Fear of falling is common in patients with type 2 diabetes and is associated with increased risk of falls.
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Aims: fear of falling is an important falls-related symptom that has received little attention in studies of falls risk in older adults with type 2 diabetes. Methods: matched pairs of participants with diabetes or with normoglycaemia (n = 186 per group) recruited from a community-based survey underwent an assessment of fear of falling and associated falls risk factors. Multivariate methods examined associations between fear of falling and risk factors for history of recent falls. Results: compared with the normoglycaemic participants, those with diabetes had worse mobility (slow timed Up and Go test times: 16.2 versus 4.9, P < 0.01), more fear of falling (24.2 versus 15.1%, P < 0.05) and more activity restriction from fear of falling (indoors: 14.0 versus 4.8, P = 0.006), but there was no increase in reported recent falls. In the combined sample, a history of recent falls was negatively associated with fear-related limitation of outdoor activities (odds ratio (95% confidence interval): 0.30 (0.15-0.58), P < 0.001) and positively associated with age (1.65 (1.20-2.28) per 10-year increase, P = 0.002) and use of antidepressants (2.14 (1.02-4.50), P = 0.044). The frequency of falls in those with recurrent falls was negatively associated with measures of balance. Conclusions: type 2 diabetes is associated with increased fear of falling and fear-associated activity restriction, and this modifies the risk of falls even in the face of increased falls risk factors including worse mobility. Future studies of falls in diabetes need to consider that fear of falling is an important modifier of the relationship between risk factors and falls.

Plasma interleukin-18 levels are a biomarker of innate immune responses that predict and characterize tuberculosis-associated immune reconstitution inflammatory syndrome.
Tan HY, Yong YK, et al.

Resident-to-resident physical aggression leading to injury in nursing homes: a systematic review.
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BACKGROUND: resident-to-resident aggression (RRA) is an understudied form of elder abuse in nursing homes.
OBJECTIVE: the purpose of this systematic review was to examine the published research on the frequency, nature, contributing factors and outcomes of RRA in nursing homes.
METHODS: in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement, this review examined all original, peer-reviewed research published in English, French, German, Italian or Spanish between 1st January 1949 and 31st December 2013 describing incidents of RRA in nursing homes. The following information was extracted for analysis: study and population characteristics; main findings (including prevalence, predisposing factors, triggers, nature of incidents, outcomes and interventions).
RESULTS: eighteen studies were identified, 12 quantitative and 6 qualitative. The frequency of RRA ranged from 1 to 122 incidents, with insufficient information across the studies to calculate prevalence. RRA commonly occurred between exhibitors with higher levels of cognitive awareness and physical functionality and a history of aggressive behaviours, and female targets who were cognitively impaired with a history of behavioural issues including wandering. RRA most commonly took place in the afternoon in communal settings, was often triggered by communication issues and invasion of space, or was unprovoked. Limited information exists on organisational factors contributing to RRA and the outcomes for targets of aggression.
CONCLUSIONS: we must continue to grow our knowledge base on the nature and circumstances of RRA to prevent harm to an increasing vulnerable population of nursing home residents and ensure a safe working environment for staff. Copyright © The Author 2015. Published by Oxford University Press on behalf of the British Geriatrics Society. All rights reserved. For Permissions, please email: journals.permissions@oup.com.

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Plasma interleukin-18 levels are a biomarker of innate immune responses that predict and characterize tuberculosis-associated immune reconstitution inflammatory syndrome.
Tan HY, Yong YK, et al.

Conclusion: Plasma interleukin-18 levels pre-ART are candidate biomarkers for predicting paradoxical and unmasking TB-IRIS. By receiver operating curve analysis, CXCL10, and/or interleukin-18 pre-ART were predictive of all-cause mortality in individuals with HIV-1 infection, assessment of plasma levels of CXCL8 might provide information about causes of mortality and/or SNAEs.

METHODS: Biomarkers were assayed pre-ART and during TB-IRIS, or equivalent time-point, in a case-control study of Malaysian HIV patients with paradoxical or unmasking TB-IRIS (n = 15), TB no IRIS (n = 14), and no TB or IRIS (n = 15). Findings for interleukin-18 were verified in another cohort of patients with paradoxical TB-IRIS (n = 26) and their controls (n = 22) from India. RESULTS: Interleukin-18 was higher in TB-IRIS patients pre-ART and during the event in both Malaysian patients (P < 0.0001) and Indian patients (P < 0.01). CXCL10 was higher pre-ART (P < 0.001), mainly in paradoxical TB-IRIS patients, and during TB-IRIS (P < 0.001), whereas CXCL8 was only higher during TB-IRIS (P < 0.001). Soluble(s) CD14 was increased in all patients with HIV/TB coinfection pre-ART and during TB-IRIS or equivalent time-point, compared with patients without TB. In contrast, interferon- was lower before and during TB-IRIS. By receiver operating curve analysis, CXCL10, and/or interleukin-18 pre-ART were predictive of TB-IRIS.

Conclusion: Plasma interleukin-18 levels pre-ART are candidate biomarkers for predicting paradoxical and unmasking TB-IRIS and should be investigated for risk stratification and elucidation of disease pathogenesis.


Plasma levels of cytokines and chemokines and the risk of mortality in HIV-infected individuals: a case-control analysis nested in a large clinical trial.


METHODS: Baseline plasma samples from 142 participants enrolled into the Strategies for Management of Antiretroviral Therapy study, who subsequently died, and 284 matched controls, were assayed for levels of 15 cytokines and chemokines. Cytokine and chemokine levels were analysed individually and when grouped according to function (innate/proinflammatory response, cell trafficking and cell activation/proliferation) for their association with the risk of subsequent death.

RESULTS: Higher plasma levels of proinflammatory cytokines (interleukin-18 and tumour necrosis factor-alpha) were associated with an increased risk of all-cause mortality but in analyses adjusted for potential confounders, only the association with interleukin-6 persisted. Increased plasma levels of the chemokine CXCL8 were also associated with all-cause mortality independently of hepatitis C virus status but not when analyses were adjusted for all confounders. In contrast, higher plasma levels of cytokines mediating cell activation/proliferation were not associated with a higher mortality risk and exhibited a weak protective effect when analysed as a group.

CONCLUSION: Whereas plasma levels of interleukin-6 are the most informative biomarker of cytokine dysregulation associated with all-cause mortality in individuals with HIV-1 infection, assessment of plasma levels of CXCL8 might provide information about causes of mortality and possibly SNAEs.


Alzheimer's Dement. 2015.

Incidence and predictors of cognitive impairment and dementia in Aboriginal Australians: A follow-up study of 5 years.


METHODS: Data were collected at baseline and annually for up to 5 years from 1993 to 2000 on 1970 Aboriginal Australians aged 45 years and older, who lived in Victoria and were living in remote communities. Information was collected on a range of physical, mental, social, and lifestyle factors that might be associated with cognitive impairment and dementia.

RESULTS: The incidence of cognitive impairment and dementia was significantly higher in Aboriginal Australians than in the general population. The incidence of dementia was highest in those with a history of alcohol use disorder and in those with a history of physical abuse.

CONCLUSION: These findings highlight the importance of addressing these risk factors in the prevention and management of cognitive impairment and dementia in Aboriginal Australians.
A germline MTOR mutation in Aboriginal Australian siblings with intellectual disability, dysmorphism, macrocephaly, and small thoraces.

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We report on three Aboriginal Australian siblings with a unique phenotype which overlaps with known megalencephaly syndromes and RASopathies, including Costello syndrome. A gain-of-function mutation in MTOR was identified and represents the first reported pathogenic mutation in this gene. The identification of this mutation in a family with a phenotype consistent with megalencephaly syndrome highlights the importance of whole-exome sequencing in identifying genetic causes of intellectual disability in Aboriginal Australian families. The incidence of cognitive impairment or dementia was 52.6 (95% confidence interval 33.9, 81.5) per 1000 person-years (380.3 total person-years) over the age 60 years. Longitudinal risk factors associated with a decline from normal cognition to impairment were age and head injury. Other associations with cognitive decline were stroke, head injury, nonaspirin analgesics, lower BMI, and higher systolic BP. CONCLUSIONS: Dementia incidence in Aboriginal Australians is among the highest in the world, and is associated with age and head injury.


A Multicenter Randomized Trial of Continuous versus Intermittent beta-Lactam Infusion in Severe Sepsis.

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RATIONALE: Continuous infusion of beta-lactam antibiotics may improve outcomes due to time-dependent antibacterial activity compared to intermittent dosing. OBJECTIVES: To evaluate the efficacy of continuous versus intermittent infusion in patients with severe sepsis. METHODS: We conducted a randomized controlled trial in 25 intensive care units (ICUs). Participants commenced on parenteral (total flavonoidUSDA and total flavonoidPE) and metoprolol were randomized to receive the prescribed antibiotic via continuous or 30-minute intermittent infusion for the remainder of the treatment course or until ICU discharge. The primary outcome was the number of alive ICU-free days at day 28. Secondary outcomes were 90-day survival, clinical cure 14 days post antibiotic cessation, alive organ failure-free days at day 14 and duration of bacteremia. MEASUREMENTS AND MAIN RESULTS: We enrolled 432 eligible participants with a median age of 64 years and an Acute Physiology and Chronic Health Evaluation II score of 20. There was no difference in ICU-free days: 18 days (IQR: 2-24) and 20 days (IQR 3-24) in the continuous and intermittent groups (P = 0.38). There was no difference in 90-day survival: 74.3% (156/210) and 72.5% (158/218); HR 0.91 (95% CI 0.63-1.31, P = 0.61). Clinical cure was 52.4% (111/212) and 49.5% (109/220); OR 1.12 (95% CI 0.77-1.63, P = 0.56). There was no difference in organ-failure free days (6 days, P = 0.27) and duration of bacteremia (0 days, P = 0.24). CONCLUSIONS: In critically ill patients with severe sepsis, there was no difference in outcomes between beta-lactam antibiotic administration by continuous and intermittent infusion.

Clinical trial registration available at www.anzctr.org.au, ID ACTRN12612000138886.


Flavonoid intake and all-cause mortality.
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BACKGROUND: Flavonoids are bioactive compounds found in foods such as tea, chocolate, red wine, fruit, and vegetables. Higher intakes of specific flavonoids and flavonoid-rich foods have been linked to reduced mortality from specific vascular diseases and cancers. However, the importance of flavonoids in preventing all-cause mortality remains uncertain.

OBJECTIVE: The objective was to explore the association between flavonoid intake and risk of 5-y mortality from all causes by using 2 comprehensive food composition databases to assess flavonoid intake.

DESIGN: The study population included 1063 randomly selected women aged ≥75 y. All-cause, cancer, and cardiovascular mortalities were assessed over 5 y of follow-up through the Western Australia Data Linkage System. Two estimates of flavonoid intake (total flavonoidUSDA and total flavonoidPE) were determined by using food composition data from the USDA and the Phenol-Explorer (PE) databases, respectively.

RESULTS: During the 5-y follow-up period, 129 (12%) deaths were documented. Participants with high total flavonoid intake were at lower risk [multivariate-adjusted HR (95% CI)] of 5-y all-cause mortality than those with low total flavonoid consumption [total flavonoidUSDA: 0.37 (0.22, 0.58); total flavonoidPE: 0.36 (0.22, 0.60)]. Similar beneficial relations were observed for both cardiovascular disease mortality [total flavonoidUSDA: 0.34 (0.17, 0.69); flavonoidPE: 0.32 (0.16, 0.61)] and cancer mortality [total flavonoidUSDA: 0.25 (0.10, 0.62); flavonoidPE: 0.26 (0.11, 0.62)].

CONCLUSIONS: Using the most comprehensive flavonoid databases, we provide evidence that high consumption of flavonoids is associated with reduced risk of mortality in older women. The benefits of flavonoids may extend to the etiology of cancer and cardiovascular disease.


Dietary saturated fat intake and atherosclerotic vascular disease mortality in elderly women: A prospective cohort study.
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Background: The reduction of saturated fatty acid (SFA) intake has been the basis of long-standing dietary recommendations. However, recent epidemiologic studies have reported conflicting evidence in the relation between SFA consumption and risk of atherosclerotic vascular disease (ASVD) mortality. Objective: We investigated the association of SFA intake with serum lipid profiles and ASVD mortality in a population-based 10-y cohort study. Design: At baseline (1998) 1469 women living in Perth, Western Australia, with a mean +/- SD age of 75.2 +/- 2.7 y had SFA intake measured by using a validated food-frequency questionnaire. Outcome data were serum lipids at baseline and ASVD deaths over 10 y (13,649 person-years of follow-up), retrieved from the Western Australian Data Linkage System. Other risk factors for ASVD were assessed and adjusted for in multivariable analyses. Results: ASVD deaths occurred in 9.1% (134) of participants. The highest quartile of SFA intake (>31.28 g/d) had an ~16% cumulative mortality risk compared with ~5% in the lowest quartile (<17.39 g/d) (HR: 3.07; 95% CI: 1.54, 6.11; P = 0.001). Baseline SFA intake was associated with baseline serum total and LDL cholesterol in multivariable-adjusted models (beta: 0.199, SE: 0.056, P < 0.001 and beta: 0.190, SE: 0.051, P < 0.001, respectively). However, baseline serum total and LDL cholesterol were not associated with ASVD mortality. Conclusions: High SFA intake was associated with the risk of ASVD mortality in this population of elderly women. Although there was a strong positive association between SFA intake and LDL cholesterol, LDL cholesterol was not associated with ASVD mortality in this cohort. Nevertheless, these data support dietary advice to reduce SFA intake.


Tea and flavonoid intake predict osteoporotic fracture risk in elderly Australian women: a prospective study.


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BACKGROUND: Observational studies have linked tea drinking, a major source of dietary flavonoids, with higher bone density. However, there is a paucity of prospective studies examining the association of tea drinking and flavonoid intake with fracture risk. OBJECTIVE: The objective of this study was to examine the associations of black tea drinking and flavonoid intake with fracture risk in a prospective cohort of women aged >75 y. DESIGN: A total of 1188 women were assessed for habitual dietary intake with a food-frequency and beverage questionnaire. Incidence of osteoporotic fracture requiring hospitalization was determined through the Western Australian Hospital Morbidity Data system. Multivariable adjusted Cox regression was used to examine the HRs for incident fracture.

RESULTS: Over 10 y of follow-up, osteoporotic fractures were identified in 288 (24.2%) women; 212 (17.8%) were identified as a major osteoporotic fracture, and of these, 129 (10.9%) were a hip fracture. In comparison with the lowest tea intake category (<1 cup/wk), consumption of >3 cups/d was associated with a 30% decrease in the risk of any osteoporotic fracture (HR: 0.70; 95% CI: 0.50, 0.96). Compared with women in the lowest tertile of total flavonoid intake (from tea and diet), women in the highest tertile had a lower risk of any osteoporotic fracture (HR: 0.65; 95% CI: 0.47, 0.88), major osteoporotic fracture (HR: 0.66; 95% CI: 0.45, 0.95), and hip fracture (HR: 0.58; 95% CI: 0.36, 0.93). For specific classes of flavonoids, statistically significant reductions in fracture risk were observed for higher intake of flavonols for any osteoporotic fracture and major osteoporotic fracture, as well as flavones for hip fracture (P < 0.05).

CONCLUSION: Higher intake of black tea and particular classes of flavonoids were associated with lower risk of fracture-related hospitalizations in elderly women at high risk of fracture.Copyright © 2015 American Society for Nutrition.


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Association of depression with sexual and daily activities: a community study of octogenarian men.
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OBJECTIVE: To determine the association between clinically significant depressive symptoms, routine function, and sexual interest and practice in a community-derived sample of octogenarian men.

METHODS: Cross-sectional study of 1,649 community-dwelling men aged 80 years or over with no history of terminal illnesses or neurodegenerative diseases. Men with Patient Health Questionnaire (PHQ-9) scores greater than or equal to 10 were deemed to be clinically depressed. Scores between 5 and 9 were considered indicative of subthreshold depression. We used standard procedures to collect self-reported sociodemographic, lifestyle, and clinical data, as well as basic and instrumental activities of daily living, and a structured questionnaire to ask men about their 12-month interest in sex, frequency, past experiences, and current sexual problems.

RESULTS: 121 men (7.3%) had clinically significant depression and 239 (14.5%) had subthreshold depression. Depressive symptoms were associated with difficulties in basic and instrumental activities of daily living, but not with sexual practice. Decreased interest in sex and anxiety before sex were associated with subthreshold depression. Clinically significant depressive symptoms were independently and positively associated with past history of diabetes (odds ratio [OR]: 2.1, 95% confidence interval [CI]: 1.1-4.0), depression (OR: 9.0; 95% CI: 4.6-17.3), impaired ability to groom (OR: 3.7, 95% CI: 1.2-11.0), carry out heavy housework duties (OR: 2.4, 95% CI: 1.1-5.1), manage finances (OR: 2.5, 95% CI: 1.1-5.7), or engage in leisure activities (OR: 4.1, 95% CI: 2.0-8.2).

CONCLUSIONS: Ability to function effectively at home, financial autonomy, and leisure are associated with clinically significant depression in octogenarian men. Maintaining daily function and autonomy may be a suitable target for interventions that aim to reduce the prevalence and incidence of depression in older age.

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The PACE Study: A Randomized Clinical Trial of Cognitive Activity Strategy Training for Older People with Mild Cognitive Impairment.

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OBJECTIVE: The role of cognition-focused interventions in reducing cognitive decline in older people remains uncertain. This study aimed to clarify whether a group cognitive activity (CA) strategy-training program would decrease the 2-year rate of cognitive decline of people with mild cognitive impairment (MCI).

DESIGN: Randomized controlled trial.

SETTING: One study site.

PARTICIPANTS: 160 older adults with MCI >65 years of age (mean: 75, SD: 5.8).

INTERVENTION: Five-week CA strategy training or a control nonspecific educational program. The primary outcome measure was change from baseline in the total score on the Cambridge Cognitive Examination-Revised (CAMCOG-R). Secondary outcomes of interest included changes in memory, attention, executive functions, mood, and quality of life. Endpoints were collected 10, 52, and 104 weeks post baseline.

RESULTS: Intention to treat analysis identified no significant difference in CAMCOG-R scores over time between the two groups (mean difference: -0.36, 95% CI: -1.02,0.29) or across secondary outcome measures. The exceptions were better performance of the CA group on immediate attention (Digit Span Forwards, adjusted mean difference: 0.15, 95% CI: 0.01,0.30) and better quality of life (adjusted mean difference: 0.57, 95% CI: 0.10,1.04) compared with controls.

CONCLUSION: The devised program of CA did not improve general cognitive performance of older adults with MCI over a period of 2 years. Although favorable, the beneficial effects of the intervention on attention and quality of life were small, and of uncertain significance.

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Insulin Resistance and Depressive Symptoms in Older Men: The Health in Men Study.

Ford AH, Flicker L, et al.


OBJECTIVE: A positive association between depression and diabetes has been reported, but the direction and nature of this association is unclear. Insulin resistance is a state of reduced responsiveness of target tissues to normal circulating levels of insulin and predisposes to diabetes in the presence of beta cell dysfunction.

METHODS: We conducted this cross-sectional and prospective study in a community representative sample of 3,140 older men free of diabetes to determine if insulin resistance was associated with prevalent and incident depressive symptoms.

RESULTS: Men with insulin resistance had increased odds of depression cross-sectionally (odds ratio [OR]: 1.61; 95% confidence interval [CI]: 1.08-2.40), although this was not significant after adjustment for possible confounding (OR: 1.32; 95% CI: 0.85-2.03).

CONCLUSION: Older men with clinically significant depressive symptoms were more likely to have higher markers of insulin resistance. Additionally, the odds of depression increased with increasing levels of insulin resistance, and insulin resistance increased the risk of developing depression over 5 years later. Because depression is now a leading cause of disability worldwide, addressing the rising challenge of insulin resistance may prove important in improving the future health of our communities.

Lifecourse Adiposity and Blood Pressure Between Birth and 17 Years Old.

Huang RC, Burrows S, et al.


OBJECTIVE: Adiposity trajectories (which comprise 27% of the population) were associated with an increased risk of decline in lifecourse BP compared to the reference adiposity trajectory.

RESULTS: The study includes 1,023 adolescents with BP measured at age 17 years. Three of 7 childhood adiposity trajectories (with accelerating adiposity) previously related to increased insulin resistance in early adolescence. Our aim was to investigate the relationship between these adiposity trajectories with childhood blood pressure (BP) development.

METHODS: Adiposity trajectories were previously developed by semiparametric modeling using serial anthropometry from birth to age 14 from the West Australian Pregnancy Cohort. The association between these trajectories and the prevalence of hypertension and prehypertension in 17 year olds was assessed by logistic regression. The relationship between adiposity trajectories and lifecourse BP was then assessed using linear mixed modeling.

RESULTS: The study includes 1,023 adolescents with BP measured at age 17 years. Three of 7 childhood adiposity trajectories (with accelerating adiposity) previously related to increased insulin resistance were associated with an increased risk of 17-year-old prehypertension or hypertension, compared to a referent trajectory of "stable average adiposity" (odds ratio (OR) = 2.9; P < 0.001; OR = 3.5; P = 0.001; and OR = 1.8; P = 0.041). One decelerating adiposity trajectory from high birth size was associated with significant interactions with age terms (P values = 0.025-0.084 and 0.011-0.027), indicating an altered slope and therefore, relative decline in lifecourse BP compared to the reference adiposity trajectory.

CONCLUSIONS: Adiposity trajectories (which comprise 27% of the population) were associated with an increased risk of hypertension/prehypertension in adolescence. Higher BP was detectable as early as 3 years old. Consequently, targeting fat loss (catch-down growth) in the preschool years may prevent the development of hypertension and related metabolic disorders.


A randomized, placebo-controlled trial of pentoxifylline on erythropoiesis-stimulating agent hyporesponsiveness in anemic patients with CKD: the Handling Erythropoietin Resistance With Oxpentifylline (HERO) trial.

Johnson DW, Pascoe EM, et al.

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BACKGROUND: Erythropoiesis-stimulating agent (ESA)-hyporesponsive anemia is common in chronic kidney disease (CKD). Pentoxifylline shows promise as a treatment for ESA-hyporesponsive anemia, but has not been rigorously evaluated.

STUDY DESIGN: Multicenter, double-blind, randomized, controlled trial.

SETTING & PARTICIPANTS: 53 adult patients with CKD stage 4 or 5 (excluding dialysis) and ESA-hyporesponsive anemia (hemoglobin<120g/L and ESA resistance index [calculated as weight-adjusted weekly ESA dose in IU/kg/wk divided by hemoglobin concentration in g/L] >1.0 IU/kg/wk/g/L for erythropoietin-treated patients and >0.005 mg/kg/wk/g/L for darbepoetin-treated patients).

INTERVENTIONS: Pentoxifylline (400 mg/d; n=26) or matching placebo (control; n=27) for 4 months.

Outcomes:

PRIMARY OUTCOME: ESA resistance index at 4 months; secondary outcomes: hemoglobin concentration, ESA dose, blood transfusion requirement, serum ferritin level and transferrin saturation, C-reactive protein level, adverse events, quality of life, and health economics.

RESULTS: There was no statistically significant difference in ESA resistance index between the pentoxifylline and control groups (adjusted mean difference, -0.39 [95%CI, -0.89 to 0.10] IU/kg/wk/g/L; P=0.1). Pentoxifylline significantly increased hemoglobin concentration relative to the control group (adjusted mean difference, 7.6 [95%CI, 1.7-13.5] g/L; P=0.01). There was no difference in ESA dose between groups (-20.8 [95%CI, -67.2 to 25.7] IU/kg/wk; P=0.4). No differences in blood transfusion requirements, adverse events, or quality of life were observed between groups. Pentoxifylline cost A$88.05 (US $82.94) per person over the trial and produced mean savings in ESA cost of A$1,332 (US $1,255). The overall economic impact over the trial period was a saving of A$1,244 (US $1,172) per person for the pentoxifylline group compared with controls.

LIMITATIONS: Sample size smaller than planned due to slow recruitment.

CONCLUSIONS: Pentoxifylline did not significantly modify ESA hyporesponsiveness, but increased hemoglobin concentration. Further studies are warranted to determine whether pentoxifylline therapy represents a safe strategy for increasing hemoglobin levels in patients with CKD with ESA-hyporesponsive anemia. Crown Copyright 2014. Published by Elsevier Inc. All rights reserved.

Publication Types: Multicenter Study
Randomized Controlled Trial
Research Support, Non-U.S. Gov't


Variation in risk and mortality of acute kidney injury in critically ill patients: A multicenter study.

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Background: Despite standardized definitions of acute kidney injury (AKI), there is wide variation in the reported rates of AKI and hospital mortality for patients with AKI. Variation could be due to actual differences in disease incidence, clinical course, or a function of data ascertainment and application of diagnostic criteria. Using standard criteria may help determine and compare the risk and outcomes of AKI across centers. Methods: In this cohort study of critically ill patients admitted to the intensive care units at...
six hospitals in four countries, we used KDIGO criteria to define AKI. The main outcomes were the occurrence of AKI and hospital mortality. Results: Of the 15,132 critically ill patients, 32% developed AKI based on serum creatinine criteria. After adjusting for differences in age, sex, and severity of illness, the odds ratio for AKI continued to vary across centers (odds ratio (OR), 2.57-6.04, p < 0.001). The overall crude hospital mortality of patients with AKI was 27%, which also varied across centers after adjusting for KDIGO stage, differences in age, sex, and severity of illness (OR, 1.13-2.20, p < 0.001). The severity of AKI was associated with incremental mortality risk across centers. Conclusions: In this study, the absolute and severity-adjusted rates of AKI and hospital mortality rates for AKI varied across centers. Future studies should examine whether variation in the risk of AKI among centers is due to differences in clinical practice or process of care or residual confounding due to unmeasured factors.


The Diagnosis of Community-acquired Pneumonia. Do We Need to Take a Big Step Backward?

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Ultra-low-dose chest computer tomography screening of an asbestos-exposed population in Western Australia.

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Wang A, McCann P, et al. (Wang, Alfonso, Reid) Liver and Kidney Transplant Unit, Sir Charles Gairdner Hospital, Perth, Australia (Swaminathan) Renal Medicine and Kidney Transplant, Fiona Stanley Hospital, Perth, Australia (He, Hamdorf, Delriviere) School of Surgery, University of Western Australia, Perth, Australia.


Delayed graft function in laparoscopic kidney transplantation: The importance of prolonged cold and warm ischemia - Response.

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Comparative survival benefits and costs of an eplet and broad antigen based matching system in deceased donor kidney transplant allocation among indigenous Australians.

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Aim: To compare the benefits and costs of incorporating an eplet-based matching algorithm to the current allocation of deceased donor kidneys to indigenous Australians. Background: The overall waiting time for transplantation among indigenous Australians is at least six times longer than the nonindigenous Australians with end-stage kidney disease. Such disparities are largely attributed to the HLA-antigen mismatch between donors and potential indigenous transplant candidates. Structural matching within the epitope level (eplets) may provide additionally accurate assessment of immunological risk compared to HLA matching at the broad antigen level.

Results: Of 34 recipients, the average waiting time for transplantation for 5 recipients (15%) was reduced by an average of 23 (SD=17) months with an algorithm using the threshold of 0-2 HLA-ABDR broad antigen mismatch with 10 HLA-DR eplet mismatch for allocation (associated with low incidence of rejection). There was an average incremental gain in 0.004 QALY with average savings of $3860 using this allocation compared to the current. There was a small consequential loss of up to 0.001 QALYs and extra costs of $2005 for non-indigenous Australians. Conclusions: Alternative allocation for indigenous kidney transplant recipients are associated with a reduction in transplant waiting-time with improved health benefits without disadvantaged non-indigenous recipients.

Evaluation of the utility of the Vigileo FloTrac, LiDCO, USCOM and CardioQ to detect hypovolaemia in conscious volunteers: A proof of concept study.

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It is important to detect and treat hypovolaemia; however, detection is particularly challenging in the conscious, spontaneously breathing patient. Eight healthy male volunteers were monitored using four minimally invasive monitors: Vigileo FloTrac<sup></sup>; LiDCO<sup></sup>; USCOM 1A; and CardioQ<sup></sup> oesophageal Doppler. Monitor output and clinical signs were recorded during incremental venesection of 2.5% estimated blood volume aliquots to a total of 20% blood volume removed. A statistically significant difference from baseline stroke volume was detected after 2.5% blood loss using the LiDCO (p = 0.007), 7.5% blood loss using the USCOM (p = 0.019), and 12.5% blood loss using the CardioQ (p = 0.046) and the FloTrac (p = 0.028). Receiver operator characteristic curves for predicting > 10% blood loss had areas under the curve of 0.68-0.82. The minimally invasive cardiac output devices tested can detect blood loss by a reduction in stroke volume in awake volunteers, and may have a role in guiding fluid replacement in conscious patients with suspected hypovolaemia.

Clinical predictors of a low central venous oxygen saturation after major surgery: a prospective prevalence study.

Litton E, Silibert B, et al.
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Optimising perioperative haemodynamic status may reduce postoperative complications. In this prospective prevalence study, we investigated the associations between standard haemodynamic parameters and a low central venous oxygen saturation (ScvO2) in patients after major surgery. A total of 201 patients requiring continuous arterial and central venous pressure monitoring after major surgery were recruited. Simultaneous arterial and central venous blood gases, haemodynamic and biochemical data and perfusion index were obtained from patients at a single time-point within 24 hours of surgery. A low ScvO2 (<70%) was observed in 109 patients (54%). Use of mechanical ventilation, mean arterial pressure, central venous pressure, haemoglobin concentrations,
arterial pH and lactate concentrations, arterial oxygen (PaO2) and carbon dioxide tensions (PaCO2) were all associated with a low ScvO2 in the univariate analyses. In the multivariate analysis, only a higher perfusion index (odds ratio [OR] 0.87, 95% confidence interval [CI] 0.78 to 0.98), PaO2 (OR 0.98 per mmHg increment, 95% CI 0.97 to 0.99) and PaCO2 (OR 0.88 per mmHg increment, 95% CI 0.82 to 0.95) and a lower central venous pressure (OR 1.14 per mmHg increment, 95% CI 1.04 to 1.25) were significantly associated with a reduced risk of a low ScvO2, all in a linear fashion. In conclusion, PaO2, PaCO2, perfusion index and central venous pressure were significant predictors of a low ScvO2 in patients after major surgery including cardiac surgery.


Near-infrared spectroscopy-based microcirculatory assessment in acute atrial fibrillation.

Barrett OS, Macdonald SP, et al.

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Near-infrared spectroscopy is a means of assessing microcirculatory function, but has not been studied in atrial fibrillation (AF). We evaluated the effect of acute AF on thenar eminence near-infrared spectroscopy-derived microcirculatory variables. Stable patients presenting to the emergency department with acute onset AF underwent dynamic near-infrared spectroscopy assessment with a three minute vascular occlusion test (VOT). This was repeated after cardioversion to sinus rhythm (SR). Each assessment included baseline tissue oxygen saturation (StO2), slope of StO2 decrease during VOT, slope of StO2 increase post VOT, minimum and maximum StO2, amplitude of StO2 response and post-ischaemic hyperperfusion. Pre and post cardioversion values were compared by Wilcoxon signed-rank test. Twelve participants (seven male, five female) with a median age of 63 years (interquartile range 52 to 70 years) were enrolled. Median baseline StO2 was 74% before and 77% after cardioversion (P=0.03). The median slope of StO2 decrease during VOT was -0.19%/second and -0.16%/second (P=0.018) and the median slope of StO2 increase post VOT was 3.03%/second and 2.56%/second (P=0.002), pre and post cardioversion, respectively. Minimum StO2 was lower (39% versus 52%, P=0.002) and the amplitude of StO2 response greater (49% versus 40%, P=0.005) in AF, but there was no significant difference in maximum StO2 or the degree of reperfusion hyperaemia. In summary, baseline and minimum StO2 were lower with a greater ischaemic decrease in StO2 during AF, reflecting reduced tissue perfusion, compared with sinus rhythm. Recovery after ischaemia was higher in AF, suggesting normalisation of capillary recruitment during ischaemia.

Publication Types: Research Support, Non-U.S. Gov't


A comparison of outcomes among hospital survivors with and without severe comorbidity admitted to the intensive care unit.

Williams TA, McConigley R, et al.

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Little is known about the experiences of patients with severe comorbidity discharged from Intensive Care Units (ICUs). This project aimed to determine the effects of an ICU stay for patients with severe comorbidity by comparing 1) quality of life (QOL), 2) the symptom profile of hospital survivors and 3) health service use after hospital discharge for patients admitted to ICU with and without severe comorbidity. A case-control study was used. Patients with severe comorbidity were matched to a contemporaneous cohort of ICU patients by age and severity of illness. Assessment tools were the Medical Outcome Study 36-item short-form and European Organisation for Research and Treatment of Cancer QOL-C15-PAL questionnaires for QOL and the Symptom Assessment Scale for symptom distress. A proportional odds assumption was performed using an ordinal regression model. The difference in QOL outcome was the dependent variable for each pair. Health service use after discharge from ICU was monitored with patient diaries. Patients aged 18+ years admitted to an ICU in a metropolitan teaching hospital between 2011 and 2012 were included. We recruited 30 cases and 30 controls. QOL improved over the six months after hospital discharge for patients with and without severe comorbidity (P <0.01) within the groups but there was no difference found between the groups (P >0.3). There was no difference in symptoms or health service use between patients with and without severe comorbidity. ICU admission for people with severe comorbidity can be appropriate to stabilise the patient's condition and is likely to be followed by some overall improvement over the six months after hospital discharge.

Publication Types: Research Support, Non-U.S. Gov't


A survey of antientemic dexamethasone administration-frequency of use and perceptions of benefits and risks.

Corcoran TB, Edwards T.
and 46.6% receive dexamethasone. No respondent gives more than a single dose of dexamethasone and there was an almost equal split between those who administer 4 and 8 mg, with a smaller number dosing on a weight basis. 5HT-3 receptor antagonists and dexamethasone are the preferred first-line PONV prophylactic agents and 5HT-3 receptor antagonists and droperidol are the preferred first-line PONV therapeutic agents. Concerns relating to the safety of dexamethasone were expressed by 80% of respondents. From this survey, we concluded that the PONV practice of the respondents is largely compliant with recent consensus guidelines, although PONV prophylaxis appears to be given more routinely. It also appears that more education is required on issues regarding dexamethasone safety.


Predictors of an increased in vitro thrombotic and bleeding tendency in critically ill trauma and non-trauma patients.

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Trauma patients are at a high risk of both bleeding and thromboembolism. This study assessed whether conventional coagulation blood tests were reliable predictors of an increased in vitro thrombotic and bleeding tendency of trauma and non-trauma patients. Conventional coagulation blood tests and thromboelastographs of 63 trauma and 63 randomly selected, critically ill non-trauma patients were compared. Increased in vitro thrombotic and bleeding tendencies were defined by a maximum amplitude >72 mm or an angle >74degree on the thromboelastograph and a maximum amplitude <54 mm or an angle <47degree, respectively. In vitro thrombotic tendency was more common than bleeding tendency and this was not different between the critically ill trauma and non-trauma patients (59% versus 67% with thrombotic tendency, P=0.461; 11% versus 10% with bleeding tendency, respectively, P=0.999). Thrombocytopenia (<150 x 109 /l) and low fibrinogen concentrations (<2 g/l) were the only two factors associated with an increased in vitro bleeding tendency (both P=0.001) and thrombocytopenia was the only factor associated with a lower risk of in vitro thrombotic tendency (21% versus 75%, P=0.001). Platelet counts (Pearson's correlation coefficient [r]: 0.59, P=0.001) and fibrinogen concentrations (r 0.61, P=0.001) both had a relatively linear association with maximum amplitude of the thromboelastograph. Prolonged International Normalized Ratio (>1.5) and activated Partial Thromboplastin Time (>40 seconds) were, however, not significantly associated with an increased in vitro thrombotic or bleeding tendency. In conclusion, in vitro thrombotic tendency was more common than bleeding tendency in critically ill trauma and non-trauma patients. Platelet counts and fibrinogen concentrations were better predictors of increased in vitro thrombotic and bleeding risks than International Normalized Ratio or activated Partial Thromboplastin Time.


Research without informed patient consent in incompetent patients.

Dobb GJ.

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Most patients needing intensive care cannot give informed consent to participation in research. This includes the most acutely and severely ill, with the highest mortality and morbidity where research has the greatest potential to improve patient outcomes. In these circumstances consent is usually sought from a substitute decision maker, but while survivors of intensive care believe substitute decision makers will look after their interests, evidence suggests substitute decision makers are poorly equipped for this task. Various models have been suggested for research without patient informed consent when intervention is urgent and cannot wait until first person consent is possible, including a waiver of consent if conditions are met. A nationally consistent model is proposed for Australia with a robust process for initial waiver of consent followed by first person consent to further research-related procedures or ongoing follow-up when this can be competently provided.


Central venous-to-arterial carbon dioxide gradient as a marker of occult tissue hypoperfusion after major surgery.

Silbert BI, Litton E, et al.

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The central venous arterio-venous carbon dioxide tension gradient (‘CO2 gap’) has been shown to correlate with cardiac output and tissue perfusion in septic shock. Compared to central venous oxygen saturation (SCVO2), the CO2 gap is less susceptible to the effect of hyperoxia and may be particularly useful as an adjunctive haemodynamic target in the perioperative period. This study investigated whether a high CO2 gap was associated with an increased systemic oxygen extraction (O2ER >0.3) or occult tissue hypoperfusion in 201 patients in the immediate postoperative period. The median CO2 gap of all patients was 8 mmHg (IQR 6 to 9), and a large CO2 gap was very common (>6 mmHg in 139 patients [69%], 95% CI 63 to 75; >5 mmHg in 170 patients [85%], 95% CI 79 to 89). A CO2 gap >5 mmHg had a higher sensitivity (93%) and negative predictive value (74%) than a CO2 gap >6 mmHg in excluding occult tissue hypoperfusion. Of the four variables that were predictive of an increased O2ER in the multivariate analysis- CO2 gap, arterial pH, haemoglobin and arterial lactate concentrations-the CO2 gap (odds ratio 4.11 per mmHg increment, 95% CI 1.7 to 11.2, P=0.002) was most important and explained about 34% of the variability in the risk of occult tissue hypoperfusion. In conclusion, a normal CO2 gap (<5 mmHg) had a high sensitivity and negative predictive value in excluding inadequate systemic oxygen delivery and may be useful as an adjunct to other haemodynamic targets in avoiding occult tissue hypoperfusion in the perioperative setting when high inspired oxygen concentrations are used.


**Iron-restricted erythropoiesis and risk of red blood cell transfusion in the intensive care unit: a prospective observational study.**

Litton E, Xiao J, et al.

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Intravenous (IV) iron can decrease transfusion requirements in selected patients with low, normal and moderately elevated ferritin. Whether the syndrome of iron-restricted erythropoiesis (IRE), diagnosed by iron studies, identifies critically ill patients at risk for subsequent red blood cell (RBC) transfusion, and hence, provides a simple method to determine response to IV iron therapy, is uncertain. We aimed to describe the characteristics of patients with IRE on admission to intensive care and determine the optimal variables to identify patients at risk of RBC transfusion who may benefit from early administration of IV iron. The study included 201 consecutive ICU admissions from a single 23-bed combined medical/surgical ICU. The prevalence of IRE on admission to ICU, defined according to ferritin <300 micro g/l and transferrin saturation <20%, was 26.2% (95% CI 19.9 to 32.4). The proportion of patients with IRE subsequently receiving RBC transfusion was significantly lower than the proportion of patients without IRE receiving RBC transfusion (absolutem difference 38.9% [95% CI 4.7 to 33.1, P <0.001]). IRE was not independently associated with risk of transfusion on multivariate analysis, however, a prognostic model with three risk factors (RBC transfusion prior to ICU admission, Hb <100 g/l and ICU length of stay >3 days), had good discrimination and calibration for predicting transfusion (receiver operator curve area under the curve 0.87 [95% CI 0.79 to 0.94, P=0.88], Hosmer-Lemeshow 6.21; P=0.1). Excluding iron overload and using simple prognostic criteria to identify patients at high risk of RBC transfusion may be a preferable strategy for identifying critically ill patients who may benefit from IV iron.


**What’s new in medical management strategies for raised intra-abdominal pressure: Evacuating intra-abdominal contents, improving abdominal wall compliance, pharmacotherapy, and continuous negative extra-abdominal pressure.**


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In the future, medical management may play an increasingly important role in the prevention and management of intra-abdominal hypertension (IAH). A review of different databases was used (PubMed, MEDLINE and EMBASE) with the search terms ‘Intra-abdominal Pressure’ (IAP), ‘IAH’, ‘Abdominal Compartment Syndrome’ (ACS), ‘medical management’ and ‘non-surgical management’. We also reviewed all papers with the search terms ‘IAH’, ‘IAP’ and ‘ACS’ over the last three years, only extracting those papers which showed a novel approach in the non-surgical management of IAH and ACS. IAH and ACS are associated with increased morbidity and mortality. Non-surgical management is an important treatment option in critically ill patients with raised IAP. There are five medical treatment options to be considered to reduce IAP: 1) improvement of abdominal wall compliance; 2) evacuation of intra-luminal contents; 3) evacuation of abdominal fluid collections; 4) optimisation of fluid administration; and 5) optimisation of systemic and regional perfusion. This paper will review the first three treatment arms of the WSACS algorithm: abdominal wall compliance; evacuation of intra-luminal contents and evacuation of abdominal fluid collections. Emerging medical treatments will be analysed and finally some alternative specific treatments will be assessed. Other treatment options with regard to optimising fluid administration and systemic and regional perfusion will be described elsewhere, and are beyond the scope of this review. Medical management of critically ill patients with raised IAP should be instigated early to prevent further organ dysfunction.

and to avoid progression to ACS. Many treatment options are available and are often part of routine daily management in the ICU (nasogastric, rectal tube, prokinetics, enema, sedation, body position). Some of the newer treatments are very promising options in specific patient populations with raised IAP. Future studies are warranted to confirm some of these findings.

Publication Types: Review


Fluid therapy and perfusional considerations during resuscitation in critically ill patients with intra-abdominal hypertension.


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Intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) are consistently associated with morbidity and mortality among the critically ill or injured. Thus, avoiding or potentially treating these conditions may improve patient outcomes. With the aim of improving the outcomes for patients with IAH/ACS, the World Society of the Abdominal Compartment Syndrome recently updated its clinical practice guidelines. In this article, we review the association between a positive fluid balance and outcomes among patients with IAH/ACS and how optimisation of fluid administration and systemic/regional perfusion may potentially lead to improved outcomes among this patient population. Evidence consistently associates secondary IAH with a positive fluid balance. However, despite increased research in the area of non-surgical management of patients with IAH and ACS, evidence supporting this approach is limited. Some evidence exists to support implementing goal-directed resuscitation protocols and restrictive fluid therapy protocols in shocked and recovering critically ill patients with IAH. Data from animal experiments and clinical trials has shown that the early use of vasopressors and inotropic agents is likely to be safe and may help reduce excessive fluid administration, especially in patients with IAH. Studies using furosemide and/or renal replacement therapy to achieve a negative fluid balance in patients with IAH are encouraging. The type of fluid to be administered in patients with IAH remains far from resolved. There is currently insufficient evidence to recommend the use of abdominal perfusion pressure as a resuscitation endpoint in patients with IAH. However, it is important to recognise that IAH either abolishes or increases threshold values for pulse pressure variation and stroke volume variation to predict fluid responsiveness, while the presence of IAH may also result in a false negative response to a negative passive leg raising test. Correct fluid therapy and perfusional support during resuscitation form the cornerstone of medical management in patients with abdominal hypertension. Controlled studies determining whether the above medical interventions may improve outcomes among those with IAH/ACS are urgently required.


Awareness and knowledge of intra-abdominal hypertension and abdominal compartment syndrome: Results of an international survey.

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Background: Surveys have demonstrated a lack of physician awareness of intra-abdominal hypertension and abdominal compartment syndrome (IAH/ACS) and wide variations in the management of these conditions, with many intensive care units (ICUs) reporting that they do not measure intra-abdominal pressure (IAP). We sought to determine the association between publication of the 2006/2007 World Society of the Abdominal Compartment Syndrome (WSACS) Consensus Definitions and Guidelines and IAH/ACS clinical awareness and management. Methods: The WSACS Executive Committee created an interactive online survey with 53 questions, accessible from November 2006 until December 2008. The survey was endorsed by the WSACS, the European Society of Intensive Care Medicine (ESICM) and the Society of Critical Care Medicine (SCCM). A link to the survey was emailed to all members of the supporting societies. Participants of the 3rd World Congress on Abdominal Compartment Syndrome meeting (March 2007, Antwerp, Belgium) were also asked to complete the questionnaire. No reminders were sent. Based on 13 knowledge questions, an overall score was calculated (expressed as percentage). Results: A total of 2,244 of the approximately 10,000 clinicians who were sent the survey responded (response rate: 22.4%). Most of the 2,244 respondents (79.2%) completing the survey were physicians or physicians in training and the majority were residing in North America (53.0%). The majority of
responders (85%) were familiar with IAP/IAH/ACS, but only 28% were aware of the WSACS consensus definitions for IAH/ACS. Three quarters of respondents considered the cut-off for IAH to be at least 15 mm Hg, and nearly two thirds believed the cut-off for ACS was higher than the currently suggested consensus definition (20 mm Hg). In 67.8% of respondents, organ dysfunction was only considered a problem with IAP of 20 mm Hg or higher. IAP was measured most frequently via the bladder (91.9%), but the majority reported that they instilled volumes well above the current guidelines. Surgical decompression was frequently used to treat IAH/ACS, whereas medical management was only attempted by about half of the respondents. Decisions to decompress the abdomen were predominantly based on the severity of IAP elevation and presence of organ dysfunction (74.4%). Overall knowledge scores were low (43 +/- 15%); respondents who were aware of the WSACS had a better score compared to those who were not (49.6% vs 38.6%, P < 0.001). Conclusions: This survey showed that although most responding clinicians claim to be familiar with IAH and ACS, knowledge of published consensus definitions, measurement techniques, and clinical management is inadequate.


**Anaesthesiology Intensive Therapy. 2015; 47(3): 191-194.**

**WSACS-The Abdominal Compartment Society. A Society dedicated to the study of the physiology and pathophysiology of the abdominal compartment and its interactions with all organ systems.**

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Publication Types: Review

**Anaesthesiology Intensive Therapy. 2015; 47(3): 241-251.**

**A user’s guide to intra-abdominal pressure measurement.**
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The intra-abdominal pressure (IAP) measurement is a key to diagnosing and managing critically ill medical and surgical patients. There are an increasing number of techniques that allow us to measure the IAP at the bedside. This paper reviews these techniques. IAP should be measured at end-expiration, with the patient in the supine position and ensuring that there is no abdominal muscle activity. The transvesicular IAP measurement is convenient and considered the gold standard. The level where the mid-axillary line crosses the iliac crest is the recommended zero reference for the transvesicular IAP measurement; moreover, marking this level on the patient increases reproducibility. Protocols for IAP measurement should be developed for each ICU based on the locally available tools and equipment. IAP measurement techniques are safe, reproducible and accurate and do not increase the risk of urinary tract infection. Continuous IAP measurement may offer benefits in specific situations in the future. In conclusion, the IAP measurement is a reliable and essential adjunct to the management of patients at risk of intra-abdominal hypertension.
Publication Types: Review

**Anaesthesiology Intensive Therapy. 2015; 47(3): 228-240.**

**Intra-abdominal hypertension and abdominal compartment syndrome in burns, obesity, pregnancy, and general medicine.**
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Intra-abdominal hypertension (IAH) is an important contributor to early organ dysfunction in trauma and sepsis. However, relatively little is known about the impact of intra-abdominal pressure (IAP) in general internal medicine, pregnant patients, and those with obesity or burns. The aim of this paper is to review the pathophysiologic implications and treatment options for IAH in these specific situations. A MEDLINE and PubMed search was performed and the resulting body-of-evidence included in the current review on the basis of relevance and scientific merit. There is increasing awareness of the role of IAH in different clinical situations. Specifically, IAH will develop in most (if not all) severely burned patients, and may contribute to early mortality. One should avoid over-resuscitation of these patients with large volumes of fluids, especially crystalloids. Acute elevations in IAP have similar effects in obese patients compared to non-obese patients, but the threshold IAP associated with organ dysfunction may be higher. Chronic elevations in IAP may, in part, be responsible for the pathogenesis of obesity-related co-morbid conditions such as hypertension, pseudotumor cerebri, pulmonary dysfunction, gastroesophageal reflux disease, and abdominal wall hernias. At the bedside, measuring IAP and considering IAH in all critical maternal conditions is essential, especially in preeclampsia/eclampsia where some have hypothesized that IAH may have an additional role. IAH in pregnancy must take into account the precautions for aorto-caval compression and has been associated with ovarian hyperstimulation syndrome. Recently, IAH has been associated with the cardioenal dilemma and hepatorenal syndrome, and this has led to the recognition of the polycompartment syndrome. In conclusion, IAH and ACS have been associated with several patient populations beyond the classical ICU, surgical, and trauma patients. In all at risk conditions the focus should be on the early recognition of IAH and prevention of ACS. Patients at risk for IAH should be identified early through measurements of IAP. Appropriate actions should be taken when IAP increases above 15 mm Hg, especially if pressures reach above 20 mm Hg with new onset organ failure. Although non-operative measures come first, surgical decompression must not be delayed if these fail. Percutaneous drainage of ascites is a simple and potentially effective tool to reduce IAP if organ dysfunction develops, especially in burn patients. Escharotomy may also dramatically reduce IAP in the case of abdominal burns.

Publication Types: Review


Intra-abdominal hypertension and abdominal compartment syndrome in pancreatitis, paediatrics, and trauma.

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Intra-abdominal hypertension (IAH) is an important contributor to early organ dysfunction among patients with trauma and sepsis. However, the impact of increased intra-abdominal pressure (IAP) among pediatric, pregnant, non-septic medical patients, and those with severe acute pancreatitis (SAP), obesity, and burns has been studied less extensively. The aim of this review is to outline the pathophysiologic implications and treatment options for IAH and abdominal compartment syndrome (ACS) for the above patient populations. We searched MEDLINE and PubMed to identify relevant studies. There is an increasing awareness of IAH in general medicine. The incidence of IAH and, to a lesser extent, ACS is high among patients with SAP. IAH should always be suspected and IAP measured routinely. In children, normal IAP in mechanically ventilated patients is approximately 7 +/- 3 mm Hg. As an IAP of 10-15 mm Hg has been associated with organ damage in children, an IAP greater than 10 mm Hg should be considered IAH in these patients. Moreover, as ACS may occur in children at an IAP lower than 20 mm Hg, any elevation in IAP higher than 10 mm Hg associated with new organ dysfunction should be considered ACS in children until proven otherwise. Monitor IAP trends and be aware that specific interventions may need to be instituted at lower IAP than the current ACS definitions accommodate. Finally, IAH and ACS can occur both in abdominal trauma and extra-abdominal trauma patients. Early mechanical hemorrhage control and the avoidance of excessive fluid resuscitation are key elements in preventing IAH in trauma patients. IAH and ACS have been associated with many conditions beyond the general ICU patient. In adults and in children, the focus should be on the early recognition of IAH and the prevention of ACS. Patients at risk for IAH should be identified early during their treatment (with a low threshold to initiate IAP monitoring). Appropriate actions should be taken when IAP increases above 20 mm Hg, especially in patients developing difficulty with ventilation. Although non-operative measures should be instituted first, one should not hesitate to resort to surgical decompression if they fail.

Publication Types: Review

Furthermore, 53% of anesthetists identified with a practice of “deeper and longer” intraoperative paralysis of patients. All 71 neuromuscular monitoring, and aminosteroidal neuromuscular blocking agents were used in 94.3% of cases (versus 77% in 2011). Data from 2011. We found that, in the 2.5 years since introduction of Sugammadex, more anesthetists (69.5 versus 38%) utilized freely available. In clinical practice Sugammadex was frequently (57%) mildly overdosed, with 200mg being the most commonly (n = 20) of respondents felt it provided “faster turnover,” less postoperative residual neuromuscular blockade (n = 23; 79%), and without the unrestricted availability of Sugammadex, and 1 colleague would refuse to work in a hospital without this drug being related to the use of neuromuscular blocking agents at the Royal Perth Hospital since this introduction. Results were compared with online survey and 1-week in-theatre snapshot audit) were undertaken to investigate the change of beliefs and clinical practice order to assess the volume status accurately and to optimize hemodynamic performance. http://www.ncbi.nlm.nih.gov/pubmed?tool=iau&term=2015420118

Anesthesiology Research and Practice. 2015; 2015: 367937.

Neuromuscular monitoring, muscle relaxant use, and reversal at a tertiary teaching hospital 2.5 years after introduction of sugammadex: changes in opinions and clinical practice. Ledowski T, Ong JS, et al. Ledowski,Thomas. Department of Anaesthesia, Royal Perth Hospital, Perth, WA 6000, Australia ; University of Western Australia, Perth, WA 6009, Australia. Ong, J.J.ing Shen. Royal Perth Hospital, Perth, WA 6000, Australia. Flett, Tom. Department of Intensive Care, The Alfred Hospital, Melbourne, VIC 3000, Australia. Sugammadex was introduced to Royal Perth Hospital in early 2011 without access restriction. Two departmental audits (26-page online survey and 1-week in-theatre snapshot audit) were undertaken to investigate the change of beliefs and clinical practice related to the use of neuromuscular blocking agents at the Royal Perth Hospital since this introduction. Results were compared with data from 2011. We found that, in the 2.5 years since introduction of Sugammadex, more anesthetists (69.5 versus 38%) utilized neuromuscular monitoring, and aminosteroidal neuromuscular blocking agents were used in 94.3% of cases (versus 77% in 2011). Furthermore, 53% of anesthetists identified with a practice of “deeper and longer” intraoperative paralysis of patients. All 71 patients observed during the 5-day in-theatre audit were reversed with Sugammadex. Since the introduction of Sugammadex, 69% (n = 20) of respondents felt it provided “faster turnover,” less postoperative residual neuromuscular blockade (n = 23; 79%), and higher anesthetist satisfaction (n = 17; 59%). 45% (n = 13) of colleagues reported that they would feel professionally impaired without the unrestricted availability of Sugammadex, and 1 colleague would refuse to work in a hospital without this drug being freely available. In clinical practice Sugammadex was frequently (57%) mildly overdosed, with 200mg being the most commonly administered dose.


Anesthesiology Research and Practice. 2015; 2015(410248).

Postoperative residual neuromuscular paralysis at an Australian tertiary children's hospital. Ledowski T, O’Dea B, et al. (Ledowski, O’Dea, Meyerkort, Von Ungern-Sternberg) School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6009, Australia (Ledowski) Department of Anaesthesia and Pain Medicine, Royal Perth Hospital, Perth, WA 6000, Australia (Hegarty, Von Ungern-Sternberg) Department of Anaesthesia and Pain Management, Princess Margaret Hospital for Children, Perth 6008, Australia B.S. Von Ungern-Sternberg, School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6009, Australia Purpose. Residual neuromuscular blockade (RNMB) is known to be a significant but frequently overlooked complication after the use of neuromuscular blocking agents (NMBA). Aim of this prospective audit was to investigate the incidence and severity of RNMB at our Australian tertiary pediatric care center. Methods. All children receiving NMBA during anesthesia were included over a 5-week period at the end of 2011 (Mondays to Fridays; 8 a.m.-6 p.m.). At the end of surgery, directly prior to tracheal extubation, the train-of-four (TOF) ratio was assessed quantitatively. Data related to patient postoperative outcome was collected in the postoperative acute care unit. Results. Data of 64 patients were analyzed. Neostigmine was given in 34 cases and sugammadex in 1 patient. The incidence of RNMB was 28.1% overall (without reversal: 19.4%; after neostigmine: 37.5%; n.s.). Severe RNMB (TOF ratio < 0.7) was found in 6.5% after both no reversal and neostigmine, respectively. Complications in the postoperative acute care unit were infrequent, with no differences between reversal and no reversal groups. Conclusions. In this audit, RNMB was frequently observed, particularly in cases where patients were reversed with neostigmine. These findings underline the well-known problems associated...
with the use of NMBA that are not fully reversed.


Intravenous iron in clinical concentrations does not impair haemoglobin measurement.
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BACKGROUND: Intravenous iron is commonly administered to anaemic patients to treat iron deficiency, but due to its ferric colouration, it may interfere with the spectrophotometric assessment of haemoglobin concentrations. This paper investigates the potential interference of three clinically used intravenous iron preparations on the measurement of haemoglobin.

METHODS: Haemoglobin concentration was measured for neat and Hartmann's solution-diluted iron polymaltose, carboxymaltose and sucrose solutions using bedside (Radiometer HemoCue(R)), point-of-care (Radiometer ABL800 Flex) and laboratory (Abbott CellDyne Sapphire) devices. Haemoglobin concentration was then assessed with the same devices utilizing anaemic whole blood with the iron solutions added.

RESULTS: Neat iron preparations registered clinically significant haemoglobin concentrations on bedside and laboratory measurements. When intravenous iron preparations were diluted to clinical concentrations, their effect on haemoglobin measurements, either in isolation or mixed with anaemic blood, was negligible.

CONCLUSION: Although neat preparations of intravenous iron do interfere with spectrophotometric analysis of haemoglobin, concentrations likely to be seen post iron infusion do not significantly interfere with haemoglobin measurement.

Ann Neurol. 2015.

Familial cortical dysplasia caused by mutation in the mTOR regulator NPRL3.
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Clinical Genetics, Austin Health, Melbourne, Australia.
Shriners Hospital Pediatric Research Center, Temple University, Philadelphia, USA.

We describe first cousin sibling pairs with focal epilepsy, one of each pair having focal cortical dysplasia (FCD) IIa. Linkage analysis and whole-exome sequencing identified a heterozygous germline frameshift mutation in the gene encoding nitrogen permease regulator-like 3 (NPRL3). NPRL3 is a component of GATOR1, a negative regulator of the mTORC1 signaling pathway.

Immunostaining of resected brain tissue demonstrated mTOR activation. Screening of 52 unrelated individuals with FCD identified two additional patients with FCDIIa and germline NPRL3 mutations. Similar to DEPDC5, NPRL3 mutations may be considered as causal variants in patients with FCD or MRI-negative focal epilepsy. This article is protected by copyright. All rights reserved.

Ann Oncol. 2015.

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Department of Medical Oncology, Port Macquarie Base Hospital, Port Macquarie.
Department of Medical Oncology, The Tweed Hospital, Tweed Heads School of Medicine & Dentistry, Griffith University, Southport.
Department of Medical Oncology, Nepean Cancer Care Centre, Kingswood.
Department of Medical Oncology, Nambour General Hospital, Nambour.
Department of Medical Oncology, Lismore Base Hospital, Lismore.
Glioblastoma adaptation traced through decline of an IDH1 clonal driver and macro-evolution of a double-minute chromosome.


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NanOmits, LLC, Santa Cruz, USA.

Illumina Ltd, Cambridge.

University College London Cancer Institute, London, United Kingdom.

Department of Molecular and Clinical Cancer Medicine, University of Liverpool, Liverpool Department of Radiation Oncology, Clatterbridge Cancer Centre NHS Foundation Trust, Bebington, United Kingdom.

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BACKGROUND: Glioblastoma (GBM) is the most common malignant brain cancer occurring in adults, and is associated with dismal outcome and few therapeutic options. GBM has been shown to predominantly disrupt three core pathways through somatic aberrations, rendering it ideal for precision medicine approaches. METHODS: We describe a 35-year-old female patient with recurrent GBM following surgical removal of the primary tumour, adjuvant treatment with temozolomide and a 3-year disease-free period. Rapid whole-genome sequencing (WGS) of three separate tumour regions at recurrence was carried out and interpreted relative to WGS of two regions of the primary tumour. RESULTS: We found extensive mutational and copy-number heterogeneity within the primary tumour. We identified a TP53 mutation and two focal amplifications involving PDGFRA, KIT and CDK4, on chromosomes 4 and 12. A clonal IDH1 R132H mutation in the primary, a known GBM driver event, was detectable at only very low frequency in the recurrent tumour. After sub-clonal diversification, evidence was found for a whole-genome doubling event and a translocation between the amplified regions of PDGFRA, KIT and CDK4, encoded within a double-minute chromosome also incorporating miR26a-2. The WGS analysis uncovered progressive evolution of the double-minute chromosome converging on the KIT/PDGFRA/PI3K/mTOR axis, superseding the IDH1 mutation in dominance in a mutually exclusive manner at recurrence, consequently the patient was treated with imatinib. Despite rapid sequencing and cancer genome-guided therapy against amplified oncogenes, the disease progressed, and the patient died shortly after. CONCLUSION: This case sheds light on the dynamic disease at recurrence and the loss of a clonal driver. Even in the era of rapid WGS analysis, cases such as this illustrate the significant hurdles for precision medicine success.

In reply,
Isbister GK, Page CB, et al.

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Publication Types: Comment

Letter


A phase II1 randomized trial of adding topical nitroglycerin to first-line chemotherapy for advanced nonsmall-cell lung cancer: the Australasian lung cancer trials group NITRO trial.


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BACKGROUND: We sought to determine whether the substantial benefits of topical nitroglycerin with first-line, platinum-based, doublet chemotherapy in advanced nonsmall-cell lung cancer (NSCLC) seen in a phase II trial could be corroborated in a rigorous, multicenter, phase III trial.

PATIENTS AND METHODS: Patients starting one of five, prespecified, platinum-based doublets as first-line chemotherapy for advanced NSCLC were randomly allocated treatment with or without nitroglycerin 25 mg patches for 2 days before, the day of, and 2 days after, each chemotherapy infusion. Progression-free survival (PFS) was the primary end point.

RESULTS: Accrual was stopped after the first interim analysis of 270 events. Chemotherapy was predominantly with carboplatin and gemcitabine (79%) or carboplatin and paclitaxel (18%). The final analysis included 345 events in 372 participants with a median follow-up of 33 months. Topical nitroglycerin had no demonstrable effect on PFS [median 5.0 versus 4.8 months, hazard ratio (HR) = 1.07, 95% confidence interval (CI) 0.86-1.22, P = 0.25; overal survival (median 11.0 versus 10.3 months, HR = 0.99, 95% CI 0.79-1.24, P = 0.84), or objective tumor response (31% versus 30%, relative risk = 1.03, 95% CI 0.82-1.29, P = 0.81). Headache, hypotension, syncope, diarrhea, dizziness, and anorexia were more frequent in those allocated nitroglycerin.

CONCLUSION: The addition of topical nitroglycerin to carboplatin-based, doublet chemotherapy in NSCLC had no demonstrable benefit and should not be used or pursued further.

CLINICAL TRIALS NUMBER: Australian New Zealand Clinical Trials Registry Number ACTRN12608000588392. Copyright © The Author 2015. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. For permissions, please email: journals.permissions@oup.com.


Aortic pseudoaneurysm eroding through the anterior chest wall.

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Publication Types: Note


Transapical Versus Transaortic Transcatheter Aortic Valve Implantation: A Systematic Review.
Dunne B, Tan D, et al.
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B. Dunne, Department of Cardiothoracic Surgery, Royal Perth Hospital, Perth, WA 6000, Australia

Two alternative approaches for transcatheter aortic valve implantation (TAVI) exist for patients unsuitable for the transfemoral approach; the transapical and the transaortic approach. It is unclear as to which approach has superior short-term outcomes. A systematic review and meta-analysis was performed to answer this question. Mortality was equivalent in the 2 groups. There was a trend toward a lower rate of stroke in the transaortic group (0.9% vs 2.1%) but this was not statistically significant. Conversion to surgical aortic valve replacement, paravalvular leak, pacemaker requirement, and major bleeding occurred at equivalent rates.


Mechanical prostheses for right ventricular outflow tract reconstruction: a systematic review and meta-analysis.
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It remains unclear as to whether mechanical valves have a role in pulmonary valve replacement. A systematic review and meta-analysis was performed to answer this question. Nineteen observational studies, including 299 pediatric and adult patients with a mean follow-up of 73 months, were analyzed. Nonstructural valve deterioration and valve thrombosis occurred in 1.5% and 2.2% of patients, respectively. Surgical reintervention was performed in 0.9% of cases and thrombosis was required in 0.5%. Mechanical valves in the pulmonary position are associated with a low incidence of valve deterioration and thrombosis, as well as freedom from reoperation and thrombosis. Copyright © 2015 The Society of Thoracic Surgeons. Published by Elsevier Inc. All rights reserved.

Publication Types: Review


A CC12 MRSA strain, West Australian MRSA-59, harbors a novel pseudo-SCCmec element.
Monecke S, Coombs GW, et al.
Alere Technologies GmbH, Jena, Germany. Institute for Medical Microbiology and Hygiene, Faculty of Medicine "Carl Gustav Carus", Technische Universitat Dresden, Dresden, Germany. InfectoGnostics Forschungscampus Jena, Germany.

An Australian MRSA strain (WA-MRSA-59) was characterized by microarray and sequencing. Its pseudo-SCCmec element comprised dcs, Q9XB68-dcs, mva5-SCC, Q5HJ W6, dru, ugpQ, ydeM, mecA+mecR+mecI, txbi mecI, tnp IS431, copA2+mco (copper resistance), ydhK, arsC+arsR (arsenic resistance), ORF PT43 and per2. Recombinase genes, xylR/mecR2 and PSM-mec (phenol-soluble modulin) were absent. We suggest that the mec complex A should be split into two subtypes. One harbors PSM-mec and xylR/mecR2. It is found in SCCmec II, III and VIII. The second subtype as described herein is present in WA-MRSA-59 and some coagulase-negative staphylococci.


Pharmacokinetics of a novel sublingual spray formulation of the antimalarial drug artemether in healthy adults.
Salman S, Bendel D, et al.

The pharmacokinetics of sublingual artemether (ArtIMist) was investigated in two open-label studies. In study 1, 16 healthy males
were randomized to each of four single-dose treatments administered in random order: (i) 15.0 mg of sublingual artemether (5 x 3.0 actuations), (ii) 30.0 mg of sublingual artemether (10 x 3.0 mg), (iii) 30.0 mg of sublingual artemether (5 x 6.0 mg), and (iv) 30.0 mg of artemether in tablet form. In study 2, 16 healthy males were randomized to eight 30.0-mg doses of sublingual artemether, Madang, Papua New Guinea. 5 days as either 10 3.0-mg or 5 6.0-mg actuations. Frequent blood samples were drawn postdose. Plasma artemether and dihydroartemisinin levels were measured using liquid chromatography-mass spectrometry. Population compartmental pharmacokinetic models were developed. In study 1, sublingual artemether absorption was biphasic, with both rate constants being greater than that of the artemether tablets (1.46 and 1.66 versus 0.43/h, respectively). Relative to the tablets, sublingual artemether had greater bioavailability (>1.24), with the greatest relative bioavailability occurring in the 30.0-mg dose groups (>1.58). In study 2, there was evidence that the first absorption phase accounted for between 32% and 69% of the total dose and avoided first-pass (FP) metabolism, with an increase in FP metabolism occurring in later versus earlier doses but with no difference in bioavailability between the dose actuations. Sublingual artemether is more rapidly and completely absorbed than are equivalent doses of artemether tablets in healthy adults. Its disposition appears to be complex, with two absorption phases, the first constants being greater than that of the artemether tablets (1.46 and 1.66 versus 0.43/h, respectively). Relative to the tablets,sublingual artemether had greater bioavailability (>1.24), with the greatest relative bioavailability occurring in the 30.0-mg dose groups (>1.58). In study 2, there was evidence that the first absorption phase accounted for between 32% and 69% of the total dose and avoided first-pass (FP) metabolism, with an increase in FP metabolism occurring in later versus earlier doses but with no difference in bioavailability between the dose actuations. Sublingual artemether is more rapidly and completely absorbed than are equivalent doses of artemether tablets in healthy adults. Its disposition appears to be complex, with two absorption phases, the first representing pregastrointestinal absorption, as well as dose-dependent bioavailability and autoinduction of metabolism with multiple dosing. Copyright © 2015, American Society for Microbiology. All Rights Reserved.

Pharmacokinetics of a novel sublingual spray formulation of the antimalarial drug artemether in African children with malaria.
Salman S, Bendel D, et al.
The pharmacokinetics of sublingual artemether (ArtiMist) was investigated in 91 young African children with severe malaria or who could not tolerate oral antimalarial therapy. Each received 3.0 mg/kg of body weight of artemether at 0, 8, 24, 36, and 48 hours after initial dose. Postdose, frequent blood samples were drawn. Plasma artemether and dihydroartemisinin (DHA) levels were measured using liquid chromatography-mass spectrometry, and the data were analyzed using established population compartmental pharmacokinetic models. Parasite clearance was prompt (median parasite clearance time, 24 h), and there were no serious adverse events. Consistent with studies in healthy adults

Pharmacokinetics of Piperaquine Transfer into the Breast Milk of Melanesian Mothers.
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Transfer of piperaquine (PQ) into breast milk was examined in 27 Papua New Guinean women given a 3-day course of dihydroartemisinin-PQ or sulfadoxine-pyrimethamine-PQ during the second/third trimester. Breast milk was sampled on days 1, 2, 3 to 5, 7 to 11, and 14 to 17 postdelivery, a median of 70 days postdose (range, 6 to 145 days). A blood sample was taken at delivery, and additional serial samples were available from 9 women who delivered within 42 days of dosing. Milk and plasma PQ were assayed by high-performance liquid chromatography. A population-based approach was used to model the loge(plasma) and milk concentration-time data. A sigmoid Emax model best described PQ breast milk transfer. The population average milk:plasma PQ ratio was 0.58, with a peak of 2.5 at delivery. The model-derived maximum milk intake (148 ml/kg of body weight/day) was similar to the accepted value of 150 ml/kg/day. The median estimated absolute and relative cumulative infant PQ doses were 22 mug and 0.07%, respectively, corresponding to absolute and relative daily doses of 0.41 mug/kg and 0.004%. Model-based simulations for PQ treatment regimens given at birth, 1 week postdelivery, and 6 weeks postdelivery showed that the highest median estimated relative total infant dose (0.36%; median absolute total dose of 101 mug/kg) was seen after maternal PQ treatment 6 weeks postpartum. The maximum simulated relative total and daily doses from any scenario were 4.3% and 2.5%, respectively, which were lower than the recommended 10% upper limit. Piperaquine is transferred into breast milk after maternal treatment doses, but PQ exposure for suckling infants appears safe. Copyright © 2015, American Society for Microbiology. All Rights Reserved.

Gametocyte Clearance Kinetics Determined by Quantitative Magnetic Fractionation in Melanesian Children with Uncomplicated Malaria Treated with Artemisinin Combination Therapy.

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Gametocyte Clearance Kinetics Determined by Quantitative Magnetic Fractionation in Melanesian Children with Uncomplicated Malaria Treated with Artemisinin Combination Therapy.

Karl,Stephan. School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia. Laman,Moses. School of Medicine and Pharmacology, University of Western Australia, Australia. Moore,Brioni R. School of Medicine and Pharmacology, University of Western Australia, Australia. Woodward,Robert C. School of Physics, University of Western Australia, Australia.

Pseudo-SCCmec Element.

Monecke S, Coombs GW, et al.


Monecke S, Coombs GW, et al.


Monecke S, Coombs GW, et al.


Monecke S, Coombs GW, et al.


Monecke S, Coombs GW, et al.


Monecke S, Coombs GW, et al.
Outcomes of open partial nephrectomies performed by Australian trainees.
Tucker PE, Rukin NJ, et al.
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Department of Urology, St John of God Hospital, Perth, Western Australia, Australia.
Department of Urology, The Royal Wolverhampton Hospital NHS Trust, Wolverhampton, UK.
Department of General Surgery, Derriford Hospital, Plymouth, UK.
Department of Urology, Rockingham Hospital, Rockingham, Western Australia, Australia.
BACKGROUND: Partial nephrectomy (PN) has become the standard of care for small renal tumours, with open partial nephrectomy (OPN) being superseded by minimally invasive PN. Advances in minimal access surgery have resulted in fewer relative contraindications, with subsequently fewer OPN being performed. Consequentially, trainees have less opportunity to gain skills and experience in open renal surgery. The aims of this study were to assess the standard of OPN performed by Australian urological trainees and to define whether OPN is a safe and suitable training opportunity. METHOD: A retrospective review was undertaken on patients who underwent OPN performed by urology trainees from 2010 to 2014 at two training hospitals in Western Australia. Data collected included patient demographics, surgical and oncological outcomes and morbidity. RESULTS: Sixty patients underwent OPN, with a mean age of 56 years. Most tumours were single, with mean size 31 mm. Mean operative time was 157 min, with a mean cold ischaemic time of 27 min. Mean pre- and post-operative creatinine levels were equivalent (77 mumol/L). The overall complication rate was 18%, with no documented urinary leaks, and 1.7% blood transfusion rate. Median length of stay was 4 days. There were no oncological positive margins or recurrence after a median follow-up of 2 years. CONCLUSION: Our data support the notion that Australian urological trainees can perform the majority of OPN cases, with equivalent oncological outcomes. We would advocate that when an OPN is being performed, the supervising consultant should use the case as an adjuvant for open renal surgery training.

Recurrence in patients with stage I colorectal cancer.
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Oncology Department, St John of God and Royal Perth Hospital, Perth, Western Australia, Australia.
Colorectal Surgical Unit, Western Health, Melbourne, Victoria, Australia.
Royal Melbourne Hospital, Melbourne, Victoria, Australia.
Department of Medical Oncology, Royal Melbourne Hospital, Melbourne, Victoria, Australia.
Colorectal Surgical Unit, Saint John of God Hospital Subiaco, Perth, Western Australia, Australia.
Department of Surgery, University of Western Australia, Perth, Western Australia, Australia.
BACKGROUND: Outcomes of patients with stage I colorectal cancer submitted to surgery with curative intent have not been thoroughly explored in contemporary series. METHODS: All patients with colon or rectal adenocarcinoma who underwent resection from the St John of God Hospital (1996-2013) and BioGrid (1991-2013) databases were identified. Patients submitted to local excision, polypectomies or neoadjuvant treatment were excluded. Outcomes included recurrence (combined local and systemic), recurrence-free and overall survival, and survival after recurrence. RESULTS: A total of 1193 patients with stage I disease were included. Median age was 67 (interquartile range 59-75) and median follow-up was 3.2 years (interquartile range 1.4-5.8). Five-year recurrence rate was 7.1% (95% confidence interval (CI) 5.4-9.4%); 5.0% for colon and 11.1% for rectal cancer). Rectal location was an independent predictor of recurrence (hazard ratio (HR) 1.97, 95% CI 1.09-3.55; P = 0.024). Lymphovascular invasion was an independent predictor of recurrence only in patients with rectal cancer (HR 3.0, 95% CI 1.2-7.6; P = 0.018). Five-year recurrence-free survival was 83.2% (95% CI 80.3-85.4%). Age (HR 1.05, 95% CI 1.03-1.07; P < 0.001), elective surgery (HR 0.41, 95% CI 0.21-0.80; P = 0.011) and the American Society of Anesthesiologists (ASA) score (HR 3.08, 95% CI 1.51-6.31; P < 0.001) were independently associated with recurrence-free survival. Median survival after recurrence was 41 months. Recurrence was attempted in 39% of patients. CONCLUSION: Patients with stage I colorectal cancers still have a clinically significant risk of recurrence. Rectal location is independently associated with higher recurrence. Age, elective surgery and ASA are independently associated with recurrence-free survival. A significant proportion of patients with recurrence underwent further resection.

Rare case of iliopsoas hernia: incidental finding at laparoscopic total extraperitoneal hernia repair.
Department of General Surgery, Fiona Stanley Hospital, Perth, Western Australia, Australia.
Department of General Surgery, Armadale Health Service, Perth, Western Australia, Australia.
Department of General Surgery, St John of God Murdoch Hospital, Perth, Western Australia, Australia.
Click it: do not risk it: lap seat belt causing extensive abdominal injuries.
Vascular Surgery, Fiona Stanley Hospital, Perth, Western Australia, Australia.

Pneumatosis intestinalis: a diagnostic dilemma.
Department of General Surgery, Fremantle Hospital, Fremantle, Western Australia, Australia.

Prognostic factors following pathological fractures.
Hill T, D'Alessandro P, et al.
Hill,Thomas. Department of Orthopaedics, Fremantle Hospital, Perth, Western Australia, Australia.

BACKGROUND: Pathological fractures are a significant and often devastating event in the progression of metastatic bone disease. They are frequently a marker of end-stage cancer and the end of functional independence. Although several studies look into prognosis following the development of metastatic lesions, few look into the prognosis after the fracture itself. This study investigates the variables affecting prognosis in patients suffering pathological fractures.

METHOD: Retrospective clinical audit of 72 patients from the Orthopaedic Unit at Fremantle Hospital in Western Australia. The variables of interest include primary cancer, fracture site, method of fixation, use of cement augmentation, appendicular metastatic load, spinal metastatic load, presence of visceral metastases, patient co-morbidities and functional scoring before and after the fracture has occurred.

RESULTS: The median time between diagnosis of cancer to pathological fracture was 8.3 months, while the median survival post-fracture was 3.3 months. There is a statistically significant correlation between patient survival and primary cancer type, spinal metastatic burden and functional performance score.

CONCLUSION: Overall, the prognosis following pathological fracture is extremely poor. We propose that these variables are scrutinized by the treating orthopaedic team preoperatively to help guide management and provide patients and their families with a realistic expectation of functional outcome and survival time.

Training models for meniscal repairs and small joint arthroscopy.
Kovac N, Grainger N, et al.
Kovac,Nikola. Clinical Services, Royal Perth Hospital, Perth, Western Australia, Australia. Grainger,Nicholas. Large Animal Laboratory, Royal Perth Hospital, Perth, Western Australia, Australia. Hurworth,Mark. Orthopaedics, Royal Perth Hospital, Perth, Western Australia, Australia.

BACKGROUND: The reduced availability of human cadavers and their associated high costs, coupled with an increasing requirement for meeting continuing professional development targets, has accentuated the need for alternative training models that meet current ethical standards. The aim of this study is to identify suitable substitutes that are accessible and cost effective for use as training models for meniscal repairs and small joint arthroscopy.

METHOD: Ovine, bovine and porcine stifles were analysed for comparable anatomy to the human knee, arthroscopic access, arthroscopic view and ease of meniscal repair.

RESULTS: The bovine stifle joint was found to be too large and offered limited access due to a large anterior fat pad and thick surrounding soft tissue. The ovine and bovine stifles were both easily available and had comparable anatomy to the human knee. Advantages of the porcine stifle include better availability and easier accessibility, comparable anatomy to the human knee and its relatively larger size that made it easier to arthroscope.

CONCLUSION: Porcine stifles are cost effective, accessible, allow for meniscal repair and are suitable for arthroscopic access and view. Our view is that they are an ideal training model for arthroscopic meniscal repair, small joint arthroscopy and anterior cruciate ligament reconstruction.

Management of complex anal fistulae.
Bartolo DC.
Bartolo,David C C. Department of Colorectal Surgery, Fiona Stanley Hospital, Murdoch, Western Australia, Australia. Bartolo,David C C. Department of Surgery, University of Western Australia, Crawley, Western Australia, Australia.

Publication Types: Editorial
and six participants to UC. No significant differences were present in baseline prognostic factors between the two groups prior to sentence production, and discourse structure. Outcomes & Results: Eight participants were assigned to the NARNIA intervention to meet the assessed needs of the participant. The Curtin University Discourse Protocol (CUDP) was used to measure verb access, everyday discourse (ED) genres. UC comprised any speech-language therapy routinely used in clinical practice, individually tailored groups across ED genres. The NARNIA group made significant gains across all language levels, while the UC made isolated gains in group gains for the NARNIA participants will provide a platform to power a larger trial to evaluate the effectiveness of this significantly different between groups, significant within-group differences were seen. While both groups significantly improved in measures than in the UC group, with no other between-group differences found. Significant changes were, however, seen within groups across ED genres. The NARNIA group made significant gains across all language levels, while the UC made isolated gains in sentence production. Few changes were seen in narrative discourse for either group. While single-word processing was not significantly different between groups, significant within-group differences were seen. While both groups significantly improved in retrieving nouns in isolation, only the NARNIA group made significant improvement in verb processing. No change was seen in constrained sentence production for either group. Conclusions: These findings are highly promising in demonstrating the use of macrostructure to scaffold production of words and sentences and improve discourse organisation. The significantly greater within-group gains for the NARNIA participants will provide a platform to power a larger trial to evaluate the effectiveness of this integrated multilevel intervention for aphasia.


A new, simple and precise method for measuring cyclotron proton beam energies using the activity vs. depth profile of zinc-65 in a thick target of stacked copper foils.

Depressive symptoms and adverse outcomes from hospitalization in older adults: secondary outcomes of a trial of falls prevention education. [Erratum appears in Arch Gerontol Geriatr. 2015 Mar-Apr;60(2):372 Note: Hill, D [corrected to Hill, Keith D]].

Haines TP, Williams CM, et al.

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Depression is common in older people and symptoms of depression are known to substantially increase during hospitalization. There is little known about predictors of depressive symptoms in older adults or impact of common interventions during hospitalization. This study aimed to describe the magnitude of depressive symptoms, shift of depressive symptoms and the impact of the symptoms of depression among older hospital patients during hospital admission and identify whether exposure to falls prevention education affected symptoms of depression. Participants (n=1206) were older adults admitted within two Australian hospitals, the majority of participants completed the Geriatric Depression Scale - Short Form (GDS) at admission (n=1168). Participants' mean age was 74.7 (+/- SD 11) years and 47% (n=551) were male. At admission 53% (619 out of 1168) of participants had symptoms of clinical depression and symptoms remained at the same level at discharge for 55% (543 out of 987). Those exposed to the low intensity education program had higher GDS scores at discharge than those in the control group (low intensity vs control n=652, adjusted regression coefficient (95% CI)=0.24 (0.02, 0.45), p=0.03). The only factor other than admission level of depression that affected depressive symptoms was if the participant was worried about falling. Older patients frequently present with symptoms of clinical depression on admission to hospital. Future research should consider these factors, whether these are modifiable and whether treatment may influence outcomes. Copyright © 2014 Elsevier Ireland Ltd. All rights reserved.

Publication Types: Randomized Controlled Trial

Research Support, Non-U.S. Gov't


Archives of Gerontology & Geriatrics. 2015; 60(1): 96-102.

Depressive symptoms and adverse outcomes from hospitalization in older adults: secondary outcomes of a trial of falls prevention education.

Haines TP, Williams CM, et al.

Haines, Terry P. Monash University/Monash Health, Allied Health Research Unit, Monash Health Kingston Hospital, Cnr Warrigal and Kingston Rds, Cheltenham, VIC 3192, Australia (Williams) Allied Health Research Unit, Monash Health Kingston Hospital, Cnr Warrigal and Kingston Rds, Cheltenham, VIC 3192, Australia (Hill) The University of Notre Dame Australia, 19 Mouat Street (PO Box 1225), Fremantle, WA 6959, Australia (McPhail) Queensland University of Technology/Queensland Health, Australia (Hill) Curtin University, School of Physiotherapy, Australia (Brauer) Queensland University of Queensland, School of Health and Rehab Sciences, Brisbane, QLD 4072, Australia (Hoffmann) Centre for Research in Evidence-Based Practice, Bond University, Faculty of Health Sciences and Medicine, QLD 4229, Australia (Etherington-Beer) University of Western Australia, School of Medicine and Pharmacology Royal Perth Hospital Unit, 35 Stirling Highway, Crawley, WA 6009, Australia.
Depression is common in older people and symptoms of depression are known to substantially increase during hospitalization. There is little known about predictors of depressive symptoms in older adults or impact of common interventions during hospitalization. This study aimed to describe the magnitude of depressive symptoms, shift of depressive symptoms and the impact of the symptoms of depression among older hospital patients during hospital admission and identify whether exposure to falls prevention education affected symptoms of depression. Participants (n = 1206) were older adults admitted within two Australian hospitals, the majority of participants completed the Geriatric Depression Scale - Short Form (GDS) at admission (n = 1168). Participants' mean age was 74.7 (+/-SD 11) years and 47% (n = 551) were male. At admission 53% (619 out of 1168) of participants had symptoms of clinical depression and symptoms remained at the same level at discharge for 55% (543 out of 987). Those exposed to the low intensity education program had higher GDS scores at discharge than those in the control group (low intensity vs control n = 652, adjusted regression coefficient (95% CI) = 0.24 (0.02, 0.45), p = 0.03). The only factor other than admission level of depression that affected depressive symptoms change was if the participant was worried about falling. Older patients frequently present with symptoms of clinical depression on admission to hospital. Future research should consider these factors, whether these are modifiable and whether treatment may influence outcomes.


Archives of Gerontology and Geriatrics. 2015; 60(2): 372.  
Haines TP, Williams CM, et al.  
Publication Types: Erratum  

Archives of Medical Science. 2015; 11(5): 915-926.  
Sleep changes following statin therapy: A systematic review and meta-analysis of randomized placebo-controlled polysomnographic trials.  
Broncel M, Gorzelak-Pabis P, et al.  
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M. Banach, Department of Hypertension, Nephrology and Hypertension, WAM University Hospital, Medical University of Lodz, 113 Zeromskiego St, Lodz 90-549, Poland  
Introduction: Statin use might be associated with an increased risk of sleep disturbances including insomnia, but the evidence regarding sleep changes following statin therapy has not been conclusive. Therefore we assessed the impact of statin therapy on sleep changes through a systematic review and meta-analysis of available randomized controlled trials (RCTs). Material and methods: We searched MEDLINE and SCOPUS up to October 1, 2014 to identify placebo-controlled RCTs investigating the effect of statin therapy on sleep changes. A meta-analysis was performed using either a fixed-effects or a random-effect model according to the I2 statistic. Effect size was expressed as weighted mean difference (WMD) and 95% confidence interval (CI). Results: Overall, the impact of statin therapy on polysomnography (PSG) indices of sleep was reported in 5 trials comprising 9 treatment arms. Overall, statin therapy had no significant effect on total sleep duration (WMD: -7.75 min, 95% CI: -18.98, 3.48, p = 0.176), sleep efficiency (WMD: 0.09%, 95% CI: -2.27, 2.46, p = 0.940), entries to stage I (WMD: 0.36, 95% CI: -0.91, 1.63, p = 0.580), or latency to stage I (WMD: -1.92 min, 95% CI: -4.74, 0.89, p = 0.181). In contrast, statin therapy significantly reduced wake time (WMD: -4.43 min, 95% CI: -7.77, -0.88, p = 0.014) and number of awakenings (WMD: -0.40, 95% CI: -0.46, -0.33, p < 0.001). Meta-regression did not suggest any correlation between changes in wake time and awakening episodes with duration of treatment and LDL-lowering effect of statins. Conclusions: The results indicated that statins have no significant adverse effect on sleep duration and efficiency, entry to stage I, or latency to stage I sleep, but significantly reduce wake time and number of awakenings.  
Publication Types: Review  

Kinetic and Related Determinants of Plasma Triglyceride Concentration in Abdominal Obesity: Multicenter Tracer Kinetic Study.  
Boren J, Watts GF, et al.  
Boren, Jan. From the Department of Molecular and Clinical Medicine, University of Gothenburg and Sahlgrenska University Hospital, Gothenburg, Sweden (J.B., M.A.); Lipid Disorders Clinic, Metabolic Research Centre, Cardiovascular Medicine, Royal Perth Hospital, School of Medicine and Pharmacology (G.F.W., D.C.C., P.H.R.B.) and Faculty of Engineering, Computing and Mathematics (P.H.R.B.), University of Western Australia, Perth, Australia; Heart and Lung Centre, Helsinki University Central Hospital and
APPRAOCH AND RESULTS: A multicenter study using dual stable isotopes (deuterated leucine and glycerol) and multicompartmental modeling was performed to elucidate the kinetics of triglycerides and apoB in VLDL1 in 46 subjects with abdominal obesity and additional cardiometabolic risk factors. Results showed that plasma triglyceride concentrations were dependent on both the secretion rate (r=0.44, P<0.01; r=0.45, P<0.01) and fractional catabolism (r=0.49, P=0.001; r=0.55, P<0.001) of VLDL1-triglycerides and VLDL1-apoB. Liver mass was independently and directly associated with secretion rates of VLDL1-triglycerides (r=0.56, P<0.001) and VLDL1-apoB (r=0.53, P=0.001). Plasma apoC-III concentration was independently and inversely associated with the fractional catabolism of VLDL1-triglycerides (r=0.48, P<0.001) and VLDL1-apoB (r=0.51, P<0.001). 

CONCLUSIONS: Plasma triglyceride concentrations in abdominal obesity are determined by the kinetics of VLDL1 subfractions, catabolism being mainly dependent on apoC-III concentration and secretion on liver fat content. Reduction in liver fat and targeting apoC-III may be an effective approach for correcting triglyceride metabolism atherogenic dyslipidemia in obesity. Copyright © 2015 American Heart Association, Inc.


Hao Y, Thakkar V, et al.

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Introduction: There is evidence that early screening for pulmonary arterial hypertension (PAH) in systemic sclerosis (SSc) improves outcomes. We compared the predictive accuracy of two recently published screening algorithms (DETECT 2013 and Australian Scleroderma Interest Group (ASiG) 2012) for SSc-associated PAH (SSc-PAH) with the commonly used European Society of Cardiology/European Respiratory Society (ESC/ERS 2009) guidelines. Methods: We included 73 consecutive SSc patients with suspected PAH undergoing right heart catheterization (RHC). The three screening models were applied to each patient. For each model, contingency table analysis was used to determine sensitivity, specificity, and positive (PPV) and negative (NPV) predictive values for PAH. These properties were also evaluated in an 'alternate scenario analysis' in which the prevalence of PAH was set at 10%. Results: RHC revealed PAH in 27 (36.9%) patients. DETECT and ASiG algorithms performed equally in predicting PAH with sensitivity and NPV of 100%. The ESC/ERS guidelines had sensitivity of 96.3% and NPV of only 91%, missing one case of PAH. These guidelines could not be applied to three patients who had absent tricuspid regurgitant (TR) jet. The ASiG algorithm had the
highest specificity (54.5%). With PAH prevalence set at 10%, the NPV of the models was unchanged, but the PPV dropped to less than 20%. Conclusions: In this cohort, the DETECT and ASIG algorithms out-perform the ESC/ERS guidelines, detecting all patients with PAH. The ESC/ERS guidelines have limitations in the absence of a TR jet. Ultimately, the choice of SSC-PAH screening algorithm will also depend on cost and ease of application.


Arthritis Rheumatol. 2015.

Interpretation of an extended auto-antibody profile in a well characterised Australian systemic sclerosis (scleroderma) cohort utilising Principle Components Analysis.

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OBJECTIVE: To determine the relationships between systemic sclerosis (SSc) related autoantibodies (AA), and their clinical associations, in a well characterised Australian patient cohort. METHODS: Serum from 505 Australian SSc patients were analysed with a line immunoassay (EUROLINE, Euroimmun, Lubeck, Germany) for AA to centromere (CENP) A and B, RNA polymerase III (RNAP3) (11 and 155 epitopes), NOR-90, Fibrillarin, Th/To, PMScl-75 and PMScl-100, Ku, Topoisomerase-1 (Topo1), TRIM21/Ro52 and PDGF-Receptor (PDGFR). Patient subgroups were identified by hierarchical clustering of the first two dimensions of a Principal Components Analysis (PCA) of quantitative AA scores. Results were compared with detailed clinical data. RESULTS: 449/505 patients were positive for at least one immunoblot AA. Heatmap visualisation of AA scores, and PCA clustering, demonstrated strong, mutually exclusive relationships between CENP, RNAP3 and Topo1. Five patient clusters were identified (CENP, RNAP3 'strong', RNAP3 'weak', Topo1, 'Other'). Clinical features associated with CENP, RNAP3 and Topo1 were consistent with previously published reports concerning limited cutaneous and diffuse cutaneous SSc. A novel finding was the statistical separation of RNAP3 into two clusters. RNAP3 'strong' patients had an increased risk of gastric antral vascular ectasia, but a lower risk of oesophageal dysmotility. "Other" patients were more likely to be males and have a history of smoking and malignancy, but less likely to have telangiectasia, Raynaud's phenomenon and joint contractures. CONCLUSION: Five major autoantibody clusters, with specific clinical and serological associations, were identified in Australian SSc patients. Sub-classification and disease stratification utilising AAs, may have clinical utility, particularly in early disease. This article is protected by copyright. All rights reserved.


Artif Organs. 2015.

Clinical Outcomes of Patients Treated With Pulmonary Vasodilators Early and in High Dose After Left Ventricular Assist Device Implantation.


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Right ventricular failure (RVF) is common after left ventricular assist device (LVAD) implantation and a major determinant of adverse outcomes. Optimal perioperative right ventricular (RV) management is not well defined. We evaluated the use of pulmonary vasodilator therapy during LVAD implantation. We performed a retrospective analysis of continuous-flow LVAD implants and pulmonary vasodilator use at our institution between September 2004 and June 2013. Preoperative RVF risk was assessed using recognized variables. Sixty-five patients (80% men, 50 +/- 14 years) were included: 52% HeartWare ventricular assist device (HVAD), 11% HeartMate II (HMII), 17% VentrAssist, 20% Jarvik. Predicted RVF risk was comparable with contemporary LVAD populations: 8% ventilated, 14% mechanical support, 86% inotropes, 25% BUN >39 mg/dL, 23% bilirubin >/=2 mg/dL, 31% RV : LV (left ventricular) diameter >/=0.75, 27% RA : PCWP (right atrium : pulmonary capillary wedge pressure) >0.63, 36% RV stroke work index <6 gm-m/m2 /beat. The majority (91%) received pulmonary vasodilators early and in high dose: 72% nitric oxide, 77% sildenafil (max 200 +/- 79 mg/day), 66% iloprost (max 126 +/- 37 mug/day). Median hospital stay was 26 (21) days. No patient required RV mechanical support. Of six (9%) patients meeting RVF criteria based on prolonged need for inotropes, four were transplanted, one is alive with an LVAD at 3 years, and one died on day 35 of intracranial hemorrhage. Two-year survival was 77% (92% for HMII/HVAD): transplanted 54%, alive with LVAD 21%, recovery/explanted 2%. A low incidence of RVF and excellent outcomes were observed for patients treated early during LVAD implantation with combination, high-dose pulmonary vasodilators. The results warrant further investigation in a randomized controlled study.

Surgical resection of a giant cardiac fibroma.
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A 42-year-old woman presented to a regional hospital emergency room with palpitations and was found to be in ventricular tachycardia. Chest radiography demonstrated a massively enlarged cardiac silhouette. Echocardiography and cardiac magnetic resonance imaging demonstrated a mass within the left ventricular free wall, consistent with a cardiac fibroma. The patient proceeded to have surgical resection of the mass. Left ventricular function was preserved postoperatively.

Impact of fibrate therapy on plasma plasminogen activator inhibitor-1: A systematic review and meta-analysis of randomized controlled trials.
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Effectiveness of genetic cascade screening for familial hypercholesterolaemia using a centrally co-ordinated clinical service: An Australian experience.
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BACKGROUND: Familial hypercholesterolaemia (FH) is a co-dominantly inherited disorder of low-density lipoprotein (LDL) catabolism, causing elevated LDL-cholesterol and premature coronary artery disease (CAD). Several guidelines recommend genetic cascade screening relatives of probands (index cases) with genetically proven FH, but experience in a clinical service setting is limited.

METHODS: Relatives from 100 index cases with genetically confirmed FH underwent genetic and lipid testing via a centralised screening program in Western Australia. The program’s effectiveness was evaluated as the number of newly diagnosed relatives with FH per index case and the proportional reduction in LDL-cholesterol after treatment.

RESULTS: Of 366 relatives tested for FH, 188 (51.4%) were found to have a pathogenic mutation. On average, 2 cases were affected per index case. Affected relatives were younger and less likely to have physical stigmata of FH and premature CAD than index cases (p < 0.001). Of the new cases, 12.8% had hypertension, 2.7% had diabetes and 16.0% were smokers; 48.4% were already on statin therapy and these were older (p < 0.001) and had more vascular risk factors and CAD (p < 0.01) than those not on therapy. Significant reductions in LDL-cholesterol (~24.3%, p < 0.001) were achieved overall, with previously untreated new cases of FH attaining a maximal average reduction of 42.5% in LDL-cholesterol after drug therapy. Over 90% of subjects were satisfied with screening and care.

CONCLUSION: Genetic cascade screening co-ordinated by a centralised service is an effective and acceptable strategy for detecting FH in an Australian setting. A significant proportion of new cases exhibit other CAD risk factors and are already on statins, but have not received a prior diagnosis of FH. Copyright 2014 Elsevier Ireland Ltd. All rights reserved.


Impact of fibrate therapy on plasma plasminogen activator inhibitor-1: A systematic review and meta-analysis of randomized controlled trials.
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Objective: The aim of this systematic review was to perform a meta-analysis of randomized controlled trials (RCTs) examining the efficacy of fibrate therapy in reducing plasma concentration or activity of plasminogen activator inhibitor 1 (PAI-1). Methods: Scopus and MEDLINE databases were searched (up to October 15, 2014) to identify RCTs investigating whether fibrates lower plasma PAI-1 concentration or activity. A random-effects model and the generic inverse variance method were used for quantitative data synthesis. Sensitivity analyses were conducted using the one-study remove approach. Random-effects meta-regression was performed to assess the impact of potential moderators on the estimated effect sizes. Results: A total of 14 RCTs examining the effects of gemfibrozil (6 trials), bezafibrate (4 trials), and fenofibrate (5 trials) were included. Meta-analysis suggested that fibrate therapy did not significantly reduce plasma PAI-1 concentration (weighted mean difference [WMD]: -11.39 ng/mL, 95% CI: 26.64, 3.85, p=0.143) or activity (WMD: 2.02 U/mL, 95% CI: -0.87, 4.90, p=0.170). These results remained unchanged after subgroup analysis according to duration of treatment (<12 and >12 weeks) and type of fibrate administered (fenofibrate, bezafibrate or gemfibrozil). The estimated effects of fibrate therapy on plasma concentration and activity of PAI-1 were independent of duration and changes in plasma triglyceride levels in the meta-regression analysis. Conclusion: This meta-analysis of RCTs suggested that fibrate therapy does not reduce plasma concentration or activity of PAI-1. The putative benefits of fibrate therapy in patients with cardiovascular disease appear to be exerted via mechanisms independent of effects on PAI-1.

Publication Types: Review


Statin therapy reduces plasma endothelin-1 concentrations: A meta-analysis of 15 randomized controlled trials.

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Objective: Raised plasma endothelin-1 (ET-1) levels may be a risk factor for vascular dysfunction and cardiovascular (CV) disease. This meta-analysis assessed the effect of statins on circulating ET-1 concentrations. Methods and results: The search included PUBMED, Cochrane Library, Web of Science, Scopus, and EMBASE up to September 30, 2014 to identify randomized controlled trials (RCTs) with ET-1 measurement during statin therapy. Quantitative data synthesis was performed using a random-effects model, with weighed mean difference (WMD) and 95% confidence interval (CI) as summary statistics. Data from 15 RCTs showed that statin therapy significantly reduces plasma ET-1 concentrations (WMD: -0.30 pg/mL, 95% CI: -0.47, -0.13; p < 0.01). This effect was robust in sensitivity analysis, and not largely affected by the duration of statin therapy (<12 weeks - WMD: -0.51 pg/mL, 95% CI: -0.89, -0.14, p < 0.01; >12 week - WMD: -0.19 pg/mL, 95% CI: -0.36, -0.02; p < 0.05) or by dose of statins (<40 mg/day - WMD: -0.27 pg/mL, 95% CI: -0.49, -0.05; p = 0.01; >40 mg/day - WMD: -0.38 pg/mL, 95% CI: -0.68, -0.08; p = 0.01). Lipophilic statin (atorvastatin, simvastatin, fluvastatin, and cerivastatin - WMD: -0.34 pg/mL, 95% CI: -0.55, -0.13; p < 0.01), but not a hydrophilic statin (pravastatin - WMD: -0.18 pg/mL, 95% CI: -0.44, -0.08; p > 0.05) had a significant effect in promoting ET-1 reduction. Conclusions: Statin therapy significantly reduces circulating ET-1 concentrations, regardless of treatment duration or dose of statins. This effect of statins may be influenced by statin lipophilicity. There is a need to establish whether lowering ET-1 levels has a beneficial effect on CV events.


Europe aspires to set the record straight on familial hypercholesterolaemia.

Watts GF, Pang J, et al. Watts, Gerald F. School of Medicine and Pharmacology, University of Western Australia, Western Australia, Australia; Lipid Disorders Clinic, Cardiovascular Medicine, Royal Perth Hospital, Western Australia, Australia. Electronic address: gerald.watts@uwa.edu.au. Pang, Jing. School of Medicine and Pharmacology, University of Western Australia, Western Australia, Australia. Santos, Raul D. Lipid Clinic Heart Institute (InCor), University of Sao Paulo Medical School Hospital, and Preventive Medicine Centre and Cardiology Program Hospital Israelita Albert Einstein, Sao Paulo, Brazil.
Tibolone decreases Lipoprotein(a) levels in postmenopausal women: A systematic review and meta-analysis of 12 studies with 1009 patients.

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Introduction: Circulating lipoprotein (a) (Lp(a)) is a recognized risk factor for cardiovascular disease (CVD). Tibolone, a synthetic steroid, may lower Lp(a) levels; however, evidence of the effects of tibolone on Lp(a) still remain to be defined. Therefore, we investigated the effects of tibolone treatment on circulating Lp(a) levels in postmenopausal women. Methods: The search included PUBMED, Web of Science, Scopus, and Google Scholar (up to January 31st, 2015) to identify controlled clinical studies investigating the effect of oral tibolone treatment on Lp(a) levels in postmenopausal women. Random-effects meta-regression was performed using unrestricted maximum likelihood method for the association between calculated weighted mean difference (WMD) and potential moderators. Results: Meta-analysis of data from 12 trials (16 treatment arms) suggested a significant reduction of Lp(a) levels following tibolone treatment (WMD:-25.28%, 95% confidence interval [CI]:-36.50,-14.06; p<0.001). This result was robust in the sensitivity analysis and its significance was not influenced after omitting each of the included studies from the meta-analysis.

When the studies were categorized according to the tibolone dose, there were consistent significant reductions of Lp(a) in the subsets of studies with doses <2.5mg/day (WMD:-17.00%, 95%CI:-30.22,-3.77; p=0.012) and 2.5mg/day (WMD:-29.18%, 95%CI:-45.02,-13.33; p<0.001). Likewise, there were similar reductions in the subsets of trials with follow-up either <24 months (WMD:-26.79%, 95%CI:-38.40,-15.17; p<0.001) or >24 months (WMD:-23.10%, 95%CI:-40.17,-6.03; p=0.008). Conclusions: This meta-analysis shows that oral tibolone treatment significantly lowers circulating Lp(a) levels in postmenopausal women. Further studies are warranted to explore the mechanism of this effect and the potential value and place of tibolone or its analogues in the treatment of elevated Lp(a) in individuals at risk of CVD.


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Lipoprotein (a) levels are not associated with carotid plaques and carotid intima media thickness in statin-treated patients with familial hypercholesterolemia.

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Background: Lipoprotein (a), also called Lp(a), is a cardiovascular disease (CVD) risk factor. Statins do not lower Lp(a), this may at least partly explain residual CVD risk in statin-treated patients with familial hypercholesterolemia (FH). We investigated the association of Lp(a) levels with atherosclerosis in these patients. Methods and results: We performed ultrasonography in 191 statin-treated FH patients (50% men; 48+/-15 years) to detect carotid plaques and determine carotid intima-media thickness (C-IMT). Patients with high versus low Lp(a) levels (<0.3g/L) had similar plaque prevalence (36 and 31%, p=0.4) and C-IMT (0.59+/-0.12 and 0.59+/-0.13mm, p=0.8). Patients with and without plaques had similar Lp(a) levels (median 0.33 (IQR: 0.57) and 0.24 (0.64) g/L, respectively, p=0.4). Conclusions: The Lp(a) levels were not associated with atherosclerosis in the carotid arteries of statin-treated FH patients. This suggests that adequate statin treatment delays carotid atherosclerosis in FH independently of Lp(a) levels.


Familial hypercholesterolaemia: A global call to arms.

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Challenges during long-term follow-up of ICU patients with and without chronic disease.

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INTRODUCTION: Reflecting on researchers' experiences during follow-up of patients enrolled in research may lead to improved understanding of the challenges faced in maintaining contact when patients leave hospital. AIM(S): (1) Describe the challenges researchers face when following-up patients who survive ICU. (2) Identify issues that influenced our ability to follow-up patients. METHODS: This sub-study was part of a larger "case-control" study investigating the quality of life of ICU survivors with and without pre-existing chronic disease. Patients completed self-assessment QLQ and symptom assessment before hospital discharge and at six months, plus they were asked to keep a paper diary of healthcare services used. Patient contact was maintained by monthly telephone calls. Each telephone call was logged and summaries of conversations documented. Our experience of conducting the study was reviewed by the identification of common issues which arose from the follow-up of patients. RESULTS: Thirty patients with a history of chronic disease and 30 patients without underlying chronic disease were followed-up. A total of 582 telephone calls were made for 60 patients discharged from hospital of which 261 (45%) calls led to a telephone interview. Only 19 (30%) of diaries were completed and returned. We identified six challenges associated with issues that arose from the follow-up of patients. CONCLUSION: We underestimated the number of telephone calls required for follow-up after discharge. Diaries were unreliable sources of data suggesting strategies are needed to improve compliance. How patients respond to follow-up is not always predictable. Processes are needed to deal with unexpected information provided during telephone follow-up.


Anticoagulant therapy and its impact on dental patients: a review.

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Several new oral anticoagulants have been studied in the past decade, and have now started to enter the market. These drugs are reported to be as effective as, or more effective than warfarin. In Australia, the Therapeutic Goods Administration has approved dabigatran, rivaroxaban, and apixaban. The use of these newer anticoagulants is likely to increase in time, and it is important for dentists to have a sound understanding of the mechanisms of action, reversal strategies, and management guidelines for patients taking oral anticoagulants. This article discusses the process of coagulation, available anticoagulants and their monitoring and reversal, and provides clinical advice on the management of patients on anticoagulants who require dental treatment. This article is protected by copyright. All rights reserved.


Cardiac 123I-meta-iodo-benzyl-guanine in a patient with bipolar affective disorder, musical hallucinations and Parkinsonism.
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Common familial risk factors for schizophrenia and diabetes mellitus.
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OBJECTIVE: The co-occurrence of type 2 diabetes and psychosis is an important form of medical comorbidity within individuals, but no large-scale study has evaluated comorbidity within families. The aim of this study was to determine whether there is evidence for familial comorbidity between type 2 diabetes and psychosis. METHOD: Data were analysed from an observational study of a nationally representative sample of 1642 people with psychosis who were in contact with psychiatric services at the time of survey (The 2010 Australian National Survey of Psychosis). Participants were aged 18-64 years and met World Health Organization's International Classification of Diseases, 10th Revision diagnostic criteria for a psychotic disorder (857 with schizophrenia, 319 with bipolar disorder with psychotic features, 293 with schizoaffective disorder, 81 with depressive psychosis and 92 with delusional disorder or other non-organic psychoses). Logistic regression was used to estimate the association between a family history of diabetes and a family history of schizophrenia. RESULTS: A positive family history of diabetes was associated with a positive family history of schizophrenia in those with a psychotic disorder (odds ratio = 1.35, p = 0.01, adjusted for age and gender). The association was different in those with an affective versus non-affective psychosis (odds ratio = 0.613, p = 0.019, adjusted for age and gender) and was significant only in those with a non-affective psychosis, specifically schizophrenia (odds ratio = 1.58, p = 0.005, adjusted for age and sex). Adjustment for demographic factors in those with schizophrenia slightly strengthened the association (odds ratio = 1.74, p = 0.001, adjusted for age, gender, diagnosis, ethnicity, education, employment, income and marital status). CONCLUSION: Elevated risk for type 2 diabetes in people with schizophrenia is not simply a consequence of antipsychotic medication; type 2 diabetes and schizophrenia share familial risk factors.


Dubious findings concerning the prevalence of late-life depression.
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Occupational therapy practice in acute physical hospital settings: Evidence from a scoping review.

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School of Occupational Therapy and Social Work, Curtin University, Perth, WA, Australia.

BACKGROUND/AIM: Increased accountability and growing fiscal limitations in global health care continue to challenge how occupational therapy practices are undertaken. Little is known about how these changes affect current practice in acute hospital settings. This article reviews the relevant literature to further understanding of occupational therapy practice in acute physical hospital settings. METHODS: A scoping review of five electronic databases was completed using the keywords Occupational therapy, acute hospital settings/acute physical hospital settings, acute care setting/acute care hospital setting, general medicine/general medical wards, occupational therapy service provision/teaching hospitals/tertiary care hospitals. Criteria were applied to determine suitability for inclusion and the articles were analysed to uncover key themes. RESULTS: In total 34 publications were included in the review. Analysis of the publications revealed four themes: (1) Comparisons between the practice of novice and experienced occupational therapists in acute care (2) Occupational therapists and the discharge planning process (3) Role of occupation in the acute care setting and (4) Personal skills needed and organisation factors affecting acute care practice. CONCLUSION: The current literature has highlighted the challenges occupational therapists face in practicing within an acute setting. Findings from this review enhance understanding of how occupational therapy department managers and educators can best support staff that practise in acute hospital settings.


Serum 25-hydroxyvitamin D increases with NB-UVB and UVA/UVB phototherapy in patients with psoriasis and atopic dermatitis in Western Australia.

Le P, Tu J, et al.
Department of Dermatology, Fremantle Hospital, Fremantle.

BACKGROUND/OBJECTIVE: The benefit of NB-UVB phototherapy on serum 25-hydroxyvitamin D [25(OH)D] levels in patients with inflammatory skin conditions has been reported in the northern hemisphere. Vitamin D status is known to differ between geographical latitudes. The objective of this study was to investigate the influence of NB-UVB and UVA/UVB phototherapy on the 25(OH)D serum levels in patients with psoriasis and atopic dermatitis in Western Australia. METHODS: A total of 35 patients with psoriasis or atopic dermatitis requiring phototherapy thrice weekly for a minimum of 4 weeks were enrolled. Of these, 20 patients completed the study. Serum vitamin D levels were measured at baseline and at approximately 6 weeks into phototherapy. Data were adjusted for season, patients' age, sex, skin condition and Fitzpatrick skin phototype. RESULTS: There was a statistically significant increase in serum 25(OH)D from pre- to post-NB-UVB and UVA/UVB phototherapy (P < 0.0001), with a mean raw increase of 34.6 (25) nmol/L; or 45.1 (7.5) nmol/L when adjusted for covariates. This was also true for patients receiving NB-UVB phototherapy with a baseline vitamin D of <80 nmol/L (P < 0.05) and >80 nmol/L (P < 0.004). CONCLUSIONS: NB-UVB and UVA/UVB phototherapy significantly increased 25(OH)D serum level in patients with psoriasis and atopic dermatitis in Western Australia. Our study cohort had a higher baseline vitamin D level and a lower percentage increase of serum 25(OH)D post-phototherapy than the increases reported in the literature from cohorts in the northern hemisphere.


Sensory testing with the sharp point of a folded piece of paper.

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Publication Types: Letter


Mycophenolic acid in dermatology a century after its discovery.

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Strathie Page,Sarah J. Royal Perth Hospital, Perth, Western Australia, Australia.

Mycophenolic acid was first discovered in 1913 and first used clinically in the 1970s as an immunosuppressant to prevent organ transplantation rejection. It was later used in the treatment of psoriasis. However due to its side-effect profile and fears over its carcinogenic potential it was abandoned. From the late 1990s a prodrug, mycophenolate mofetil (MMF), was developed and more recently, enteric-coated mycophenolate sodium (EC-MPS), both of which have gained increasing use in the field of dermatology for a variety of skin conditions. This review discusses the pharmacology, mechanisms of action, side-effects and current clinical applications in dermatology of MMF and EC-MPS. Copyright © 2014 The Australasian College of Dermatologists.


Mycosis fungoides: An important differential diagnosis for acquired palmoplantar keratoderma.

Mycosis fungoides is the most common subtype of primary cutaneous lymphoma and has several clinical variants. We report a 74-year-old man presenting with an acquired palmoplantar keratoderma initially diagnosed and treated as psoriasis with suboptimal improvement. Several months later the patient developed patches and plaques that were histologically consistent with mycosis fungoides. These lesions were ameliorated with the treatment of the underlying mycosis fungoides and the palmoplantar keratoderma resolved promptly with radiotherapy. This case highlights the importance of considering mycosis fungoides as an infrequent but serious cause of acquired palmoplantar keratoderma.

OBJECTIVES: Research can seem daunting, especially for trainees and early career researchers. This paper focuses on how to formulate and begin a research project such as the RANZCP Scholarly Project.

METHODS: We outline an approach to framing a research question, developing theses and hypotheses, choosing a supervisor and conducting a literature review.

CONCLUSIONS: Through systematic planning early career researchers and other clinicians can plan and conduct research suitable for the Scholarly Project or other research activity. Copyright The Royal Australian and New Zealand College of Psychiatrists 2014.


Prevalence and nature of antipsychotic polypharmacy among inpatients with schizophrenia spectrum disorders at an Australian mental health service.

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Objective: Though antipsychotic polypharmacy (APP) is widely utilised in many clinical settings for the treatment of people with schizophrenia, the extent of this practice varies considerably between different regions, countries and clinical settings. Studies from Australasia exploring the prevalence and factors associated with APP are sparse and have yielded inconsistent results. Methods: We conducted a systematic retrospective audit of the medical records of all admissions in 2010 in the adult wards of a metropolitan public mental health service in Western Australia, having a diagnosis of schizophrenia or schizoaffective disorder. We analysed the rates of APP use, and its association with selected demographic and clinical variables. Results: The prevalence of APP among our sample of 229 patients was high, at 43.2%. APP was associated with a longer hospital stay (p = 0.033) and voluntary admission (p = 0.027); but APP was not significantly related to: age, gender, diagnosis and treatment by different psychiatrists. Conclusions: Substantial difference exists between everyday clinical practice and recommendations of practice guidelines of schizophrenia, regarding the use of APP. Prospective studies from different settings exploring the relevant clinical, patient, prescriber and system-related issues are warranted, to comprehend the rationale behind high utilisation of APP in clinical practice.


Getting started in research: Systematic reviews and meta-analyses.

Kisely S, Chang A, et al. (Kisely, Chang, Crowe, Galletly, Jenkins, Looi, Macfarlane, McVie, Parker, Power, Siskind, Smith, Merry, Macfarlane) Committee for Research, Royal Australian and New Zealand College of Psychiatrists (RANZCP), Melbourne, VIC, Australia (Kisely) School of Medicine, University of Queensland, MacGregor Building, Number 64, Woolloongabba, QLD 4072, Australia (Loi) Academic Unit for Psychiatry of Old Age, Saint Vincent's Health, Saint George's Hospital, University of Melbourne, Melbourne, VIC, Australia (Looi) Academic Unit of Psychiatry and Addiction Medicine, Australian National University Medical School, Canberra, ACT, Australia (Looi) ACT Health Direc., Mental Health Service, Canberra Hospital, Woden, ACT, Australia (Macfarlane) Graduate School of Medicine, University of Wollongong, Wollongong, NSW, Australia (Macfarlane) Illawarra Shoalhaven Local Health District, NSW, Australia (Power) School of Psychiatry and Clinical Neurosciences, University of Western Australia, Perth, WA, Australia (Power) South Metropolitan Area Health Service, Perth, WA, Australia (Siskind) School of Medicine, University of Queensland, Woolloongabba, QLD, Australia (Smith) WA Centre for Mental Health Policy Research, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Perth, WA, Australia (Smith) Curtin University, Perth, WA, Australia (Merry) Psychological Medicine, University of Auckland, Auckland, New Zealand (Macfarlane) Aged Psychiatry Service, Alfred Health, Caulfield, VIC, Australia S. Kisely, School of Medicine, University of Queensland, MacGregor Building, Number 64, Woolloongabba, QLD 4072, Australia

Objectives: Systematic reviews are one of the major building blocks of evidence-based medicine. This overview introduces readers to conducting systematic reviews and meta-analyses. Conclusions: Systematic reviews and meta-analyses are not as daunting as they may appear to be, provided the scope is sufficiently narrow and an appropriate supervisor available.


Cardiovascular risk factor associations in adults with psychosis and adults in a national comparator sample.


Objectives: Systematic reviews are one of the major building blocks of evidence-based medicine. This overview introduces readers to conducting systematic reviews and meta-analyses. Conclusions: Systematic reviews and meta-analyses are not as daunting as they may appear to be, provided the scope is sufficiently narrow and an appropriate supervisor available.


Effectiveness of CTOs applied by PaRK mental health services.

Eatt J, Yint Y, et al.
Background: Following the UK-based OCTET study there has been debate about the effectiveness of Community Treatment Orders (CTOs). Australia and New Zealand have comparatively high numbers of patients on CTOs. Objectives: Our study aims to examine the effectiveness of all the CTOs applied by Peel and Rockingham (PaRK) mental health services over the past years. Outcome measures will include readmission rate, time to readmission and length of stay in hospital. We will look at adverse incidents and risks before and after the person was subject to a CTO. Methods: Twenty-five patients who were under CTO were identified. Information from the PSOLIS database regarding the current and previous Mental Health Act orders was compared with mental health admission dates recorded on the ISOFT Clinical Manager Program. There was also access to clinical notes. The number of admissions prior to and since the first CTO were recorded. Data was also collected to examine and compare the length of admission before and after the commencement of CTO, the time to readmission and the occurrence of significant clinical incidents pre and post CTO. We endeavour to have access approved for the same clients at other services in the state. Findings: Our preliminary impression from the data is that following being subject to a CTO, the majority of patients had a reduced number of admissions and fewer adverse incidents. Conclusions: Yet to be reached.

Publication Types: Conference Abstract

Eating best outcomes for migrant women with mental disorders: A successful partnership between government and nongovernment agencies.
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(Moore, Yeak) South Metropolitan Health Service, Mental Health Strategy and Leadership Unit, Perth, Australia (Korica) Fremantle Multicultural Centre, Fremantle, Australia

Background: Migration is associated with significant mental disorder. The complexity of the migrant experience may include language difficulties, different cultural expectations, limited family support and the need to navigate around different systems to access health care, financial assistance and legal systems. Method: This review defined the collaborative pathways and analysed outcomes over the last 10 years achieved by our publicly funded mental health services and a dynamic community-managed organisation delivering services to migrant women. Findings: The findings included: Staff at the Fremantle Multicultural Centre (FMC) gained skills in appropriately recognising mental disorder that required specialist intervention; Staff at South Metropolitan Health Service were more aware of the trauma associated with migration and more likely to choose appropriate socialisation through the FMC rather than "medicalise" the response to migration; Pathways to appropriate care for migrant women were facilitated; Family and carer needs were identified and supported. The strategies needed to develop and sustain the partnership included: Strong and stable leadership; Clear role delineation; Regular review of roles; Joint staff development opportunities; Co-production with carers and consumers. Conclusion: The successful strategies in this long-standing partnership can be applied in other jurisdictions to improve outcomes for this cohort and their families.

Publication Types: Conference Abstract

Does therapeutic temperature management after cardiac arrest increase the risk of bleeding?
Williams TA, McKenzie N, et al.
Williams,Teresa A. School of Nursing and Midwifery, Prehospital Resuscitation and Emergency Care Research Unit (PRECRU), Curtin University, Australia; Intensive Care Unit, Royal Perth Hospital, Perth, Western Australia, Australia. Electronic address: teresa.williams@curtin.edu.au. McKenzie,Nicole. School of Nursing and Midwifery, Prehospital Resuscitation and Emergency Care Research Unit (PRECRU), Curtin University, Australia; Intensive Care Unit, Royal Perth Hospital, Perth, Western Australia, Australia. Inoue,Madoka. School of Nursing and Midwifery, Prehospital Resuscitation and Emergency Care Research Unit (PRECRU), Curtin University, Australia.


Don't rush to crash.
Simmons C.
(Simmons) Fremantle Hospital and Health Service, WA, Australia

Cancer services in Western Australia: A comparison of regional outcomes with metropolitan Perth.
Martin HL, Ohara K, et al.
Martin, Hillary L. Department of Medical Oncology, Royal Perth Hospital, University of Western Australia, Perth, Western Australia, Australia. Ohara,Kanako. Department of Medical Oncology, Royal Perth Hospital, Perth, Western Australia, Australia. Chin, Wee.
Department of Medical Oncology, Royal Perth Hospital, Perth, Western Australia, Australia. Davidson, Andrew. Department of Medical Oncology, Royal Perth Hospital, University of Western Australia, Perth, Western Australia, Australia. Bayliss, Evan. Department of Medical Oncology, Royal Perth Hospital, Perth, Western Australia, Australia. Redfern, Andrew. Department of Medical Oncology, Royal Perth Hospital, University of Western Australia, Perth, Western Australia, Australia. Khattak, Muhammad Adnan. Department of Medical Oncology, Royal Perth Hospital, University of Western Australia, Perth, Western Australia, Australia.

OBJECTIVE: To investigate whether any survival differences existed between advanced cancer patients treated in metropolitan Perth and those treated in regional Western Australia (WA).

DESIGN: Retrospective study.

SETTING: Advanced cancer patients treated through medical oncology clinics at Royal Perth Hospital and regional cancer centres (Kalgoorlie, Albany, Geraldton and Northam).

PARTICIPANTS: Patients diagnosed with advanced melanoma, breast, colorectal, gastro-oesophageal, prostate, lung and pancreatic cancers between 1 January 2007 and 31 December 2011.

INTERVENTIONS: Nil.

MAIN OUTCOME MEASURE: Median survival.

RESULTS: Data were available for 1581 patients with 75% living in a metropolitan setting and 25% in rural WA. Median overall survival was 8.3 months for metropolitan patients and 7.6 months for regional patients (P=0.06, HR 0.89; 95% CI, 0.78-1.01).

There was no statistically significant difference in median survival for different tumour types except pancreatic cancer: breast 22.1 months versus 21.3 months, colorectal 13.1 months versus 16.4 months, lung 5.1 months versus 3.1 months, upper GI 5.6 months versus 7.2 months, pancreatic 4.5 months versus 3 months (P=0.02, HR 0.57; 95% CI, 0.32-0.99), melanoma 10.4 months versus 10.5 months, prostate 28.6 months versus 15.3 months. Rural cancer patients with breast and pancreatic cancers received fewer lines of anti-cancer therapy compared to metropolitan patients. The three-year survival rates for metropolitan compared to rural breast cancer patients were 34 and 23%, respectively (not statistically significant).

CONCLUSION: Our findings suggest a trend towards inferior survival for regional cancer patients in WA compared with metropolitan-based patients.


Measuring vitamin D.

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P. Glendenning, Department of Clinical Biochemistry, Royal Perth Hospital, School of Medicine and Pharmacology, University of Western Australia, Australia

When assessing vitamin D status, measure serum 25-hydroxyvitamin D concentration as this reflects total body vitamin D reserves. Recent Australasian guidelines outline who should be tested for vitamin D deficiency, who should be treated and when repeat testing should be performed. A 25-hydroxyvitamin D threshold of at least 50 nanomol/L at the end of winter is a suitable treatment target. Measurement can be repeated after three months of repletion, and thereafter less frequently unless new risk factors for vitamin D deficiency arise. When interpreting vitamin D pathology reports, practitioners should be aware that some laboratories quote reference limits which are based on overseas rather than Australian guidelines.


Imaging for chronic abdominal pain in adults.

Mendelson R. (Mendelson) Royal Perth Hospital Clinical professor, The University of Western Australia, Australia (Mendelson) Royal Perth Hospital, Australia

Diagnostic imaging is often not indicated in chronic abdominal pain. In particular, undifferentiated abdominal pain is rarely an indication for a CT scan. CT scanning is overused even when imaging is required. Other modalities may be preferable. A normal CT scan does not rule out cancer. Alarm symptoms, including anaemia, blood in the stool, waking at night with gastrointestinal symptoms, and weight loss, should be investigated. The most appropriate modality depends on the symptoms. Clinical information on request forms for CT scans should be specific and include the suspected condition as this helps the radiologist to determine an appropriate imaging protocol.


Modeling C-reactive protein kinetic profiles for use as a clinical prediction tool in patients with Staphylococcus aureus bacteremia.

Gliddon, T, Salman, S, et al. Gliddon, Thomas. Pathwest Laboratory Medicine, Nedlands, WA, Australia. Gliddon, Thomas. Sir Charles Gairdner Hospital, Nedlands, WA, Australia. Gliddon, Sam. Sir Charles Gairdner Hospital, Nedlands, WA, Australia. Salman, Sam. Harry Perkins Research Institute, School of Medicine & Pharmacology, University of Western Australia, Fiona Stanley Hospital, Western Australia, University of Western Australia, WA, Australia. Robinson, James Owen. Pathwest Laboratory Medicine, Nedlands, WA, Australia. Robinson, James Owen. Harry Perkins Research Institute, School of Veterinary & Life Sciences, Murdoch University & School of Biomedical Sciences, Curtin University, Perth, WA, Australia.
RESULTS: There were significant differences between the G0 and identified GB values in this cohort (prs and pks<0.0001), compared using a Kolmogorov-Smirnov (KS) and signed rank (RS) test for the cohort. A total of 36 tests were conducted across 12 participants throughout the study. Measured G0 and identified GB values were intravenous glucose tolerance tests (IM-IVGTT) were undertaken at week 0, 12 and 24 and were used with DISST model to identify the suitability the DISST model has for individuals with established type 2 diabetes.

METHODS: 14 participants with established T2D were recruited to take part in a dietary intervention study. Insulin-modified normoglycaemic cohort. We sought to determine the DISST model captures the behaviour of the participants more accurately than the original model.

CONCLUSIONS: This analysis has shown that GB is an important variable for modelling the glycaemic behaviour in T2D. These findings suggest that the original DISST model, while appropriate for normoglycaemic cohorts, needs to model basal glucose level as a variable for assessing individuals with established type 2 diabetes (T2D).

MATERIALS & METHODS: We constructed and validated a nonlinear mixed effects model using CRP values obtained during the first week of illness.

RESULTS: Hematological malignancy, prosthetic heart valves and metastatic seeding were identified as major covariates that influenced CRP kinetics. When considering the presence of metastatic infection as an 'unknown', the model could predict its presence through analysis of the observed CRP profile with an Area-under-the-Receiver-Operator-Characteristic curve of 0.81, indicating some diagnostic accuracy.

CONCLUSION: We conclude that early CRP kinetics can be accurately modeled and can help identify patients with metastatic seeding in S. aureus bacteremia. Further validation is required.


Biomedical Engineering Online. 2015; 14(1): 18. The necessity of identifying the basal glucose set-point in the IVGTT for patients with Type 2 Diabetes.

Othman NA, Docherty PD, et al. Othman,Nor Azlan. Department of Mechanical Engineering, Centre for Bio-Engineering, University of Canterbury, Private Bag 4800, Christchurch, 8054, New Zealand. azlan.othman@pg.canterbury.ac.nz. Docherty,Paul D. Department of Mechanical Engineering, Centre for Bio-Engineering, University of Canterbury, Private Bag 4800, Christchurch, 8054, New Zealand. paul.docherty@canterbury.ac.nz. Krebs,Jeremy D. Department of Medicine, University of Otago, Wellington, 6242, New Zealand. Jeremy.Krebs@cdh.org.nz. Bell,Damon A. School of Medicine and Pharmacology Royal Perth Hospital Unit, The University of Western Australia, Perth, Western Australia, 6009, Australia. damon.bell@uwa.edu.au. Chase,Geoffrey. Department of Mechanical Engineering, Centre for Bio-Engineering, University of Canterbury, Private Bag 4800, Christchurch, 8054, New Zealand. geoff.chase@canterbury.ac.nz.

BACKGROUND: The model-based dynamic insulin sensitivity and secretion test (DISST) uses fasting glucose (G0) as the basal glucose (GB) concentration when assessing insulin sensitivity (SI). However, this model was developed in a healthy, normoglycaemic cohort. We sought to determine the suitability the DISST model has for individuals with established type 2 diabetes (T2D).

METHODOLOGY: 14 participants with established T2D were recruited to take part in a dietary intervention study. Insulin-modified intravenous glucose tolerance tests (IM-IVGTT) were undertaken at week 0, 12 and 24 and were used with DISST model to identify GB. A total of 36 tests were conducted across 12 participants throughout the study. Measured G0 and identified GB values were compared using a Kolmogorov-Smirnov (KS) and signed rank (RS) test for the cohort.

RESULTS: There were significant differences between the G0 and identified GB values in this cohort (prs and pks<0.0001), although both values were well correlated (R=0.70). The residual plot demonstrates that the modified model captures the behaviour of the participants more accurately than the original model.

CONCLUSIONS: This analysis has shown that GB is an important variable for modelling the glycaemic behaviour in T2D. These findings suggest that the original DISST model, while appropriate for normoglycaemic cohorts, needs to model basal glucose level as a variable for assessing individuals with established T2D.


Yang JZ, Hu XZ, et al. (Yang, Hu, Sultana, Edward Day) School of Mechanical and Chemical Engineering, University of Western Australia, Perth, WA 6009, Australia (Yang) Harvard-MIT Division of Health Science and Technology, Harvard Medical School, Cambridge, MA 02139, United States (Edward Day) Department of Medical Engineering and Physics, Royal Perth Hospital, Perth, WA 6000, Australia (Ichim) School of Dentistry, University of Western Australia, Perth, WA 6009, Australia.

Bioceramic scaffolds with desired bone regeneration functions have the potential to become real alternatives to autologous bone grafts for reconstruction of load-bearing and critical-sized segmental bone defects. The aim of this paper was to develop a layered scaffold structure that has the biodegradable function of common monolithic scaffolds and adequate mechanical function for surgical fixing and after surgery support. The exemplary case of this study is assumed to be a large-segment tibia or femur bone repair. The layered scaffold structure consists of a macroporous hydroxyapatite-wollastonite layer and a strong dense zirconia matrix dense layer. The bio-functional scaffold layer with interconnected freeze-dried porous structures shows excellent apatite formation, cell attachment, and cell proliferation capabilities. The mechanical functional layer provides a bending strength matching that of the compact bone.


Frayne J, Allen S, et al. (Frayne, Allen) King Edward Memorial Hospital, Perth, Australia (Frayne) School of Primary, Aboriginal and Rural Healthcare, University of Western Australia, Perth, Australia (Nguyen) School of Psychiatry and Clinical Neurosciences, University of Western Australia.
Introduction Women with severe mental illness (SMI) appear to be a vulnerable obstetric population. Antenatal care is often complicated by psychiatric instability, and the use of psychotropic medication. Our aim is to explore metabolic and nutritional status in order to define necessary intervention strategies. Methods A retrospective study was conducted between December 2007 and January 2014 (n = 323) from the Childbirth and Mental Illness Antenatal Clinic (CAMI) clinic at King Edward Memorial Hospital in Perth, Western Australia, on pregnant women with SMI aged 18-44 years. Descriptive statistics, one way ANOVA, logistic regression and Chi Squared tests were conducted using SPSS version 22. Data were compared between three diagnostic groups (bipolar, schizophrenia and non-psychotic SMI). Results Overall, 208/321 (64.8%) of women with SMI have Body Mass Indices (BMI) in the overweight or obese categories at their booking appointments. Women with schizophrenia had significantly elevated body mass index (BMI) (P = 0.044) compared to other diagnostic groupings. Mean gestational weight gain in women in this cohort was measured as 0.56 kg/week (95% CI: 0.51-0.61), which was significantly more than the recommended 0.42 kg/week for normal weight individuals (P < 0.001), with no significant difference between diagnostic groups (P = 0.091) or use of antipsychotic medication (P = 0.773). Significantly elevated weight gain was reported with EPDS >12, psychiatric admission in pregnancy and psychiatric relapse in pregnancy (0.61, 0.62 and 0.64 kg/week respectively). Other findings include a high rate of gestational diabetes mellitus (GDM) (13.3%), with a higher GDM rate and antipsychotic use (16.1% versus 8.9%, P = 0.064), but after adjusting for BMI and age with logistic regression analysis this trend reduced (P = 0.1027). Preconception folic acid supplementation was taken by 44/284 (15.5%) of women, with a significant decrease in those with schizophrenia (4.5%, P = 0.041). Folic acid was taken in pregnancy by 211/297 (71%), again with a significant decrease in those with schizophrenia (P = 0.001). Anaemia was present in 125/323 (38.7%) of women with SMI with a mean ferritin of 21.25 mug/L (95% CI: 18.42-24.09) across all women. Conclusion Pregnant women with SMI have an elevated BMI and excessive gestational weight gain in pregnancy, which appears to be associated with symptoms of psychiatric distress. They also have high rates of GDM. Antenatal services should aim to optimise metabolic health for women with SMI. The low rates of folic acid supplementation would be best addressed through preconception counseling.

(Karkhanis, Malarselvi, Patni) Princess of Wales Maternity Unit, Birmingham Heartlands Hospital, Birmingham, United Kingdom (Khawaja) New Queen Elizabeth Hospital, Birmingham, United Kingdom (Sunanda) Fiona Stanley Hospital, Perth, WA, Australia (Sunanda) University Notre Dame, Fremantle, WA, Australia
P. Karkhanis, Malarselvi, M, et al. performed. Referral criteria included on-going singleton pregnancy with (1) Previous spontaneous mid trimester miscarriage (MTM)/PTB or PPROM between 14-34 weeks of a singleton pregnancy, (2) Previous cervical cerclage or surgery. Information regarding outcomes of all patients registered with the clinic by determining the proportion of patients who were able to reach a gestation beyond 34 weeks. Methods Retrospective case-note analysis of PPC patients from 1 November 2007 to 31 October 2013 was performed. Referral criteria included on-going singleton pregnancy with (1) Previous spontaneous mid trimester miscarriage (MTM)/PTB or PPROM between 14-34 weeks of a singleton pregnancy, (2) Previous cervical cerclage or surgery. Information regarding demographics, scanfindings, intervention, gestation at delivery and neonatal outcomes was collected. The results were analysed using two-tailed test for proportion. Results 712 pregnancies were referred to PPC during the study period. 33 patients were excluded because of inappropriate referral or missing data leaving 679 patients for analysis. The patients were divided into 4 groups. Group I - Past history of cervical surgery, or incidental finding of shortened cervix without MTM or PTB Group II - Previous one MTM or PTB Group III - Previous two MTMs or PTBs Group IV - Previous more than two MTMs or PTBs 11.9% of babies required admission to the neonatal unit and 1% of babies died. A term delivery rate (>37 weeks) was achieved in 78%, 77%, 66% and 53% in Groups I, II, III and IV respectively. Conclusion With counselling and appropriate patient selection, PPC has significantly reduced prematurity related morbidity and mortality in patients at high risk of preterm birth. We propose establishing such dedicated clinics across the United Kingdom to tackle the problem of prematurity.

Publication Types: Conference Abstract

Flukes S, Hayne D, et al.
Flukes,Stephanie. Department of Urological Surgery, Fremantle Hospital, Perth, Australia.
OBJECTIVES: To quantify the outcomes of retrograde ureteric stenting in the setting of infected hydrenephrosis secondary to ureteric calculi.

PATIENTS AND METHODS: Prospective analysis of all patients over a 15-month period admitted with infected obstructed kidneys secondary to ureteric calculi. Inclusion criteria were based on clinical evidence of systemic inflammatory response syndrome (SIRS) and radiological evidence of obstructing ureteric calculi. Outcome measures included success of procedure, admission to intensive care unit (ICU), length of hospital stay, morbidity, and all-cause mortality during hospital admission.

RESULTS: In all, 52 patients were included. Success of retrograde ureteric stenting was 98%. In all, 17% of patients required an
ICU admission, with a post ureteric instrumentation ICU admissions rate of 6%. The mean white cell count and serum creatinine improved significantly after the procedure. Major complication rate included septic shock 6%, but there were no episodes of major haemorrhage and no deaths.

CONCLUSION: Retrograde ureteric stenting is safe and effective in infected obstructed kidneys with results comparable to percutaneous nephrostomy tube insertion. Post instrumentation ICU admissions occur in 6% of retrograde stentings.

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The development of a radical cystectomy enhanced recovery pathway at fremantle hospital.

McCombie S, Nak T, et al.

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Introduction & Objectives: Radical cystectomy (RC) with bilateral pelvic lymph node dissection and urinary diversion is associated with a high incidence of complications and a prolonged length of stay. These can both be safely reduced through the introduction of a RC enhanced recovery pathway. In 2013, the Enhanced Recovery After Surgery (ERAS) society conducted a systematic review into peri-cystectomy care and made several recommendations. Our objectives were to audit our recent practice, review the relevant literature, and design and introduce a RC integrated care pathway incorporating enhanced recovery principles at our institution.

Methods: Stage one involved a case note audit of 14 patients who underwent RC at Fremantle Hospital between June 2012 and December 2013. Stage two involved a detailed literature review, with relevant articles published from 1980 to present identified using Medline and Embase. Stage three involved the development and introduction of a RC integrated care pathway. Results: Of the 14 patients undergoing RC, urinary diversion consisted of either ileal conduit (12/14) or neo-bladder (2/14). Naso-gastric tubes were used routinely and remained in situ for a median of 3.5 days (range 1-14). Whilst use of gastrointestinal ulcer prophylaxis (12/14) and extended thromboprophylaxis (14/14) was good, other areas of care were less consistent. These included the timing of removal of ureteric stents (median 12 days, range 7-18), use of prokinetics (7/14), and physiotherapy input on day 1 (9/14) and day 2 (8/14). Median time to bowel opening and achieving normal diet were 5 days and 5.5 days respectively; the median length of stay was 13 days. Three major complications were noted (all Clavien 3), and postoperative ileus was the commonest minor complication encountered. Following a review of the literature and multidisciplinary discussion several key changes were introduced including: * Routine use of carbohydrate drinks, metoclopramide and chewing gum * Avoidance of naso-gastric tubes * Removal of ureteric stents on day 7 * Earlier progression of oral intake * Compulsory physiotherapy review for first three days * Automatically prompting key care (e.g. neo-bladder flushes) * Clarifying what is expected for neobladder patients at re-admission Conclusions: In light of increasing evidence, we have conducted a thorough process in order to introduce a RC integrated care pathway at our institution. This pathway incorporates multiple enhanced recovery principles, and it is hoped that this will result in improved patient outcomes and a reduced length of stay. A prospective multicentre trial concept, adapting this pathway with sequential randomised interventions, has been presented to the ANZUP bladder cancer sub-committee and may be supported for development as a future ANZUP bladder cancer trial.

Publication Types: Conference Abstract


BJU International. 2015; 115: 92.

Is there a significant learning curve for fellowship trained Australian laparoscopic radical prostatectomists? Comparison of first 100 to second 100 cases.

Handmer MM, Chabert C, et al.

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Introduction & Objectives: The challenging learning curve for Laparoscopic Radical Prostatectomy (LRP) is well recognised with a multicentre analysis demonstrating the learning curve for surgical margins plateaus at 200 to 250 cases (Secin et al. J Urol 2010). We sought to analyse the perioperative and positive surgical margin (PSM) outcomes of nine Australian LRP surgeons. Methods: Prospectively collected data was obtained from nine Australian surgeons who had performed 2943 consecutive LRP cases with a mean annual case load of 45 patients. Their combined initial experience of 100 cases each (n = 900) was compared to their combined second 100 cases (n = 782) with two of nine surgeons having not completed a total of at least 200 cases. Results: The mean age (61.1 vs 61.2 years) and mean PSA (7.4 vs 7.8 ng/mL) were similar between first 100 cases (F100) and second 100 cases (S100). There was a greater proportion of D’Amico’s high risk patients in the S100 with high, intermediate and low risk cases being 15%, 59% and 26% for the F100 vs 20%, 59% and 21% for the S100 respectively. Blood transfusions (0.8% vs 2.4%), mean blood loss (378 mL vs 413 mL), mean operating time (163 min vs 193 min) and length of stay (2.4 days vs 2.7 days) were all lower in the S100. The histopathological specimens had organ confined disease (pT2) in 76% of F100 and 71% of S100. There was no significant difference in overall PSM being 18.4% in F100 vs 17.5% S100 (P = 0.62). There was also no significant difference between F100 and S100 PSM rates according to pathological stage with pT2 PSM 12.2% vs 9.5% (P = 0.13), pT3a PSM 34.8% vs 40.5% (P = 0.29) and pT3b PSM 52.9% vs 36.4% (P = 0.14). Conclusions: Although the significant learning curve for LRP is well
recognised, especially for PSMs, there was no significant difference in PSMs for the first 100 vs second 100 cases for Fellowship trained Australian surgeons. Perioperative outcomes were acceptable in F100 and further improved with experience in S100. This suggests the learning curve for LRP can be minimised with mentoring and LRP remains a valid minimally invasive surgical treatment for prostate cancer in Australia even in the early experience of Fellowship trained surgeons.

Publication Types: Conference Abstract

BJU International. 2015; 115: 78.

**Disharmony from trainee underperformance: A systematic management process.**


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P. Rashid & Objectives: Underperformance and the disharmony it can cause is not commonly faced by trainees. However, when it surfaces, significant disharmony can engulf a surgical teaching unit. A process to recognise and manage this compassionately must be put in place. Method: A literature review was undertaken to outline processes and themes in addressing and resolving these types of conflicts. A PUBMED search using ‘surgical underperformance’ and ‘remedial teaching’ was used as a broad template to find articles that illustrated key concepts. 1415 articles were identified. 294 abstracts were reviewed in articles where the titles were in line with the stated topic. Key articles were used to develop narrative themes. Additional cross-referenced articles were also included where relevant. Results: There can be a variety of reasons for trainee underperformance. The root cause is not always clear. Disharmony within a surgical teaching unit can occur at this time. A variety of stressors may coexist. A systematic process of management is offered and can be used to evaluate the situation. This process can bring some resolution to difficulties in working relationships. Conclusion: Early constructive intervention improves outcomes. A process is offered, to systematically and compassionately resolve underlying issues. This paper outlines the disharmony that can result from trainee underperformance and offers some guidance to those involved to help bring about resolution.

Publication Types: Conference Abstract


**Should we be investing in the training of laparoscopic radical prostatectomy in Australia? A cost analysis based on the Australian experience of 2735 cases.**


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Introduction & Objective: It is recognised that the increased costs of minimally invasive surgical treatments for prostate cancer of laparoscopic radical prostatectomy (LRP) and robotic assisted laparoscopic prostatectomy (RALP) maybe offset by the potential cost savings from decreased hospital stay, convalescence and transfusion rates. There has been a worldwide decline in the training and uptake of LRP despite its trainability in preference for RALP. We sought to evaluate the relative cost effectiveness of LRP based on a large Australian multiprofessional series of 2735 LRPs, compared to published Australian data of 820 RALP from the Victorian Prostate Cancer Registry. Methods: A decision analytic model was developed in TreeAge Pro 2014 to model the relative cost effectiveness of both surgical approaches. The procedures were weighted with an identical post-operative utility value as there is no conclusive evidence that either LRP or RALP produces superior functional outcomes. Adjuvant/salvage therapy rates were also assumed to be similar, as positive surgical margins for LRP and RALP were overall 15.7% and 20.4% respectively. Costs were drawn from Australian sources with episode costs included procedure cost, cost of consumables, and using mean hospital length of stay 2.45 and 2.86 days for LRP and RALP. Costs for blood transfusion were calculated from Red Cross data with transfusion rates of 1.0% and 1.7% for LRP and RALP respectively. Capital costs for laparoscopic tower and scopes and Da Vinci Si robot and interface were annuitised over 7 years at a 5% interest rate. Results: In the base case analysis RALP was dominated by LRP. Although the relative procedure cost discrepancy between RALP and LRP was reduced by higher patient numbers, even at high volumes of 750 cases per year, the incremental cost was $5502 for each RALP performed (Fig. 1). In the sensitivity analysis all values were varied at 20% above and below the base case value. Even at the limits of the confidence intervals cost per case never approached equivalence with LRP always proving significantly more cost effective. Conclusion: Based on contemporary Australian data LRP is cost-superior to RALP. Given LRP is a cost effective minimally invasive surgical treatment for prostate cancer, formal training programs in LRP should be enhanced with continued dissemination of this skill in Australasia especially with the limited healthcare resources. (Figure Presented).

Publication Types: Conference Abstract
Consultant radiologists experienced in MRI reporting of the prostate. Each 'region of interest' on the mpMRI was rated according to a method for the incorporation of this technology into standard biopsy technique remains undefined. This study is a retrospective review of pathology and correlation was made to the MRI imaging and report. Results: Mean age was 62 (range 46-83). 41 underwent mpMRI for increasing PSA with a mean trigger of 10.7 (standard deviation 7.8). 18 had an mpMRI completed in 3, low likelihood 21, moderate likelihood 27 and high likelihood 9. 11 were subsequently diagnosed with significant prostate cancer disease based on Epstein's criteria. 9 out of 11 had MRI findings consistent with moderate to high likelihood. The remaining two with low likelihood demonstrated significant volume of Gleason 6 disease from the systematic biopsy. 39 patients had a normal ultrasound scan revealed that the left testis had shrunk to 9 cc in volume and was relatively hypovascular compared with the right testis (15.0 cc). Scrotal exploration surgery was performed. Results: No testicular torsion was found. The right testis appeared normal. Bilateral orchidectomy was performed. A biopsy of the left testis was taken and sent fresh for histopathology which revealed moderately severe chronic LO with reduced spermatogenesis and marked atrophy of seminiferous tubules. Tests to exclude potential autoimmune and infectious causes were normal. There was a moderate degree of improvement with oral prednisolone and opiate analgesia. However, significant left testicular pain recurred after 1-2 months. After six months of chronic testicular pain, he underwent left orchidectomy. Histopathology findings were similar to the initial biopsy. He was pain-free after the post-operative period and has been weaned off all medications. He is now leading a normal life. Conclusions: LO is rarely reported condition that in this case responded well to corticosteroids but subsequently required orchidectomy due to chronic pain. Early diagnosis and management is crucial to reduce the risk of impaired spermatogenesis or infertility seen with this condition. When conventional management for more common causes of orchitis fails, urologists may consider a case of LO and diagnose and treat accordingly.

Publication Types: Conference Abstract

Does MRI-informed free hand transperineal biopsy of the prostate improve the detection of significant prostate cancer where clinical concern?

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Introduction & Objectives: There is increasing evidence supporting the use of MRI directed prostate biopsy. However the optimal method for the incorporation of this technology into standard biopsy technique remains undefined. This study is a retrospective review of our experience with MRI informed transperineal biopsy in a major tertiary public hospital in Western Australia. Methods: Between January 2012 and December 2013, 60 patients were referred to Royal Perth Hospital for MRI-informed transperineal biopsy of the prostate due to ongoing clinical suspicion for significant prostatic cancer disease despite previous biopsies. Multiparametric magnetic resonance imaging (mpMRI: T2 and diffusion-weighted imaging) was performed and co-reported by two consultant radiologists experienced in MRI reporting of the prostate. Each 'region of interest' on the mpMRI was rated according to the likelihood of it being moderate to high risk prostatic cancer disease. A free hand transperineal biopsy technique with transrectal ultrasound assistance was subsequently performed to sample 'regions of interest' in addition to a routine systematic core biopsy. Retrospective review of pathology and correlation was made to the MRI imaging and report. Results: Mean age was 62 (range 46-83). 41 underwent mpMRI for increasing PSA with a mean trigger of 10.7 (standard deviation 7.8). 18 had an mpMRI completed prior to entrance onto active surveillance, 1 was an incidental finding on MRI for another indication. mpMRI was reported as normal in 3, low likelihood 21, moderate likelihood 27 and high likelihood 9. 11 were subsequently diagnosed with significant prostate cancer disease based on Epstein's criteria. 9 out of 11 had MRI findings consistent with moderate to high likelihood. The remaining two with low likelihood demonstrated significant volume of Gleason 6 disease from the systematic biopsy. 39 patients had a normal biopsy; this was despite 23 of these demonstrating MRI findings of moderate to high likelihood. Conclusions: Our experience appears to be similar to that encountered in other methods of prostatic biopsy utilising MRI, however a larger cohort needs to be assessed to confirm this. Nevertheless it appears that MRI-informed free hand transperineal biopsy potentially offers a cheaper and yet viable alternative to other methods such as MRI guided in-gantry and fusion techniques.

Publication Types: Conference Abstract

Delays in the diagnosis and treatment of bladder cancer in Western Australia.

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Introduction & Objectives: The expeditious detection and treatment of bladder cancer is vital. Whilst 'one stop' haematuria clinics can reduce delay, there may be the potential for further reductions to be achieved in both pre-referral and post-referral delays. This
study sought to quantify pre-referral and post-referral delays, examine reasons for and predictors of delay, and identify strategies to reduce delay. Methods: Patients diagnosed with bladder cancer through Fremantle Hospital’s ‘one stop’ haematuria clinic between May 2008 and April 2014 were identified retrospectively; patients who were contactable and able to communicate telephonically were invited to participate, resulting in 100 participants. Standardised telephonic questionnaires were used to collect data. Results: Data were provided in the table on pre-referral and post-referral delays for the 72 out of 100 participants who presented with visible haematuria. No significant differences in total delay in days were observed based on sex (143 [male] vs. 183 [female]), remoteness (155 [urban] vs. 98 [rural]), or age (145 [≤70] vs. 156 [>70]). Longer total delays observed in those presenting at a higher T-stage did not reach statistical significance (115 [T1a] vs. 179 [T1+], P = 0.22). Analysis suggested that poor public awareness, misconceptions in primary care, an over-reliance on imaging, and multi-step administrative processes may be contributing to excessive delays. Conclusions: The pathway that could result in delay. Ethical approval was obtained and funding was provided by the Cancer and Palliative Care Research and Evaluation Unit (CapCReU). Results: Data are provided in the table on pre-referral and post-referral delays for the 72 out of 100 participants who presented with visible haematuria. No significant differences in total delay in days were observed based on sex (143 [male] vs. 183 [female]), remoteness (155 [urban] vs. 98 [rural]), or age (145 [≤70] vs. 156 [>70]). Longer total delays observed in those presenting at a higher T-stage did not reach statistical significance (115 [T1a] vs. 179 [T1+], P = 0.22). Analysis suggested that poor public awareness, misconceptions in primary care, an over-reliance on imaging, and multi-step administrative processes may be contributing to excessive delays. pathways, education of general practitioners, and public health measures.

Publication Types: Conference Abstract

BJU International. 2015; 115: 23.

The Australian laparoscopic non robotic radical prostatectomy experience-analysis of 2943 cases.
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Introduction & Objectives: Laparoscopic Radical Prostatectomy (LRP) is a proven effective, trainable minimal invasive surgical treatment option for localised prostate cancer. Despite the increasing trend towards Robotic Assisted Laparoscopic Prostatectomy (RALP), LRP continues to be performed in Australian centres due to local surgeon experience, as well as geographical and financial barriers to robotic access. We analysed the Australian experience of high volume Fellowship trained LRP surgeons. Methods: 2943 LRP cases were performed by nine Australian surgeons. The criteria for inclusion into the study were a prospectively collected database with a minimum of 100 consecutive LRP cases. The surgeons' LRP experience commenced at various times from July 2003 to September 2009. Six of the nine surgeons continue to perform LRP as of August 2014. Mean surgeon annual case load was 45 ranging from 22 to 95 cases per year. Data were analysed for demographic, perioperative, oncological and functional outcomes. Results: The mean age of patients were 61.5 (39-83) years and mean preoperative prostate specific antigen (PSA) was 7.4 (0.1-87) ng/mL. 19%, 63% and 18% were preoperative D’Amico’s low, intermediate and high risk respectively. Mean operating time was 168 min (range of operator means 117-224 min) with conversion to open surgery in 0.5% (range of operator means, 0-1.5%) and a blood transfusion rate of 1.1% (range of operator means, 0-2.5%). The overall mean length of stay was 2.5 days (range of operator means 1.7-3 days). Pathological specimens were 73.6% pT2, 20.7% pT3a, 5.5% pT3b and 0.1% pT4. Overall positive surgical margins (PSM) occurred in 15.9% of cases with pT2 PSM 9.8% (range of operator means 2.7%-18.5%), pT3a PSM 30.8% (range of operator means 16.7%-52.9%) and pT3b PSM 39.2% (range of operator means 0-75% {<5 cases for minimum and maximum range}). 86.3% had a final Gleason Score > 7. Mean urinary continence at 12 months was 91.4% (range of operator means 89.9%-99.7%) with data available from five surgeons. Mean 12 months potency (preoperative potency defined as IIEF > 17) after unilateral and bilateral nerve sparing was 35.2% and 47.2% respectively with data available from four surgeons. Biochemical recurrence occurred in 10.6% with a mean follow up of 17 months and data available from seven surgeons. Conclusions: The Australian experience of Fellowship trained surgeons performing LRP demonstrates favourable perioperative, oncological and functional outcomes in comparison to published data for open, laparoscopic and robotic assisted radical prostatectomy. In our Australian centres, LRP remains an acceptable minimal invasive surgical treatment for prostate cancer despite the increasing use of robotic assisted surgery.

Publication Types: Conference Abstract


Long term follow-up of renal oncocytoma diagnosed by percutaneous needle biopsy.
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Introduction & Objectives: In Western Australia, incidentally found localised renal masses are routinely biopsied under imaging guidance for tissue diagnosis to differentiate between benign and malignant pathologies. However routine biopsy is not endorsed by current major guidelines as up to 22% of core biopsies were deemed non-diagnostic in traditional series. Oncocytoma is radiologically indistinguishable from renal cell carcinoma and represents the commonest benign renal mass encountered and can potentially be managed conservatively. This study evaluates the management, the long-term outcome and the safety of conservative management in patients diagnosed with biopsy-proven oncocytoma. Methods: The database of a major specialist urological practice (Uropath) in Perth was accessed. Of the 841 specimens of percutaneous renal biopsy that were submitted
between January 1999 and January 2014, the diagnosis of oncocytoma was made in 106 samples from 97 patients. To date retrospective data of 53 patients were collected and analysed. The medical records of those who were subjected to active surveillance were reviewed to obtain information about patient characteristics, mode of presentation, subsequent radiological findings and the presence or absence of disease progression on follow-up. Patients who went on to have resection or ablation of their renal mass were also evaluated for reason for intervention and the ensuing oncological outcome. When available, correlation was made between the final surgical and the initial biopsy specimens. Results: Mean follow-up was 29.5 months (range 6 to 109 months). Mean tumour size at the time of diagnosis was 34 mm (range 13 to 87 mm). Average age of diagnosis was 64 years (range 20 to 85). All patients were initially placed under active surveillance. Of those who remained under surveillance (47 of 53), no pathological disease progression was identified. Average growth rate was 1.1 mm per year. Of the 6 remaining patients who subsequently received intervention, the average annual growth was 5.8 mm. 4 had partial nephrectomy, 1 radical nephrectomy and 1 radiofrequency ablation. All 5 patients who had surgical resection were diagnosed with oncocytoma on final histopathological specimen. Conclusions: Most patients (88.7%) in our series remained on active surveillance at the time of last follow-up. Our study suggests that it appears to be safe to monitor biopsy proven oncocytoma with imaging surveillance.

OBJECTIVE: To report on the structure and outcomes of a new 'One Stop' Prostate Clinic (OSPC) designed specifically for rural and remote men.

PATIENTS AND METHODS: Prospective cohort study of the first 200 rural or remote men to access a new OSPC at a public tertiary-level hospital in Western Australia between August 2011 and August 2014. Men attended for urological assessment, and proceeded to same-day transrectal ultrasonography-guided prostate biopsies, if appropriate. Referral criteria were either two abnormal age-related prostate-specific antigen (PSA) levels in the absence of urinary tract infection (UTI), or an abnormal digital rectal examination (DRE) regardless of PSA level.

RESULTS: The median (range) distance travelled was 1545 (56-3229) km and median (range) time from referral to assessment was 33 (2-165) days. The median (range) age was 62 (38-85) years. PSA level was 6.7 (0.5-360) ng/mL and 39% (78/200) had a suspicious DRE. In all, 92% (184/200) of men proceeded to prostate biopsies, and 60% (111/184) of these men were diagnosed with prostate cancer. Our complication rate was 3.5% (6/172). Radical prostatectomy (46/111), active surveillance (28/111) and external beam radiation therapy (26/111) were the commonest subsequent treatment methods. A $1045 (Australian dollars) cost-saving per person was estimated based on the reduced need for travel with the OSPC model.

CONCLUSION: The OSPC is an effective and efficient model for assessing men suspected of having prostate cancer living in rural and remote areas of Western Australia, and this model may be applicable to other areas.
BACKGROUND: Despite adequate trans-urethral resection of the bladder tumour (TURBT), non-muscle-invasive bladder cancer (NMIBC) is associated with high rates of recurrence and progression. Instillation of Bacillus Calmette-Guerin (BCG) into the urinary bladder after TURBT (adjuvant intravesical administration) reduces the risk of both recurrence and progression, and this is therefore the standard of care for high-risk tumours. However, over 30% of people still recur or progress despite optimal delivery of BCG. Our meta-analysis suggests that outcomes might be improved further by using an adjuvant intravesical regimen that includes both mitomycin and BCG. These promising findings require corroboration in a definitive, large scale, randomised phase III trial using standard techniques for intravesical administration.

METHODS AND DESIGN: The BCG + MMC trial (ANZUP 1301) is an open-label, randomised, stratified, two-arm multi-centre phase III trial comparing the efficacy and safety of standard intravesical therapy (BCG alone) against experimental intravesical therapy (BCG and mitomycin) in the treatment of adults with resected, high-risk NMIBC. Participants in the control group receive standard treatment with induction (weekly BCG for six weeks) followed by maintenance (four-weekly BCG for ten months). Participants in the experimental group receive induction (BCG weeks 1, 2, 4, 5, 7, and 8; mitomycin weeks 3, 6, and 9) followed by four-weekly maintenance (mitomycin weeks 13, 17, 25, 29, 37, and 41; BCG weeks 21, 33, and 45). The trial aims to include 500 participants who will be centrally randomised to one of the two treatment groups in a 1:1 ratio stratified by T-stage, presence of CIS, and study site. The primary endpoint is disease-free survival; secondary endpoints are disease activity, time to recurrence, time to progression, safety, health-related quality of life, overall survival, feasibility, and resource use.

TRIAL REGISTRATION: This trial is registered with the Australian New Zealand Clinical Trials Registry (ACTRN1261300513718).

Publication Types: Research Support, Non-U.S. Govt


Epidemiological, clinical, outcome and antibiotic susceptibility differences between PVL positive and PVL negative Staphylococcus aureus infections in Western Australia: a case control study.

Boan P, Tan HL, et al.


BACKGROUND: Panton Valentine Leukocidin (PVL) has been associated with invasive Staphylococcus aureus soft tissue and pneumonic infections.

METHODS: From September 2007 to January 2009 at Royal Perth Hospital we tested for the PVL gene in S. aureus isolates from an invasive site, a suspected PVL-related soft tissue infection and all MRSA isolates. We could access medical records for 141 PVL positive (PVL+ve) infections and compared these to a control group comprised of 148 PVL negative (PVL-ve) infections.

RESULTS: In the PVL+ve group 62 isolates were MRSA (48 were ST93-MRSA-IV) and 79 isolates were methicillin-sensitive S. aureus, and in the PVL-ve group 56 were MRSA (50 were WA-MRSA strains) and 92 were methicillin-sensitive S. aureus. We found the presence of PVL to be significantly associated with younger age, aboriginality, intravenous drug use, community acquisition, shorter length of hospital stay and lower mortality at 1 year. Overall PVL+ve infections more often required surgical intervention (73.0% versus 44.6%, p<0.001) and were less often polymicrobial (8.5% versus 41.2%, p<0.001). PVL+ve isolates were more often susceptible to clindamycin (87.9% versus 73.0%, p=0.002).

CONCLUSIONS: This study demonstrates that PVL+ve infections are associated with a distinct clinical picture, predominantly pyogenic skin and soft tissue infections often requiring surgery, disproportionately affecting patients who are younger, indigenous or with fewer health-care risk factors.
Antiretroviral treatment use, co-morbidities and clinical outcomes among Aboriginal participants in the Australian HIV Observational Database (AHOD).

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Background: There are few data regarding clinical care and outcomes of Indigenous Australians living with HIV and it is unknown if these differ from non-Indigenous HIV-positive Australians. Methods: AHOD commenced enrolment in 1999 and is a prospective cohort of HIV-positive participants attending HIV outpatient services throughout Australia, of which 20 (74 %) sites report Indigenous status. Data were collected up until March 2013 and compared between Indigenous and non-Indigenous participants. Person-year methods were used to compare death rates, rates of loss to follow-up and rates of laboratory testing during follow-up between Indigenous and non-Indigenous participants. Factors associated with time to first combination antiretroviral therapy (cART) regimen change were assessed using Kaplan Meier and Cox Proportional hazards methods. Results: Forty-two of 2197 (1.9 %) participants were Indigenous. Follow-up amongst Indigenous and non-Indigenous participants was 332 & 16270 person-years, respectively. HIV virological suppression was achieved in similar proportions of Indigenous and non-Indigenous participants 2 years after initiation of cART (81.0 % vs 76.5 %, p = 0.635). Indigenous status was not independently associated with shorter time to change from first- to second-line cART (ahR 0.95, 95 % CI 0.51-1.76, p = 0.957). Compared with non-Indigenous participants, Indigenous participants had significantly less frequent laboratory monitoring of CD4 count (rate:2.76 tests/year vs 2.97 tests/year, p = 0.025) and HIV viral load (rate:2.53 tests/year vs 2.93 tests/year, p < 0.001), while testing rates for lipids and blood glucose were almost half that of non-Indigenous participants (rate:0.43/year vs 0.71 tests/year, p < 0.001). Loss to follow-up (23.8 % vs 19.0 %, p = 0.496) and death (2.4 % vs 7.1 %, p = 0.361) occurred in similar proportions of Indigenous and non-Indigenous participants, respectively, although causes of death in both groups were mostly non-HIV-related. Conclusions: As far as we are aware, these are the first data comparing clinical outcomes between Indigenous and non-Indigenous HIV-positive Australians. The forty-two Indigenous participants represent over 10 % of all Indigenous Australians ever diagnosed with HIV. Although outcomes were not significantly different, Indigenous patients had lower rates of laboratory testing for HIV and lipid/glucose parameters. Given the elevated risk of cardiovascular disease in the general Indigenous community, the additional risk factor of HIV infection warrants further focus on modifiable risk factors to maximise life expectancy in this population.


BMC Infectious Diseases. 2015; 15(1).

Impact of statin therapy on coronary plaque composition: a systematic review and meta-analysis of virtual histology intravascular ultrasound studies.

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BACKGROUND: Virtual histology intravascular ultrasound (VH-IVUS) imaging is an innovative tool for the morphological evaluation of coronary atherosclerosis. Evidence for the effects of statin therapy on VH-IVUS parameters has been inconclusive. Consequently, we performed a systematic review and meta-analysis to investigate the impact of statin therapy on plaque volume and its composition using VH-IVUS. METHODS: The search included PubMed, Cochrane Library, Scopus, and Embase (through 30 November 2014) to identify prospective studies investigating the effects of statin therapy on plaque volume and its composition using VH-IVUS. RESULTS: We identified nine studies with 16 statin treatment arms and 830 participants. There was a significant effect of statin therapy on reducing plaque volume (standardized mean difference (SMD): -0.137, 95% confidence interval (CI): -0.255, -0.019; P = 0.023), external elastic membrane volume (SMD: -0.097, 95% CI: -0.183, -0.011; P = 0.027) but not lumen volume (SMD: -0.025, 95% CI: -0.110, +0.061; P = 0.574). There was a significant reduction in fibrous plaque volume (SMD: -0.129, 95% CI: -0.255, -0.003; P = 0.045) and an increase of dense calcium volume (SMD: +0.229, 95% CI: +0.008, +0.450; P = 0.043), while changes in fibro-fatty (SMD: -0.247, 95% CI: -0.592, +0.098; P = 0.16) and necrotic core (SMD: +0.011, 95% CI: -0.144, +0.165; P = 0.892) tissue volumes were not statistically significant. CONCLUSIONS: This meta-analysis indicates a significant effect of statin therapy on plaque and external elastic membrane volumes and fibrous and dense calcium volumes. There was no effect on lumen volume, fibro-fatty and necrotic tissue volumes.


BMC Medical Education. 2015; 15: 5.
Graduate entry and undergraduate medical students’ study approaches, stress levels and ways of coping: a five year longitudinal study.
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BACKGROUND: Incorporating graduate students into undergraduate medical degree programs is a commonly accepted practice. However, it has only recently been recognized that these two types of students cope with their studies in various ways. The aim was to compare the learning approaches, stress levels and ways of coping of undergraduate (UG) and graduate entry medical students (GEMP) throughout their medical course.

METHODS: From 2007-2011 each of the five year cohorts of undergraduate and GEMP students completed four components of the study. The components included demographics, The Biggs' R-SPQ-2 F questionnaire which determines students' approaches to learning, the Perceived Stress Scale (PSS) used to rate students perceived stress during the past four weeks, and the Ways of Coping (WOC) questionnaire used to assess students' methods of coping with everyday problems.

RESULTS: There was a consistent difference between UG and GEMP students approaches to learning over the five years. GEMP students preferred a deep approach while the UG students preferred a superficial approach to learning. There was a significant effect of statin therapy on reducing plaque volume (standardized mean difference (SMD): -0.137, 95% confidence interval (CI): -0.255, -0.019; P = 0.023), external elastic membrane volume (SMD: -0.097, 95% CI: -0.183, -0.011; P = 0.027) but not lumen volume (SMD: -0.025, 95% CI: -0.110, +0.061; P = 0.574). There was a significant reduction in fibrous plaque volume (SMD: -0.129, 95% CI: -0.255, -0.003; P = 0.045) and an increase of dense calcium volume (SMD: +0.229, 95% CI: +0.008, +0.450; P = 0.043), while changes in fibro-fatty (SMD: -0.247, 95% CI: -0.592, +0.098; P = 0.16) and necrotic core (SMD: +0.011, 95% CI: -0.144, +0.165; P = 0.892) tissue volumes were not statistically significant. CONCLUSIONS: This meta-analysis indicates a significant effect of statin therapy on plaque and external elastic membrane volumes and fibrous and dense calcium volumes. There was no effect on lumen volume, fibro-fatty and necrotic tissue volumes.


BMC Nephrology. 2015; 16: 89.
The Omega-3 fatty acids (Fish Oils) and Aspirin in Vascular access Outcomes in REnal Disease (FAVOURED) study: the updated final trial protocol and rationale of post-initiation trial modifications.
APOE epsilon4 moderates abnormal CSF-abeta-42 levels, while neurocognitive impairment is associated with abnormal CSF tau levels in HIV+ individuals - a cross-sectional observational study.

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Comparison of the effects of sun exposure and vitamin D supplementation on vitamin D insufficiency, and immune and cardio-metabolic function: the Sun Exposure and Vitamin D Supplementation (SEDS) Study.

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METHODS/DESIGN: The SEDS Study is a multi-centre, randomised controlled trial of two different daily doses of vitamin D supplementation, and placebo, in conjunction with guidance on two different patterns of sun exposure. Participants recruited from across Australia are aged 18-64 years and have a recent vitamin D test result showing a serum 25(OH)D level of 40-60 nmol/L.

DISCUSSION: This paper discusses the rationale behind the study design, and considers the challenges but necessity of data collection within a non-institutionalised adult population, in order to address the study aims. We also discuss the challenges of participant recruitment and retention, ongoing engagement of referring medical practitioners and address issues of compliance and

METHODS: A total of 604 HIAs, sampled across three geographical regions of China at three administrative levels, participated in a cross-sectional survey conducted in 2013. Descriptive statistics were used to analyze the status of mandated operations, manpower, financial allocations were the main sources of revenue. Three primary personnel employment models coexisted and most employed manpower, financial allocations were the main sources of revenue. Three primary personnel employment models coexisted and most employed personnel. Personnel management and training were considered to be important for meeting service delivery objectives of the HIA in the People's Republic of China. Personnel training and development, including course planning, were considered important for the development of the HIA in the People's Republic of China.

RESULTS: On average, the HIAs had not fully implemented the 11 mandated functions at any administrative levels. Governmental financial allocations were the main sources of revenue. Three primary personnel employment models coexisted and most employed personnel. Personnel management and training were considered to be important for meeting service delivery objectives of the HIA in the People's Republic of China. Personnel training and development, including course planning, were considered important for the development of the HIA in the People's Republic of China.

CONCLUSIONS: In 2012, the majority of the HIAs in China at the provincial, municipal, and county levels did not meet the mandated requirements, although positive indications toward meeting these requirements were observed. It is necessary for the government to pay more attention to institutional resources (buildings, equipment, and the level of the staff's educational attainment) and ensure that the HIAs can meet their service delivery objectives.


Rationale, design and methods for the 22 year follow-up of the Western Australian Pregnancy Cohort (Raine) Study. Straker LM, Hall GL, et al.

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BACKGROUND: Young adulthood is a critical life period for health and health behaviours. Related measurements collected before and after birth, and during childhood and adolescence can provide a life-course analysis of important factors that contribute to health and behaviour in young adulthood. The Western Australian Pregnancy Cohort (Raine) Study has collected a large number of such measurements during the fetal, perinatal, infancy, childhood and adolescence periods and plans to relate them to common health issues and behaviours in young adults, including spinal pain, asthma, sleep disorders, physical activity and sedentary behaviour and, work absence and presenteeism. The aim of this paper is to describe the rationale, design and methods of the 22 year follow-up of the Raine Study cohort.

METHODS/DESIGN: The Raine Study is a prospective cohort study. Participants still active in the cohort (n=2,086) were contacted around the time of their 22nd birthday and invited to participate in the 22 year follow-up. Each was asked to complete a questionnaire, attend a research facility for physical assessment and an overnight sleep study, wear activity monitors for a week, and to maintain a sleep and activity diary over this week. The questionnaire was broad and included questions related to sociodemographics, medical history, quality of life, psychological factors, lifestyle factors, spinal pain, respiratory, sleep, activity and work factors. Physical assessments included anthropometry, blood pressure, back muscle endurance, tissue sensitivity, lung function, airway reactivity, allergic status, 3D facial photographs, cognitive function, and overnight polysomnography.

DISCUSSION: Describing the prevalence of these health issues and behaviours in young adulthood will enable better recognition of the issues and planning of health care resources. Providing a detailed description of the phenotype of these issues will provide valuable information to help educate health professionals of the needs of young adults. Understanding the life-course risk factors of health issues and behaviours in young adulthood will have important health planning implications, supporting the development of targeted interventions to improve current health status and reduce the onset and development of further ill-health across adulthood.


Aspects of the Health Inspection Authority in the People's Republic of China.

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BACKGROUND: In China, there was a pressing need to establish a governmental agency to oversee the organizations that provide public health and medical services. The Chinese Health Inspection Authority (HIA), a relatively independent organization functioning at each administrative level (provincial, municipal, and county), was mandated to conduct 11 health inspection functions to maintain efficient public health and medical services. These functions include issuing health permit, conducting health supervision and inspection, health testing and evaluation, case investigation, complaint handling, managing public health crisis, monitoring and safeguarding public health at major public events, enforcing supervision and inspection compliance, public health education, information management, and team training and management. Since the reform of the health inspection system by the Ministry of Health in 2000, the HIA underwent a series of changes and transitions. This study aimed to describe and assess the five factors that were considered to be important for meeting service delivery objectives of the HIA in the People's Republic of China.

METHODS: A total of 604 HIAs, sampled across three geographical regions of China at three administrative levels, participated in a cross-sectional survey conducted in 2013. Descriptive statistics were used to analyze the status of mandated operations, manpower, revenue and expenditures, and institutional infrastructure. Differences in these characteristics across the geographical regions and administrative levels were compared.

RESULTS: On average, the HIAs had not fully implemented the 11 mandated functions at any administrative levels. Governmental financial allocations were the main sources of revenue. Three primary personnel employment models coexisted and most employed personnel. Personnel management and training were considered to be important for meeting service delivery objectives of the HIA in the People's Republic of China. Personnel training and development, including course planning, were considered important for the development of the HIA in the People's Republic of China.

CONCLUSIONS: In 2012, the majority of the HIAs in China at the provincial, municipal, and county levels did not meet the mandated requirements, although positive indications toward meeting these requirements were observed. It is necessary for the government to pay more attention to institutional resources (buildings, equipment, and the level of the staff's educational attainment) and ensure that the HIAs can meet their service delivery objectives.


TRIAL REGISTRATION: Australia New Zealand Clinical Trials Registry: ACTRN1261300290796 Registered 14 March 2013.
BMJ Case Reports. 2015; 2015(206827).

**What to look for on a breast specimen radiograph: Lessons learnt.**
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Two women underwent stereotactic sampling of mammographically detected lesions with insertion of breast biopsy markers. Localisation of the malignant lesions was performed using iodine 125 seeds, with bracketing of the edges of the larger lesion. The seeds/lesions were located and excised using a probe. Liga clips attached to peripheral sutures at the edges of the specimen enabled radiographic orientation. Surgeon and radiologist found the specimen radiographs difficult to interpret. In one case the surgeon thought the lesion had been removed, mistaking the iodine seed for the biopsy marker. The radiologist noted absence of the biopsy marker and marginal calcifications but was concerned the seed was absent. Widening the window level allowed seed identification, revealing a characteristic rectangular radiolucent area in what had been interpreted as a Liga clip. Correct interpretation of the findings helped guide lesion removal, intraoperative margin re-excision and confirmed 125I seed retrieval.

BMJ Case Reports. 2015.

**Parotid epithelial-myoepithelial carcinoma: an unexpected intraoperative finding.**
Davidoss NH, Khaleel Z, et al.

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We present a case of a 72-year-old man with a parotid mass which was initially diagnosed as a pleomorphic adenoma. Intraoperatively, the tumour was found to be invading the facial nerve. It was later found to be an epithelial-myoepithelial carcinoma, a rare salivary gland tumour. Despite invasion of the facial nerve, function of the nerve remained intact. Copyright 2015 BMJ Publishing Group Ltd.

BMJ Case Reports. 2015.

**Glomus tumour: a rare differential for subungual lesions.**

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A 21-year-old, usually fit and well man, presented with a 10-year history of intermittent, paroxysmal pain and temperature sensitivity to his right thumb. He felt this was associated with a subungual lesion present on the same digit. He was diagnosed as having a glomus tumour and was referred to the hand surgeons for surgical excision. Copyright 2015 BMJ Publishing Group Ltd.

BMJ Case Reports. 2015.

**Functional movement disorder: a long journey to diagnosis.**

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A 61-year-old man presented to a country clinic with involuntary orofacial movements and progressive cognitive decline, causing significant disability and psychosocial distress. Review of records uncovered a 7-year history of presentations to several specialties, including memory clinics, neurology, internal medicine and emergency departments, with varied symptoms, extensive complex work up and inconclusive diagnosis. Comprehensive review at our hospital highlighted inconsistent neurological signs, fluctuating cognition and psychosocial stressors, which preceded symptom onset, leading to the diagnosis of a functional movement disorder (FMD), which subsequently improved with relaxation therapy, cognitive-behavioural therapy and physiotherapy. We illustrate a variety of somatic symptoms, diagnostic clues and management outcomes for FMDs, and the importance of diagnostic criteria to minimise costly, time-consuming and ultimately unnecessary tests of exclusion. Copyright 2015 BMJ Publishing Group Ltd.

BMJ Case Reports. 2015.

**Novel presentation of a cricket ball-related intra-abdominal injury: genitofemoral nerve referred pain.**
Philippoff AC, Rowcroft A, et al.

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CONCLUSIONS: A model which explores person, place, and setting and practice factors can provide important information about those with severe stroke (OR=10.4, p<0.001, 95% CI 9.27 to 11.65). Were excluded for most of the reasons, including refusal. The odds of exclusion due to early deterioration were particularly high for arrival to hospital (ie, >24 h). Overall, being older and female reduced the odds of recruitment to the trial. More women than men a licence) please go to http://group.bmj.com/group/rights-licensing/permissions.

RESULTS: The demographics and stroke characteristics of the included patients in the trial were broadly similar to population-based exploratory analysis of the demographic, clinical, site and process factors associated with recruitment.

MODEL: We use the Proximal Similarity Model, which considers the person, place, and setting and practice, as a framework for considering generalisability. As well as comparing the recruited patients with the target population, we also performed an

Ongoing,contact with the ball or bat, another player, the ground or boundary) or overuse injuries (due to running, throwing, batting, bowling, repetitive movements and overexertion). This case report describes a rare case of small bowel perforation and suspected genitofemoral nerve injury secondary to the direct impact of a cricket ball, and includes a brief review of blunt abdominal injuries resulting in isolated small bowel perforations. Copyright 2015 BMJ Publishing Group Ltd.


Exploring threats to generalisability in a large international rehabilitation trial (AVERT).
Bernhardt,J. Raffelt, A. et al.
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OBJECTIVE: The purpose of this paper is to examine potential threats to generalisability of the results of a multicentre randomised controlled trial using data from A Very Early Rehabilitation Trial (AVERT).

RESEARCH DESIGN: AVERT is a prospective, parallel group, assessor-blinded randomised clinical trial. This paper presents data assessing the generalisability of AVERT.

SETTING: Acute stroke units at 44 hospitals in 8 countries.

PARTICIPANTS: The first 20 000 patients screened for AVERT, of whom 1158 were recruited and randomised.

MODEL: We use the Proximal Similarity Model, which considers the person, place, and setting and practice, as a framework for considering generalisability. As well as comparing the recruited patients with the target population, we also performed an exploratory analysis of the demographic, clinical, site and process factors associated with recruitment.

RESULTS: The demographics and stroke characteristics of the included patients in the trial were broadly similar to population-based norms, with the exception that AVERT had a greater proportion of men. The most common reason for non-recruitment was late arrival to hospital (ie, >24 h). Overall, being older and female reduced the odds of recruitment to the trial. More women than men were excluded for most of the reasons, including refusal. The odds of exclusion due to early deterioration were particularly high for those with severe stroke (OR=10.4, p<0.001, 95% CI 9.27 to 11.65).

CONCLUSIONS: A model which explores person, place, and setting and practice factors can provide important information about the external validity of a trial, and could be applied to other clinical trials.

TRIAL REGISTRATION NUMBER: Australian New Zealand Clinical Trials Registry (ACTRN12606001855611) and Clinicaltrials.gov (NCT01846247). Copyright Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to http://group.bmj.com/group/rights-licensing/permissions.


Should HFE p.C282Y homozygotes with moderately elevated serum ferritin be treated? A randomised controlled trial comparing iron reduction with sham treatment (Mi-iron).
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SUBJECTS: Records of 17,753 persons aged at least 20 years when hospitalised for a first burn injury in Western Australia during the period 1980-2012, and 70,758 persons who were age and gender-frequency matched with no injury admissions randomly selected from Western Australia's electoral roll.

MAIN OUTCOME MEASURES: Admission rates and cumulative length of stay for musculoskeletal diseases. Negative binomial and Cox proportional hazards regression modelling were used to generate incidence rate ratios (IRR) and HRs with 95% CIs, respectively.

RESULTS: After adjustment for pre-existing health status and demographic characteristics, the burn cohort had almost twice the hospitalisation rate for a musculoskeletal condition (IRR, 95% CI 1.98, 1.86 to 2.10), and spent 3.70 times as long in hospital with a musculoskeletal diagnosis (95% CI 3.10 to 4.42) over the 33-year period, than the uninjured comparison cohort. Adjusted survival analyses of incident post-burn musculoskeletal disease admissions found significant increases for the 15-year post burn discharge period (0-6 months: HR, 95% CI 2.51, 2.04 to 3.11; 6 months-2 years: HR, 95% CI 1.77, 1.53 to 2.05; 2-15 years: HR, 95% CI 1.32, 1.23 to 1.42). Incident admission rates were significantly elevated for 20 years post-burn for minor and severe burn injury for a range of musculoskeletal diseases that included arthropathies, dorsopathies, osteopathies and soft tissue disorders.

CONCLUSIONS: Minor and severe burn injuries were associated with significantly increased post-burn incident admission rates, long-term hospital use and prolonged length of stay for a range of musculoskeletal diseases. Further research is required that facilitates identification of at-risk patients and appropriate treatment pathways, to reduce the long-term morbidity associated with burns.


BMJ Open. 2015; 5(9): e009395.


Randall SM, Fear MW, et al.

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OBJECTIVE: To investigate if adults who are hospitalised for a burn injury have increased long-term hospital use for musculoskeletal diseases.

DESIGN: A population-based retrospective cohort study using linked administrative health data from the Western Australian Data Linkage System.

SUBJECTS: Records of 17,753 persons aged at least 20 years when hospitalised for a first burn injury in Western Australia during the period 1980-2012, and 70,758 persons who were age and gender-frequency matched with no injury admissions randomly selected from Western Australia's electoral roll.

MAIN OUTCOME MEASURES: Admission rates and cumulative length of stay for musculoskeletal diseases. Negative binomial and Cox proportional hazards regression modelling were used to generate incidence rate ratios (IRR) and HRs with 95% CIs, respectively.

RESULTS: After adjustment for pre-existing health status and demographic characteristics, the burn cohort had almost twice the hospitalisation rate for a musculoskeletal condition (IRR, 95% CI 1.98, 1.86 to 2.10), and spent 3.70 times as long in hospital with a musculoskeletal diagnosis (95% CI 3.10 to 4.42) over the 33-year period, than the uninjured comparison cohort. Adjusted survival analyses of incident post-burn musculoskeletal disease admissions found significant increases for the 15-year post burn discharge period (0-6 months: HR, 95% CI 2.51, 2.04 to 3.11; 6 months-2 years: HR, 95% CI 1.77, 1.53 to 2.05; 2-15 years: HR, 95% CI 1.32, 1.23 to 1.42). Incident admission rates were significantly elevated for 20 years post-burn for minor and severe burn injury for a range of musculoskeletal diseases that included arthropathies, dorsopathies, osteopathies and soft tissue disorders.

CONCLUSIONS: Minor and severe burn injuries were associated with significantly increased post-burn incident admission rates, long-term hospital use and prolonged length of stay for a range of musculoskeletal diseases. Further research is required that facilitates identification of at-risk patients and appropriate treatment pathways, to reduce the long-term morbidity associated with burns.


BMJ Open. 2015; 5(9): e009395.
Bone Marrow Transplantation. 2015; 50: S320-S321.

**Survival after mesenchymal stromal cell therapy in steroid resistant acute graft-versus-host-disease. A systematic review and meta-analysis.**

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Introduction: Graft-versus-host-disease (GVHD) is the major limitation of allogeneic transplants. Due to the results of compelling phase I-II studies (including the EBMT trial) in acute GVHD, the use of mesenchymal stromal cells (MSC) has become standard practice in many countries even though a phase III trial in the United States (Prochymal) reported negative results. We conducted a meta-analysis of currently available published and unpublished data using the PRISMA Statement to formulate the reporting.

Materials (or patients) and methods: A literature search (1996-2013) included the Medline, EMBASE, Ovid & Cochrane CENTRAL databases. Outcomes measured were response rates (RR) & 6 month survival. Unpublished studies/ conference abstracts from ASBMT, SIOP, EBMT, ASH were also searched. Quality Appraisal for the Risk of Bias was done via RoBANS since most of the studies were non-randomized. A random-effects model was used to pool outcomes across studies due to anticipated heterogeneity. Survival was assessed at 6 months and at the end of the study. Subgroup analyses included (a) pediatric vs adult (b) dosage of MSCs delivered (c) type of MSC lysate utilized and (d) source of MSCs. Results: Searches yielded 628 published & unpublished studies, 562 were excluded mainly due to usage of MSCs for non-GVHD conditions. Additional information at 6 months was obtained for 13 studies from investigators which was included in the final cohort. Because of the absence of survival data from the Prochymal Study, this study was not included in the meta-analysis. For the survival meta-analysis, 292 patients were included. The median number of days from the onset of acute GVHD to MSC infusion varied between studies (2-46d). The MSC dose delivered was variable in different studies (0.3-9 x 10^6/kg). The 6m survival was 0.63 (range 0.50-0.74; 1<sup>-</sup>2<sup>=</sup>41); survival (end of study) was 0.52 (range 0.41-0.64; 1<sup>-</sup>2<sup>=</sup>67). There was no significant difference in relative risks (RR) based on age, lysate type, dose of MSC delivered, and no significant correlation in survival between adult vs pediatric groups (P=0.43), or between the dosage of MSCs (P=0.48). MSC studies which had utilized Fetal Bovine Serum (FBS) lysate compared to platelet lysate for culture demonstrated a superior response (0.8 vs 0.62 respectively; P=0.02). MSC responders had a 6m survival of 0.63 (0.51-0.74); nonresponders had a 6m survival of 0.16 (0.07-0.35), with no heterogeneity (1<sup>-</sup>2<sup>=</sup>0). ORR and CR were significantly associated with time from diagnosis with early administration of MSCs favoring better responses (P= 0.03 and P=0.02 respectively). The 6m survival from non-MSC studies which have been analyzed in recent ASBMT guidelines was compared with that of MSC studies. The average weighted event rate was found to be 0.42 from the onset of GVHD in non-MSC studies, compared to 0.63 with MSCs. Additional work is in progress to analyze the comparisons of survival from the onset of MSC and non-MSC treatments. Conclusion: Totality of evidence from this meta-analysis indicates that MSCs are an acceptable treatment for acute steroid refractory GVHD. Randomized clinical trials are urgently needed for comparison of MSC vs non-MSC modalities.

Publication Types: Conference Abstract


**Br J Hosp Med (Lond).** 2015; 76(9): 542-3.

**Lower limb lymphoedema and obesity: a much-neglected association.**

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**Br J Ophthalmol.** 2015.

**Cerebrospinal fluid pressure and the eye.**

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Royal Perth Hospital, Perth, Western Australia, Australia.

Cerebrospinal fluid pressure (CSFP) interacts with intraocular pressure (IOP) and blood pressure to exert a major influence upon the eye, particularly the optic nerve head region. There is increased interest regarding the influence of CSFP upon disorders affecting this region, in particular glaucoma and idiopathic intracranial hypertension. Additionally, a high proportion of astronauts develop features similar to idiopathic intracranial hypertension that persist for years after returning to Earth. The factors that affect the CSFP influence upon the optic nerve and globe are likely to influence the outcome of various ophthalmic disorders.

Dystroglycanopathies are a heterogeneous group of diseases with a broad phenotypic spectrum ranging from severe disorders with congenital muscle weakness, eye and brain structural abnormalities and intellectual delay to adult-onset limb-girdle muscular dystrophies without mental retardation. Most frequently the disease onset is congenital or during childhood. The exception is FKRP mutations, in which adult onset is a common presentation. Here we report eight patients from five non-consanguineous families with GMPPB mutations, one presented with isolated episodes of rhabdomyolysis, and one as a congenital muscular dystrophy. This report expands the phenotypic spectrum of GMPPB mutations to include limb-girdle muscular dystrophies with adult onset with or without intellectual disability, or isolated rhabdomyolysis. Copyright © The Author (2015). Published by Oxford University Press on behalf of the Guarantors of Brain.


Epidemiology of ductal carcinoma in situ in Western Australia: implications for surgical margins and management.


BACKGROUND: In 2010, the Australian Institute of Health and Welfare published a report examining the characteristics of Australian women diagnosed with ductal carcinoma in situ (DCIS). This study identified the characteristics of women who were diagnosed with DCIS in Western Australia (WA) 1996-2005, and built on a national study by determining the rate of second operation and breast cancer events (BCE) in WA.

METHODS: A retrospective analysis of data from the WA Cancer Registry and the Hospital Morbidity Database was undertaken. The main outcome measures were histological characteristics, second operation rate, breast cancer events.

RESULTS: A total of 1356 cases of DCIS were diagnosed in WA between 1996 and 2005, with a minimum 5-year follow-up. The age-standardised incidence rate in 2005 was 15.4 per 100,000 women. 72 % of patients received breast-conserving therapy for primary treatment, 18 % of patients requiring a second operation to obtain adequate margins and 35 % of patients received postoperative radiotherapy. 17.3 % of cases had a subsequent BCE, with the 5- and 10-year probabilities being 4.36 and 8.27 %, respectively. A BCE was significantly associated with age (p < 0.001), no second operation (p < 0.001) and no radiotherapy (p = 0.049 recurrence, p = 0.043 invasion).

CONCLUSION: This study supports the need to ensure adequate margins during primary surgery for DCIS is obtained to reduce the need for a second operation or the risk of a subsequent BCE. The consideration of mastectomy versus radiotherapy should be made in conjunction with the identified risk factors, specifically age and whether a second operation was performed.

Venous thrombotic, thromboembolic, and mechanical complications after retrievable inferior vena cava filters for major trauma.

Ho KM, Tan JA, et al.
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Background: The ideal thromboprophylaxis in patients at risk of bleeding is uncertain. This retrospective cohort study assessed the risk factors for complications after using retrievable inferior vena cava (IVC) filters for primary or secondary thromboembolism prophylaxis in patients after major trauma. Methods: Using data from radiology, trauma and death registries, the incidence of and risk factors for subsequent deep venous thrombosis (DVT), venous thromboembolism (VTE), and mechanical complications related to retrievable IVC filters in patients, admitted between 2007 and 2012, were assessed in a single trauma centre. Results: Of the 2940 major trauma patients admitted during the study period, a retrievable IVC filter was used in 223 patients (7.6%). Thirty-six patients (16%) developed DVT or VTE subsequent to placement of IVC filters (median 20 days, interquartile range 9-33), including 27 with lower limb (DVT), 8 upper limb DVT, and 4 pulmonary embolism. A high Injury Severity Score, tibial/fibular fractures, and a delay in initiating pharmacological thromboprophylaxis after insertion of the filters (14 vs 7 days, \( P=0.001 \)) were significant risk factors. Thirty patients were lost to follow-up (13%) and their filters were not retrieved. Mechanical complications - including filters adherent to the wall of IVC (4.9%), IVC thrombus (4.0%), and displaced or tilted filters (2.2%) - were common when the filters were left in situ for >50 days. Conclusions: A delay in initiating pharmacological thromboprophylaxis or filter removal were associated with an increased risk of subsequent DVT, VTE, and mechanical complications of retrievable IVC filters in patients after major trauma.


A comparative study examining the management of squamous cell carcinoma in situ (Bowen disease) in the U.K. and Australia.

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Squamous cell carcinoma (SCC) in situ, or Bowen disease (BD), is an intraepidermal malignancy that may progress to invasive SCC. A wide range of treatments are used, but the existing literature is unable to make clear assertions regarding optimum management. Given this uncertainty, it is important to assess how BD is managed in clinical practice. Therefore, this study will endeavour to describe and compare current clinical practice for the management of BD in two centres, one in the U.K. and one in Australia. This retrospective comparison study selected patients from a centre in West Midlands, U.K. and a centre in Western Australia. All cases of BD diagnosed in each centre's histopathology department, in a 12-month period (1 July 2012 to 30 June 2013), were identified from the histopathology departmental databases. The medical records of those patients with BD were analysed to collect data regarding patient age and sex, site of lesion and treatment modality used. In 1 year there were a total of 185 patients with 193 BD lesions in the U.K. centre and 124 patients with 200 lesions in the Australian centre. Of these lesions, 155 in the U.K. and 151 in Australia had notes available for analysis. Patients from both centres were, on average, in their eighth decade: mean age 79 +/- 9 years in the U.K. and 76 +/- 12 years in Australia (\( P = 0.03 \)). There were further demographic similarities between the two centres, as each cohort consisted of a small majority of men: 56% of the U.K. cohort and 59% of the Australian cohort (\( P = 0.58 \)). The site at which BD lesions were most frequently observed was the face, both in the U.K. with 70 (45%) and in Australia with 83 (55%) (\( P = 0.08 \)). The management of the majority of lesions in the U.K. centre was fulfilled by the plastic surgery department, 72 (46%) lesions. This contrasts with the Australian centre in which most lesions were managed by the dermatology department, 121 (80%) lesions. However, the therapy utilized most frequently was surgical excision, in both centres, with 103 (67%) lesions in the U.K. centre and 102 (67%) in the Australian centre. In both the U.K. and Australia BD arises in the older population on sun-exposed sites. The most common therapy was surgical excision, which was performed by a number of different specialties.

Publication Types: Conference Abstract


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Does mindfulness improve outcomes in patients with chronic pain? Systematic review and meta-analysis.

Bawa FL, Mercer SW, et al.

BACKGROUND: Chronic pain and its associated distress and disability are common reasons for seeking medical help. Patients with chronic pain use primary healthcare services five times more than the rest of the population. Mindfulness has become an increasingly popular self-management technique.

AIM: To assess the effectiveness of mindfulness-based interventions for patients with chronic pain.

DESIGN AND SETTING: Systematic review and meta-analysis including randomised controlled trials of mindfulness-based
interventions for chronic pain. There was no restriction to study site or setting.

METHOD: The databases MEDLINE(I), Embase, AMED, CINAHL, PsycINFO, and Index to Theses were searched. Titles, abstracts, and full texts were screened iteratively against inclusion criteria of: randomised controlled trials of mindfulness-based intervention; patients with non-malignant chronic pain; and economic, clinical, or humanistic outcome reported. Included studies were assessed with the Yates Quality Rating Scale. Meta-analysis was conducted.

RESULTS: Eleven studies were included. Chronic pain conditions included: fibromyalgia, rheumatoid arthritis, chronic musculoskeletal pain, failed back surgery syndrome, and mixed aetiology. Papers were of mixed methodological quality. Main outcomes reported were pain intensity, depression, physical functioning, quality of life, pain acceptance, and mindfulness. Economic outcomes were rarely reported. Meta-analysis effect sizes for clinical outcomes ranged from 0.12 (95% confidence interval [CI] = -0.05 to 0.30) (depression) to 1.32 (95% CI = -1.19 to 3.82) (sleep quality), and for humanistic outcomes 0.03 (95% CI = -0.66 to 0.72) (mindfulness) to 1.58 (95% CI = -0.57 to 3.74) (pain acceptance). Studies with active, compared with inactive, control groups showed smaller effects.


Does mindfulness improve outcomes in patients with chronic pain? Systematic review and meta-analysis.

Marikar Bawa FL, Mercer SW, et al.

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Background: Chronic pain and its associated distress and disability are common reasons for seeking medical help. Patients with chronic pain use primary healthcare services five times more than the rest of the population. Mindfulness has become an increasingly popular self-management technique. Aim: To assess the effectiveness of mindfulness-based interventions for patients with chronic pain. Design and setting: Systematic review and meta-analysis including randomised controlled trials of mindfulness-based interventions for chronic pain. There was no restriction to study site or setting. Method: The databases MEDLINE, Embase, AMED, CINAHL, PsycINFO, and Index to Theses were searched. Titles, abstracts, and full texts were screened iteratively against inclusion criteria of: randomised controlled trials of mindfulness-based intervention; patients with non-malignant chronic pain; and economic, clinical, or humanistic outcome reported. Included studies were assessed with the Yates Quality Rating Scale. Meta-analysis was conducted. Results: Eleven studies were included. Chronic pain conditions included: fibromyalgia, rheumatoid arthritis, chronic musculoskeletal pain, failed back surgery syndrome, and mixed aetiology. Papers were of mixed methodological quality. Main outcomes reported were pain intensity, depression, physical functioning, quality of life, pain acceptance, and mindfulness. Economic outcomes were rarely reported. Meta-analysis effect sizes for clinical outcomes ranged from 0.12 (95% confidence interval [CI] = -0.05 to 0.30) (depression) to 1.32 (95% CI = -1.19 to 3.82) (sleep quality), and for humanistic outcomes 0.03 (95% CI = -0.66 to 0.72) (mindfulness) to 1.58 (95% CI = -0.57 to 3.74) (pain acceptance). Studies with active, compared with inactive, control groups showed smaller effects. Conclusion: There is limited evidence for effectiveness of mindfulness-based interventions for patients with chronic pain. Better-quality studies are required. Copyright © British Journal of General Practice 2015. http://www.ncbi.nlm.nih.gov/pubmed?tool=iaufhhslib&term=2015108408

Use of the dietary guideline index to assess cardiometabolic risk in adolescents.

Chan She Ping-Delfos WL, Beilin LJ, et al.

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W.L. Chan She Ping-Delfos, School of Medicine and Pharmacology, Royal Perth Hospital Unit, University of Western Australia, Perth, WA 6000, Australia

The long-term adherence to the dietary guidelines has not been evaluated against emergence of cardiometabolic risks in adolescents with increasing rates of obesity. The present study aimed to (1) determine the level of adherence to the guidelines using the Australian Dietary Guideline Index for Children and Adolescents (DGI-CA) in adolescents of age 14 and 17 years and to (2) examine the relationship between their assessed diet quality and concurrently measured cardiometabolic risk factors over time. Data were analysed from the Western Australian Pregnancy Cohort (Raine) Study. The DGI-CA was determined from a FFQ. Anthropometry and fasting biochemical measures were taken using standard procedures. Hierarchical linear mixed models examined associations between cardiometabolic risk factors and DGI-CA, adjusting for socio-economic status, physical activity, BMI, and sex, and examining for interactions. The mean DGI-CA scores were 471 (sd 102) at 14 years (n 1419) and 477 (sd 110) at 17 years (n 843), and were not different between sex. There was a significant inverse association between DGI-CA and insulin, homeostasis model assessment score and heart rate. The DGI-CA was positively associated with BMI (P= 0029) but negatively with waist:hip ratio (P= 0026). It was not associated with lipids or blood pressure, with the exception of a negative association with TAG (P= 0011). The degree of adherence in the Raine Study adolescents was suboptimal but similar to the Australian Children's
Nutrition and Physical Activity Survey. The present study shows that, at any particular time, better diet quality was associated with better insulin sensitivity and TAG levels and decreased abdominal fatness.


**Swimming goggle wear is not associated with an increased prevalence of glaucoma.**

Franchina M, Yazar S, et al.

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**BACKGROUND/AIMS:** Previous studies have demonstrated a small but significant transient increase in intraocular pressure (IOP) in individuals wearing certain types of swimming goggles. These findings suggested that wearing goggles could represent a significant risk factor for developing and/or worsening of glaucoma in people who swim regularly. The aim of this study was to determine if glaucoma prevalence is increased among adult swimmers.

**METHODS:** A comprehensive ocular examination was performed on 231 members of local swimming clubs and 118 non-swimmers. IOP was measured using iCare tonometry and visual field testing was performed using Humphrey SITA fast 24-2. Retinal nerve fibre layer thickness was assessed using spectral domain optical coherence tomography.

**RESULTS:** Based on measurements of IOP and visual fields, we did not detect any new cases of glaucoma in our cohort of frequent swimmers. Similarly, we found no difference in the thickness of the retinal nerve fibre layer between swimmers and non-swimmers; the mean right global thickness (GT) was 94.0 μm (IQR 88.0, 100.3) vs 93.0 μm (IQR 89.0, 101.0), respectively (p=0.976), and the median left GT was 93.7 μm (IQR 88.0, 101.0) in both groups (p=0.799).

**CONCLUSIONS:** These findings suggest that frequently wearing swim goggles does not lead to an increased risk of glaucoma over time in adults. Copyright Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to http://group.bmj.com/group/rights-licensing/permissions.


**Long-term mortality among older adults with burn injury: A population-based study in Australia.**

Duke JM, Boyd JH, et al.

(Duke) Burn Injury Research Unit, School of Surgery, Dentistry and Health Sciences, University of Western Australia, M318 35 Stirling Highway, Crawley, Perth, WA 6009, Australia (Boyd, Randall) Centre for Data Linkage, Curtin University, Perth, Australia (Rea, Wood) Burns Service of Western Australia, Royal Perth Hospital and Princess Margaret Hospital, Perth, Australia (J. M. Duke, Burn Injury Research Unit, School of Surgery, Dentistry and Health Sciences, University of Western Australia, M318 35 Stirling Highway, Crawley, Perth, WA 6009, Australia) Objective To assess if burn injury in older adults is associated with changes in long-term all-cause mortality and to estimate the increased risk of death attributable to burn injury. Methods We conducted a population-based matched longitudinal study - based on administrative data from Western Australia's hospital morbidity data system and death register. A cohort of 6014 individuals who were aged at least 45 years when hospitalized for a first burn injury in 1980-2012 was identified. A non-injury comparison cohort, randomly selected from Western Australia's electoral roll (n = 25 759), was matched to the patients. We used Kaplan-Meier plots and Cox proportional hazards regression to analyse the data and generated mortality rate ratios and attributable risk percentages. Findings For those hospitalized with burns, 180 (3%) died in hospital and 2498 (42%) died after discharge. Individuals with burn injury had a 1.4-fold greater mortality rate than those with no injury (95% confidence interval, CI: 1.3-1.5). In this cohort, the long-term mortality attributable to burn injury was 29%. Mortality risk was increased by both severe and minor burns, with adjusted mortality rate ratios of 1.3 (95% CI: 1.1-1.9) and 2.1 (95% CI: 1.9-2.3), respectively. Conclusion Burn injury is associated with increased long-term mortality. In our study population, sole reliance on data on in-hospital deaths would lead to an underestimate of the true mortality burden associated with burn injury.


**A survey of skin substitute use in United Kingdom and Australasia.**


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Publication Types: Letter

Scald burns in children aged 14 and younger in Australia and New Zealand - An analysis based on the Burn Registry of Australia and New Zealand (BRANZ).

Riedlinger D., Jennings PA, et al.

Scalds are a common injury in children and a frequent reason for hospitalisation despite being a preventable injury. Effective burn first aid reduces hospital stay and reinforces the need to encourage, carers and bystanders to deliver effective first aid and the importance of targeted prevention campaigns that reduce the burden of pediatric scald burns in Australia and New Zealand.


Patient confidentiality and new technologies in burn care.

Dunne JA, Rawlins JM.

Patient confidentiality and new technologies in burn care.


Non-severe burn injury leads to depletion of bone volume that can be ameliorated by inhibiting TNF-alpha.

O'Halloran E, Kular J, et al.

Non-severe burn injury leads to depletion of bone volume that can be ameliorated by inhibiting TNF-alpha.


Transfer time to a specialist burn service and influence on burn mortality in Australia and New Zealand: A multicentre, hospital based retrospective cohort study.

Cassidy TJ, Edgar DW, et al.

Transfer time to a specialist burn service and influence on burn mortality in Australia and New Zealand: A multicentre, hospital based retrospective cohort study.

**The Brief Fatigue Inventory is reliable and valid for the burn patient cohort.**

Toh C, Li M, et al.
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D.W. Edgar, Burn Service of WA, Royal Perth Hospital, WA, Australia

Objective After burn, patients are at risk of fatigue which may influence negatively their capacity to participate in activity, rehabilitation and other treatments. Fatigue may stem from the wound healing and systemic responses to burn which drive a hypermetabolic state that may persist for months. However, an established method is not available for objectively measuring fatigue after burns. The Brief Fatigue Inventory (BFI) was hypothesised to be an appropriate option for assessments following severe burn. The primary aim of the study was to establish if the BFI was reliable and valid in a burn patient sample. Methods Adult patients admitted between 2009 and 2013 to Royal Perth Hospital Burn Center were included. Patients completed the BFI and Burns Specific Health Scale Brief (BSHS-B) in tandem at one, three, six and 12 months after burn. Reliability was assessed using Cronbach’s alpha; construct validity using factor analysis and multi-variable regression of BFI; and, criterion validity with longitudinal regression of BFI with BSHS-B. Results The sample (n = 587) had a median TBSA of 3% (range = <1-75%). The BFI demonstrated excellent reliability (alpha > 0.90). The factor analysis confirmed a single-domain construct, centred around the first scale item. Good correlation between BFI and BSHS-B scores (p < 0.001) on longitudinal analysis confirmed criterion validity. There was a significant difference in fatigue scores between minor and major burn patients and a significant association of fatigue levels over time with TBSA. Conclusion The BFI is a reliable and valid tool for fatigue measurement in patients during the first 12 months after burn.


**Interpretation of the DermaLab Combo() pigmentation and vascularity measurements in burn scar assessment: An exploratory analysis.**

Gankande TU, Duke JM, et al.

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BACKGROUND: The DermaLab Combo() measures pigmentation and vascularity of a burn scar more reliably than the modified Vancouver Scar Scale (mVSS). This study aims to examine how the DermaLab Combo() continuous measurements of pigmentation and vascularity of burns scars relate to the mVSS, a standard clinical scar assessment method; and secondly, to obtain evidence to support the concurrent validity of DermaLab Combo() measurements for pigmentation and vascularity.

METHOD: Scar assessments were performed on an index burn scar of 100 subjects using two methods: the mVSS (two raters) and...
the DermaLab Combo() device (one rater). Using the DermaLab Combo(), measurements of pigmentation and vascularity for the index scar and an adjacent normal skin site were obtained. Indices were generated to represent the scar pigmentation (melanin index, MI%) and scar vascularity (erythema index, EI%) relative to the patient’s matched normal skin. Exploratory univariate and bivariate analyses were conducted and the concordance of classification by mVSS score using DermaLab() cut-off values was assessed.

RESULTS: For pigmentation, the results suggest a 80% classification concordance for the DermaLab Combo() MI% values into mVSS pigmentation categories (hypopigmentation, normal pigmentation and hyperpigmentation) using two predictors (MI% and EI%) and visually fitted discriminant axis cut-offs. Due to the high degree of overlap of EI% values between the vascularity categories, meaningful classification of EI% values using the mVSS was not possible.

CONCLUSION: Quantifying percentage changes in melanin and erythema relative to matched normal skin improved understanding of the DermaLab Combo() pigmentation and vascularity measurements. The DermaLab Combo() pigmentation MI% values were able to be classified into pigmentation categories of the mVSS, and pigmentation classification concordance was further improved with consideration of the scar's DermaLab Combo() vascularity EI% values. The DermaLab Combo() is an objective tool; however, while the nusenfmet provides continuous numerical data that may be useful for identifying change over time in clinical scar monitoring of pigmentation and vascularity, further work will be useful to understand the DermaLab Combo() measurements to optimise the interpretation of these data.Copyright © 2015 Elsevier Ltd and ISBI. All rights reserved. http://www.ncbi.nlm.nih.gov/pubmed?tool=iaufhhslib&term=25703660

Burns. 2015.

Increased admissions for musculoskeletal diseases after burns sustained during childhood and adolescence.

Duke JM, Randall SM, et al.

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BACKGROUND: Severe burn triggers systemic responses that result in reduced muscle mass and bone formation, with recent evidence also suggesting systemic effects on bone after minor burn. The aim of this study was to assess if children and adolescents who are hospitalised with a burn have increased long-term hospital service use for musculoskeletal conditions. METHODS: A population-based longitudinal study using linked hospital morbidity and death data from Western Australia was undertaken of those younger than 20 years when hospitalized for a first burn (n=13,244) during the period 1980-2012 and a frequency matched non-injury comparison cohort, randomly selected from Western Australia's birth registrations and electoral roll (n=51,021). Crude admission rates and cumulative length of stay for musculoskeletal diseases were calculated. Negative binomial and Cox proportional hazards regression modelling were used to generate incidence rate ratios (IRR) and hazard ratios (HR), respectively. RESULTS: After adjusting for demographic characteristics and pre-existing health status, those who were hospitalised for a burn had a 1.87 times as many hospital admissions for a musculoskeletal disease (95%CI: 1.69-2.08) and spent 2.61 times as long in hospital with musculoskeletal disease (95%CI: 2.09-3.27), than the uninjured comparison cohort. The burn cohort had significantly higher rates of first time admissions over the study period for arthropathies (HR, 95%CI: 1.14, 1.00-1.29, p=0.047), dorsopathies (HR, 95%CI: 1.64, 1.29-2.08) and for soft tissue disorders (HR, 95%CI: 1.33, 1.11-1.60); results were not statistically significant for incident admissions for osteopathies and chondropathies (HR, 95%CI: 1.07, 0.71-1.59) or connective tissue disorders (HR, 95%CI: 0.54, 0.24-2.09). CONCLUSIONS: These results identified elevated post-discharge hospital service use for diseases of the musculoskeletal system for a prolonged period after discharge for those with both severe and minor burns.


Towards more efficient burn care: Identifying factors associated with good quality of life post-burn.


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BACKGROUND: As minor burn patients constitute the vast majority of a developed nation case-mix, streamlining care for this group can promote efficiency from a service-wide perspective. This study tested the hypothesis that a predictive nomogram model that
estimates likelihood of good long-term quality of life (QoL) post-burn is a valid way to optimise patient selection and risk management when applying a streamlined model of care.

METHOD: A sample of 224 burn patients managed by the Burn Service of Western Australia who provided both short and long-term outcomes was used to estimate the probability of achieving a good QoL defined as 150 out of a possible 160 points on the Burn Specific Health Scale-Brief (BSHS-B) at least six months from injury. A multivariate logistic regression analysis produced a predictive model provisioned as a nomogram for clinical application. A second, independent cohort of consecutive patients (n=106) was used to validate the predictive merit of the nomogram.

RESULTS AND DISCUSSION: Male gender (p=0.02), conservative management (p=0.03), upper limb burn (p=0.04) and high BSHS-B score within one month of burn (p<0.001) were significant predictors of good outcome at six months and beyond. A Receiver Operating Curve (ROC) analysis demonstrated excellent (90%) accuracy overall. At 80% probability of good outcome, the false positive risk was 14%. The nomogram was validated by running a second ROC analysis of the model in an independent cohort. The analysis confirmed high (86%) overall accuracy of the model, the risk of false positive was reduced to 10% at a lower (70%) probability. This affirms the stability of the nomogram model in different patient groups over time. An investigation of the effect of missing data on sample selection determined that a greater proportion of younger patients with smaller TBSA burns were excluded due to loss to follow up.

CONCLUSION: For clinicians managing comparable burn populations, the BSWA burns nomogram is an effective tool to assist the selection of patients to a streamlined care pathway with the aim of improving efficiency of service delivery.


Prostaglandin agonist effect on matrix metalloproteinase aqueous levels in glaucoma patients.

Pradhan S, Dalvi RA, et al.

OBJECTIVE: To determine whether the aqueous levels of matrix metalloproteinases (MMPs) differ between patients with glaucoma treated with topical prostaglandin analogues and normal, nonglaucomatous control patients. Also, to note any difference in MMP levels between latanoprost, travoprost, and bimatoprost that might suggest a difference in efficacy or mechanism of action between these drugs.

DESIGN: Prospective, observational study.

PARTICIPANTS: Patients who were scheduled to undergo routine intraocular surgery (phacoemulsification or combined phacotrabeculectomy) as part of their standard clinical care were included. Eighteen eyes of 18 patients with glaucoma using any 1 prostaglandin analogue (latanoprost, travoprost, or bimatoprost) were compared with 8 normal control patients.

METHODS: This was a multicentre study. Aqueous humour (0.2 mL) was aspirated at the beginning of the intraocular surgery through a clear corneal paracentesis. MMP-2 and -9 were quantified in the aqueous of all participants using enzyme-linked immunosorbent assay.

RESULTS: There was no significant difference in the levels of either MMP-2 (p = 0.216) or MMP-9 (p = 0.552) between the control patients and the patients with glaucoma on prostaglandins. There was no difference in the levels of MMP-2 or -9 between the latanoprost, travoprost, or bimatoprost groups.

CONCLUSIONS: The levels of MMP-2 and -9 in aqueous of glaucomatous eyes on topical prostaglandin analogues were the same as those of normal age-matched control patients. This could reflect either a return to normal levels with efficacious treatment or a lack of difference between disease and nondisease states.Copyright 2015 Canadian Ophthalmological Society. Published by Elsevier Inc. All rights reserved.


The case of the shrinking testis.

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We report the case of a man with idiopathic lymphocytic orchitis (LO) manifested by undifferentiated testicular pain and atrophy. Conventional investigation results were unremarkable. Oral ciprofloxacin only improved the pain temporarily. Scrotal exploration surgery was performed to exclude acute testicular torsion and a biopsy was taken during surgery for histological examination. Histology revealed severe LO with reduced spermatogenesis. A trial of oral steroids was initially effective but the effect was temporary. Due to chronic pain, he eventually underwent unilateral orchidectomy. Histology confirmed the initial diagnosis of LO. He was pain-free postoperatively. Idiopathic LO is a rarely reported cause of testicular atrophy.


NeuroEndocrine Tumor Therapy with Lutetium-177-octreotate and Everolimus (NETTLE): A Phase I Study.

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OBJECTIVE: To establish the optimal safe dose of everolimus in combination with (177)Lu-octreotate peptide receptor radionuclide therapy (PRRT) of advanced progressive gastro-entero pancreatic neuroendocrine tumors (GEP-NETS) and to define dose-limiting toxicity.

PATIENTS AND METHODS: Patients with advanced unresectable progressive well-differentiated GEP-NETS avid for (68)Ga-octreotate on positron emission tomography-computed tomography imaging underwent PRRT with four cycles of 7.8GBq (177)Lu-octreotate at 8 week intervals. Successful cohorts of 3 patients received escalating doses of everolimus comprising 5, 7.5, and 10mg daily for 24 weeks.

RESULTS: Sixteen patients comprised 4 at 5mg, 9 at 7.5mg, and 3 at 10mg everolimus. Patient cohorts at 5 and 7.5mg received 83% and 80% of the total planned dose of everolimus over 24 weeks. All patients required dose reduction or complete cessation of everolimus at the 10mg level, which induced neutropenia and thrombocytopenia, and reduced creatinine clearance. The overall response rate was 44% (7 of 16 patients), and no patient progressed over the 6 month period of treatment. Four of 5 pancreatic NET patients achieved PR 80%. No patient progressed on study.

CONCLUSION: In combination, PRRT with (177)Lu-octreotide, the maximum tolerated dose of everolimus is 7.5mg daily.


The Inositol Polyphosphate 5-Phosphatase PIPP Regulates AKT1-Dependent Breast Cancer Growth and Metastasis.

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Metastasis is the major cause of breast cancer mortality. Phosphoinositide 3-kinase (PI3K) generated PtdIns(3,4,5)P3 activates AKT, which promotes breast cancer cell proliferation and regulates migration. To date, none of the inositol polyphosphate 5-phosphatases that inhibit PI3K/AKT signaling have been reported as tumor suppressors in breast cancer. Here, we show depletion of the inositol polyphosphate 5-phosphatase PIPP (INPP5J) increases breast cancer cell transformation, but reduces cell migration and invasion. Pipp ablation accelerates oncogene-driven breast cancer tumor growth in vivo, but paradoxically reduces metastasis by regulating AKT1-dependent tumor cell migration. PIPP mRNA expression is reduced in human ER-negative breast cancers associated with reduced long-term outcome. Collectively, our findings identify PIPP as a suppressor of oncogenic PI3K/AKT signaling in breast cancer.


Survivors of childhood cancer in the United States: prevalence and burden of morbidity.


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BACKGROUND: No studies have estimated the population-level burden of morbidity in individuals diagnosed with cancer as children (ages 0-19 years). We updated prevalence estimates of childhood cancer survivors as of 2011 and burden of morbidity in this population reflected by chronic conditions, neurocognitive dysfunction, compromised health-related quality of life, and health status (general health, mental health, functional impairment, functional limitations, pain, and fear/anxiety). METHODS: Surveillance, Epidemiology, and End Results (SEER) Program data from 1975 to 2011 were used to update the prevalence of survivors of childhood cancers in the United States. Childhood Cancer Survivor Study data were used to obtain estimates of morbidity burden indicators, which were then extrapolated to SEER data to obtain population-level estimates. RESULTS: There were an estimated 388,501 survivors of childhood cancer in the United States as of January 1, 2011, of whom 83.5% are >/=5 years after diagnosis. The prevalence of any chronic condition among >/=5-year survivors ranged from 66% (ages 5-19) to 88% (ages 40-49). Estimates for specific morbidities ranged from 12% (pain) to 35% (neurocognitive dysfunction). Generally, morbidities increased by age. However, mental health and anxiety remained fairly stable, and neurocognitive dysfunction exhibited initial decline and then remained stable by time since diagnosis. CONCLUSIONS: The estimated prevalence of survivors of childhood cancer is increasing, as is the estimated prevalence of morbidity in those >/=5 years after diagnosis. IMPACT: Efforts to understand how to effectively decrease morbidity burden and incorporate effective care coordination and rehabilitation models to optimize longevity and well-being in this population should be a priority.


The aggregation of early-onset melanoma in young Western Australian families.

Ward SV, Dowty JG, et al.
Background: Few studies have examined the familial aggregation of melanoma or its co-aggregation with other cancers using whole-population based designs. This study aimed to investigate aggregation patterns in young Western Australian families, using population-based linked health data to identify individuals born in Western Australia between 1974 and 2007, their known relatives, and all incident cancer diagnoses within the resulting 1,506,961 individuals. Methods: Cox proportional hazards regression models were used to compare the risk of melanoma for first-degree relatives of melanoma cases to that for first-degree relatives of controls, with bootstrapping used to account for correlations within families. The risk of (i) developing melanoma based on the number of first-degree relatives with other cancers, and (ii) developing non-melanoma cancers based on the number of first-degree relatives diagnosed with melanoma was also investigated. Results: First-degree relatives of melanoma cases had a significantly greater incidence of melanoma than first-degree relatives of individuals not affected with melanoma (Hazard Ratio (HR) = 3.58, 95% bootstrap confidence interval (CI): 2.43-5.43). Sensitivity analyses produced a higher hazard ratio estimate when restricted to greater incidence of melanoma than first-degree relatives of individuals not affected with melanoma (HR = 3.58, bootstrap 95% CI: 2.49-6.39) and a lower estimate when only melanoma cases diagnosed before 40 years of age (HR = 3.77, bootstrap 95% CI: 2.49-6.39) and a lower estimate when only melanoma cases diagnosed before 40 years of age (HR = 3.77, bootstrap 95% CI: 2.49-6.39) and a lower estimate when only melanoma cases diagnosed before 40 years of age (HR = 3.77, bootstrap 95% CI: 2.49-6.39) and a lower estimate when only melanoma cases diagnosed before 40 years of age (HR = 3.77, bootstrap 95% CI: 2.49-6.39) and a lower estimate when only melanoma cases diagnosed before 40 years of age (HR = 3.77, bootstrap 95% CI: 2.49-6.39) and a lower estimate when only melanoma cases diagnosed before 40 years of age (HR = 3.77, bootstrap 95% CI: 2.49-6.39). A significant evidence was found for co-aggregation between melanoma and any other cancers. Conclusions: Results indicated a strong familial basis of melanoma, with the higher than expected hazard ratio observed likely to reflect early-age at onset cases in this young cohort, supported by the results of the sensitivity analyses. Exploratory analyses suggested that the determinants of melanoma causing the observed aggregation within families may be independent of other malignancies, although these analyses were limited by the young age of the sample. Determining familial aggregation patterns will provide valuable knowledge regarding improved clinical risk prediction and the underlying biological mechanisms of melanoma and other cancers.


Folate pathway gene polymorphisms, maternal folic acid use, and risk of childhood acute lymphoblastic leukemia.
(Milne, Greenop, Jamieson, Bower, Bailey, Dawson, De Klerk) Telethon Kids Institute, University of Western Australia, PO Box 855, West Perth, WA 6872, Australia (Scott, Attia) Hunter Medical Research Institute, John Hunter Hospital, New Lambton, NSW, Australia (Scott) School of Biomedical Sciences and Pharmacy, Faculty of Health, University of Newcastle, Newcastle, NSW, Australia (Scott) Hunter Area Pathology Service, HNEHealth, Newcastle, NSW, Australia (Haber, Norris) Children's Cancer Institute Australia for Medical Research, Lowy Cancer Research Centre, University of New South Wales, Sydney, NSW, Australia (Attia) School of Medicine and Public Health, Faculty of Health and Medicine, University of Newcastle, Newcastle, NSW, Australia (Miller) School of Exercise and Health Sciences, Edith Cowan University, Mount Lawley, WA, Australia (Bailey) Section of Environment and Radiation, International Agency for Research on Cancer, Lyon, France (McCowage) Oncology Unit, Children's Hospital at Westmead, Sydney, Australia (Van Bockxmeer) Department of Clinical Biochemistry, Royal Perth Hospital and the School of Surgery, University of Western Australia, Perth, WA, Australia (Armstrong) Sax Institute, Haymarket, NSW, Australia (Armstrong) Sydney School of Public Health, University of Sydney, Sydney, NSW, Australia (E. Milne, Telethon Kids Institute, University of Western Australia, PO Box 855, West Perth, WA 6872, Australia (E. Milne, Telethon Kids Institute, University of Western Australia, PO Box 855, West Perth, WA 6872, Australia Background: Several studies suggest that maternal folic acid supplementation before or during pregnancy protects against childhood acute lymphoblastic leukemia (ALL). We investigated associations between ALL risk and folate pathway gene polymorphisms, and their modification by maternal folic acid supplements, in a population-based case-control study (2003-2007). Methods: All Western Australian pediatric oncology centers provided cases; controls were recruited by national random digit dialing. Data from 392 cases and 535 controls were included. Seven folate pathway gene polymorphisms (MTHFR 677C>T, MTHFR 1298A>C, MTRR 66A>G, MTR 2756 A>C, MTR 5049 C>A, CBS 844 Ins68, and CBS 2199 T>C) were genotyped in children and their parents. Information on prepregnancy maternal folic acid supplement use was collected. ORs were estimated with unconditional logistic regression adjusted for frequency-matched variables and potential confounders. Case-parent trios were also analyzed. Results: There was some evidence of a reduced risk of ALL among children who had, or whose father had, the MTRR 66G genotype: ORs 0.60 [95% confidence interval (CI) 0.39-0.91] and 0.64 (95% CI, 0.40-1.03), respectively. The ORs for paternal MTHFR 677CT and TT genotypes were 1.41 (95% CI, 1.02-1.93) and 1.81 (95% CI, 1.06-3.07). ORs varied little by maternal folic acid supplementation. Conclusions: Some folate pathway gene polymorphisms in the child or a parent may influence ALL risk. While biologically plausible, underlying mechanisms for these associations need further elucidation. Impact: Folate pathway polymorphisms may be related to risk of childhood ALL, but larger studies are needed for conclusive results.


Folate pathway gene polymorphisms and risk of childhood brain tumors: results from an Australian case-control study.
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Information on prepregnancy maternal folic acid supplement use was collected. ORs were estimated with unconditional logistic regression adjusted for frequency-matched variables and potential confounders. Case-parent trios were also analyzed. Results: There was some evidence of a reduced risk of ALL among children who had, or whose father had, the MTRR 66G genotype: ORs 0.60 [95% confidence interval (CI) 0.39-0.91] and 0.64 (95% CI, 0.40-1.03), respectively. The ORs for paternal MTHFR 677CT and TT genotypes were 1.41 (95% CI, 1.02-1.93) and 1.81 (95% CI, 1.06-3.07). ORs varied little by maternal folic acid supplementation. Conclusions: Some folate pathway gene polymorphisms in the child or a parent may influence ALL risk. While biologically plausible, underlying mechanisms for these associations need further elucidation. Impact: Folate pathway polymorphisms may be related to risk of childhood ALL, but larger studies are needed for conclusive results.


The achievement of ideal informed and voluntary consent is difficult when patients are confronted with the trauma of newly diagnosed illness. Innovative approaches are implicated to obtain consent while protecting the autonomy and dignity of patients.

METHODS: The qualitative method of Grounded Theory was used, and data were gathered through digitally recorded semistructured interviews with 18 participants. Data were analyzed using the constant comparative method to the descriptive level.

RESULTS: Four major categories were identified describing the response to the consent process used for donating tissue for cancer research. These categories were: (1) The donation experience; (2) The role of the research team; (3) The choice of donation; and (4) The impact of donation.

CONCLUSIONS: This finding has potential to improve the process for the donation of tissue for cancer research. Further research is needed to determine how best to involve patients in the decision-making process.

IMPLICATIONS FOR PRACTICE: The results from this study can contribute to further development of processes for the donation of biospecimens for research purposes that respect the needs and views of patients.


Cancer Res. 2015; 75(16): 3236-45.

Investigation of Optical Coherence Microelastography as a Method to Visualize Cancers in Human Breast Tissue.

Assessing the carcinogenic potential of low-dose exposures to chemical mixtures in the environment: the challenge ahead.

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An accurate intraoperative identification of malignant tissue is a challenge in the surgical management of breast cancer. Imaging techniques that help address this challenge could contribute to more complete and accurate tumor excision, and thereby help reduce the current high reexcision rates without resorting to the removal of excess healthy tissue. Optical coherence microelastography (OCME) is a three-dimensional, high-resolution imaging technique that is sensitive to micrascule variations of the mechanical properties of tissue. As the tumor modifies the mechanical properties of breast tissue, OCME has the potential to identify, on the microscale, involved regions of fresh, unstained tissue. OCME is based on the use of optical coherence tomography (OCT) to measure tissue deformation in response to applied mechanical compression. In this feasibility study on 58 ex vivo samples from patients undergoing mastectomy or wide local excision, we demonstrate the performance of OCME as a means to visualize tissue microarchitecture in benign and malignant human breast tissues. Through a comparison with corresponding histology and OCT images, OCME is shown to enable ready visualization of features such as ducts, lobules, microcysts, blood vessels, and arteries and to identify invasive tumor through distinctive patterns in OCME images, often with enhanced contrast compared with OCT. These results lay the foundation for future intraoperative studies. Cancer Res; 75(16): 3236-45. (c)2015 AACR.

Paclitaxel-eluting balloon and everolimus-eluting stent for provisional stenting of coronary bifurcations: 12-month results of the multicenter BIOLUX-I study.

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Cardiovascular Research Centre, Monash Medical Centre, Clayton, Australia.

BACKGROUND: Several studies investigated the combination of bare metal stents in the main branch and drug-eluting balloons in the side branch in bifurcation lesions, but data on the combination of drug-eluting stents and drug-eluting balloons are scarce. We aim to assess the feasibility of provisional stenting with an everolimus-eluting stent in the main branch and a paclitaxel-eluting balloon in the side branch. METHODS: In this prospective, multi-center study conducted in 5 Australian sites, 35 patients with bifurcation lesions were enrolled. Angiographic and intravascular ultrasound assessments were conducted at 9months; clinical follow-up was conducted until 12months. RESULTS: The primary endpoint, late lumen loss in the side branch measured by quantitative coronary angiography, was 0.10 +/- 0.43mm. No binary restenosis was observed. One patient died; 3 myocardial infarctions (one suspected and two in non-target vessels) and one target lesion revascularization occurred. No probable or definite stent thrombosis was observed. CONCLUSION: The combination of an everolimus-eluting stent in the main branch and a paclitaxel-
eluting balloon in the side branch appears to be a safe, effective and novel treatment option for bifurcation lesions. 


Cardiovasc Ther. 2015.  
**The Effect of a Cardiovascular Polypill Strategy on Pill Burden.**

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AIMS: Recent trials of cardiovascular polypills in high-risk populations show improvements in use of cardiovascular preventive treatments, compared to usual care. We describe patterns of pill burden in Australian practice, define the impact of polypill therapy on pill burden and explore how physicians add medication to polypill therapy.  
METHODS: The Kanyini Guidelines Adherence with the Polypill study was an open-label trial involving 623 participants in Australia which randomised participants to a polypill strategy (containing a statin, anti-platelet agent and 2 blood pressure lowering medications) or usual care. Participants either had established cardiovascular disease or were at high calculated risk (>15% over 5 years). Current medications, daily pill burden, and self-reported use of combination treatment were recorded prior to randomisation and at study end. Median pill burden at baseline and study end were compared in both arms. Subgroup analysis of the polypill strategy on trial primary outcomes was conducted by pill burden at baseline. RESULTS: Median total and cardiovascular pill burdens of the polypill group decreased from 7 to 5 and from 4 to 2 respectively (median change -2; IQR -3, 0) with no change in the usual care group (comparison of change; p<0.001). No change was seen for non-cardiovascular medications. Of those still using the polypill at study end, 43.8% were prescribed additional medications; 84.5% of these additional medications were blood pressure lowering medications. Within the polypill group, lower pill burden at baseline was associated with greater increases in the use of indicated cardiovascular preventive medications at study end compared to those with higher pill burdens. No trend was observed between the level of baseline pill burden and the effect of polypill treatment on systolic blood pressure or total cholesterol. CONCLUSION: A cardiovascular polypill in contemporary Australian practice reduces cardiovascular and total pill burdens, despite frequent prescription of additional medications. This article is protected by copyright. All rights reserved.  

Case Reports in Ophthalmological Medicine. 2015; 2015: 796381.  
**Posterior Cortical Atrophy Presenting with Superior Arcuate Field Defect.**

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An 80-year-old female with reading difficulty presented with progressive arcuate field defect despite low intraocular pressure. Over a 5-year period, the field defect evolved into an incongruous homonymous hemianopia and the repeated neuroimaging revealed progressive posterior cortical atrophy. Further neuropsychiatric assessment demonstrated symptoms and signs consistent with Benson's syndrome.  

**Kounis syndrome with Samter-Beer triad treated with intracoronary adrenaline.**

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Kounis syndrome is a well-described clinical condition characterized by the simultaneous occurrence of chest pain and an allergic reaction accompanied by clinical and laboratory findings of angina caused by inflammatory mediators released during an allergic insult. We present the case of a 50-year-old male with the Samter-Beer triad of asthma, nasal polyps, and salicylate intolerance with an ST elevation myocardial infarction complicated with cardiac arrest due to multi-vessel coronary artery spasm secondary to aspirin anaphylaxis. Adrenaline is recommended during anaphylaxis but is controversial in Kounis syndrome as it may worsen coronary spasm. We report the use of intracoronary adrenaline in successfully reversing coronary artery spasm in this hemodynamically unstable patient. (c) 2015 Wiley Periodicals, Inc.  
Stimulus-dependent differences in signalling regulate epithelial-mesenchymal plasticity and change the effects of drugs in breast cancer cell lines.

INTRODUCTION: The normal process of epithelial mesenchymal transition (EMT) is subverted by carcinoma cells to facilitate metastatic spread. Cancer cells rarely undergo a full conversion to the mesenchymal phenotype, and instead adopt positions along the epithelial-mesenchymal axis, a propensity we refer to as epithelial mesenchymal plasticity (EMP). EMP is associated with metastatic spread. Cancer cells rarely undergo a full conversion to the mesenchymal phenotype, and instead adopt positions along the epithelial-mesenchymal axis, a propensity we refer to as epithelial mesenchymal plasticity (EMP). EMP is associated with increased risk of metastasis in breast cancer and consequent poor prognosis. Drivers towards the mesenchymal state in malignant cells include growth factor stimulation or exposure to hypoxic conditions.

METHODS: We have examined EMP in two cell line models of breast cancer: the PMC42 system (PMC42-ET and PMC42-LA sublines) cells include growth factor stimulation or exposure to hypoxic conditions.

 RESULTS: We found that EGF and hypoxia both drive MDA-MB-468 cells to phenotypically similar mesenchymal states. Comparing the transcriptional response to EGF and hypoxia, we have identified differences in the cellular signalling pathways that mediate, and are influenced by, EMT. Significant differences were observed for a number of important cellular signalling components previously implicated in EMT, such as HBEFGF and VEGFA. We have shown that EGF- and hypoxia-induced transitions respond differently to treatment with chemical inhibitors (presented individually and in combinations) in these breast cancer cells. Unexpectedly, MDA-MB-468 cells grown under hypoxic growth conditions became even more mesenchymal following exposure to certain kinase inhibitors that prevent growth-factor induced EMT, including the mTOR inhibitor everolimus and the AKT1/2/3 inhibitor AZD5363.

 CONCLUSIONS: While resulting in a common phenotype, EGF and hypoxia induced subtly different signalling systems in breast cancer cells. Transition to a mesenchymal phenotype was induced across all three cell lines using epidermal growth factor (EGF) stimulation, and in MDA-MB-468 cells by hypoxia. We used RNA sequencing to identify gene expression changes that occur as cells transition to a more-mesenchymal phenotype, and identified the cell signalling pathways regulated across these experimental systems. We then used inhibitors to modulate signalling through these pathways, verifying the conclusions of our transcriptomic analysis.

RESULTS: We found that EGF and hypoxia both drive MDA-MB-468 cells to phenotypically similar mesenchymal states. Comparing the transcriptional response to EGF and hypoxia, we have identified differences in the cellular signalling pathways that mediate, and are influenced by, EMT. Significant differences were observed for a number of important cellular signalling components previously implicated in EMT, such as HBEFGF and VEGFA. We have shown that EGF- and hypoxia-induced transitions respond differently to treatment with chemical inhibitors (presented individually and in combinations) in these breast cancer cells. Unexpectedly, MDA-MB-468 cells grown under hypoxic growth conditions became even more mesenchymal following exposure to certain kinase inhibitors that prevent growth-factor induced EMT, including the mTOR inhibitor everolimus and the AKT1/2/3 inhibitor AZD5363.

CONCLUSIONS: While resulting in a common phenotype, EGF and hypoxia induced subtly different signalling systems in breast cancer cells. Our findings have important implications for the use of kinase inhibitor-based therapeutic interventions in breast cancers, where these heterogeneous signalling landscapes will influence the therapeutic response.


Levels of CMV-reactive antibodies correlate with the induction of CD28+ T cells and systemic inflammation in chronic obstructive pulmonary disease (COPD).

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Irrigated Needle Ablation Creates Larger and More Transmural Ventricular Lesions Compared to Standard Unipolar Ablation in an Ovine Model.
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BACKGROUND: VT recurrence can occur after VT ablation due to incomplete and/or non-transmural ventricular lesion formation.

We sought to compare the lesions made by a novel irrigated needle catheter to conventional radiofrequency (RF) lesions. METHODS AND RESULTS: Thirteen female sheep (4.6 +/- 0.7 yrs, 54 +/- 8 kg) were studied. In 7 sheep, 60 s RF applications were performed using an irrigated needle catheter. In 6 sheep, conventional lesions were made using a 4 mm-irrigated catheter. 1.5 T in vivo and high-density MRI (9.4 Tesla) were performed on explanted hearts from animals receiving needle RF. Conventional lesion volume was calculated as (1/6) *pi *(A *B^2+C *D^2/2). Needle lesion volume was measured as Sigma(pi *r^2)/2 with a slice thickness of 1 mm. The dimensions of all lesions were also measured on gross pathology. Additional histological analysis of the needle lesions was performed. 120 endocardial left ventricular ablation lesions (conventional, n=60; needle, n=60) were created. At necropsy, more irrigated needle lesions were found using needle vs. conventional RF (90% vs. 75%, p<0.05). Comparing needle vs. conventional RF: Lesion volume was larger (1030 +/- 362 mm^3 vs. 488 +/- 384 mm^3, p<0.001), lesion depth was increased (9.9 +/- 2.7 mm vs. 5 +/- 2.4 mm, p<0.001) and more transmural lesions were created (62.5% vs. 17%, p<0.01). Pericardial contrast injection was observed in 4 apical attempts using needle RF, however with no adverse effects. Steam pops occurred in 3 attempts using conventional RF.

CONCLUSIONS: Irrigated needle ablation is associated with more frequent, larger, deeper, and more often transmural lesions compared to conventional irrigated ablation. This technology might be of value to treat intramural or epicardial VT substrates resistant to conventional ablation.
apolipoprotein B-containing lipoproteins in the circulation. Knowledge of the molecular basis for abetalipoproteinemia has led to the development of therapies for dyslipidemia that inhibit MTP. Partial MTP inhibition using small molecule inhibitors, such as lomitapide, can effectively lower plasma low-density lipoprotein-cholesterol and apolipoprotein B levels, but is associated with gastrointestinal side effects. Long-term gastrointestinal side effects that could limit their use in humans. We review contemporary aspects of the biology and therapeutic regulation of MTP and their significance for lipid metabolism and cardiovascular disease.

HDL Particle Size is a Critical Determinant of ABCA1-Mediated Macrophage Cellular Cholesterol Export.

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Burnett JR, Hegele RA.

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METHODS AND RESULTS: We used reconstituted HDL particles of defined size and composition, isolated subfractions of human plasma HDL, cell lines stably expressing ABCA1 or ABCG1, and both mouse and human macrophages in which ABCA1 or ABCG1 expression was deleted. We show that ABCA1 is the major mediator of macroparticle cholesterol efflux to HDL, demonstrating most marked efficiency with small, dense HDL subfractions (HDL3b and HDL3c). ABCG1 has a lesser role in cholesterol efflux and a negligible role in efflux to HDL3b and HDL3c subfractions.

CONCLUSIONS: Small, dense HDL subfractions are the most efficient mediators of cholesterol efflux, and ABCA1 mediates cholesterol efflux to small dense HDL and to lipid-free apolipoprotein A-I. HDL-directed therapies should target increasing the concentrations or the cholesterol efflux capacity of small, dense HDL species in vivo.
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BACKGROUND: In vitro laboratory and animal studies demonstrate a synergistic role for the combination of vancomycin and anti-staphylococcal beta-lactams for methicillin-resistant Staphylococcus aureus (MRSA) bacteremia. Prospective clinical data are lacking.

METHODS: In this open-label, multicenter, clinical trial, adults with MRSA bacteremia received vancomycin 1.5g intravenously (IV) twice daily and were randomly assigned (1:1) to flucloxacillin 2g IV 6 hourly for seven days (combination group) or no additional therapy (standard therapy group). Participants were stratified by hospital and randomized in permuted blocks of variable size. Randomization codes were kept in sealed, sequentially numbered, opaque envelopes. The primary outcome was the duration of MRSA bacteremia in days. RESULTS: We randomly assigned 60 patients to receive vancomycin (n=29), or vancomycin plus flucloxacillin (n=31). The mean duration of bacteremia was 3.00 days in the standard therapy group and 1.94 days in the combination group. According to a negative binomial model, the mean time to resolution of bacteremia in the combination group was 65% (95% confidence interval [CI] 41%, 102%; P=0.06) of that in the standard therapy group. There was no difference in the secondary endpoints of 28 and 90 day mortality, metastatic infection, nephrotoxicity, or hepatotoxicity. CONCLUSIONS: Combining an anti-staphylococcal beta-lactam with vancomycin may shorten the duration of MRSA bacteremia. Further trials with a larger sample size and objective clinically relevant endpoints are warranted.


Clin Microbiol Infect. 2015.

Strain features and distributions in pneumococci from children with invasive disease before and after 13 valent conjugate vaccine implementation in the United States.

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The effect of second generation pneumococcal conjugate vaccines on invasive pneumococcal disease (IPD) strain distributions have not yet been well described. We analyzed IPD isolates recovered from children <5 years of age through Active Bacterial Core surveillance before (2008-2009; n=828) and after (2011-2013; n=600) 13-valent vaccine (PCV13) implementation. We employed conventional testing, PCR/electrospray ionization mass spectrometry, and whole genome sequence (WGS) analysis to identify serotypes, resistance features, genotypes, and pilus types. PCV13, licensed in February of 2010, effectively targeted all major 19A and 7F genotypes and decreased antimicrobial resistance primarily due to removal of the 19A/ST320 complex. The strain complex contributing most to remaining beta-lactam resistance during 2011-2013 was 35B/ST558. Significant emergence of non-vaccine clonal complexes was not evident. Due to the removal of vaccine serotype strains, positivity for one or both pili types (PI-1 and PI-2) decreased in the post PCV13 years 2011-2013 relative to 2008-2009 (decreases of 32-55% for PI-1, > 95% for PI-2 and combined PI-1 + PI-2), beta-lactam susceptibility phenotypes correlated consistently with transpeptidase region sequence combinations of the three major penicillin binding proteins (PBPs) determined through WGS. Other major resistance features were predictable by DNA signatures from WGS. Multilocus sequence data combined with PBP combinations identified progeny, serotype donors, and recipient strains in serotype switch events. PCV13 decreased all PCV13 serotype clones and concurrently decreased strain subsets with resistance and/or adherence features conducive for successful carriage. Our results serve as a reference describing key features of current pediatric IPD strains in the United States after PCV13 implementation.


Clin Nutr. 2015.

Effects of flaxseed supplements on blood pressure: A systematic review and meta-analysis of controlled clinical trial.

Ursoniu S, Sahebkar A, et al.

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A randomized controlled trial of the effects of n-3 fatty acids on resolvins in chronic kidney disease.

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BACKGROUND & OBJECTIVE: The high incidence of cardiovascular disease (CVD) in chronic kidney disease (CKD) is related partially to chronic inflammation. n-3 Fatty acids have been shown to have anti-inflammatory effects and to reduce the risk of CVD. Specialized Poreforming Lipid Mediators (SPMs) derived from the n-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) actively promote the resolution of inflammation. This study evaluates the effects of n-3 fatty acid supplementation on plasma SPMs in patients with CKD.

METHODS: In a double-blind, placebo-controlled intervention of factorial design, 85 patients were randomized to either n-3 fatty acids (4 g), Coenzyme Q10 (CoQ) (200 mg), both supplements, or control (4 g olive oil), daily for 8 weeks. The SPMs 18-HEPE, 17-HDHA, RvD1, 17R-RvD1, and RvD2, were measured in plasma by liquid chromatography-tandem mass spectrometry before and after intervention. RESULTS: Seventy-four patients completed the 8 weeks intervention. n-3 Fatty acids but not CoQ significantly increased (P < 0.0001) plasma levels of 18-HEPE and 17-HDHA, the upstream precursors to E- and D-series resolvins, respectively. RvD1 was significantly increased (P = 0.036) after n-3 fatty acids, but no change was seen in other SPMs. In regression analysis the increase in 18-HEPE and 17-HDHA after n-3 fatty acids was significantly predicted by the E- and D-series resolvins, respectively. RvD1 was significantly increased (P = 0.036) after n-3 fatty acids, but no change was seen in other SPMs. In regression analysis the increase in 18-HEPE and 17-HDHA after n-3 fatty acids was significantly predicted by the E- and D-series resolvins, respectively. RvD1 was significantly increased (P = 0.036) after n-3 fatty acids, but no change was seen in other SPMs. In regression analysis the increase in 18-HEPE and 17-HDHA after n-3 fatty acids was significantly predicted by the E- and D-series resolvins, respectively. RvD1 was significantly increased (P = 0.036) after n-3 fatty acids, but no change was seen in other SPMs. In regression analysis the increase in 18-HEPE and 17-HDHA after n-3 fatty acids was significantly predicted by the E- and D-series resolvins, respectively. RvD1 was significantly increased (P = 0.036) after n-3 fatty acids, but no change was seen in other SPMs. In regression analysis the increase in 18-HEPE and 17-HDHA after n-3 fatty acids was significantly predicted by the E- and D-series resolvins, respectively. RvD1 was significantly increased (P = 0.036) after n-3 fatty acids, but no change was seen in other SPMs. In regression analysis the increase in 18-HEPE and 17-HDHA after n-3 fatty acids was significantly predicted by the E- and D-series resolvins, respectively.

CONCLUSION: SPMs are increased after 8 weeks n-3 fatty acid supplementation in patients with CKD. This may have important implications for limiting ongoing low grade inflammation in CKD.

Antioxidant and anti-inflammatory effects of curcuminoid-piperine combination in subjects with metabolic syndrome: A randomized controlled trial and an updated meta-analysis.

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BACKGROUND: Oxidative stress and inflammation have been proposed as emerging components of metabolic syndrome (MetS). Curcuminoids are natural polyphenols with strong antioxidant and anti-inflammatory properties. OBJECTIVE: To study the effectiveness of supplementation with a bioavailable curcuminoid preparation on measures of oxidative stress and inflammation in...
patients with MetS. Our secondary aim was to perform a meta-analysis of data from all randomized controlled trials in order to estimate the effect size of curcuminoids on plasma C-reactive protein (CRP) concentrations. METHODS: In this randomized double-blind placebo-controlled trial, 117 subjects with MetS (according to the NCEP-ATPIII diagnostic criteria) were randomly assigned to curcuminoids (n = 59; drop-outs = 9) or placebo (n = 58; drop-outs = 8) for eight weeks. Curcuminoids were administered at a daily dose of 1 g, and were co-supplemented with piperine (10 mg/day) in order to boost oral bioavailability. Serum activities of superoxide dismutase (SOD) and concentrations of malondialdehyde (MDA) and CRP were measured at baseline and at study end. Regarding the importance of CRP as a risk marker and risk factor of cardiovascular disease, a random-effects meta-analysis of clinical trials was performed to estimate the overall impact of curcuminoid therapy on circulating concentrations of CRP. The robustness of estimated effect size was evaluated using leave-one-out sensitivity analysis. RESULTS: Supplementation with curcuminoid-piperine combination significantly improved serum SOD activities (p < 0.001) and reduced MDA (p < 0.001) and CRP concentrations compared with placebo. Quantitative data synthesis revealed a significant effect of curcuminoids vs. placebo in reducing circulating CRP concentrations (weighted mean difference: -2.20 mg/L; 95% confidence interval [CI]: -3.96, -0.44; p = 0.01). This effect was robust in sensitivity analysis. CONCLUSIONS: Short-term supplementation with curcuminoid-piperine combination significantly improves oxidative and inflammatory status in patients with MetS. Curcuminoids could be regarded as natural, safe and effective CRP-lowering agents.


SPG11 mutation in a Turkish familial hypobetalipoproteinemia family with hereditary spastic paraplegia.
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Publication Types: Letter

The potential role of an expert computer system to augment the opportunistic detection of individuals with familial hypercholesterolaemia from a community laboratory.
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Background: Familial hypercholesterolaemia (FH) is the most common monogenic cause of premature atherosclerotic cardiovascular disease (CVD). However, most individuals with FH remain undiagnosed. We sought to determine if an expert system (ES) at a community laboratory could identify information relevant for estimating an individual's likelihood of FH using the Dutch Lipid Clinic Network criteria (DLCNC). Methods: An ES (RippleDown) retrospectively analysed laboratory results and clinical details on the current and previous lipid requests from a community laboratory in Western Australia, over 12. months. Results: 84,823 individuals had > 1 LDL-cholesterol request with data available on 84,083 (99.1%). Clinical details were provided on 71,282 (84.8%) individuals' current or previous requests. History relevant to the DLCNC was present in 883 (1.1%) individuals, with premature CVD and non-cardiac vascular disease present in 177 and 64 individuals, respectively. Statin therapy was reported in 5118 individuals; 112 individuals with a current LDL-cholesterol of < 6.5. mmol/L had a previous LDL-cholesterol of > 6.5. mmol/L. Conclusions: The ES was able to identify information that increased the likelihood of FH in 5471 cases. The ability to detect individuals with premature CVD and to classify them based on their highest LDL-cholesterol may augment FH detection, although further investigation is required to confirm this.

Survival from uveal melanoma in Western Australia 1981-2005.
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BACKGROUND: The survival rates for patients diagnosed with uveal melanoma in Australia are unknown. Few long-term studies of uveal melanoma are available, and it is unclear whether their results are applicable to the Australian population.

METHODS: All patients had SSc-ILD defined by HRCT chest. All PFTs during follow-up, including FVC (L), DLCO (ml/min/mmHg) and KCO (DLCO/alveolar volume ratio; DLCO/VA) (ml/min/mmHg/L) were retrieved. The rate of change over the first four years, and percentage change in the first year of follow-up were used in ROC curve analysis to determine the best cut-off points to predict disease.

OBJECTIVES: Clinically meaningful change in systemic sclerosis (SSc) related interstitial lung disease (SSc-ILD) disease is unknown. The aim of this study was to quantify change in pulmonary function as a predictor of outcome in SSc-ILD.

METHODS: Three hundred eighty cases were included. Relative survival and Cox regression were performed. Variables tested for their predictive ability included patient age and sex, tumour-specific variables, and treatment modality.

MAIN OUTCOME MEASURES: All-cause survival rates and relative survival rates of patients with diagnosed uveal melanoma.

RESULTS: Relative survival rates for the entire cohort were 88.2%, 81.4% and 71.4% at 3, 5 and 10 years, respectively. Predictors of worse survival included mixed-cell tumour morphology (hazard ratio [HR]=2.1; P-value=0.002), tumour location at the ciliary body (HR=1.7; P-value=0.029) and tumour apical height more than 5mm (HR 1.9, P-value=0.026). Of all patients who underwent enucleation, those diagnosed in 1998-2005 died twice as fast (HR=2.3; P-value=0.004). In the 17 patients with metastasis, the median survival time from date of diagnosis of metastasis was 3.1 months.

CONCLUSIONS: These survival estimates are comparable to those reported for the USA, and more optimistic than those reported for most European-based studies. Tumour apical height, tumour site, tumour morphology and having an enucleation in certain calendar periods of diagnosis were independent predictors of survival. Survival prognosis for patients with diagnosed metastatic uveal melanoma is very poor. Copyright © 2014 Royal Australian and New Zealand College of Ophthalmologists.


Quantifying change in pulmonary function as a prognostic marker in systemic sclerosis-related interstitial lung disease.

Moore OA, Proudman SM, et al.

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OBJECTIVES: Clinically meaningful change in systemic sclerosis (SSc) related interstitial lung (SSc-ILD) disease is unknown. The aim of this study was to quantify change in pulmonary function as a predictor of outcome in SSc-ILD.

METHODS: All patients had SSc-ILD defined by HRCT chest. All PFTs during follow-up, including FVC (L), DLCO (ml/min/mmHg) and KCO (DLCO/alveolar volume ratio; DLCO/VA) (ml/min/mmHg/L) were retrieved. The rate of change over the first four years, and percentage change in the first year of follow-up were used in ROC curve analysis to determine the best cut-off points to predict
adverse outcome (home oxygen, lung transplantation, or death).

RESULTS: Among 264 patients, there were 49 events (38 deaths, 10 supplemental oxygen, one lung transplant) over a mean (+/- SD) follow-up of 3.0 (+/-1.7) years. The rates of decline over time and percentage change over one year in each of FVC, DLCO and KCO were predictive of adverse outcome. Stable PFTs over four years gave the optimal negative predictive values (NPVs) of 88-96%. The best sensitivity-specificity trade-off was a decline in FVC of 10% and in DLCO and KCO of 15% with NPVs of 92-93%.

CONCLUSIONS: The course that SSC-ILD takes is evident within the first 1-4 years of follow up. Patients who have no decline in PFTs over 4 years have better outcomes. A decline within one year in DLCO or KCO of 15% or more is a poor prognostic factor, and identifies patients who should be monitored more closely and considered for therapy.


Novel optical coherence tomography classification of torpedo maculopathy.

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Background: Torpedo maculopathy is a rare condition with a twofold clinical significance. Firstly, it is a differential of atypical congenital hypertrophy of the retinal pigment epithelium. Secondly, visual field loss has been reported. We demonstrate the spectrum of structural abnormality of torpedo maculopathy as seen on optical coherence tomography, and correlate this with age of presentation, fundus autofluorescence, retinal sensitivity loss and visual field abnormality. Design: A retrospective, observational case series. Participants: Five Australian patients seen between 2008 and 2013. Methods: Fundus photography, optical coherence tomography, fundus autofluorescence and visual field analysis. One patient underwent fluorescein angiography. Main Outcome Measures: Lesion appearance on each imaging modality, and visual field analysis. Results: We consistently observed a flat, hypopigmented lesion located in the temporal macula, with a distinctive tip pointing toward the fovea. Optical coherence tomography demonstrated variable retinocochiodal features ranging from mild outer retinal disturbance (type 1) to outer retinal cavitation (type 2). Lesion appearance on short-wave autofluorescence showed varying degrees of hypo-autofluorescence. Near-infrared autofluorescence was performed in two patients and showed a well-defined region of hypo-autofluorescence. Microperimetry showed normal sensitivity over the lesion in one patient and a dense paracentral scotoma over the temporal portion of the lesion in another. On Humphrey field analysis, only one of two patients tested had a paracentral scotoma. Conclusion: Two types of torpedo maculopathy lesions are described here with unique optical coherence tomography, demographic, fundus autofluorescence and retinal sensitivity features. These may represent different stages of the same disease that evolve over several decades.


Comparison of results from commercial assays for plasma CTX: The need for harmonization.

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INTRODUCTION: Plasma C-terminal telopeptide of type I collagen (CTX) is the nominated reference bone resorption marker. We set out to test the agreement of patients' results between the available plasma CTX assays.

METHODS: Samples were collected from patients attending tertiary hospitals and clinics for investigation and management of metabolic bone disease. Plasma (EDTA) samples were collected from fasted patients between 7.00am and 11.00am, divided into three portions and stored at -20degreeC until analysis. Plasma CTX was measured by enzyme-linked immunosorbent assay (ELISA) (Immunodiagnostic Systems plc), E170 (Roche Diagnostics) and IDS-iSYS (Immunodiagnostic Systems plc) methods. Agreement of patient sample results was assessed by Passing and Bablok regression. Commutability of the calibrators in each kit was assessed by assaying each calibrator in the alternate methods and comparing the observed results with those expected based on the relevant patients' samples method comparison; +/-8.1% was set as the criterion for commutability.

RESULTS: 161 specimens were analysed. Regression parameters (slope, intercept) were 0.788, 0.2ng/L for Roche vs ELISA, 1.266 and -109ng/L for iSYS vs ELISA and 1.605 and -109ng/L for iSYS vs Roche. Only the ELISA calibrator assayed in the Roche assay gave a result within 8.1% of the expected value.
CONCLUSIONS: There is significant disagreement between the results generated for patient samples by the 3 CTX assays and limited commutability of the currently supplied calibrator materials between assays. Harmonization of the results from the different assays would greatly enhance the value of CTX as the reference bone resorption marker. Copyright © 2015 The Canadian Society of Clinical Chemists. Published by Elsevier Inc. All rights reserved.


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The provision of clinical interpretation of results, either verbally or in the printed report, may be considered an integral part of clinical biochemistry diagnostic service. Proficiency testing or external quality assessment (EQA) of such activity may be useful in education, training, continuing professional development and ensuring the quality of such service. Details of the Patient Report Comments Program (RPCProgram) developed by the Royal College of Pathologists of Australasia (RCPA) Chemical Pathology Quality Assurance Programs Pty Ltd (QAP) is described in this review. The program is aimed at pathologists, clinical scientists and trainees. Registered participants are provided a report with case details and a set of clinical biochemistry results at monthly intervals and submit an interpretative comment for the report. Comments received are broken up into components that are translated into common key phrases. An expert panel evaluates the key phrases, classifies them according to appropriateness and drafts a suggested comment, a case summary and a rationale, which are included in a summary report returned to participants. There is considerable diversity in the quality of interpretative comments received from participants of the RPCProgram. The primary purpose of EQA of interpretative commenting is educational self-assessment, and they are recognized as a continuing professional development activity. Whilst there is some evidence for the utility of interpretative comments in improving patient outcomes, evidence for the utility of EQA in improving quality of comments is awaited. Copyright © 2014 The Canadian Society of Clinical Chemists. Published by Elsevier Inc. All rights reserved.

Publication Types: Review


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Publication Types: Editorial


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BACKGROUND: Monoclonal antibodies targeting epidermal growth factor receptor (EGFR) or vascular endothelial growth factor (VEGF) have demonstrated efficacy in combination with chemotherapy in the first-line therapy of advanced colorectal cancer (CRC). Data from randomized studies comparing these monoclonal antibodies as initial therapy is conflicting, and their comparative efficacy remains unclear. We aimed to evaluate the impact of these targeted therapies on patient outcomes by combining the data from randomized clinical trials.

MATERIALS AND METHODS: MEDLINE, PubMed, EMBASE, and meeting proceedings within the past 12 months were searched to identify relevant studies. All randomized phase II/III clinical trials of advanced CRC comparing an anti-EGFR therapy with an anti-VEGF agent in the first-line setting were included. Data were extracted on sample size, objective response rate (ORR), progression-free survival (PFS), and overall survival (OS).

RESULTS: Three randomized studies comprising 2014 participants were included in the meta-analysis. For patients with KRAS wild type (KRAS-WT) CRC, the ORR was superior in patients who received first-line anti-EGFR therapy compared with those who received anti-VEGF therapy (odds ratio [OR], 1.31; 95% confidence interval [CI], 1.09-1.58; P = .004). This effect was even stronger for all RAS-WT patients (OR, 1.46; 95% CI, 1.13-1.90; P = .004). There was no difference in PFS overall irrespective of the KRAS-WT (HR, 1.03; 95% CI, 0.93-1.13; P = .61) or all RAS-WT (HR, 0.92; 95% CI, 0.71-1.18; P = .50) status. The OS was
significantly longer in the patients who received first-line anti-EGFR therapy compared with those who received anti-VEGF therapy (KRAS-WT: HR, 0.79; 95% CI, 0.65-0.97; P = .026; all RAS-WT: HR, 0.77; 95% CI, 0.63-0.95; P = .016).

CONCLUSION: The results of our research show superior ORR and OS with first-line anti-EGFR therapy compared with anti-VEGF therapy in both KRAS-WT and all RAS-WT patients with advanced CRC. These results suggest that anti-EGFR monoclonal antibodies may be a real alternative to anti-VEGF therapy as initial treatment of advanced CRC. Copyright © 2015 Elsevier Inc. All rights reserved.


Higher ferritin levels, but not serum iron or transferrin saturation, are associated with Type 2 diabetes mellitus in adult men and women free of genetic haemochromatosis.

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Context Iron overload predisposes to diabetes and higher ferritin levels have been associated with diabetes. However, it is unclear whether ferritin reflects differences in iron-related parameters between diabetic and nondiabetic persons. We examined associations of serum ferritin, iron and transferrin saturation with Type 2 diabetes in adults without genetic predisposition to iron overload. Design, participants and measurements Cross-sectional analysis of community-dwelling men and women aged 17-97 years from the Busselton Health Survey, Western Australia. Men and women carrying genotypes associated with haemochromatosis (C282Y/C282Y or C282Y/H63D) were excluded. Serum ferritin, iron and transferrin saturation were assayed. Results There were 1834 men (122 with diabetes, 66%) and 2351 women (141 with diabetes, 6%). In men, higher serum ferritin was associated with diabetes after adjusting for age, smoking, alcohol, cardiovascular history, body mass index (BMI), waist, blood pressure, lipids, C-reactive protein (CRP), adiponectin, alanine transaminase (ALT) and gamma-glutamyl transeptidase (GGT) [odds ratio (OR): 129 per 1 unit increase log ferritin, 95% confidence interval (CI) = 101-165, P = 0043]. In women, higher serum ferritin was associated with diabetes [fully adjusted OR: 131 per 1 unit increase log ferritin, 95% CI = 104-163, P = 0020; 184 for tertile (T) 3 vs T1, 95% CI = 109-311]. Neither iron levels nor transferrin saturation were associated with diabetes risk in men or women. Higher ferritin was not associated with insulin resistance in nondiabetic adults. Conclusions In adults, higher ferritin levels are independently associated with prevalent diabetes while iron and transferrin saturation are not. Ferritin is a robust biomarker for diabetes risk, but further investigation is needed to clarify whether this relationship is mediated via iron metabolism.


Clinical Endocrinology. 2015; 83(2): 268-76.

Higher serum testosterone and dihydrotestosterone, but not oestradiol, are independently associated with favourable indices of lung function in community-dwelling men.

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OBJECTIVES: Lower circulating androgens and poorer lung function are associated with increased cardiovascular risk and mortality in men. The association between androgens and lung function is unclear. We tested the hypothesis that circulating testosterone (T) and its metabolites dihydrotestosterone (DHT) and oestradiol (E2) are differentially associated with lung function in men.

METHODS: Early-morning serum T, DHT and E2 were assayed using mass spectrometry in 1768 community-dwelling men from Busselton, Western Australia. Forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were measured using spirometry. Line regression models adjusting for age, height, smoking, exercise, body mass index, respiratory conditions and cardiovascular risk factors were used.

RESULTS: Mean age was 50.1 +/- 168 years. 160% were current smokers, 141% reported a history of asthma and 27% reported chronic obstructive pulmonary disease. Current smokers had higher T compared with never smokers (age-adjusted mean 145 vs 135 nmol/l, P = 0002) and higher E2 (653 vs 601 pmol/l, P = 0017). In fully adjusted analyses, T was associated with FEV1 (51 ml
per 1 SD increase, \( P < 0.001 \) as was DHT (62 ml, \( P < 0.001 \), DHT: 65 ml, \( P < 0.001 \); \( E_2 \) P = 0.664). Higher DHT was marginally associated with the ratio FEV1/FVC (0.3% per 1 SD increase, \( P = 0.047 \)).

CONCLUSIONS: Both T and DHT were independently associated with higher FEV1 and FVC in predominantly middle-aged community-dwelling men. Androgens may contribute to, or be biomarkers for, better lung function in men. Further research is needed to clarify whether androgens preserve lung function in ageing men. Copyright © 2015 John Wiley & Sons Ltd.


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Effects of testosterone treatment on glucose metabolism and symptoms in men with type 2 diabetes and the metabolic syndrome: a systematic review and meta-analysis of randomized controlled clinical trials.


CONTEXT: The effects of testosterone treatment on glucose metabolism and other outcomes in men with type 2 diabetes (T2D) and/or the metabolic syndrome are controversial.

OBJECTIVE: To perform a systematic review and meta-analysis of placebo-controlled double-blind randomized controlled clinical trials (RCT) of testosterone treatment in men with T2D and/or the metabolic syndrome.

DATA SOURCES: A systematic search of RCTs was conducted using Medline, Embase and the Cochrane Register of controlled trials from inception to July 2014 followed by a manual review of the literature.

STUDY SELECTION: Eligible studies were published placebo-controlled double-blind RCTs published in English.

DATA EXTRACTION: Two reviewers independently selected studies, determined study quality and extracted outcome and descriptive data.

DATA SYNTHESIS: Of the 112 identified studies, seven RCTs including 833 men were eligible for the meta-analysis. In studies using a simple linear equation to calculate the homeostatic model assessment of insulin resistance (HOMA1), testosterone treatment modestly improved insulin resistance, compared to placebo, pooled mean difference (MD) -1.58 [-2.25, -0.91], \( P < 0.001 \). The treatment effect was nonsignificant for RCTs using a more stringent computer-based equation (HOMA2), MD -0.019 [-0.086, 0.049], \( P = 0.058 \). Testosterone treatment did not improve glycaemic (HbA1c) control, MD -0.015 [-0.039, 0.010], \( P = 0.25 \), or constitutional symptoms, Aging Male Symptom score, MD -2.49 [-5.81, 0.03], \( P = 0.14 \).

CONCLUSIONS: This meta-analysis does not support the routine use of testosterone treatment in men with T2D and/or the metabolic syndrome without classical hypogonadism. Additional studies are needed to determine whether hormonal interventions are warranted in selected men with T2D and/or the metabolic syndrome. Copyright © 2014 John Wiley & Sons Ltd.


If only my celiac patients and I knew that.

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Publication Types: Letter


Screening for familial hypercholesterolemia: Primary care applications.

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Publication Types: Review


Alcoholic liver disease - the extent of the problem and what you can do about it.

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It takes upwards of ten years for alcohol-related liver disease to progress from fatty liver through fibrosis to cirrhosis to acute on chronic liver failure. This process is silent and symptom free and can easily be missed in primary care, usually presenting with advanced cirrhosis. At this late stage, management consists of expert supportive care, with prompt identification and treatment of bleeding, sepsis and renal problems, as well as support to change behaviour and stop harmful alcohol consumption. There are opportunities to improve care by bringing liver care everywhere up to the standards of the best liver units, as detailed in the Lancet Commission report. We also need a fundamental rethink of the technologies and approaches used in primary care to detect and intervene in liver disease at a much earlier stage. However, the most effective and cost-effective measure would be a proper evidence-based alcohol strategy. Copyright © 2015 Royal College of Physicians.


**What Doesn't Kill You Makes You Fitter: A Systematic Review of High-Intensity Interval Exercise for Patients with Cardiovascular and Metabolic Diseases.**

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High-intensity interval exercise (HIIE) has gained popularity in recent years for patients with cardiovascular and metabolic diseases. Despite potential benefits, concerns remain about the safety of the acute response (during and/or within 24 hours postexercise) to a single session of HIIE for these cohorts. Therefore, the aim of this study was to perform a systematic review to evaluate the safety of acute HIIE for people with cardiometabolic diseases. Electronic databases were searched for studies published prior to January 2015, which reported the acute responses of patients with cardiometabolic diseases to HIIE (>80% peak aerobic power output or >85% peak aerobic power, VO2peak). Eleven studies met the inclusion criteria (n = 156; clinically stable, aged 27-66 years), with 13 adverse responses reported (~8% of individuals). The rate of adverse responses is somewhat higher compared to the previously reported risk during moderate-intensity exercise. Caution must be taken when prescribing HIIE to patients with cardiometabolic disease. Patients who wish to perform HIIE should be clinically stable, have had recent exposure to at least regular moderate-intensity exercise, and have appropriate supervision and monitoring during and after the exercise session.

Publication Types: Review


**Animal models of IBD-Associated CRC and colorectal cancer tumorigenesis.**

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Colorectal cancer (CRC) is a highly prevalent disease, and despite advances in medical research, much remains unknown about CRC. As such, it is important to improve our current understanding of CRC. Several animal models for CRC exist, and they provide an excellent tool for studying CRC tumorigenesis. These models, however, have limitations, and a good understanding of the pathophysiology of these models is required in order to fully understand how closely they mimic human sporadic and colitis-associated CRC.


**Disagreement in high-grade/ low-grade intraepithelial neoplasia and high-risk/ low-risk HPV infection: Clinical implications for anal cancer precursor lesions in HIV-positive and HIV-negative MSM.**

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Invasive infections due to filamentous fungi other than Aspergillus: Epidemiology and determinants of mortality.


Clinical Microbiology and Infection. 2015; 21(5): 444-450.

**ST2249-MRSA-III: A second major recombinant methicillin-resistant Staphylococcus aureus clone causing healthcare infection in the 1970s.**

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Typing of healthcare-associated methicillin-resistant Staphylococcus aureus (MRSA) from Australia in the 1970s revealed a novel clone, ST2249-MRSA-III (CC45), present from 1973 to 1979. This clone was present before the Australian epidemic caused by the recombinant clone, ST239-MRSA-III. This study aimed to characterize the genome of ST2249-MRSA-III to establish its relationship to other MRSA clones. DNA microarray analysis was conducted and a draft genome sequence of ST2249 was obtained. The recombinant structure of the ST2249 genome was revealed by comparisons to publicly available ST239 and ST45 genomes. Microarray analysis of genomic DNA of 13 ST2249 isolates showed gross similarities with the ST239 chromosome in a segment around the origin of replication and with ST45 for the remainder of the chromosome. Recombination breakpoints were precisely determined by the changing pattern of nucleotide polymorphisms in the genome sequence of ST2249 isolate SK1585 compared with ST239 and ST45. One breakpoint was identified to the right of orfC, between sites 1014 and 1065 of the gene D484_00045. Another was identified to the left of orfC, between sites 1185 and 1248 of D484_01632. These results indicate that ST2249 inherited approximately 35.3% of its chromosome from an ST239-like parent and 64.7% from an ST45-like parent. ST2249-MRSA-III resulted from a major recombination between parents that resemble ST239 and ST45. Although only limited Australian archival material is available, the oldest extant isolate of ST2249 predates the oldest Australian isolate of ST239 by 3 years. It is therefore plausible that these two recombinant clones were introduced into Australia separately.


**The Role of 18F-Fluorocholine PET/CT in Biochemically Relapsed Prostate Cancer: A Case of Osteolytic Prostate Metastasis.**

Tabrizipour, Amir Iravani. From the *WA PET Service, Nuclear Medicine Department, Sir Charles Gairdner Hospital, Nedlands; and +Nuclear Medicine Department, Royal Perth Hospital, Perth, Western Australia, Australia.

We present the case of a 60-year-old male patient with T3b-N1, Gleason score 8, adenocarcinoma prostate with biochemical relapse (prostate-specific antigen, 5.2 mug/L) 1 year after radical treatment with 50.4-Gy 3-dimensional conformal radiotherapy and androgen deprivation therapy. Conventional imaging including contrast-enhanced abdominal CT and whole-body bone scintigraphy did not reveal any local recurrence or distant metastases. F-flourocholine PET/CT demonstrated a solitary, intensely avid (SUVmax, 9.2) osteolytic metastasis in the manubrium. Histopathology confirmed metastatic prostate adenocarcinoma.


**Bleeding Small Intestine Pyogenic Granuloma on 18F-FDG PET/CT.**

Iravani, Amir. From the *WA PET Service, Department of Nuclear Medicine, Sir Charles Gairdner Hospital; ++Department of Nuclear Medicine, Royal Perth Hospital; ++University of Western Australia; Departments of Oncology, General Surgery, and PANatomical Pathology, PathWest, Sir Charles Gairdner Hospital, Perth, Australia.

A 53-year-old man with metastatic melanoma, in remission, presented with an 8-week history of melena and anemia. Initial investigations including upper and lower gastrointestinal endoscopy, capsule endoscopy, and Tc-labeled red blood cell scan did not reveal a source of bleeding. Given the concern over melanoma recurrence, F-FDG PET/CT was performed that demonstrated a focus of intense uptake in the small bowel. Uncomplicated surgical resection of the segment of jejunum containing the lesion was performed, after which the patient reported no further gastrointestinal bleeding. Histopathological assessment of the lesion was consistent with pyogenic granuloma.


**Abnormal Quantitative Sensory Testing is Associated With Persistent Pain One Year After TKA.**

Wright A, Moss P, et al.

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P. Moss, School of Physiotherapy and Exercise Science, Curtin University, Kent Street, Bentley, Perth, WA 6102, Australia

Background: Up to 15% of patients report at least moderate persistent pain after TKA. Such pain may be associated with the

Indications for diagnostic open biopsy of mammographic screen-detected lesions preoperatively diagnosed as fibroadenomas by needle biopsy and their outcomes.

Sala M A. The University of Western Australia, Stirling Hwy, Crawley, WA 6009, Australia. Electronic address: sala_ma@iinet.net.au. Dhillon R. BreastScreen WA, Australia. Brookes D. The University of Western Australia, Stirling Hwy, Crawley, WA 6009, Australia. Lagrange C. The University of Western Australia, Stirling Hwy, Crawley, WA 6009, Australia. Metcalf C. Department of Anatomical Pathology, Royal Perth Hospital, WA, Australia. Wylie E. The University of Western Australia, Stirling Hwy, Crawley, WA 6009, Australia.

AIM: To identify the clinical, radiological, and histopathological factors that resulted in a diagnostic open biopsy of mammographic screen-detected lesions diagnosed preoperatively as fibroadenomas by needle biopsy.

MATERIALS AND METHODS: BreastScreen WA data over 10 year period from 1 January 1999 to 31 December 2008 was reviewed. RESULTS: Among the 760,027 women screened in Western Australia between 1999 and 2008, 31 had a fine-needle aspiration (FNA) or a core biopsy (CB) diagnosing a fibroadenoma and subsequently underwent a diagnostic open biopsy (DOB). Three were preoperatively diagnosed as fibroadenoma by initial FNA but subsequent CB showed that these were not fibroadenomas and, therefore, were excluded from the present series. Of the 28 cases, DOB identified 21 fibroadenomas, two cellular fibroadenomas, two benign phyllodes tumours, one malignant phyllodes tumour, one fibroadenoma containing ductal carcinoma in situ (DCIS), and one case of a 40mm adenosis tumour with a small 5mm fibroadenoma. The lesions ranged from 5-100mm in size with an average size of 28mm. DOB and CB results were concordant in 25 (89%) of the cases. The primary clinical indications for undergoing DOB included indeterminate histopathological findings of cellular fibroadenomas versus phyllodes tumour (n = 10), enlarging size (n = 4), large size (n = 5), fibroadenomas with atypia (n = 1), discordant radiological and pathological findings (n = 3), patient preference (n = 1), association with a second screen-detected lesion requiring excision (n = 2), and an unknown indication (n = 1). CONCLUSION: CB diagnosis of fibroadenomas is a safe diagnosis unless it has atypical clinical, radiological, or pathological features. Copyright © 2015 The Royal College of Radiologists. All rights reserved.


Intracranial involvement by multiple myeloma.


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Intracranial involvement is a rare complication of multiple myeloma. It results either from direct extra-osseous spread from adjacent skeletal plasmacytomas or extra-medullary disease via haematogenous dissemination. The imaging appearances are non-specific, and dural, leptomeningeal, and parenchymal involvement can all occur. The purpose of this review is to illustrate the various neuroimaging appearances of this rare entity, focusing on MRI. Copyright © 2015 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.

Publication Types: Review


Retrospective preoperative assessment of the axillary lymph nodes in patients with breast cancer and literature review.

Saffar B, Bennett M, et al.

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Recent advances in the understanding and care of familial hypercholesterolaemia: significance of the biology and therapeutic regulation of proprotein convertase subtilisin/kexin type 9.

Page MM, Stefanutti C, et al.

A low-risk group of women was identified with screen-detected, low-grade small cancers with LN involvement, and to determine which clinical, pathological, and imaging findings best predict LN involvement.

RESULTS: Using a cut-off point of 3 mm versus >3 mm, abnormal cortical thickness had a sensitivity and specificity of 56.3% and 86.7%, respectively. Breast cancer size was significantly associated with the odds of LN metastasis (p<0.001). There were 69 patients with breast cancers of <10 mm and 18% had positive axillary LNs. A much higher rate of malignancy was observed in breast cancers located in multiple sites and in a central location.

CONCLUSION: The likelihood of axillary LN metastasis increases with cortical thickness >3 mm and this concurs with the literature. A low-risk group of women was identified with screen-detected, low-grade small cancers with LN involvement, and to determine which clinical, pathological, and imaging findings best predict LN involvement. Whether using genetic testing or not, cholesterol screening of family members of index patients with abnormally raised LDLC must be used to determine the need for early treatment to prevent the development of CAD. The metabolic defects in FH extend beyond LDL, and may affect triacylglycerol-rich and high-density lipoproteins, lipoprotein(a) and oxidative stress. Achievement of the recommended targets for LDL-C with current treatments is difficult, but this may be resolved at present logistically feasible. Whether using genetic testing or not, cholesterol screening of family members of index patients with abnormally raised LDLC must be used to determine the need for early treatment to prevent the development of CAD. The metabolic defects in FH extend beyond LDL, and may affect triacylglycerol-rich and high-density lipoproteins, lipoprotein(a) and oxidative stress. Achievement of the recommended targets for LDL-C with current treatments is difficult, but this may be resolved at present logistically feasible.


Moore A, Schug SA.

Moore, Andrew. Pain Research, Nuffield Division of Anaesthetics The Churchill, Oxford, United Kingdom. Schug, Stephan A. School of Medicine and Pharmacology University of Western Australia; Director of Pain Medicine, Royal Perth Hospital, Perth, Western Australia, Australia.

Clinical Therapeutics. 2015; 37(8): 1866-1867.

Letters to the Editor.

Moore A, Schug SA.

(Moore) Pain Research, Nuffield Division of Anaesthetics, Churchill, Oxford, United Kingdom (Schug) School of Medicine and Pharmacology, University of Western, Australia (Schug) Royal Perth Hospital, Perth, WA, Australia.
were tested at different doses (50, 100 or 200 mumole/g weight) using a tyloxapol-induced hyperlipidemic mouse model. Blood labeled immunoliposomes were assessed for their uptake by J774.A1 macrophages. Lipid-modifying effects of immunoliposomes conjugating a monoclonal antibody against apoB-100 to the liposomal surface using a post-insertion technique. Fluorescently-

Publication Types: Review

reserved.

mechanisms. This study aimed to evaluate the lipid-modifying effects of anionic immunoliposomes targeted against apoB, an important component of atherogenic lipoproteins. Methods: Two sets of nanoliposomes (20. mM) were prepared with low (including hydrogenated soy phosphatidylcholine [SPC] and egg phosphatidylglycerol [EPG]) and high (including hydrogenated soy phosphatidylcholine [HSPC] and distearyl phosphatidylglycerol [DSPG]) phase transition temperature values without cholesterol. In each set, the anionic phospholipid (EPG or DSPG) constituted 75% of total phospholipid content. Immunoliposomes were prepared by conjugating a monoclonal antibody against apoB-100 to the liposomal surface using a post-insertion technique. Fluorescently-labeled immunoliposomes were assessed for their uptake by J774.A1 macrophages. Lipid-modifying effects of immunoliposomes were tested at different doses (50, 100 or 200. mumole/g weight) using a tyloxapol-induced hyperlipidemic mouse model. Blood

Clinical Toxicology. 2015; 53 (4): 313.

Isoniazid poisoning: Pharmacokinetics and effect of dialysis after massive ingestion.

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Objective: Isoniazid is a rare overdose that causes seizures; there is limited evidence, mainly case reports, to guide treatment. We describe ingestion of a massive dose of isoniazid in a patient who was dialysed. Case report: We report a 20-year-old female migrant who presented with recurrent seizures after ingesting 25 g isoniazid. She was treated with activated charcoal, repeated doses of midazolam for the seizures and given multiple doses of pyridoxine (14 mg), limited by availability. She was admitted to intensive care 5.5 hours post-ingestion and commenced on continuous veno-venous haemodiafiltration (CVVHDF). She had further seizures which were treated with parenteral benzodiazepines and pyridoxine. Dialysis was continued until 30 hours post-overdose and then ceased. She gradually recovered, was extubated on day 3 and had no long-term sequelae. Five serum samples from the patient were available and isoniazid was quantified using a liquid chromatography-mass spectrometry (LC-MS/MS) method. A two compartment model with first order input (with fixed absorption co-efficient Ka) adequately described the timed concentration data. The effect of CVVHDF was modelled as a time-dependent covariate, best described by an exponential decay in clearance due to CVVHDF. Pharmacokinetic analysis suggests that there was initially good clearance with CVVHDF (four times endogenous clearance) which rapidly declined within hours. Conclusion: In patients with isoniazid poisoning early presentation, good supportive care and high dose benzodiazepines are likely to be sufficient treatment, including pyridoxine, if available. Dialysis did appear to increase isoniazid clearance for a few hours after commencement, and the earlier it is used the more effective it will be. Publication Types: Conference Abstract


Colloids and Surfaces B: Biointerfaces. 2015; 129: 71-78.

Apolipoprotein B-100-targeted negatively charged nanoliposomes for the treatment of dyslipidemia.

Background: Anionic nanoliposomes can interact with serum lipoproteins and regulate lipid metabolism through several mechanisms. This study aimed to evaluate the lipid-modifying effects of anionic immunoliposomes targeted against apoB, an important component of atherogenic lipoproteins. Methods: Two sets of nanoliposomes (20. mM) were prepared with low (including soy phosphatidylcholine [SPC] and egg phosphatidylglycerol [EPG]) and high (including hydrogenated soy phosphatidylcholine [HSPC] and distearyl phosphatidylglycerol [DSPG]) phase transition temperature values without cholesterol. In each set, the anionic phospholipid (EPG or DSPG) constituted 75% of total phospholipid content. Immunoliposomes were prepared by conjugating a monoclonal antibody against apoB-100 to the liposomal surface using a post-insertion technique. Fluorescently-labeled immunoliposomes were assessed for their uptake by J774.A1 macrophages. Lipid-modifying effects of immunoliposomes were tested at different doses (50, 100 or 200. mumole/g weight) using a tyloxapol-induced hyperlipidemic mouse model. Blood


Current Attitudes on Cardiac Devices in Heart Failure: A Review.

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PURPOSE: Despite significant advances in optimizing drug therapy, heart failure-related mortality and morbidity remain high. There has been great progression with regard to device therapy in heart failure, and device use continues to increase. The aims of this review were to critically re-examine the evidence base and to highlight recent refinements in device therapy in heart failure.

METHODS: Significant contemporary clinical trials and registries of device therapy in heart failure were examined and critically reviewed to draw conclusions on the clinical applications of implantable cardioverter-defibrillators, cardiac resynchronization therapy, remote monitoring of devices, and hemodynamic monitoring.

FINDINGS: Advances regarding patient selection, technology, and implementation for the use of devices in heart failure have significantly improved outcomes.

IMPLICATIONS: This review article provides a contemporary guide to the current attitudes toward the use of devices in heart failure. Device therapy is an important adjuvant to optimal pharmacologic therapy. The role of devices continues to increase, and devices have a positive impact on patients' quality of life and survival. Crown Copyright © 2015. Published by Elsevier Inc. All rights reserved.

Publication Types: Review


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Background: Anionic nanoliposomes can interact with serum lipoproteins and regulate lipid metabolism through several mechanisms. This study aimed to evaluate the lipid-modifying effects of anionic immunoliposomes targeted against apoB, an important component of atherogenic lipoproteins. Methods: Two sets of nanoliposomes (20. mM) were prepared with low (including soy phosphatidylcholine [SPC] and egg phosphatidylglycerol [EPG]) and high (including hydrogenated soy phosphatidylcholine [HSPC] and distearyl phosphatidylglycerol [DSPG]) phase transition temperature values without cholesterol. In each set, the anionic phospholipid (EPG or DSPG) constituted 75% of total phospholipid content. Immunoliposomes were prepared by conjugating a monoclonal antibody against apoB-100 to the liposomal surface using a post-insertion technique. Fluorescently-labeled immunoliposomes were assessed for their uptake by J774.A1 macrophages. Lipid-modifying effects of immunoliposomes were tested at different doses (50, 100 or 200. mumole/g weight) using a tyloxapol-induced hyperlipidemic mouse model. Blood

Current Attitudes on Cardiac Devices in Heart Failure: A Review.
A novel folic acid-conjugated TiO(2)-SiO(2) photosensitizer for cancer targeting in photodynamic therapy.

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In this paper, a novel folic acid-conjugated silica-coated titanium dioxide (TiO2-SiO2) photosensitizer was synthesized and characterized using various analytical instruments. The photosensitizer was further assessed with regards to its photoreactivity, cellular and hemocompatibility, cell internalization, and phototoxicity. Conjugating folic acid with TiO2-SiO2 has shown a significantly improved compatibility of the nanoparticles with the mouse fibroblast cells (L929) at 24 h. An improved compatibility with the human nasopharyngeal epidermoid cancer (KB) cells was also demonstrated, but to a slightly reduced degree. Enhanced cell internalization was well demonstrated in the TiO2-SiO2 folate nanoparticles. Upon exposure to UV light, TiO2-SiO2 folate nanoparticles maintained a high level photodynamic reactivity and yielded a 38-43% photo-killing of KB cells. The photo-killing effect increased with increasing dosage in the investigated concentration range of 50-100 μg ml(-1).

A randomized controlled trial of 6-week Chlorella vulgaris supplementation in patients with major depressive disorder.

Panahi Y, Badeli R, et al.
(Panahi) Chemical Injuries Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran, Islamic Republic of (Badeli) Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, Iran, Islamic Republic of (Karami) Department of Psychiatry, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran, Islamic Republic of (Badeli) Department of Microbiology, Islamic Azad University, Tonekabon branch, Tonekabon, Iran, Islamic Republic of (Sahebkar) Biotechnology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran, Islamic Republic of (Sahebkar) Metabolic Research Center, Royal Perth Hospital, School of Medicine and Pharmacology, University of Western Australia, Perth, Australia

A. Sahebkar, Department of Medical Biotechnology, School of Medicine, Mashhad University of Medical Sciences, P.O. Box: 91779-48564, Mashhad, Iran, Islamic Republic of

Background: Major depressive disorder (MDD) is a widespread psychiatric disorder with incapacitating symptoms. Oxidative stress has been identified to play a role in the pathophysiology of MDD. Objective: To evaluate the therapeutic effectiveness of a chemically defined and antioxidant-rich Chlorella vulgaris extract (CVE) as adjunct to standard treatment in patients suffering from MDD. Methods: Subjects with MDD diagnosis according to DSM-IV criteria who were receiving standard antidepressant therapy were assigned to add-on therapy with CVE (1800 mg/day; n = 42), or continued standard antidepressant therapy alone (n = 50) for a period of 6 weeks. Changes in the frequency of depressive symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS) and Beck Depression Inventory II (BDI-II) scale. Results: There were significant reductions in total and subscale BDI-II and HADS scores in both CVE and control groups by the end of trial. The magnitude of reductions in total BDI-II score [-4.14 (-5.30 to -2.97)] as well as physical [-2.34 (-2.84 to -1.84)] and cognitive [-1.12 (-1.62 to -0.61)] subscales were significantly greater in the CVE versus control group, however, reduction of the affective symptoms was greater in the control

sampling was performed 1 h after the injection of each immunoliposomal formulation. Results: ApoB-targeted HSPC/DSPG and SPC/EPG nanoliposomes were both taken up by cultured macrophages but the uptake rate was higher with the former formulation. Both immunoliposomal formulations significantly reduced serum LDL-cholesterol concentrations of hyperlipidemic animals at all tested doses (p< 0.001) and this effect lasted for at least 48 h. Significant reductions of serum levels of apoB, non-HDL-C, total cholesterol and triglycerides, and elevations of HDL-C levels were also observed. Conclusion: Intravenous injection of a single dose of apoB-targeted anionic nanoliposomes improves serum lipid profile parameters. These findings might have implications for the treatment of patients with severe dyslipidemias or statin intolerance.

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A. Sahebkar, Department of Medical Biotechnology, School of Medicine, Mashhad University of Medical Sciences, P.O. Box: 91779-48564, Mashhad, Iran, Islamic Republic of
Early mobilisation in intensive care units in Australia and Scotland: a prospective, observational cohort study examining mobilisation practises and barriers.

Harrold ME, Salisbury LG, et al.

INTRODUCTION: Mobilisation of patients in the intensive care unit (ICU) is an area of growing research. Currently, there is little data on baseline mobilisation practises and the barriers to them for patients of all admission diagnoses. METHODS: The objectives of the study were to (1) quantify and benchmark baseline levels of mobilisation in Australian and Scottish ICUs, (2) compare mobilisation practises between Australian and Scottish ICUs and (3) identify barriers to mobilisation in Australian and Scottish ICUs. We conducted a prospective, observational, cohort study with a 4-week inception period. Patients were censored for follow-up upon ICU discharge or after 28 days, whichever occurred first. Patients were included if they were >18 years of age, admitted to an ICU and received mechanical ventilation in the ICU. RESULTS: Ten tertiary ICUs in Australia and nine in Scotland participated in the study. The Australian cohort had a large proportion of patients admitted for cardiothoracic surgery (43.3%), whereas the Scottish cohort had none. Therefore, comparison analysis was done after exclusion of patients admitted for cardiothoracic surgery. In total, 60.2% of the 347 patients across 10 Australian ICUs and 40.1% of the 167 patients across 9 Scottish ICUs mobilised during their ICU stay (p < 0.001). Patients in the Australian cohort were more likely to mobilise than patients in the Scottish cohort (hazard ratio 1.83, 95% confidence interval 1.38-2.42). However, the percentage of episodes of mobilisation where patients were receiving mechanical ventilation was higher in the Scottish cohort (41.1% vs 16.3%, p < 0.001). Sedation was the most commonly reported barrier to mobilisation in both the Australian and Scottish cohorts. Physiological instability and the presence of an endotracheal tube were also frequently reported barriers. CONCLUSIONS: This is the first study to benchmark baseline practise of early mobilisation internationally, and it demonstrates variation in early mobilisation practises between Australia and Scotland.

Clinical and renal function, thrombocytopaenia and SOFA score over the first 2, 3, 5 and 7 days of the ICU stay were consistently associated with mortality at all endpoints. These findings may help to inform clinical decision making in patients with deterioration in renal function, thrombocytopaenia and SOFA score at day 90. 


Controversy and consensus regarding vitamin D: Recent methodological changes and the risks and benefits of vitamin D supplementation.

Glendenning P, Inderjeeth CA.

A dramatic and sustained surge in vitamin D test numbers has been attributed to the extraskeletal and probable intra/paracrine effects of vitamin D and not the important role of vitamin D in the regulation of extracellular calcium homeostasis and bone metabolism. This review summarizes recent data regarding the skeletal and extraskeletal effects of vitamin D, provides an overview of current methods of 25-hydroxyvitamin D measurement and includes the beneficial and adverse effects of vitamin D replacement. The role of 1,25-dihydroxyvitamin D, 24,25-dihydroxyvitamin D, vitamin D binding protein and free hormone levels are explored and potential future developments in this area are discussed. The adoption of a reference method for the measurement of 25-hydroxyvitamin D, certified reference standards and an independent certification program administered by the Centre for Disease Control is expected to improve routine analytical performance and is a major, crucial step forward. Improvements in accuracy, precision and sensitivity of 25-hydroxyvitamin D measurement is an important prelude to accurately defining the desirable level of 25-hydroxyvitamin D that is associated with the lowest risk for falls and fractures. Finally, the results of ongoing large, prospective, randomized clinical trials such as the Australian D-Health study should clarify the role of vitamin D supplementation in the prevention and management of skeletal and nonskeletal disorders, including vitamin D effects on mortality risk.


Early mobilization and recovery in mechanically ventilated patients in the ICU: A bi-national, multi-centre, prospective cohort study.


Introduction: The aim of this study was to investigate current mobilization practice, strength at ICU discharge and functional recovery at 6 months among mechanically ventilated ICU patients. Method: This was a prospective, multi-centre, cohort study conducted in 12 ICUs in Australia and New Zealand. Patients were previously functionally independent and expected to be ventilated for >48 hours. We measured mobilization during invasive ventilation, sedation depth using the Richmond Agitation and Sedation Scale (RASS), co-interventions, duration of mechanical ventilation, ICU-acquired weakness (ICUAW) at ICU discharge, mortality at day 90, and 6-month functional recovery including return to work. Results: We studied 192 patients (mean age 58.1+/−15.8 years; mean Acute Physiology and Chronic Health Evaluation (APACHE) II score, 18.0 (14 to 24)). Mortality at day 90 was 26.6% (51/192). Over 1,351 study days, we collected information during 1,288 planned early mobilization episodes in patients on mechanical ventilation for the first 14 days or until extubation (whichever occurred first). We recorded the highest level of early mobilization. Despite the presence of dedicated physical therapy staff, no mobilization occurred in 1,079 (84%) of these episodes. Where mobilization occurred, the maximum levels of mobilization were exercises in bed (N=94, 7%), standing at the bed side (N=11, 0.9%) or walking (N=26, 2%). On day three, all patients who were mobilized were mechanically ventilated via an endotracheal tube (N=10), whereas by day five 50% of the patients mobilized were mechanically ventilated via a tracheostomy tube (N=18). Conclusions: Early mobilization of patients receiving mechanical ventilation was uncommon. More than 50% of patients discharged from the ICU had developed ICU-acquired weakness, which was associated with death between ICU discharge and hospital discharge.
Critical Care. 2015; 19: S143

**Prehospital factors associated with an ICU admission from the emergency department.**

Williams TA, Finn J, et al.

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T.A. Williams, Curtin University, Bentley, Australia

Introduction This study aimed to describe the patient characteristics and prehospital factors associated with an ICU admission from the ED. There is a paucity of information about the early recognition of critical illness by paramedics; especially in the Australian prehospital setting. Methods A retrospective cohort study, July 2012 to June 2014, conducted in the Perth metropolitan area, which is served by a single ambulance service. Adult patients were included if transported to a public hospital ED that used the ED information system (EDIS) (seven of eight EDs) and were admitted to the ICU from the ED (ED-ICU group). Patients aged <16 years, those from rural areas or transfers were excluded. We used existing ambulance clinical data linked to EDIS data. Prehospital cohort characteristics are described using univariate statistical techniques. Logistic regression was conducted with admission to the ICU from the ED (critical illness surrogate) as the outcome variable. Variables included in regression models were age, sex, paramedic-identified urgency, that is the time patients should be seen by a doctor based on the Australasian Triage Scale, paramedic-identified patient problem and the time taken from the ambulance service receiving the call to hospital arrival.

Physiological variables: systolic blood pressure (SBP), heart rate (HR), respiratory rate (RR), temperature, oxygen saturation, and GCS were included in the logistic models. Results Of the 142,448 eligible patients transported by ambulance, 1,076 (0.75%) were admitted to the ICU from the ED: the ED-ICU group was younger (mean 53 vs. 61 years, P <0.001). Seventeen percent of ICU patients were transported as Urgency 1 (resuscitation/immediate) and 58% as Urgency 2 (within 10 minutes) while 70% of non-ICU patients were transported as Urgency 3 to 5 (P <0.001). Thirteen percent of ICU patients had a SBP <90 mmHg, 15% had a HR >130 and 19% had a RR >30. Drug overdose (21%) and respiratory conditions (18%) were the most common ICU conditions identified by paramedics for the ED-ICU group. All variables entered into the logistic models were significant (all P <0.001) except the time taken from receiving the call to hospital arrival (P = 0.48). Conclusion Three-quarters of the ED-ICU patients were transported to the ED with high urgency. Currently no prehospital severity of illness or early warning system (EWS) is used in our ambulance service. Given the small proportion of ED-ICU patients who presented with abnormal observations, it is unlikely that introducing an EWS would alter practice or patient outcome.

Publication Types: Conference Abstract


**Putting Critical Care Medicine on Trial.**

Webb SA.

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**Management of inflammatory bowel disease using stem cell therapy.**

Irhimeh MR, Cooney J.

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Inflammatory bowel diseases (IBD) are a collection of diseases associated with chronic inflammation in the intestinal mucosa and/or transmural involvement. IBD is divided into two main categories Crohn's disease (CD) and ulcerative colitis (UC). While there is no cure for IBD, current therapies can only reduce the inflammatory process that causes the signs and symptoms of IBD and hopefully induce long-term remission. Improved treatment modalities for the complex IBD are still evolving. The increased understanding of the underlying immunopathology has helped identify new targeted treatment options in particular the use of stem cell treatments that are capable of modulating the immune system. Haematopoietic stem cells (HSC) and mesenchymal stromal cells (MSC) therapy are both being investigated as a treatment for IBD. MSC therapy is well tolerated and associated with minimal established side-effects compared to HSC therapy, which involves ablative chemotherapy. Currently, such stem cell therapy is not a standard of care regimen for IBD. However, it promises to become the next generation treatment of choice, especially for severe refractory IBD patients.


**Pathogenesis and Management of the Diabetogenic Effect of Statins: a Role for Adiponectin and Coenzyme Q<inf>10</inf>?**

Chan DC, Pang J, et al.

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There is growing evidence to suggest that statin therapy is associated with an increased risk of incident diabetes. The risk for statin-related diabetes depends upon many factors including age, pre-existing diabetic risk, type and potency of statin. Several mechanisms have been suggested for the diabetogenic effects of statins involving processes that alter islet cell function, resulting in impaired glucose metabolism. Recent evidence suggests that the association of statin therapy with the development of diabetes may be partly mediated by a statin-induced decrease in circulating adiponectin and coenzyme Q\textsubscript{10}. The available evidence suggests the benefit of statins in reducing cardiovascular events outweigh the risk of developing diabetes. Moreover, statin therapy does not impair glycemic control in diabetic patients. Expert recommendations for the use of statins in people at risk of developing diabetes have recently been published. However, further research is required to elucidate both the association between statin use and incident diabetes as well as underlying mechanisms.

Publication Types: Review

**Statin therapy and cognition in older people: What is the evidence?**

Gnjidic D, Naganathan V, et al.

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D. Gnjidic, University of Sydney, The University of Sydney, Bank Building A15, Science Rd, Sydney, NSW 2006, Australia Whether to start, continue or discontinue statins in older people remains a clinical and ethical dilemma. While there is clinical trial evidence that statins reduce cardiovascular morbidity in older people, recently concerns have been raised about side effects in this population. Adverse effects of statins reported in older people include muscle-related symptoms, diabetes, impaired physical function and cognitive impairment. The cognitive effects of statins are not well understood and remain contentious. In younger and healthier people with baseline intact cognitive function, short-term data suggest no adverse effects of statins on cognition whereas long-term data support a beneficial role for statins in delaying dementia. Insufficient evidence is currently available to establish causality in relation to statins and cognitive function in older people specifically. The objective of this narrative review is to analyse the current evidence in relation to statin therapy and cognition, and discuss challenges in translating the current evidence to older people.


Current Hypertension Reports. 2015; 17(8): 58.
**The Role of Central Nervous System Mechanisms in Resistant Hypertension.**

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Arterial hypertension remains a primary global health problem with significant impact on cardiovascular morbidity and mortality. The low rate of hypertension control and failure to achieve target blood pressure levels particularly among high-risk patients with resistant hypertension has triggered renewed interest in unravelling the underlying mechanisms to implement therapeutic approaches for better patient management. Here, we summarize the crucial role of neurogenic mechanisms in drug-resistant hypertension, with a specific focus on central control of blood pressure, the factors involved in central integration of afferent signalling to increase sympathetic drive in resistant hypertension, and briefly review recently introduced interventional strategies distinctively targeting sympathetic activation.

Publication Types: Review

Current Hypertension Reports. 2015; 17(10): 80.
**Role of the Sympathetic Nervous System in Stress-Mediated Cardiovascular Disease.**

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A high incidence of acute cardiovascular events and sudden cardiac death following unexpected acute emotional stress or a natural catastrophic disaster has been well-documented over the past decades. Chronic psychosocial factors have been shown to be directly linked to the development of hypertension, cardiovascular disease and stroke. Activation of various neurogenic pathways is an important mediator of acute and chronic stress-induced hypertension and heart disease. Heightened sympathetic activation has been shown to be a critical contributor linking psychogenic effects on cardiovascular regulation to serious and often fatal CV outcomes. Accordingly, several therapeutic approaches that attenuate autonomic imbalance via modulation of increased sympathetic outflow by either non-pharmacological or interventional means have been shown to alleviate clinical symptoms. Likewise stress reduction per se achieved with transcendental medicine has been linked to improved patient outcomes. Therapies
that oppose adrenergic activity and/or have the potential to attenuate negative emotions are likely to reduce cardiovascular risk and its adverse consequences attributable to chronic mental stress.


**Testosterone and cardiovascular disease risk.**

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Purpose of review Ageing is accompanied by a reduction in circulating testosterone and progressive accumulation of medical morbidities. There is an intense debate whether low testosterone contributes to ill-health as opposed to being a biomarker for its presence. Prescriptions for testosterone are rising on a background of concern over potential adverse effects. This review examines evidence relating androgens to cardiovascular risk in older men. Recent findings Observational studies show lower risk of cardiovascular events in older men with higher testosterone, and lower mortality from ischaemic heart disease in men with higher concentrations of its more potent androgenic metabolite dihydrotestosterone. However, randomized controlled trials of testosterone supplementation have been underpowered for the outcome of cardiovascular events. Recent meta-analyses have reached contrasting conclusions regarding cardiovascular adverse events associated with testosterone therapy. Retrospective studies of prescription databases have produced controversial and conflicting results. Summary Additional randomized controlled trials are required to clarify the role of testosterone supplementation in older men in the absence of pituitary or gonadal disease. Pending such studies, testosterone therapy should be considered in androgen-deficient men, with evaluation of potential benefits and risks.


**Normal personality, personality disorder and psychosis: current views and future perspectives.**

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Purpose of review: The purpose of this article is to review recent literature examining the occurrence of psychotic experiences in normal population and those with personality disorders. Recent findings: Up to 15% of individuals in the general population report some type or degree of psychotic experience. Most of these individuals function adequately, do not require psychiatric treatment and do not receive diagnosis of a psychotic illness. A significant number of individuals diagnosed with borderline personality disorder (25-50%) also report psychotic symptoms. These are not easily differentiated from the psychotic symptoms reported by individuals with schizophrenia, nor are they always transient. However, emerging research has confirmed that individuals with schizotypal personality disorder are dimensionally related to those with schizophrenia and are at an increased risk of transition to psychosis. Summary: Psychotic symptoms are best considered as ‘trans-diagnostic’ entities on a continuum from normal to pathological. There is also a significant amount of research showing that psychotic symptoms in borderline personality disorder are frequent, nontransient and represent a marker of illness severity. This review highlights the need to move beyond traditional assumptions and categorical boundaries when evaluating psychotic experiences and psychopathological phenomena. © Lippincott Williams & Wilkins.


**Improving outcomes from community-acquired pneumonia.**

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Purpose of review: We are entering into a new era of healthcare wherein patient outcomes are increasingly being publicly reported, not just by institution, but by individual clinicians. This review focuses on the issue of quality of care of patients with community-
acquired pneumonia (CAP), in particular the choice of outcome, quality of data needed and recommendations of the current bundle of care suggested by the available literature as delivering the best chance of favourable outcomes for patients. Recent findings there is increasing evidence that pneumonia outcomes have improved over the past decade, particularly mortality. However, we have been oversimplistic in setting quality targets and that a bundle of care is required to deliver best outcomes, such as has been shown with the surviving sepsis campaign. Equally, the quality of data available to compare outcomes needs to be significantly improved on what is currently available. Summary To achieve best outcomes for their patients, physicians must be actively comparing their outcomes against other institutions and not rely on historical data. A bundle of care that includes rapid administration of antibiotics, use of combination antibiotic therapy including a macrolide and early mobilization is a good starting point.

Publication Types: Review


Characterisation of mesenchymal stem cells in use in clinical trials in Australia.
Holmes LM, Shaw K, et al.
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L.M. Holmes, Cell and Tissue Therapies WA (CTTWA), Royal Perth Hospital, Perth, WA, Australia
The clinical use of mesenchymal stem cells (MSC) has exploded over the last couple of years, with over 400 clinical trials currently being undertaken around the world. However, variation in MSC products used in the trials, resulting from differences in MSC source, manufacturing processes, passage number, donor variation and, for some clinical trials, selection based on cell surface marker subsets, may be responsible for discrepant clinical outcomes amongst clinical researchers. Our laboratory currently has 7 clinical trials underway, using allogeneic bone marrow derived MSC, for multiple clinical indications including GVHD, lung and kidney transplant rejection, Crohn's disease and cranial reconstruction. We have seen significant efficacy with our CTTWA manufactured MSC across the various indications. Due to the disparity amongst groups in treatment outcomes and potential variation in quality of MSC products, it is important to identify the phenotype, differentiation potential and potency of the MSC used in clinical trials. To further characterise our cells, whole genome expression was performed using RNA-seq (Ilumina) on four donor MSC products currently used in our clinical trials, to identify expression of cell surface makers, chemokines and cytokines. Cell surface marker expression was confirmed by screening 242 markers using the BD Lyoplate Human Cell Surface Marker kit, identifying 34 cell surface markers expressed on more than 90% of the MSC population and 43 markers expressed on 10%-90% of the MSC population. Our results demonstrated different levels of expression for several markers compared to previous studies, for example STRO-1 and CD271. Additionally, differential expression of markers between different donor MSC products was identified. These initial results demonstrate the variation of MSC products and the need for characterisation of MSC used in clinical trials which will allow for direct comparison of phenotype and potency with treatment outcome.

Publication Types: Conference Abstract

Dermatology Research & Practice. 2015; 2015: 421460.
A Comparative Study Examining the Management of Bowen's Disease in the United Kingdom and Australia.
Morley GL, Matthews JH, et al.
Morley, G L. College of Medical and Dental Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK. Matthews, J H. College of Medical and Dental Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK. Verpetinske, I. Russells Hall Hospital, Pensnett Road, Dudley, West Midlands DY1 2HQ, UK. Thom, G A. Royal Perth Hospital, 197 Wellington Street, Perth, WA 6000, Australia.
Background and Aim. The optimum management of Bowen's Disease (BD) is undefined. A review of current practice is required to allow the development of best practice guidelines. Methods. All BD cases, diagnosed in one UK centre and one Australian centre over a year (1 July 2012-30 June 2013), were analysed retrospectively. Patients with BD were identified from histopathology reports and their medical records were analysed to collect demographic data, site of lesion, and treatment used. Results. The treatment of 155 lesions from the UK centre and 151 lesions from the Australian centre was analysed. At both centres BD was most frequently observed on the face: UK had 70 (45%) lesions and Australia had 83 (55%) lesions (P = 0.08). The greatest number of lesions was managed by the plastic surgery department in the UK centre, 72 (46%), and the dermatology department in the Australian centre, 121 (80%). The most common therapy was surgical excision at both centres. Conclusions. In both UK and Australia, BD arises on sun-exposed sites and was most commonly treated with surgical excision despite a lack of robust evidence-based guidelines.

Deutsche Medizinische Wochenschrift. 2015; 140(18): e176-85.
[Cross-sectional study of satisfaction with studies and lifestyle among medical students in Austria, Germany and Switzerland].
Baschera D, Westermann L, et al.
Background: The aim was to examine potential differences in various aspects of life as well as study satisfaction amongst medical
students of three German speaking countries.

METHOD: Data was collected between February and June 2010 using an online survey with the open source survey tool Limesurvey (Version 1.85 RC3).

RESULTS: 1179 medical students in year 4-6 completed the online questionnaire (798 in Germany (Ger), 265 in Austria (A) and 116 in Switzerland (CH)). Mean age was similar (25.0-25.3) for the countries (p = 0.14). Respondents from Austria were significantly more often (17.4 %) smoking than Swiss (12.1 %) or German (10 %) medical students (p = 0.002). The average number of hours spent studying per week and desired weekly work hours varied significantly between countries. The average desired working week post-graduation was 42 hours. The perceived ability to work as junior doctor post-graduation was below 5 on a visual analogue scale of 1-10.

CONCLUSION: RESULTS of consumption, work life balance and activity were similar to statistics of the population of each country. With regard to the desired work time after graduation this is in clear contrast to the reality as a doctor. Improvement of medical courses can be achieved with better preparation for the internship. Copyright © Georg Thieme Verlag KG Stuttgart New York.


Diabetes Care. 2015.

The Relationship Between Levels of Advanced Glycation End-Products and Their Soluble Receptor and Adverse Outcomes in Adults With Type 2 Diabetes.

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The George Institute for Global Health, University of Sydney, Sydney, New South Wales, Australia
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The George Institute for Global Health, University of Sydney, Sydney, New South Wales, Australia
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OBJECTIVES: This study explored whether activation of the receptor for advanced glycation end products (RAGE) is implicated in the development of diabetes complications. RESEARCH DESIGN AND METHODS: A case-cohort study was performed in 3,763 participants with prevalent diabetes in the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial. The hazard ratios (HRs) for death, major cardiovascular events, and new or worsening nephropathy were derived using Cox regression models, and the ability of sRAGE and AGE levels to reclassify the risk of nephropathy was assessed. RESULTS: After adjustment for a range of possible confounders and other risk factors, sRAGE levels were associated with all-cause mortality (HR 1.11 for a 1-SD increase of log sRAGE [95% CI 1.00-1.22]; P = 0.045) and new or worsening nephropathy (HR 1.20 for a 1-SD increase of log sRAGE [95% CI 1.02-1.41]; P = 0.032). Circulating AGE levels were also independently associated with new or worsening nephropathy (HR 1.21 for a 1-SD increase [95% CI 1.08-1.36]; P = 0.001). Both markers also significantly improved the accuracy with which the 5-year risk of new or worsening nephropathy could be predicted (net reclassification index in continuous model, 0.25 for sRAGE and 0.24 for AGE levels). CONCLUSIONS: In adults with type 2 diabetes, increased levels of sRAGE are independently associated with new or worsening kidney disease and mortality over the next 5 years. Higher levels of AGE are also associated with an increased risk of adverse renal outcomes. The AGE/RAGE axis may be of importance in the prevention and management of diabetes complications.


Relationship Between Levels of Advanced Glycation End Products and Their Soluble Receptor and Adverse Outcomes in Adults With Type 2 Diabetes.

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Cooper, Mark E. Baker IDI Heart & Diabetes Institute, Melbourne, Victoria, Australia.
Hillis, Graham S. The George Institute for Global Health, The University of Sydney, Sydney, New South Wales, Australia.

OBJECTIVE: This study explored whether activation of the receptor for advanced glycation end products (RAGE) is implicated in the
Development of diabetes complications.

**RESEARCH DESIGN AND METHODS:** A case-cohort study was performed in 3,763 participants with prevalent diabetes in the Action in Diabetes and Vascular Disease: Preterax and Diamicro Modified Release Controlled Evaluation (ADVANCE) trial. The hazard ratios (HRs) for death, major cardiovascular events, and new or worsening nephropathy were derived using Cox regression models, and the ability of sRAGE and AGE levels to reclassify the risk of nephropathy was assessed.

**RESULTS:** After adjustment for a range of possible confounders and other risk factors, sRAGE levels were associated with all-cause mortality (HR 1.11 for a 1-SD increase of log sRAGE [95% CI 1.00-1.22]; \( P = 0.045 \)) and new or worsening nephropathy (HR 1.20 for a 1-SD increase of log sRAGE [95% CI 1.02-1.41]; \( P = 0.032 \)). Circulating AGE levels were also independently associated with new or worsening nephropathy (HR 1.21 for a 1-SD increase [95% CI 1.08-1.36]; \( P = 0.001 \)). Both markers also significantly improved the accuracy with which the 5-year risk of new or worsening nephropathy could be predicted (net reclassification index in continuous model, 0.25 for sRAGE and 0.24 for AGE levels).

**CONCLUSIONS:** In adults with type 2 diabetes, increased levels of sRAGE are independently associated with new or worsening kidney disease and mortality over the next 5 years. Higher levels of AGE are also associated with an increased risk of adverse renal outcomes. The AGE/RAGE axis may be of importance in the prevention and management of diabetes complications.

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**Diabetes Prevalence and its Associations with Cardio-Metabolic Control in Aboriginal and Anglo-Celt Patients with Type 2 Diabetes:** The Fremantle Diabetes Study Phase II.

**Aims:** To determine the prevalence and associates of depression in Aboriginal and Anglo-Celt (AC) Australians with type 2 diabetes.

**Methods:** Community-based patients were screened using the Patient Health Questionnaire (PHQ-9) as part of detailed assessment. The prevalence of any current depression, major depression and antidepressant use by racial group was compared after adjustment for age, sex, educational attainment and marital status. Multiple logistic regression was used to determine associates of current depression.

**Results:** The 107 Aboriginal participants were younger (mean±SD 54.3±/−11.8 vs. 67.2+/−10.6 years), less often male (34.6% vs. 50.9%) and married (39.3% vs. 61.7%), and more likely to smoke (44.6% vs. 8.1%) than the 793 AC subjects (P<0.002). Fifty-two Aboriginal (48.5%) and 772 AC participants (97.4%) completed the PHQ-9; these Aboriginals had similar socio-demographic, anthropometric and diabetes-related characteristics to those without PHQ-9 data. A quarter of the Aboriginals had current depression vs 10.6% of ACs (P=0.16), 15.4% vs. 4.1% had major depression (P=0.029), and 68.8% vs. 29.7% had untreated depression (P=0.032). Compared with non-depressed participants, patients with current depression were younger and more likely to smoke, to be overweight/obese and to have worse glycaemic control (P<0.024). Significant independent associates of current depression were educational attainment (inversely), smoking status, body mass index and fasting plasma glucose in the AC group and alcohol use in the Aboriginal group.

**Conclusions:** Although prevalence of depression was not significantly increased in the Aboriginal patients, it was more likely to be major and untreated. Depression complicating type 2 diabetes is associated with adverse cardiovascular risk.

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**Effect of Statin Therapy on Plasma Proprotein Convertase Subtilisin Kexin 9 (PCSK9) Concentrations: A Systematic Review and Meta-Analysis of Clinical Trials.**

**Aims:** To evaluate the magnitude of the effect of statin therapy on plasma proprotein convertase subtilisin kexin 9 (PCSK9) levels...
CONCLUSION: Higher maximum VGE grades and longer durations of VGE following decompression were associated with a history of DCS.

**Prostaglandin E<sub>2</sub> and Polyenylphosphatidylcholine Protect Against Intestinal Fibrosis and Regulate Myofibroblast Function.**

Baird AC, Lloyd F, et al.

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Background: Intestinal fibrosis is a serious and often recurrent complication of inflammatory bowel disease despite surgical intervention. The anti-fibrotic potential of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) and polyenylphosphatidylcholine (PC) was investigated using the murine model of 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced chronic intestinal inflammation and fibrosis, and murine and human intestinal myofibroblasts. Methods: Mice were treated with TNBS enemas weekly for 2 or 6 weeks +/- PGE<sub>2</sub> (10 mg/kg/day orally) or PC (200 mg/kg/day orally). Inflammation and fibrosis were histologically assessed and scored. Pro-inflammatory cytokines, TLR4, and ECM-related gene expression from the colonic tissue and cultured myofibroblasts were assessed by RT-qPCR. The levels of alpha-SMA<sup>+</sup> staining and endogenous PGE<sub>2</sub> in vivo were also assessed. Results: Both PGE<sub>2</sub> and PC treatment significantly decreased TNBS-induced intestinal inflammation and excess collagen deposition in vivo. This was accompanied by decreased alpha-SMA<sup>+</sup> staining in the lamina propria and lower collagen type I (COL1alpha1) expression. Endogenous PGE<sub>2</sub> levels demonstrated that PC was not being converted into PGE<sub>2</sub>, thus mediating its effects primarily via PGE<sub>2</sub>-independent pathways. Both PGE<sub>2</sub> and the PC isoform, 1,2-dilinoleoylphosphatidylcholine (DLPC), regulated primary mouse myofibroblast and CCD-180C COL1alpha1 production, and induced lower collagen type I to III and TGF-beta1 to TGF-beta3 ratios, demonstrating their ability to induce normal healing in the presence of phorbol 12-myristate 13-acetate (protease kinase C-dependent inducer of collagen production). Conclusion: PGE<sub>2</sub> and PC both have potent anti-fibrogenic potentials in their ability to regulate inflammatory cell and myofibroblast accumulation within inflamed tissue, to decrease pro-inflammatory cytokine expression and to maintain normal healing in an inflammatory environment.


**Joint position statement on persistent foramen ovale (PFO) and diving. South Pacific Underwater Medicine Society (SPUMS) and the United Kingdom Sports Diving Medical Committee (UKSDMC).**

Smart D, Mitchell S, et al.

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This consensus statement is the result of a workshop at the SPUMS Annual Scientific Meeting 2014 with representatives of the UK Sports Diving Medical Committee (UKSDMC) present, and subsequent discussions including the entire UKSDMC. Right-to-left shunt across a persistent or patent foramen ovale (PFO) is a risk factor for some types of decompression illness. It was agreed that routine screening for PFO is not currently justifiable, but certain high risk sub-groups can be identified. Divers with a history of cerebral, spinal, inner-ear or cutaneous decompression illness, migraine with aura, a family history of PFO or atrial septal defect and those with other forms of congenital heart disease are considered to be at higher risk. For these individuals, screening should be considered. If screening is undertaken it should be by bubble contrast transthoracic echocardiography with provocative manoeuvres, including Valsalva release and sniffing. Appropriate quality control is important. If a shunt is present, advice should be provided by an experienced diving physician taking into account the clinical context and the size of shunt. Reduction in gas load by limiting depth, repetitive dives and avoiding lifting and straining may all be appropriate. Divers may consider transcatheter device closure of the PFO in order to return to normal diving. If transcatheter PFO closure is undertaken, repeat bubble contrast echocardiography must be performed to confirm adequate reduction or abolition of the right-to-left shunt, and the diver should have stopped taking potent anti-platelet therapy (aspirin is acceptable).

**Drugs. 2015; 75(15): 1715-24.**

**Challenges in the Diagnosis and Treatment of Homozygous Familial Hypercholesterolemia.**

Ito MK, Watts GF.

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Homozygous familial hypercholesterolemia (HoFH) is a rare, genetic disorder characterized by an absence or impairment of low-density lipoprotein receptor (LDLR) function resulting in significantly elevated low-density lipoprotein cholesterol (LDL-C) levels. The cholesterol exposure burden beginning in utero greatly increases the risk for atherosclerotic cardiovascular disease (ASCVD) and premature death. The genetic heterogeneity of HoFH results in a wide range of LDL-C levels among both untreated and treated patients. Diagnosis of HoFH should, therefore, be based on a comprehensive evaluation of clinical criteria and not exclusively LDL-C levels. As treatment goals, the European Atherosclerosis Society and International FH Foundation suggest target LDL-C levels of <100 mg/dL (<2.5 mmol/L) in adults or <70 mg/dL (<1.8 mmol/L) in adults with clinical coronary artery disease or diabetes. The National Lipid Association (NLA) recommends that LDL-C levels be reduced to <100 mg/dL (<2.5 mmol/L) or by at least >50 % from pretreatment levels. Conventional therapy combinations that lower atherogenic lipoproteins levels in the blood, such as statins, ezetimibe, bile acid sequestrants and niacin, as well as lipoprotein apheresis, are usually unable to reduce LDL-C levels to recommended targets. Two recently approved agents that reduce lipoprotein synthesis and secretion by the liver are lomitapide, a microsomal triglyceride transfer protein inhibitor, and mipomersen, an apolipoprotein B antisense oligonucleotide. The newly approved inhibitor of proprotein convertase subtilisin/kexin type 9 (PCSK9), evolocumab, also shows promise for the management of FH. Because of the extremely high risk for ASCVD, HoFH patients should be identified early.

**EMA - Emergency Medicine Australasia. 2015; 27(1): 16-21.**

**Predicting the number of emergency department presentations in Western Australia: A population-based time series analysis.**

Mai Q, Aboagy-Sarfo P, et al.

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Objective: To predict the number of ED presentations in Western Australia (WA) in the next 5 years, stratified by place of treatment, age, triage and disposition. Methods: We conducted a population-based time series analysis of 7 year monthly WA
statewide ED presentation data from the financial years 2006/07 to 2012/13 using univariate autoregressive integrated moving average (ARIMA) and multivariate vector-ARIMA techniques. Results: ED presentations in WA were predicted to increase from 990342 in 2012/13 to 1250991 (95% CI: 982265-1519718) in 2017/18, an increase of 260649 (or 26.3%). The majority of this increase would occur in metropolitan WA (84.2%). The compound annual growth rate (CAGR) in metropolitan WA in the next 5 years was predicted to be 6.5% compared with 2.0% in the non-metropolitan area. The greatest growth in metropolitan WA would be in ages 65 and over (CAGR, 6.9%), triage categories 2 and 3 (8.3% and 7.7%, respectively) and admitted (9.8%) cohorts. The only predicted decrease was triage category 5 (-5.3%). Conclusions: ED demand in WA will exceed population growth. The highest growth will be in patients with complex care needs. An integrated system-wide strategy is urgently required to ensure access, quality and sustainability of the health system.


Red-back spider bite to the tympanic membrane with 21 day follow up.
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Publication Types: Letter


The uncertainty of truth.
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Final frontier.
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Asia, Australia and New Zealand Dyspnoea in Emergency Departments (AANZDEM) study: Rationale, design and analysis.
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An avulsion fracture of the anterior superior iliac spine is a rare and interesting injury: It can be an easily missed diagnosis.

O'Brien G, Mukherjee A. (O'Brien, Mukherjee) Armadale Hospital, Perth, WA, Australia

An avulsion fracture of the anterior superior iliac spine is a rare and interesting injury. It can be an easily missed diagnosis if the practitioner is not looking for it on the plain film or the x-ray is inconclusive. It is most commonly found in the competitive adolescent playing running and kicking sports, namely sprinting, distance running, various codes of football and gymnastics. Severely displaced fragments may compress the lateral cutaneous nerve leading to pain and/or altered sensation in that nerves peripheral distribution. It is usually discovered on plain film (AP Pelvis), but MRI or CT may be required if unsure but clinical suspicion exists for a fracture. Differentials include Ewing sarcoma, osteosarcoma or infective process, especially where trauma seems trivial in nature. If the clinical suspicion exists for one of above then this must be pursued prior to initiating management for fracture. Treatment consists of surgical or conservative management: Surgical treatment is reserved for high grade lesions and/or neurological deficit or where early return to play is required, such as in professional sports. Open reduction and internal fixation comes with inherent risks of surgery and anaesthesia but showed earlier progression to all recovery milestones. Final outcomes at one year follow-up showed no advantage of one method versus the other.

Publication Types: Conference Abstract

Facet joint septic arthritis is an easily missed diagnosis of back pain-a case report.

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We present the interesting case of a 65 yr female who had multiple presentations to the local health service with acute on chronic back pain. At least 70% of adults will have low back pain during their lifetime. Acute on chronic low back pain is a common presentation to Emergency Departments world-wide. In Western Australia it represents approximately 2% of presentations to Emergency Departments. In the absence of trauma, research shows that the vast majority of those will be benign. Patients presenting with back pain should have detailed histories and examinations to tease out potential serious causes, such as neoplasia and infection, which account for only 1% of cases. Facet joint septic arthritis (SAF) is a rare cause of back pain, accounting for less than 0.01% of cases in the primary care setting. Spinal infections, such as facet joint septic arthritis, are rare. SAF presents rarely, accounting for approx 0.2-2.0 in 10,000 hospital admissions. There are only 40 to 50 cases documented in the literature world-wide. It can present insidiously and atypically without neurological sequelae until very late. It can be caused by direct inoculation or haematogenous spread while spontaneous SAF is rare but possible. The average time from onset to diagnosis is approximately 4 weeks (2 days to 5 months). It is most common in vulnerable patient groups, those with chronic medical conditions, those who are...
immunosuppressed and the elderly, who are also more likely to have concurrent degenerative spinal disease. The presentation can range from back pain through to confusion and sepsis and can mimic other illnesses. Early and appropriate imaging is essential. MRI and Bone scan have been shown to be the imaging modalities of choice with MRI having a higher sensitivity and specificity and better delineating the structures involved than Bone scan. Mortality is 14% due to late diagnosis and treatment. Complications such as epidural abscess and paraspinal muscle abscess are frequent. In the elderly population secondary bacteraemia can have serious consequences in those with grafts, prostheses and artificial valves. These patients require significant periods of hospitalisation, multiple input from specialist teams and often long periods of rehabilitation following diagnosis as with the patient in this report. It may be easily missed by the inexperienced practitioner. It requires a high degree of clinical suspicion to ensure timely diagnosis, commencement of treatment and avoidance of complications.

Publication Types: Conference Abstract


RESPOND-a patient-centred program to prevent secondary falls in older people presenting to the emergency department with a fall: Protocol for a program evaluation.
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Background: Program evaluations conducted alongside randomised controlled trials (RCTs) have potential to enhance understanding of trial outcomes. This paper describes a program evaluation to be conducted alongside a multicentre RCT of a patient-centred program designed to improve older people's participation in falls prevention activities in order to reduce falls, falls-injuries and emergency department (ED) re-presentations (RESPOND). Objectives: 1) To assess the degree to which RESPOND was implemented as planned. 2) To identify barriers and facilitators to implementation. 3) To identify whether RESPOND increases participation in falls prevention activities, compared with standard care. 4) To determine the degree to which demographic and program factors influence participation in falls prevention activities, and identify barriers and facilitators to participation. 5) To investigate the degree to which demographic, participatory and program factors influence RESPOND RCT outcomes; falls, falls-injuries and ED re-presentations. Method: 528 community-dwelling adults aged 60-90 years presenting to two EDs with a fall will be recruited and randomly allocated to the RESPOND intervention or standard care. A mixed methods design will be used and a program logic model will frame the program evaluation. Data from interviews, focus groups, questionnaires, clinician case notes, participant-completed daily calendars, and audio-recordings of intervention contacts will be collected and merged. Quantitative data will be analysed via descriptive and inferential statistics and qualitative data will be interpreted using thematic analysis. An inter-site comparison will be conducted to identify differences and similarities between the trial sites. Results: N/A: Protocol paper Conclusion: The RESPOND program evaluation will provide insights into contextual and influencing factors of RCT outcomes. The results will assist researchers, clinicians, policy makers and funding providers to make decisions about falls prevention interventions targeting older people at risk of recurrent falls and recurrent ED presentations.

Publication Types: Conference Abstract


Adrenaline in asthma-evidence not into action.
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Y. Nagree, Fremantle Hospital, University of Western Australia, Fremantle, WA, Australia

Background: Despite there being poor evidence for the use of adrenaline in severe and life threatening asthma, many Emergency Physicians still use it citing anecdotal evidence of its superiority over other agents. Objectives: To determine what agents Emergency Physicians use in severe and life threatening asthma. This presentation will also present the current evidence for & against the use of adrenaline in severe and life threatening asthma Method: Using the database of the Australasian College for Emergency Medicine, a survey was emailed to all Emergency Physicians (EP) and Emergency Medicine Trainees in 2012 to determine their current practice of severe asthma management against the 2006 guidelines. The email invited them to participate in a short online survey hosted by the SurveyMonkey website. EPs were asked about various agents they used in the management of severe asthma as per the 2006 handbook. Options available were never (0%), rarely (<40% of the time), usually (41-80%) and almost-always (>80%). Responses were dichotomised into never & rarely and usually & almost-always Results: 94% of EPs regularly used continuous short acting bronchodilators (SABA) nebulisations as per the guidelines with 70% EPs escalating to intravenous SABA if nebulisations failed as per the guidelines. Intravenous magnesium was used by 77% of EPs although the guidelines noted that the evidence is not strong. Adrenaline is recommended only in anaphylaxis or respiratory arrest but was used by 42% of EPs in some form (IM, IV, or infusion). Aminophylline is suggested as an alternative to SABA and was only used by 12%
of respondents. Ketamine was used by 18%. Conclusion: Despite minimal evidence in the literature for the use of adrenaline in asthma, 42% of respondents used adrenaline in some form (IM, IV or infusion). A short review of the literature will be presented.

Publication Types: Conference Abstract


Validation and impact of the four hour rule/ NEAT in the emergency department: A large data linkage study-progress update.
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Background: In 2008, the Australasian College for Emergency Medicine confirmed and ratified that Access block and Emergency Department overcrowding are the most serious issues confronting EDs in the developed world because they compromise quality and timeliness of patient care. Since then, there have been significant changes and innovations in and outside the ED. In 2012 we obtained anNHMRCPartnership Grant (AP1029492) to study this issue as we still need to understand which policy interventions are most effective in promoting improvement in patient care while reducing the impact of access block and overcrowding on patients.

Objectives: The main aims are to: (1) evaluate the effectiveness and outcomes of the Four Hour Rule/ National Emergency Access Target (NEAT) as a policy intervention; (2) identify strategies implemented under the Four Hour Rule/NEAT; (3) develop a framework for improving ED performance; and (4) design a long term strategy for maintaining and sustaining performance through the use of dynamic modelling of interventions that can be implemented in Emergency systems. Method: We will use a multilevel model study design using a reference point model and data linkage methodology to explore the impact of the policy before, during and after the implementation of the Four Hour Rule/NEAT in WA, NSW, ACT and Qld. The study will also use qualitative research to identify key areas of implementation and dynamic modelling to develop, calibrate, test and refine computer models using relevant data.

Results: To date we have obtained data linkage approval in WA and NSW, and ethics approval in NSW, WA and Queensland. The main issue to date is that access block and ED overcrowding still remain a major system problem. Conclusion: Through this study, a framework for improving ED performance will be tested together with a long term strategy for maintaining and sustaining improvements in the system. We anticipate that the findings will enable us to effectively assess the drivers of policy interventions at the ED, hospital and state level; and to develop strategies to inform policy changes and translate this.

Publication Types: Conference Abstract


Appropriateness and determinants of antibiotic prescribing in an Australian emergency department.
O'Brien AP, Rawlins MD, et al.
O’Brien, Aine P. Emergency Department, Royal Perth Hospital, Perth, Western Australia, Australia.

Publication Types: Letter


Growth in Western Australian emergency department demand during 2007-2013 is due to people with urgent and complex care needs.
Aboagye-Sarfo P, Mai Q, et al.
Aboagye-Sarfo, Patrick. Clinical Modelling, Health System Improvement Unit, Innovation and Health System Reform, Department of Health, Perth, Western Australia, Australia. Mai, Qun. Clinical Modelling, Health System Improvement Unit, Innovation and Health System Reform, Department of Health, Perth, Western Australia, Australia. Mai, Qun. Centre for Health Services Research, School of Population Health, The University of Western Australia, Perth, Western Australia, Australia. Sanfilippo, Frank M. Clinical Epidemiology Unit, School of Population Health, The University of Western Australia, Perth, Western Australia, Australia. Preen, David B. Centre for Health Services Research, School of Population Health, The University of Western Australia, Perth, Western Australia, Australia. Stewart, Louise M. Centre for Population Health Research, Curtin University, Perth, Western Australia, Australia. Fatovich, Daniel M. Emergency Medicine, Royal Perth Hospital, The University of Western Australia, Perth, Western Australia, Australia.
OBJECTIVES: To determine the magnitude and characteristics of the increase in ED demand in Western Australia (WA) from 2007 to 2013.

METHODS: We conducted a population-based longitudinal study examining trends in ED demand, stratified by area of residence, age group, sex, Australasian Triage Scale category and discharge disposition. The outcome measures were annual number and rate of ED presentations. We calculated average annual growth, and age-specific and age-standardised rates. We assessed the statistical significance of trends, overall and within each category, using the Mann-Kendall trend test and analysis of variance ANOVA. We also calculated the proportions of growth in ED demand that were attributable to changes in population and utilisation rate.

RESULTS: From 2007 to 2013, ED presentations increased by an average 4.6% annually from 739742 to 945244. The rate increased 1.4% from 354.1 to 382.6 per 1000 WA population ($P = 0.02$ for the trend). The main increase occurred in metropolitan WA, age 45+ years, triage category 2 and 3 and admitted cohorts. Approximately three-quarters of this increase was due to population change (growth and ageing) and one-quarter due to increase in utilisation.

CONCLUSION: Our study reveals a 4.6% annual increase in ED demand in WA in 2007-2013, mostly because of an increase in people with urgent and complex care needs, and not a shift (demand transfer) from primary care. This indicates that a system-wide integrated approach is required for demand management. Copyright © 2015 Australasian College for Emergency Medicine and Australasian Society for Emergency Medicine.


Interrater agreement between expert and novice in measuring inferior vena cava diameter and collapsibility index.

Bowra J, Uwagboe V, et al.

Bowra,Justin. Emergency Department, Royal North Shore Hospital, St Leonards, New South Wales, Australia. Uwagboe,Victor. Emergency Department, Royal North Shore Hospital, St Leonards, New South Wales, Australia. Goudie,Adrian. Emergency Department, Fremantle Hospital, Fremantle, Western Australia, Australia. Reid,Cliff. Emergency Department, Mona Vale Hospital, Sydney, New South Wales, Australia. Gillett,Mark. Emergency Department, Royal North Shore Hospital, St Leonards, New South Wales, Australia.

BACKGROUND: In critical care medicine, US views of the inferior vena cava (IVC) and its change with respiration are used to estimate the intravascular volume status of unwell patients and, in particular, to answer the question: 'Is this patient likely to be fluid responsive?' Most commonly in the literature, the subxiphisternal (SX) window in the longitudinal plane is utilised. To date, no study has specifically assessed interrater agreement in estimating IVC diameter between emergency medicine specialists (experts) and trainees (learners).

OBJECTIVES: To determine the interrater agreement between an expert (senior emergency specialist with US qualifications) and learner (emergency medicine trainee) when measuring IVC diameter (IVCD) and IVC collapsibility index (IVCCI) in the SX longitudinal US window in healthy volunteers.

METHODS: Healthy volunteers (ED staff) were scanned in the supine position using a sector (cardiac) probe of a portable US machine, in the SX longitudinal position. The maximum and minimum diameters of the IVC were measured in each of these positions and the IVCCI calculated. Results were analysed using Bland-Altman plots.

RESULTS: In the longitudinal SX window, the operators' measurements of maximum IVCD differed by an average of 1.9mm (95% limits of agreement -9.4mm to +5.5mm) and their measurement of IVCCI differed by an average of 4% (95% limits of agreement -30% to 38%).

CONCLUSIONS: The wide 95% limits of agreement demonstrate a poor interrater agreement between the IVC US measurements obtained by expert and learner users in the assessment of fluid status. These ranges are greater than clinically acceptable. Copyright © 2015 Australasian College for Emergency Medicine and Australasian Society for Emergency Medicine.


Near-infrared spectroscopy in the assessment of suspected sepsis in the emergency department.

MacDonald SP, Brown SG.

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BACKGROUND AND AIMS: The conventional approach to sepsis resuscitation involves early interventions targeting global oxygenation and macro-haemodynamic variables such as central venous and systemic arterial pressures. There is increasing recognition of the importance of microcirculatory changes in shock states, including sepsis, and the relationship of these to outcome. Near-infrared spectroscopy (NIRS) is a recently developed non-invasive technology that measures tissue oxygen saturations (StO2), which may be an indirect measure of the adequacy of the microcirculation. StO2 measurements, therefore, have the potential to identify patients who are at risk of progressing to organ dysfunction and could be used to guide resuscitation. This article reviews the current state of knowledge of NIRS in the setting of sepsis, examining its application, validity and prognostic value.

METHODS: A search of the relevant literature was performed using Medline, Embase and Cochrane databases, and a qualitative analysis was undertaken.

RESULTS: A limited number of observational studies, mostly conducted among patients with severe sepsis, have shown that NIRS may correlate with severity of illness but demonstrate a variable relationship between StO2 and outcome.


Near-infrared spectroscopy in the assessment of suspected sepsis in the emergency department.

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CONCLUSIONS: Outstanding questions still remain as to whether NIRS can help to risk-stratify patients with suspected sepsis in the emergency department and the utility of StO2 as a resuscitation target. Copyright Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to http://group.bmj.com/group/rights-licensing/permissions.

Publication Types: Review

Testosterone, dihydrotestosterone and estradiol are differentially associated with carotid intima-media thickness and the presence of carotid plaque in men without and with coronary artery disease.
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Clarifying the relationship of sex hormones to preclinical atherosclerosis could illuminate pathways by which androgens are associated with cardiovascular events and mortality. Our aim was to determine hormone profiles associated with carotid intima-media thickness (CIMT) and carotid atheroma, in men with and without known coronary artery disease (CAD). We included 492 community-based men aged 20-70 years (Group A) and 426 men with angiographically proven CAD aged <60 years (Group B). Fasting early morning sera were assayed for testosterone (T), dihydrotestosterone (DHT) and estradiol (E2) using mass spectrometry. CIMT and carotid plaque were assessed ultrasonographically. Mean (+/-SD) age was Group A: 53.8 +/- 12.6 and Group B: 49.6 +/- 5.1 years. Higher T was associated with reduced CIMT (-0.011 mm per 1-SD increase, p=0.042) and lower prevalence of carotid plaque (odds ratio [OR] per 1-SD increase, 0.68, p=0.012) in Group A, but not B. E2 was associated with increased CIMT in Group A (0.013 mm, p=0.011) but not B. Higher DHT and E2 were associated with reduced carotid plaque in Group B (DHT: OR=0.77, p=0.024; E2: OR=0.75, p=0.008), but not A. In community-dwelling men, higher T is associated with increased CIMT and lower prevalence of carotid plaque, while higher E2 is associated with worse CIMT. In men with CAD, higher DHT or E2 are associated with lower carotid plaque. T, DHT and E2 are differentially associated with preclinical carotid atherosclerosis in a cardiovascular phenotype-specific manner. Interventional studies are needed to examine effects of exogenous T and its metabolites DHT and E2, on atherogenesis.

Epilepsia. 2015; 56(9): 1425-31.
Is the first seizure epilepsy-and when?
Lawn N, Chan J, et al. Lawn,Nicholas. Department of Neurology, Royal Perth Hospital, Perth, Western Australia, Australia. Chan,Josephine. Department of Neurology, Royal Perth Hospital, Perth, Western Australia, Australia. Lee,Judy. Department of Neurology, Royal Perth Hospital, Perth, Western Australia, Australia. Dunne,John. Department of Neurology, Royal Perth Hospital, Perth, Western Australia, Australia. OBJECTIVE: Epilepsy has recently been redefined to include a single unprovoked seizure if the probability of recurrence is >60% over the following 10 years. This definition is based on the estimated risk of a third seizure after two unprovoked seizures, using the lower-limit 95% confidence interval (CI) at 4 years, and does not account for the initially high recurrence rate after first-ever seizure that rapidly falls with increasing duration of seizure freedom. We analyzed long-term outcomes after the first-ever seizure, and the influence of duration of seizure freedom on the likelihood of seizure recurrence, and their relevance to the new definition of epilepsy.
METHODS: Prospective analysis of 798 adults with a first-ever unprovoked seizure seen at a hospital-based first seizure clinic between 2000 and 2011. The likelihood of seizure recurrence was analyzed according to the duration of seizure freedom, etiology, electroencephalography (EEG), and neuroimaging findings.
RESULTS: The likelihood of seizure recurrence at 10 years was >60% in patients with epileptiform abnormalities on EEG or neuroimaging abnormalities, therefore, meeting the new definition of epilepsy. However, the risk of recurrence was highly time dependent; after a brief period (<12 weeks) of seizure freedom, no patient group continued to fulfill the new definition of epilepsy. Of 407 patients who had a second seizure, the likelihood of a third seizure at 4 years was 65% (95% CI 60-70%) and at 10 years was 85% (95% CI 79-91%).
SIGNIFICANCE: The duration of seizure freedom following first-ever seizure substantially influences the risk of recurrence, with none of our patients fulfilling the new definition of epilepsy after a short period of seizure freedom. When a threshold was applied based on the 10-year risk of a third seizure from our data, no first-seizure patient group ever had epilepsy. These data may be utilized in a definition of epilepsy after a first-ever seizure. Copyright Wiley Periodicals, Inc. © 2015 International League Against Epilepsy.

Familial hypercholesterolaemia (FH) is a common genetic cause of premature coronary heart disease (CHD). Globally, one baby is born with FH every minute. If diagnosed and treated early in childhood, individuals with FH can have normal life expectancy. This consensus paper aims to improve awareness of the need for early detection and management of FH children. Familial hypercholesterolaemia is diagnosed either on phenotypic criteria, i.e. an elevated low-density lipoprotein cholesterol (LDL-C) level plus a family history of elevated LDL-C, premature coronary artery disease and/or genetic diagnosis, or positive genetic testing.

Childhood is the optimal period for discrimination between FH and non-FH using LDL-C screening. An LDL-C >/=3.5 mmol/L (130 mg/dL) plus a family history of elevated LDL-C, premature coronary artery disease and/or genetic diagnosis, or positive genetic testing is considered FH.

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Familial hypercholesterolaemia (FH) is a common genetic cause of premature coronary heart disease (CHD). Globally, one baby is born with FH every minute. If diagnosed and treated early in childhood, individuals with FH can have normal life expectancy. This consensus paper aims to improve awareness of the need for early detection and management of FH children. Familial hypercholesterolaemia is diagnosed either on phenotypic criteria, i.e. an elevated low-density lipoprotein cholesterol (LDL-C) level plus a family history of elevated LDL-C, premature coronary artery disease and/or genetic diagnosis, or positive genetic testing.

Childhood is the optimal period for discrimination between FH and non-FH using LDL-C screening. An LDL-C >/=3.5 mmol/L (190 mg/dL) or an LDL-C >/=3.5 mmol/L (160 mg/dL) with family history of premature CHD and/or high baseline cholesterol in one parent, make the phenotypic diagnosis. If a parent has a genetic defect, the LDL-C cut-off for the child is >/=3.5 mmol/L (130 mg/dL). We recommend cascade screening of families using a combined phenotypic and genotypic strategy. In children, testing is recommended from age 5 years, or earlier if homozygous FH is suspected. A healthy lifestyle and statin treatment (from age 8 to 10 years) are the cornerstones of management of heterozygous FH. Target LDL-C is <3.5 mmol/L (130 mg/dL) if >10 years, or ideally 50% reduction from baseline if <10 years, especially with very high LDL-C, elevated lipoprotein(a), a family history of premature CHD or other cardiovascular risk factors, balanced against the long-term risk of treatment side effects. Identifying FH early and optimally lowering LDL-C over the lifespan reduces cumulative LDL-C burden and offers health and socioeconomic benefits. To drive policy change for timely detection and management, we call for further studies in the young. Increased awareness, early identification, and optimal treatment from childhood are critical to adding decades of healthy life for children and adolescents with FH.


Impact of nurse-mediated management on achieving blood pressure goal levels in primary care: Insights from the Valsartan Intensified Primary carE Reduction of Blood Pressure Study.

Carrington MJ, Jennings GL, et al.
mediated intervention patients achieved the greatest blood pressure falls and the highest level of blood pressure goal attainment. Practice nurse-mediated patients had a stricter blood pressure goal of 125/75 mmHg (33.7% vs. 27.3%, p=0.026). Practice nurse-intervention) and standard care management patients (150 +/- 16/88 +/- 11 vs. 150 +/- 17/89 +/- 11 mmHg, respectively).

Mean age was 59.3 +/- 12.0 years and 62% were men. Baseline blood pressure was similar in practice nurse-mediated (usual care or nurse-mediated intervention (n=283, 19.0%). Blood pressure goal attainment at 26-week follow-up was then compared. RESULTS: Mean age was 59.3 +/- 12.0 years and 62% were men. Baseline blood pressure was similar in practice nurse-mediated (usual care or intervention) and standard care management patients (150 +/- 16/88 +/- 11 vs. 150 +/- 17/89 +/- 11 mmHg, respectively).

Practice nurse-mediated patients had a stricter blood pressure goal of 125/75 mmHg (33.7% vs. 27.3%, p=0.026). Practice nurse-mediated intervention patients achieved the greatest blood pressure falls and the highest level of blood pressure goal attainment (39.2% vs. 35.0%). Practice nurse-mediated usual care (32.1%) and standard usual care (25.3%; p<0.001). Practice nurse-mediated intervention patients were almost two-fold more likely to achieve their blood pressure goal compared with standard usual care patients (adjusted odds ratio 1.92, 95% confidence interval 1.32 to 2.78; p=0.001).

CONCLUSION: There is greater potential to achieve blood pressure targets in primary care with practice nurse-mediated hypertension management.


Age-specific population centiles for androgen status in Australian men.

Handelsman DJ, Yeap B, et al.

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CONTEXT: The age-specific population profiles in men of circulating testosterone (T) and its two bioactive metabolites dihydrotestosterone (DHT) and estradiol (E2) across the adult lifespan and its determinants are not well described. OBJECTIVE: To deduce smoothed age-specific centiles of circulating testosterone T, DHT and E2 in men using pooled data from population-based studies in 3 Australian cities from liquid chromatography-mass spectrometry (LC-MS) steroid measurements in a single laboratory. DESIGN, SETTING AND PARTICIPANTS: Pooled data of 10,904 serum samples (serum T, DHT, E2, age, height, weight) from observational population-based studies in 3 major cities across Australia. MAIN OUTCOME MEASURES: Age-specific smoothed centiles for serum T, DHT and E2 in men aged 35 to 100 years deduced by large sample data analysis methods. RESULTS: Serum T, DHT and E2 decline gradually from ages 35 onwards with a more marked decline after 80 years of age. Higher weight, body mass index (BMI) and body surface area (BSA) as well as shorter stature are associated with reduced serum T, DHT and E2. CONCLUSIONS: Among Australian men, there is gradual progressive population-wide decline in androgen status during male ageing until the age of 80 years after which there is a more marked decline. Obesity and short stature are associated with reduced androgen status. Research into the age-related decline in androgen status should focus on the progressive accumulation of age-related comorbidities to better inform optimal clinical trial design.


Reply to Pembrey et al: 'ZNF277 microdeletions, specific language impairment and the meiotic mismatch methylation (3M) hypothesis'.

Ceroni F, Simpson NH, et al.

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Renal artery denervation for treatment of patients with obstructive sleep apnoea and resistant hypertension: Results from the Global SYMPLICITY Registry.

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Department of Medicine, University of Milano-Bicocca, St Gerardo Hospital, Monza, Italy (Narkiewicz) Medical University of Gdansk, Department of Hypertension and Diabetology, Gdansk, Poland (Ruliope) Hypertension Unit, Department of Nephrology, Hospital 12 de Octubre, Madrid, Spain (Schlaich) Royal Perth Hospital Unit, University of Western Australia, Perth, Australia (Schmieder) Universität Erlangen-Nürnberg, Medizinische Klinik 4, Nürnberg, Germany (Williams) Institute of Cardiovascular Sciences, University College London, London, United Kingdom

Aims: The Global SYMPLICITY Registry has prospectively enrolled over 2,000 patients with uncontrolled hypertension and with a high proportion of multiple comorbidities from around the world including obstructive sleep apnoea, which, like hypertension, is associated with increased sympathetic tone. This analysis of obstructive sleep apnoea aimed to determine if there is a difference in the blood pressure lowering effect of renal denervation based on the presence of obstructive sleep apnoea.

Methods and results: Patients were enrolled at the discretion of their treating physician according to local guidelines and treated per the SymplicityTM renal denervation system Instructions for Use. Office and 24-hour ambulatory blood pressure was collected for all patients and analysed for those with and without obstructive sleep apnoea. In 998 patients the mean age was 61 +/-12 years, 60% were male and mean body mass index was 31 +/-6 kg/m. A history of obstructive sleep apnoea was reported in 116 patients who were more likely to be male than the 752 patients without obstructive sleep (83% vs. 56%, p<0.0001), had a larger body mass index (34 +/-6 kg/m vs. 30 +/-5 kg/m, p<0.0001) more atrial fibrillation (19% vs. 11%, p=0.020), more left ventricular hypertrophy (25% vs. 15%, p=0.008) and more diabetes (52% vs. 39%, p<0.0001). Additionally, obstructive sleep apnoea patients were taking more antihypertensive medications (4.9 +/-1.4 vs. 4.4 +/-1.3, p<0.001) including a higher proportion of aldosterone antagonists (39% vs. 20%, p<0.0001), alpha 2 agonists (54% vs. 36%, p<0.001) and vasodilators (24% vs. 13%, p=0.001). Overall baseline office blood pressure was 164/89 +/-24/17 mm Hg and baseline 24-hour blood pressure was 152/85 +/-17/13 mm Hg. At 6 months, office systolic blood pressure reduction was -11.6 +/-25.3 mm Hg (p<0.001) and was -6.6 +/-18.0 mm Hg (p<0.001) for 24-hr systolic blood pressure change. Among obstructive sleep apnoea patients the baseline office systolic blood pressure was 166 +/-23 mm Hg which was reduced by -15.5 +/-24.4 mm Hg at 6 month (p<0.0001). Ambulatory 24-hr systolic blood pressure was reduced by -4.6 +/-17.1 mm Hg (n=73, p=0.024) from 156 +/-20 mm Hg at baseline. The 6 month change from baseline was not statistically different at 6 months between obstructive sleep apnoea and no obstructive sleep apnoea patients. Conclusions: Renal artery denervation resulted in significant blood pressure reductions in patients with and without obstructive sleep apnoea. The absence of a difference in BP change between obstructive sleep apnoea and non- obstructive sleep apnoea patients is surprising and it will be of interest to determine if this result is confirmed in the larger cohort of 2,100 patients that will be available for presentation in May. Confirmation of a significant blood pressure reduction may be particularly important for obstructive sleep apnoea patients who have a much higher proportion of comorbidities that put them at greater risk for cardiovascular events.

Publication Types: Conference Abstract

Fremantle experience of patients undergoing bioresorbable vascular scaffold implantation.

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Aims: Contemporary percutaneous coronary intervention (PCI) with current generation drug-eluting stents delivers anti-proliferative drugs to reduce instant restenosis. Stents have potential disadvantages such as late and very late stent thrombosis (ST), and the need for long-term antiplatelet therapy. Bioresorbable Vascular Scaffold (BVS) represents a novel approach to provide short term vessel support, maintain drug-delivery capability, without some of the long term limitations of metallic stents. To retrospectively assess the in-hospital MACE and clinical outcome [ST and target lesion revascularisation (TLR)] in the first 101 patients undergoing PCI using 2 generation BVS at our institution. Methods and results: We retrospectively analysed the PCI data of all patients undergoing BVS to evaluate the safety and efficacy of BVS in the real world clinical setting from August 2012 to October 2014. In-hospital MACE, ST, TLR events were identified from systematic review of case notes and our PCI database. Clinical follow-up was conducted by letters and telephone interview at an average of 18 months post index procedure. A total of 122 BVS were implanted in 101 patients (72% male; mean age 56 years; median number BVS 1.27/patient). Clinical presentation was with angina in 34/101, ACS- NSTEMI 45/101 and STEMI 22/101. Deployment was successful in 100/101 patients (121/122 BVS; 99%). Angiographic success
was achieved in 101 (100%) patients. The majority of lesions were located in the left anterior descending artery (35/101) and right coronary artery (41/101). In total 122 lesions were treated, the majority comprised of ACC/AHA type B lesion classification 76 (62%). There was angiographic evidence of mild or moderate calcification by visual assessment in 7/101 (6.9%) cases. Minimum coronary artery (41/101). In total 122 lesions were treated, the majority comprised of ACC/AHA type B lesion classification 76 (62%).

Methods and results: The Global SYMPLICITY Registry is a prospective, open-label, multicentre registry. Aims: We evaluated the long-term follow-up of a large cohort of hypertensive patients with a high proportion of comorbidities including renal dysfunction. Methods and results: The Global SYMPLICITY Registry is a prospective, open-label, multicentre registry. Patients are enrolled from 245 centres in 37 countries and are treated per the SymplicityTM renal denervation system protocol. Office and 24-hour ambulatory blood pressure change, laboratory values and protocol-defined safety events are collected. Patient selection is at the discretion of the treating physician according to local guidelines. In the first 1,000 enrolled patients, the mean age was 61 +/-12 years, 61% were male and mean body mass index was 30+/-6 kg/m. Comorbidities included diabetes mellitus (39%), renal dysfunction (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m, 23%), and history of cardiac disease (51%). Baseline office blood pressure was 165/89 +/-24/16 mm Hg and baseline 24-hour blood pressure was 154/86 +/-18/14 mmHg. At 1-year post-denervation, the composite safety endpoint was 3.9% (34/862), comprising 0.8% cardiovascular death, 1.6% hospitalisation for hypertensive crisis, 0.2% new renal artery stenosis >70%, 0.4% renal artery re-intervention, and 0.4% new-onset end-stage renal disease. The 1-year office systolic blood pressure reduction (n=740) was -13.0 +/-26.3 mmHg (p<0.001) and 24-hr systolic blood pressure change (n=740) was -8.3 +/-17.8 mmHg (p<0.001). Among the 231 patients with baseline renal dysfunction, the office systolic blood pressure reduction was -10.6 +/-26.8 mmHg at 1 year (p<0.001). Ambulatory 24-hr systolic blood pressure reduction was by -9.7 +/-20.1 mmHg (n=99, p<0.001). Mean eGFR of the total population decreased from 76.4+/-.25.1 at baseline to 71.9 +/-24.6 ml/min/1.73 m at 1-year. The subgroup of patients with chronic kidney disease at baseline had a mean eGFR of 48.7 +/-16.5 ml/min/1.73 m which declined slightly at 1-year to 45.7 +/-17.4 ml/min/1.73 m for 149 patients in this group. Conclusions: Renal denervation in a large real-world population resulted in significant blood pressure reductions 1-year post-procedure. Renal function, even among patients with baseline renal dysfunction, declined to a much lesser extent than would be expected based on published observations of renal function change in patients with uncontrolled hypertension. There were no long-term safety concerns following the denervation procedure. Two-year follow-up data for approximately 600 patients will be available for presentation in May.

Publication Types: Conference Abstract

Sustained treatment effect of alirocumab on Lp(a): Pooled analyses from 4,915 patients in ten phase 3 trials in the ODYSSEY program.

Gaudet D, Watts GF, et al.

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Background: Lipoprotein (a) [Lp(a)] is an independent risk factor for cardiovascular (CV) disease. Current treatment options for elevated Lp(a) levels are limited. Statins have not shown any effect on Lp(a). Purpose: To evaluate the treatment effect of alirocumab on serum Lp(a) using data from 10 Phase 3 trials of 24-78 week duration, conducted in patients with heterozygous familial hypercholesterolemia, high CV risk, and/or statin intolerance, as monotherapy or on a variety of background lipid-lowering therapies (LLTs). Methods: Pooled analyses were conducted across 2 trials (LONG TERM, HIGH FH, n=2,416) that compared alirocumab 150 mg every two weeks (Q2W) versus placebo and 8 trials that evaluated alirocumab 75 mg Q2W (increasing to 150 mg Q2W at Week 12 if LDL-C goals not achieved at Week 8) versus control. In 5 trials (COMBO I, OPTIONS I and II, ALTERNATIVE and MONO, n=1,456) the comparator was ezetimibe and in 3 trials (COMBO I, FH I and II, n=1,043) the comparator was placebo. Results: After 24 weeks, Lp(a) levels were reduced from baseline by 25% with alirocumab 150 mg Q2W (vs. control) and by up to 23.5% (Week 12, vs. control) in studies using 75 mg Q2W (p<0.0001; Table). Reductions were observed at Week 12...
and sustained through the end of the observation period (either Week 24 or 52, depending on the study). Treatment-emergent adverse event (TEAE) rates were generally similar between alirocumab and control patients. Common TEAEs in alirocumab-treated patients include influenza, headache, myalgia, and mild injection site reactions. Data up to 78 weeks will be available for presentation. Conclusions: Across the ODYSSEY program, alirocumab therapy resulted in a sustained and significant reduction in Lp(a) maintained for at least 1 year independent of statin use. The mechanism for this effect requires further investigation. (Table presented).


A contemporary model of cardiac rehabilitation improves accessibility and uptake.

Smith J, Briffa T, et al.

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Background and introduction: Following acute coronary syndrome (ACS), cardiac rehabilitation (CR) is guideline-advocated but widely underutilised and under-resourced. An alternative model of CR for cost effective secondary prevention (ACCES) was implemented and evaluated at a tertiary hospital in Western Australia. Purpose: Through service redesign, ACCES aimed to increase the proportion of patients receiving four guideline-advocated components of CR: an initial assessment, individualised plan, education and follow-up. Methods: A comparative group (historical) implementation study design evaluated effects on service accessibility and uptake. Patients from cardiology wards with a primary diagnosis of ACS discharged 1/4/2013-31/3/2014 (ACCES) were compared to controls discharged 1/4/2011-31/3/2012. Patients transferred directly to another hospital for continuing cardiology care, aged >80 years, or deceased within four weeks of discharge were excluded. A participatory action research approach helped guide service redesign. Surveys with ward staff (n pre/n post=44/21) and patients (76/66) occurred, supplemented with phone interviews (11/8) and focus groups (11/8) and feedback from CR staff (8), cardiologists (4), hospital management (4), associated external CR services (20) and general practitioners (18). CR, its components and associated processes of care were standardised. Results: ACCES was associated with a significant increase in the provision of each of the four CR components (Table 1) and resulted in almost twice as many patients receiving all four components, culminating in follow-up, by 6 months post discharge. Conclusion: ACCES compared with controls, engaged twice as many patients in CR, incorporating standardisation of care to improve in and post-hospital care. This increase in service utilisation was achieved with no additional staffing. These findings have important implications for the many CR programs with limited staff resources or relatively low levels of uptake. (Table Presented).


A comparison of paediatric and adult infectious diseases consultations in Australia and New Zealand.

Blyth CC, Walls T, et al.

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T. Walls, Department of Paediatrics, University of Otago, P.O. Box 4345, Christchurch Mail Centre, Christchurch 8140, New Zealand

The objective of this paper is to describe paediatric infectious diseases consultations across Australia and New Zealand. We surveyed infectious diseases physicians at 51 hospitals over a period of 2 weeks in 2012. Compared with adult consultations, paediatric consultations were more frequently received from general paediatricians/physicians and intensive care, yet less frequently from surgeons and emergency. Respiratory, skin/soft tissue and bone/joint infections were the most frequent consultations in children. These data demonstrate the breadth of formal infectious diseases consultations in children. Differences between paediatric and infectious diseases consultations need to be considered when planning both paediatric and adult physician training and future curriculum development.

European Journal of Human Genetics. 2015; 23(6).

Clinical utility gene card for: Familial hypobetalipoproteinaemia (APOB) - Update 2014.
25 days post initial injury a free rectus flap was used to cover the predominantly forehead defect. The second patient had a free reconstructions were performed on the two patients. The first patient had a free gracilis flap which failed five days post-operatively. We describe the flap reconstruction and outcomes of these patients and review the relevant literature. Three free flap electrical burns is reported infrequently in the literature. This case series looks at two patients with full thickness burns to the scalp and forehead requiring free flap reconstruction over 11 years at the Burns Unit at Royal Perth Hospital in Perth, Western Australia. The outcomes of both of the patients in this case series was positive and both have had satisfactory flap survival at the time of writing. Due to rare nature of this type of burn there is little published evidence outlining the definitive management of this type of injury. Level of Evidence: Level V, therapeutic study.

European Journal of Plastic Surgery. 2015; 38(3): 229-234. The reconstructive challenges of electrical burns to the scalp: A case series. Page SS, Murray A, et al. (Page, Murray, Jovic, Ball, Rawlins) Burns Unit, Royal Perth Hospital, Wellington Street, Perth, WA 6000, Australia. Soft tissue or bony loss to the scalp and forehead present a reconstructive challenge, especially in the young patient. Much literature is available on scalp and forehead reconstruction for primary malignant pathologies, however reconstruction for contact electrical burns is reported infrequently in the literature. This case series looks at two patients with full thickness burns to the scalp and forehead requiring free flap reconstruction over 11 years at the Burns Unit at Royal Perth Hospital in Perth, Western Australia. We describe the flap reconstruction and outcomes of these patients and review the relevant literature. Three free flap reconstructions were performed on the two patients. The first patient had a free gracilis flap which failed five days post-operatively. 25 days post initial injury a free rectus flap was used to cover the predominantly forehead defect. The second patient had a free latissimus dorsi flap completed one week after initial injury. Free flap reconstruction of scalp and forehead following contact electrical burns is complicated and challenging. The outcomes of both of the patients in this case series was positive and both have had satisfactory flap survival at the time of writing. Due to rare nature of this type of burn there is little published evidence outlining the definitive management of this type of injury. Level of Evidence: Level V, therapeutic study.

European Journal of Preventive Cardiology. 2015; 1: 592. Improved efficiencies in cardiac rehabilitation through service redesign. Maioran A, Julie Smith J, et al. (Maioran, Julie Smith, Rankin) Royal Perth Hospital, Cardiology, Perth, Australia (Garton-Smith) Royal Perth Hospital, Perth, Australia (Redfern) George Institute for Global Health, Sydney, Australia (Bremner, Briffa) University of Western Australia, Perth, Australia (Hendrie) Curtin University, Perth, Australia (Dimer) Heart Foundation, Perth, Australia A. Maioran, Royal Perth Hospital, Cardiology, Perth, Australia Purpose: Cardiac rehabilitation (CR) is widely recommended following acute coronary syndrome (ACS) but is both underutilised and under-resourced. An alternative model of CR for cost effective secondary prevention (ACCES) was implemented and evaluated at a West Australian tertiary hospital. The project aimed to increase the proportion of patients receiving four guideline-advocated CR components: an initial assessment, individualised plan, education and follow-up, through service redesign in an environment of unchanged staff resources. Methods: Patients discharged from cardiology wards with a primary diagnosis of ACS 1/4/ 2013-
31/3/2014 (ACCES group) were compared to patients discharged 1/4/2011-31/3/2012 (controls). Patients transferred directly to another hospital for continuing cardiology care, aged >80 years, or deceased within four weeks of discharge were excluded. A quality improvement framework involving key stakeholders (74 patients, 52 hospital staff, 18 General Practitioners) was undertaken to inform processes to support change. Ward nurses assumed a more active role in inpatient CR, supported by a new CR needs assessment tool. This enabled CR specialist nurses to focus on post discharge service provision. An automated referral process was established that generated a daily list of eligible patients for follow-up by CR staff post discharge. Results: The ACCES model was associated with a significant increase in the provision of each one of the four CR components (Table 1) and resulted in a near doubling in the proportion of patients who received all four components, culminating in follow-up. This equates to an increase of 264 patients per 1000 admissions. Conclusion: Clinical service redesign was associated with efficiencies in CR, doubling patient numbers serviced for no additional staffing. This finding has important implications for the many CR programs that have limited staff resources or relatively low levels of uptake. Improved access to CR is associated with changing the clinical course post ACS. (Table Presented).

Publication Types: Conference Abstract


**Integrated guidance on the care of familial hypercholesterolaemia from the International FH Foundation.**

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G.F. Watts, Department of Internal Medicine, University of Western Australia, Royal Perth Hospital, GPO Box X2213, Perth, WA 6847, Australia

Familial hypercholesterolaemia (FH) is a dominantly inherited disorder present from birth that markedly elevates plasma low-density lipoprotein (LDL) cholesterol and causes premature coronary heart disease. There are at least 20 million people with FH worldwide, but the majority remains undetected and current treatment is often suboptimal. To address this major gap in coronary prevention we present, from an international perspective, consensus-based guidance on the care of FH. The guidance was generated from seminars and workshops held at an international symposium. The recommendations focus on the detection, diagnosis, assessment and management of FH in adults and children, and set guidelines for clinical care of FH. They also refer to best practice for cascade screening and risk notifying and testing families for FH, including use of genetic testing. Guidance on treatment is based on risk stratification, management of non-cholesterol risk factors and safe and effective use of LDL lowering therapies. Recommendations are given on lipoprotein apheresis. The use of emerging therapies for FH is also foreshadowed. This international guidance acknowledges evidence gaps, but aims to make the best use of contemporary practice and technology to achieve the best outcomes for the care of FH. It should accordingly be employed to inform clinical judgment and be adjusted for country-specific and local healthcare needs and resources.

Publication Types: Review

European Psychiatry. 2015; 30: 1318.

**B-vitamins and depression.**

Ford A, Almeida OP, et al. (Ford, Almeida, Hirani) School of Psychiatry and Clinical Neurosciences, University of Western Australia, Perth, Australia (Flicker) School of Medicine, University of Western Australia, Perth, Australia (McCaul) WA Centre for Health and Ageing, University of Western Australia, Perth, Australia (Singh) Psychiatry, Royal Perth Hospital, Perth, Australia (Van Bockxmeer) Clinical Biochemistry, Royal Perth Hospital, Perth, Australia

A. Ford, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Perth, Australia

Introduction B-vitamin insufficiency is associated with depression but it is uncertain if treatment with these is effective in prevention or treatment. Objectives and Aims 1. To determine if daily supplementation with B-vitamins enhances response to antidepressants. 2. Systematic review and meta-analysis of randomised, placebo-controlled trials of B-vitamins for depressive symptoms in adults.

Methods 1. The B-VITAGE trial is a 52 week randomised, double-blind, placebo-controlled trial of citalopram together with vitamin...
various times from July 2003 to September 2009. Six of the nine surgeons continue to perform LRP as of August 2014. Mean 
MATERIAL & METHODS: 2943 LRP cases were performed by nine Australian surgeons. The criteria for inclusion into the study were 
Prostatectomy (RALP), LRP continues to be performed in Australian centres due to local surgeon experience, as well as geographical 
surgical treatment option for localized prostate cancer. Despite the increasing trend towards Robotic Assisted Laparoscopic 
means 0-75% {>7. Mean urinary continence at 12 months was 91.4% (range of operator means 89-97%) with data available from 
operator means 2.7%-18.5%), pT3a PSM 30.8% (range of operator means 16.7%-52.9%) and pT3b PSM 39.2% (range of operator 
respectively. Mean operating time was 168 minutes (range of operator means 117-224 minutes) with conversion to open surgery in 
mean length of stay was 2.5 days (range of operator means 1.7 - 3.0 days). Pathological specimens were 73.6%% pT2, 20.7% 
and data available from seven surgeons. CONCLUSIONS: The Australian experience of Fellowship trained surgeons performing LRP 
INTRODUCTION & OBJECTIVES: Laparoscopic Radical Prostatectomy (LRP) is a proven effective, trainable minimally invasive 
B12, B6 and folic acid in older adult participants with major depression. 2. Systematic review of 13 eligible trials of B-vitamin 
supplementation for the reduction, remission and prevention of clinically significant depressive symptoms. Results Remission was 
achieved by 78.1% and 79.4% of participants treated with placebo (n=76) and vitamins (n=77) by week 12 (p=0.328), and by 
75.8% and 85.5% at week 52 (effect of intervention over 52 weeks: odds ratio, OR=2.49; 95% confidence interval, 
95%CI=1.12,5.51). The risk of subsequent relapse among those who had achieved remission of symptoms at week 12 was lower in the 
vitamin group (OR=0.33, 95%CI=0.12,0.94). Short-term use of vitamins did not improve depressive symptoms in adults with 
major depression treated with antidepressants (standardised mean difference=-0.12, 95% CI=-0.45,0.22), but more prolonged 
consumption decreased the risk of relapse (OR=0.33, 95% CI=0.12,0.94) and the onset of clinically significant symptoms in people at risk (risk ratio=0.65, 95% CI=0.43,0.98). Conclusions Short-term use of B-vitamins does not appear to benefit depressive 
symptoms although longer use may enhance and sustain antidepressant response and decrease the risk of relapse or onset of 
clinically significant depression.

Defining the appropriate waiting time between multiple-breath nitrogen washout measurements.
Salamon ER, Gain KR, et al. 
Salamon,Elizabeth R. Respiratory Medicine, Royal Perth Hospital, Perth, Australia. Gain,Kevin R. Respiratory Medicine, Royal Perth 
Hospital, Perth, Australia. Hall,Graham L. Respiratory Medicine, Princess Margaret Hospital for Children, Perth, Australia Telethon 
Kids Institute, University of Western Australia, Perth, Australia graham.hall@telethonkids.org.au. 
Publication Types: Letter 

The Australian laparoscopic non robotic radical prostatectomy experience-analysis of 2943 cases. 
(Louie-Johnsun, Handmer) Gosford, Wyoong and Gosford Private Hospitals, Dept. of Urology, Gosford, Australia (Chabert) Pindara 
Private Hospital, Dept. of Urology, Benowa, Australia (Cohen) Uropath and University of Western Australia, Dept. of Pathology, 
Perth, Australia (Gianduzzo) Wesley Hospital, Dept. of Urology, Brisbane, Australia (Kearns) Barwon Health University Hospital, 
Dept. of Urology, Geelong, Australia (Moon) Epworth Healthcare, Dept. of Urology, Melbourne, Australia (Ooi) St Vincents Private 
Hospital, Dept. of Urology, East Melbourne, Australia (Shannon) Hollywood Private Hospital, Dept. of Urology, Perth, Australia 
(Sofield) Bethesda Hospital, Dept. of Urology, Perh, Australia (Tan) Royal Perth Hospital, Dept. of Urology, Perth, Australia 
M.W. Louie-Johnsun, Gosford, Wyoong and Gosford Private Hospitals, Dept. of Urology, Gosford, Australia 
INTRODUCTION & OBJECTIVES: Laparoscopic Radical Prostatectomy (LRP) is a proven effective, trainable minimally invasive 
surgical treatment option for localized prostate cancer. Despite the increasing trend towards Robotic Assisted Laparoscopic 
Prostatectomy (RALP), LRP continues to be performed in Australian centres due to local surgeon experience, as well as geographical 
and financial barriers to robotic access. We analysed the Australian experience of high volume Fellowship trained LRP surgeons. 
MATERIAL & METHODS: 2943 LRP cases were performed by nine Australian surgeons. The criteria for inclusion into the study were a 
processively collected database with a minimum of 100 consecutive LRP cases. The surgeons' LRP experience commenced at 
various times from July 2003 to September 2009. Six of the nine surgeons continue to perform LRP as of August 2014. Mean 
surgeon annual case load was 45 ranging from 22 to 95 cases per year. Data were analysed for demographic, perioperative, 
oncological and functional outcomes. RESULTS: The mean age of patients were 61.5 (39-83) years and mean preoperative prostate 
specific antigen (PSA) was 7.4 (0.1-87) ng/ml. 19%, 63% and 18% were preoperative D'Amico's low, intermediate and high risk 
respectively. Mean operating time was 168 minutes (range of operator means 117-224 minutes) with conversion to open surgery in 
0.5% (range of operator means, 0-1.5%) and a blood transfusion rate of 1.1% (range of operator means, 0-2.5%). The overall 
mean length of stay was 2.5 days (range of operator means 1.7 - 3.0 days). Pathological specimens were 73.6% pT2, 20.7% 
pt3a, 5.5% pt3b and 0.1% pt4. Overall positive surgical margins (PSM) occurred in 15.9% of cases with pT2 PSM 9.8% (range of 
operator means, 0-15.9%) and pT3a PSM 30.8% (range of operator means, 16.7%-52.9%) and pT3b PSM 39.2% (range of operator 
means 0-75% {>7. Mean urinary continence at 12 months was 91.4% (range of operator means 89-97%) with data available from 
five surgeons. Mean 12 months potency (preop IIEF >17) after unilateral and bilateral nerve spare was 35.2% and 47.2% 
respectively with data available from four surgeons. Biochemical recurrence occurred in 10.6% with a mean follow up of 17 months 
and data available from seven surgeons. CONCLUSIONS: The Australian experience of Fellowship trained surgeons performing LRP 
demonstrates favourable perioperative, oncological and functional outcomes in comparison to published data for open, laparoscopic 
and robotic assisted radical prostatectomy. In our Australian centres, LRP remains an acceptable minimally invasive surgical 
treatment for prostate cancer despite the increasing use of robotic assisted surgery.

Publication Types: Conference Abstract 

Angiography reveals novel features of the retinal vasculature in healthy and diabetic mice. 
McLenachan S, Magno AL, et al. 
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WA 6009, Australia (McLenachan, Chen) Ocular Tissue Engineering Laboratory, Lions Eye Institute, 2 Verdun Street, Nedlands, WA 
6009, Australia (Magno, Rakoczy) Department of Molecular Ophthalmology, Lions Eye Institute, Nedlands, WA 6009, Australia 
The mouse retina is a commonly used animal model for the study of pathogenesis and treatment of blinding retinal vascular diseases such as diabetic retinopathy. In this study, we aimed to characterize normal and pathological variations in vascular anatomy in the mouse retina using fluorescein angiography visualized with scanning laser ophthalmoscopy and optical coherence tomography (SLO-OCT). We examined eyes from C57BL/6j wild type mice as well as the Ins2<sup>Akita</sup>/sup> and Akimba mouse models of diabetic retinopathy using the Heidelberg Retinal Angiography (HRA) and OCT system. Angiography was performed on three focal planes to examine distinct vascular layers. For comparison with angiographic data, ex vivo analyses, including indocyanine green angiography, histology and 3D confocal scanning laser microscopy were performed in parallel. All layers of the mouse retinal vasculature could be readily visualized during fluorescein angiography by SLO-OCT. Blood vessel density was increased in the deep vascular plexus (DVP) compared with the superficial vascular plexus (SVP). Arteriolar and venular topographies were established and structural differences were observed between venular types. Unexpectedly, the hyaloid artery was found to persist in 15% of C57BL/6j mice, forming anastomoses with peripheral retinal capillaries. Fluorescein leakage was easily detected in Akimba retinae by angiography, but was not observed in Ins2<sup>Akita</sup>/sup> mice. Blood vessel density was increased in the DVP of 6 month old Ins2<sup>Akita</sup>/sup> mice, while the SVP displayed reduced branching in precapillary arterioles. In summary, we present the first comprehensive characterization of the mouse retinal vasculature by SLO-OCT fluorescence angiography. Using this clinical imaging technique, we report previously unrecognized variations in C57BL/6j vascular anatomy and novel features of vascular retinopathy in the Ins2<sup>Akita</sup> mouse model of diabetes.


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**Expert Opinion On Drug Metabolism & Toxicology. 2015; 11(9): 1505-15.**

**Evolocumab in the treatment of dyslipidemia: pre-clinical and clinical pharmacology.**

Page MM, Watts GF.

Page,Michael M. a 1 Royal Perth Hospital, Lipid Disorders Clinic, Cardiovascular Medicine, Perth, Australia.

INTRODUCTION: Statins are the mainstay of lipid-lowering therapies targeted at reducing cardiovascular risk. However, they do not completely obviate risk, not all patients tolerate them, and they are not sufficiently effective in patients with very high plasma levels of low-density lipoprotein-cholesterol (LDL-C) such as those with familial hypercholesterolemia (FH) or patients with elevated plasma levels of lipoprotein(a) [Lp(a)]. Recent advances in the understanding of lipoprotein metabolism have led to the development of the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors including evolocumab, which lowers plasma levels of LDL-C by 50 - 75% as monotherapy or in combination with statin therapy.

AREAS COVERED: We discuss in this review the rationale and background behind the development of evolocumab, and its pharmacodynamics and pharmacokinetics. We then discuss the current state-of-play of relevant clinical trials.

EXPERT OPINION: The dramatic reduction in plasma levels of LDL-C attributable to evolocumab is anticipated to translate into lower rates of atherosclerotic cardiovascular disease, but this hypothesis remains to be proven. Also to be established are the long-term safety and economic benefits of evolocumab. PCSK9 inhibitors will also probably provide a valuable option for patients with statin intolerance, those with FH and patients with elevated plasma levels of Lp(a).


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**Expert Opinion on Emerging Drugs. 2015; 20(2): 299-312.**

**Emerging PCSK9 inhibitors for treating dyslipidemia: buttressing the gaps in coronary prevention.**

Page MM, Watts GF.

Page,Michael M. Lipid Disorders Clinic, Cardiovascular Medicine, Royal Perth Hospital, Perth, Australia.

INTRODUCTION: Atherosclerotic cardiovascular disease (ACVD) is the leading cause of mortality worldwide. An abnormally high plasma level of low-density lipoprotein-cholesterol is a major contributor to ACVD, an effect that can be attenuated by cholesterol-lowering therapies, particularly statins. A new class of drugs, the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, will add another option for further reducing cardiovascular events in patients at high risk of ACVD, including those with familial hypercholesterolaemia (FH) and intolerance to statins. Patients with elevated levels of lipoprotein(a) [Lp(a)] are difficult to treat with conventional therapies, and may also benefit from PCSK9 inhibitors.

AREAS COVERED: This paper discusses the medical need for additional cholesterol-lowering therapies and the scientific rationale and current therapeutic status of PCSK9 inhibitors.

EXPERT OPINION: The use of anti-PCSK9 mAbs is the leading form of therapy for inhibiting PCSK9 and is likely to provide genuine hope for patients with FH, statin intolerance and elevated Lp(a). Their ability to reduce cardiovascular events in patients maximally treated with statins and other existing therapies remains to be proven, and is the subject of major ongoing clinical trials.


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**Expert Opinion on Investigational Drugs. 2015; 24(6): 761-8.**

**Early Investigational TNF receptor antagonists for the treatment of ulcerative colitis.**

Lawrence IC.

Lawrence,Ian C. University of Western Australia, Harry Perkins Institute for Medical Research, School of Medicine and
Familial hypercholesterolemia (FH) remains under-diagnosed and under-treated in the community setting. Earlier evidence suggested a prevalence of 1:500 worldwide but newer evidence suggests it is more common. Less than 15% of FH patients are ever diagnosed, with children and young adults rarely tested despite having the most to gain given their lifetime exposure. Increasing awareness among primary care teams is critical to improve the detection profile for FH. Cascade testing in the community setting needs a sustainable approach to be developed to facilitate family tracing of index cases. The use of the Dutch Lipid Clinic Network Criteria score to facilitate a phenotypic diagnosis is the preferred approach adopted in Australia and eliminates the added competition, medications costs should fall allowing for greater patient access.


Challenges in the care of familial hypercholesterolemia: a community care perspective.
Brett T, Watts GF, et al.
Brett, Tom. a 1 General Practice and Primary Health Care Research, School of Medicine, The University of Notre Dame Australia, Fremantle, Western Australia, Australia. Watts, Gerald F. b 2 School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia. Watts, Gerald F. c 3 Lipid Disorders Clinic, Cardiometabolic Services, Royal Perth Hospital, Western Australia, Australia. Arnold-Reed, Diane E. a 1 General Practice and Primary Health Care Research, School of Medicine, The University of Notre Dame Australia, Fremantle, Western Australia, Australia. Garton-Smith, Jacquie. f 6 Cardiovascular Health Network, Department of Health Western Australia, Perth, Western Australia, Australia. Garton-Smith, Jacquie. g 7 Clinical Services, Royal Perth Hospital, Perth, Western Australia, Australia. Vickery, Alistair W. h 8 School of Primary, Aboriginal and Rural Health Care, University of Western Australia, CRAWLEY, Western Australia, Australia. Ryan, Jacqueline Dm. b 2 School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia. Pang, Jing. b 2 School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia. Perera, C, Chakrabarti R, et al.
The Eye Phone Study: reliability and accuracy of assessing Snellen visual acuity using smartphone technology.


An evaluation of Admedus’ tissue engineering process-treated (ADAPT) bovine pericardium patch (CardioCel) for the repair of cardiac and vascular defects.
(Strange) University of Notre Dame, Fremantle, WA, Australia (Strange) Royal Prince Alfred Hospital, Sydney, NSW, Australia (Strange) Pulmonary Hypertension Society Australia and New Zealand (PHSANZ), Sydney, Australia (Brizard) Cardiac Surgery Unit, Royal Children's Hospital, Melbourne, VIC, Australia (Karl) Queensland Paediatric Cardiac Service, Mater Children's Hospital, Brisbane, QLD, Australia (Neethling) Department of Cardiothoracic Surgery, School of Surgery, Fremantle Hospital, Fremantle, WA, Australia

G. Strange, University of Notre Dame, Fremantle, WA, Australia
Tissue engineers have been seeking the 'Holy Grail' solution to calcification and cytotoxicity of implanted tissue for decades. Tissues with all of the desired qualities for surgical repair of congenital heart disease (CHD) are lacking. An anti-calcification tissue engineering process (ADAPT TEP) has been developed and applied to bovine pericardium (BP) tissue (CardioCel, AdmedusRegen Pty Ltd, Perth, WA, Australia) to eliminate cytotoxicity, improve resistance to acute and chronic inflammation, reduce calcification and facilitate controlled tissue remodeling. Clinical data in pediatric patients, and additional pre-market authorized prescriber data demonstrate that CardioCel performs extremely well in the short term and is safe and effective for a range of congenital heart deformations. These data are supported by animal studies which have shown no more than normal physiologic levels of calcification, with good durability, biocompatibility and controlled healing.


Eye. 2015; 29(7): 888-94.

Publication Types: Review

Australia, University of Melbourne, Victoria, Australia [2] Department of Psychological Sciences and Statistics, Faculty of Health, Arts and Design, Swinburne University of Technology, Victoria, Australia. Crowston, J. Department of Ophthalmology, Centre for Eye Research Australia, University of Melbourne, Victoria, Australia.

PurposeSmartphone-based Snellen visual acuity charts have become popularized; however, their accuracy has not been established. This study aimed to evaluate the equivalence of a smartphone-based visual acuity chart with a standard 6-m Snellen visual acuity (6SVVA) chart.MethodsFirst, a review of available Snellen chart applications on iPhone was performed to determine the most accurate application based on optotype size. Subsequently, a prospective comparative study was performed by measuring conventional 6SVVA and then iPhone visual acuity using the ‘Snellen’ application on an Apple iPhone 4. ResultsEleven applications were identified, with accuracy of optotype size ranging from 4.4-39.9%. Eighty-eight patients from general medical and surgical wards in a tertiary hospital took part in the second part of the study. The mean difference in logMAR visual acuity between the two charts was 0.02 logMAR (95% limit of agreement -0.332, 0.372 logMAR). The largest mean difference in logMAR acuity was noted in the subgroup of patients with 6SVVA worse than 6/18 (n=5), who had a mean difference of two Snellen visual acuity lines between the charts (0.276 logMAR). Conclusion We did not identify a Snellen visual acuity app at the time of study, which could predict a patient’s standard Snellen visual acuity within one line. There was considerable variability in the optotype accuracy of apps. Further validation is required for assessment of acuity in patients with severe vision impairment. 


Malnutrition and infant and young child feeding in informal settlements in Mumbai, India: findings from a census. Bentley A, Das S, et al. UCL Institute for Global Health, Institute of Child Health 30 Guilford Street, London, WC1N 1EH, UK. SNEHA (Society for Nutrition, Education and Health Action), Urban Health Centre, Chota Sion Hospital 60 Feet Road, Shahunagar, Dharavi, Mumbai, 400017, Maharashtra, India.

Childhood malnutrition remains common in India. We visited families in 40 urban informal settlement areas in Mumbai to document stunting, wasting, and overweight in children under five, and to examine infant and young child feeding (IYCF) in children under 2 years. We administered questions on eight core WHO IYCF indicators and on sugary and savory snack foods, and measured weight and height of children under five. Stunting was seen in 45% of 7450 children, rising from 15% in the first year to 56% in the fifth. About 16% of children were wasted and 4% overweight. 46% of infants were breastfed within the first hour, 63% were described as exclusively breastfed under 6 months, and breastfeeding continued for 12 months in 74%. The indicator for introduction of solids was met for 41% of infants. Only 13% of children satisfied the indicator for minimum dietary diversity, 43% achieved minimum meal frequency, and 5% had a minimally acceptable diet. About 63% of infants had had sugary snacks in the preceding 24 h, rising to 78% in the second year. Fried and salted snack foods had been eaten by 34% of infants and 66% of children under two. Stunting and wasting remain unacceptably common in informal settlements in Mumbai, and IYCF appears problematic, particularly in terms of dietary diversity. The ubiquity of sugary, fried, and salted snack foods is a serious concern: substantial consumption begins in infancy and exceeds that of all other food groups except grains, roots, and tubers.


Vitamin E and oxidative stress in abetalipoproteinemia and familial hypobetalipoproteinemia. Burnett JR, Hooper Aj. Burnett, J. Department of Clinical Biochemistry, PathWest Laboratory Medicine, Royal Perth Hospital, Perth, Australia; School of Medicine & Pharmacology, University of Western Australia, Perth, Australia. Electronic address: john.burnett@health.wa.gov.au. Hooper, Amanda J, Department of Clinical Biochemistry, PathWest Laboratory Medicine, Royal Perth Hospital, Perth, Australia; School of Medicine & Pharmacology, University of Western Australia, Perth, Australia; School of Pathology & Laboratory Medicine, University of Western Australia, Perth, Australia.

Abetalipoproteinemia (ABL) and familial hypobetalipoproteinemia (FHBL) are genetic diseases characterized by low density lipoprotein deficiency. ABL presents early in life with the gastroenterological manifestations of fat malabsorption, steatorrhea, and failure to thrive, and later in life, with progressive ophthalmopathy and neuropathy as a result of deficiency of the fat-soluble vitamins A and E. Heterozygous FHBL subjects are usually asymptomatic, but may develop fatty liver disease. In homozygous (compound heterozygous) FHBL, the clinical and biochemical features are indistinguishable from those of ABL and treatment recommendations are the same: dietary fat restriction to prevent steatorrhea, and long-term high-dose vitamin E and A supplementation to prevent or at least slow the progression of neuromuscular and retinal degenerative disease. Despite their low plasma vitamin E levels, individuals with heterozygous FHBL do not require vitamin E supplementation. There are conflicting reports on whether increased oxidative stress is seen in ABL; these differences may relate to the small size of patient groups as well as differences in patient age and dose of vitamin E supplementation, or the contribution from dietary sources of vitamin E. High density lipoproteins in ABL appear to be severely oxidized yet able to inhibit platelet aggregation by binding to scavenger receptor
B1. We review the role of vitamin E and oxidative stress in ABL and FHBL. Crown Copyright © 2015. Published by Elsevier Inc. All rights reserved.
Publication Types: Review

Frontiers in Oncology. 2015; 5: 42.
Clinical implications of circulating tumor cells of breast cancer patients: role of epithelial-mesenchymal plasticity.
McInnes LM, Jacobson N, et al. McInnes,Linda M. School of Surgery, The University of Western Australia, Perth, WA, Australia. Jacobson,Natalie. School of Surgery, The University of Western Australia, Perth, WA, Australia. School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia. Dowling,Anthony. Department of Medical Oncology, St Vincent’s Hospital Melbourne, Melbourne, VIC, Australia. Thompson,Erik W. Institute of Health and Biomedical Innovation, School of Biomedical Sciences, Queensland University of Technology, Brisbane, QLD, Australia; St. Vincent's Institute, Melbourne, VIC, Australia; Department of Surgery, St Vincent's Hospital, University of Melbourne, Melbourne, VIC, Australia; University of Melbourne, Melbourne, Australia. Saunders,Christobel M. School of Surgery, The University of Western Australia, Perth, WA, Australia.

There is increasing interest in circulating tumor cells (CTCs) due to their purported role in breast cancer metastasis, and their potential as a "liquid biopsy" tool in breast cancer diagnosis and management. There are, however, questions with regards to the reliability and consistency of CTC detection and to the relationship between CTCs and prognosis, which is limiting their clinical utility. There is increasing acceptance that the ability of CTCs to alter from an epithelial to mesenchymal phenotype plays an important role in determining the metastatic potential of these cells. This review examines the phenotypic and genetic variation, which has been reported within CTC populations. Importantly, we discuss how the detection and characterization of CTCs provides additional and often differing information from that obtained from the primary tumor, and how this may be utilized in determining prognosis and treatment options. It has been shown for example that hormone receptor status often differs between the primary tumor and CTCs, which may help to explain failure of endocrine treatment. We examine how CTC status may introduce alternative treatment options and also how they may be used to monitor treatment. Finally, we discuss the most interesting current clinical trials involving CTC analysis and note further research that is required before the breast cancer "liquid biopsy" can be realized.
Publication Types: Review

Device-based approaches for renal nerve ablation for hypertension and beyond.
Thorp AA, Schlaich MP. Thorp,Alicia A. Neurovascular Hypertension and Kidney Disease Laboratory, Baker IDI Heart and Diabetes Institute Melbourne, VIC, Australia; School of Public Health and Preventive Medicine, Monash University Melbourne, VIC, Australia. Schlaich,Markus P. Neurovascular Hypertension and Kidney Disease Laboratory, Baker IDI Heart and Diabetes Institute Melbourne, VIC, Australia; Department of Cardiovascular Medicine, Alfred Hospital Melbourne, VIC, Australia; Faculty of Medicine, Nursing and Health Sciences, Monash University Melbourne, VIC, Australia; Royal Perth Hospital Unit, School of Medicine and Pharmacology, University of Western Australia Perth, WA, Australia.

Animal and human studies have demonstrated that chronic activation of renal sympathetic nerves is critical in the pathogenesis and perpetuation of treatment-resistant hypertension. Bilateral renal denervation has emerged as a safe and effective, non-pharmacological treatment for resistant hypertension that involves the selective ablation of efferent and afferent renal nerves to lower blood pressure. However, the most recent and largest randomized controlled trial failed to confirm the primacy of renal denervation over a sham procedure, prompting widespread re-evaluation of the therapy's efficacy. Disrupting renal afferent sympathetic signaling to the hypothalamus with renal denervation lowers central sympathetic tone, which has the potential to confer additional clinical benefits beyond blood pressure control. Specifically, there has been substantial interest in the use of renal denervation as either a primary or adjunct therapy in pathological conditions characterized by central sympathetic overactivity such as renal disease, heart failure and metabolic-associated disorders. Recent findings from pre-clinical and proof-of-concept studies appear promising with renal denervation shown to confer cardiovascular and metabolic benefits, largely independent of changes in blood pressure. This review explores the pathological rationale for targeting sympathetic renal nerves for blood pressure control. Latest developments in renal nerve ablation modalities designed to improve procedural success are discussed along with prospective findings on the efficacy of renal denervation to lower blood pressure in treatment-resistant hypertensive patients. Preliminary evidence in support of renal denervation as a possible therapeutic option in disease states characterized by central sympathetic overactivity is also presented.
Publication Types: Review

Measurement of fecal calprotectin improves monitoring and detection of recurrence of Crohn's disease after surgery.
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Wright,Emily K. Department of Gastroenterology, St Vincent's Hospital, Melbourne, Australia; University of Melbourne, Melbourne, Australia. Kamm,Michael A. Department of Gastroenterology, St Vincent's Hospital, Melbourne, Australia; University of Melbourne, Melbourne, Australia. Electronic address: mkamm@unimelb.edu.au. De Cruz,Peter. Department of Gastroenterology, St Vincent's Hospital, Melbourne, Australia; University of Melbourne, Melbourne, Australia. Hamilton,Amy L. Department of Gastroenterology, St


Chandran, Sujievvan. Department of Gastroenterology, Austin Health Melbourne, Victoria, Australia. Efthymiou, Marios. Department of Gastroenterology, Austin Health Melbourne, Victoria, Australia. Kaffes, Arthur. Department of Gastroenterology, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia. Chen, John Wei. Department of Surgery, Flinders Medical Centre, Adelaide, South Australia, Australia. Kwan, Vu. Department of Gastroenterology, Westmead Hospital, Sydney, New South Wales, Australia. Murray, Michael. Department of Gastroenterology, Pindara Private Hospital, Gold Coast, Queensland, Australia. Williams, David. Department of Gastroenterology, St. Vincent's Hospital, Sydney, New South Wales, Australia. Nguyen, Nam Quoc. Department of Gastroenterology, Royal Adelaide Hospital, Adelaide, South Australia, Australia. Tam, William. Department of Gastroenterology, Lyell McEwin Hospital, Adelaide, South Australia, Australia. Welsh, Christine. Department of Gastroenterology, Townsville Hospital, Townsville, Queensland, Australia. Chong, Andre. Department of Gastroenterology, Fremantle Hospital, Fremantle, Western Australia, Australia. Gupta, Saurabh. Department of Gastroenterology, Princess Alexandra Hospital, Brisbane, Queensland, Australia. Devereaux, Ben. Department of Gastroenterology, Royal Brisbane Hospital, Brisbane, Queensland, Australia. Tagkalis, Peter. Department of Gastroenterology, Royal Melbourne Hospital, Melbourne, Victoria, Australia. Parker, Frank. Department of
BACKGROUND: Recent medical literature on novel lumen-apposing stents for the treatment of pancreatic fluid collections (PFCs) is limited by small numbers, solo operators, and single-center experience.

OBJECTIVE: To evaluate a recently developed lumen-apposing, fully covered self-expandable metal stent (FCSEMS) in the management of PFCs.

DESIGN: Retrospective case series.

SETTING: Thirteen tertiary and private health care centers across Australia.

PATIENTS: Forty-seven patients (median age 51 years) who underwent endoscopic management of PFCs.

INTERVENTION: Insertion of FCSEMS after PFC puncture under EUS guidance. A subgroup of 9 patients underwent direct endoscopic necrosectomy.

MAIN OUTCOME MEASUREMENTS: Technical and clinical success rate, adverse event rate.

RESULTS: The technical success rate was 53 of 54 patients (98.1%), and the initial clinical success rate was 36 of 47 (76.6%), which was sustained for more than 6 months in 36 of 36 (94.4%). Early adverse events included 4 cases (7.4%) of stent migration during direct endoscopic necrosectomy, 4 cases (7.4%) of sepsis, 1 case (1.9%) of bleeding, and 1 case (1.9%) of stent migration into the fistula tract. Late adverse events were 6 (11.1%) spontaneous stent migrations, 3 (5.6%) recurrent stent occlusions, 3 (5.6%) tissue ingrowth/overgrowth, and 2 (3.7%) bleeding into PFC. The majority of stents inserted (48 of 54, 88.9%) and removed (31 of 35, 88.6%) in our study were described by the operator as superior to pigtail stents with regard to ease of use.

LIMITATIONS: Retrospective study.

CONCLUSION: Although FCSEMSs are technically easier to insert and remove compared with traditional pigtail stents, there are significant limitations to the widespread use of FCSEMSs in the management of PFCs. These include cost, adverse events, and lower-than-expected resolution rates.

Corrigendum to "Hospital costs associated with depression in a cohort of older men living in Western Australia" [General Hospital Psychiatry 36, (2014) 33-37].

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Publication Types: Erratum


Evolutionary dynamics of methicillin-resistant Staphylococcus aureus within a healthcare system.

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OBSTIQUE: Developing a vaccine that is cross-reactive between HCV genotypes requires data on T cell antigenic targets that extend beyond genotype-1. We characterised T cell immune responses against HCV genotype-3, the most common infecting protein. Additional responses to wild type but not variant HLA predicted peptides were defined. Major sequence viral variability was targeted non-structural proteins at a high magnitude, whereas in chronic disease T cells were absent or skewed to target structural between genotype-1 and genotype-3 variants was assessed. RESULTS: In resolved genotype-3 infection, T cells preferentially targeted non-structural proteins at a high magnitude, whereas in chronic disease T cells were absent or skewed to target structural proteins. Additional responses to wild type but not variant HLA predicted peptides were defined. Major sequence viral variability was observed within genotype-3 and between genotypes 1 and 3 HCV at T cell targets in resolved infection and at dominant epitopes, with limited T cell cross-reactivity between viral variants. Overall 41 CD4+/CD8+ genotype-3 T cell targets were identified with limited T cell cross-reactivity between viral variants. Overall 41 CD4+/CD8+ genotype-3 T cell targets were identified with limited T cell cross-reactivity in resolved and chronic disease. Therefore, viral regions targeted in natural HCV infection may not be attractive targets for a vaccine that aims to protect against multiple HCV genotypes.

CONCLUSIONS: Our results clearly demonstrate that, alongside clinical practice and antibiotic usage, competition between clones also has an important role in driving the evolution of nosocomial pathogen populations.


Choroidal involvement in Rosai-Dorfman syndrome may be depicted and followed using enhanced depth imaging optical coherence tomography (EDI-OCT).

Isaacs TW, Veerumeen TL, et al.
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Gut. 2015.
The broad assessment of HCV genotypes 1 and 3 antigenic targets reveals limited cross-reactivity with implications for vaccine design.

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Institute of Immunology and Infectious Diseases, Murdoch University, Perth, Western Australia, Australia School of Anatomy, Physiology and Human Biology, University of Western Australia, Perth, Western Australia, Australia.

OBJECTIVE: Developing a vaccine that is cross-reactive between HCV genotypes requires data on T cell antigenic targets that extend beyond genotype-1. We characterised T cell immune responses against HCV genotype-3, the most common infecting genotype in the UK and Asia, and assessed within genotype and between genotype cross-reactivity. DESIGN: T cell targets were identified in 140 subjects with either acute, chronic or spontaneously resolved HCV genotype-3 infection using (1) overlapping peptides and (2) putative human leucocyte antigens (HLA)-class-I wild type and variant epitopes through the prior assessment of polymorphic HCV genomic sites associated with host HLA, in IFNgamma-ELISpot assays. CD4+/CD8+ T cell subsets were defined and viral variability at T cell targets was determined through population analysis and viral sequencing. T cell cross-reactivity between genotype-1 and genotype-3 variants was assessed. RESULTS: In resolved genotype-3 infection, T cells preferentially targeted non-structural proteins at a high magnitude, whereas in chronic disease T cells were absent or skewed to target structural proteins. Additional responses to wild type but not variant HLA predicted peptides were defined. Major sequence viral variability was observed within genotype-3 and between genotypes 1 and 3 HCV at T cell targets in resolved infection and at dominant epitopes, with limited T cell cross-reactivity between viral variants. Overall 41 CD4+/CD8+ genotype-3 T cell targets were identified with minimal overlap with those described for HCV genotype-1. CONCLUSIONS: HCV T cell specificity is distinct between genotypes with limited T cell cross-reactivity in resolved and chronic disease. Therefore, viral regions targeted in natural HCV infection may not serve as attractive targets for a vaccine that aims to protect against multiple HCV genotypes.


Haematologica. 2015; 100: 566.

Diagnosis and management of thrombotic thrombocytopenic purpura (TTP) in Australia-findings from the first five years of the Australian TTP registry (2009-2014).

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Results of a phase 3 randomized controlled study evaluating the efficacy and safety of idelalisib (IDELA) in combination with ofatumumab (OFA) for previously treated chronic lymphocytic leukemia (CLL).

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Background: IDELA is a selective oral PI3Kdelta inhibitor approved in combination with rituximab for previously treated patients with CLL. Aims: This open-label study (NCT01659021) compared the safety and efficacy of IDELA plus OFA vs OFA in patients with relapsed or refractory CLL. Methods: Patients with CLL progressing <24 months from last therapy, and who had received >2 cycles of a purine analogue or bendamustine, were randomized 2:1 to either Arm A (IDELA 150 mg BID continuously plus OFA, 300 mg IV week 1, then 1 gm IV weekly x 7 and q 4 week x 4) or Arm B (OFA, same as Arm A except 2 gm was substituted for 1 gm dosing). Stratification was performed for relapsed vs refractory, del17p and/or TP53 mutation, and IGHV mutation. Response and progression were assessed by an independent review committee (IRC) based on clinical data and imaging using modified IWCLL 2008 criteria. The primary endpoint was PFS and alpha-protected secondary endpoints were confirmed ORR, lymph node response (LNR), OS, PFS in patients with del17p and/or TP53 mutation, and CR rate. Results are from the final analysis of the primary endpoint. Results: Patient characteristics were balanced in the 2 arms: median age 68; Rai III/IV 18/13%. Median number of prior regimens 3, refractory disease 49%, del17p/TP53 mut 40%, IGHV unm 78%. The median exposure to IDELA was 12.3 months (range: 0.2-23.9). Disposition and efficacy are shown in the Table 1. There was a disproportionate dropout rate with an excess of Arm B patients discontinuing prior to PD or death. Efficacy results, demonstrating superiority of the combination, were consistent across risk groups. The median duration of response was 14.9 months in Arm A and 6.7 months in Arm B patients, respectively. The most frequent non-haematologic Gr 3 AEs in Arm A patients were diarrhea/collitis (20.2%), pneumonia (12.7%), and febrile neutropenia (11.6%). Grade 3/4 ALT/AST elevation occurred in 12.9% of Arm A patients. Infusion-related reactions of any Grade/Gr >3 were reported in 16.8% / 2.3% and 26.7%/1.2% of patients in Arms A and B, respectively. Deaths in Arm A occurred in 16.8% of patients (until 30 days post-discontinuation) and 6.9% off-study; and in Arm B in 9.3% of patients on-study and 16.3% offstudy. TEAEs leading to death were reported in 10.4% (exposure-adjusted rate=0.10/yr) and 7.0% (exposure-adjusted rate=0.18/yr) of patients in Arms A and B, respectively. (Table Presented) Summary and Conclusions: IDELA plus OFA yielded superior PFS, ORR, and LNR compared to OFA in patients with previously treated CLL, including within high-risk subgroups. Safety was manageable with a profile similar to that previously observed with IDELA in CLL trials. Publication Types: Conference Abstract

Evaluation of health promotion training for the Western Australian Aboriginal maternal and child health sector.

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ISSUE ADDRESSED: The evaluation of health promotion training for the Western Australian (WA) Aboriginal maternal and child health (MCH) sector. METHODS: Fifty-one MCH professionals from five regions in WA who attended one of three health promotion short courses in 2012-2013 were invited to complete an online survey or a telephone interview, between 4 to 17 months post-course. Respondents were asked how they had utilised the information and resources from the training and to identify the enabling factors or barriers to integrating health promotion into their work practices subsequently. RESULTS: Overall response rate was 33% (n=17). 94% of respondents reported they had utilised the information and resources from the course and 76% had undertaken health promotion activities since attending the course. Building contacts with other MCH providers and access to planning tools were identified as valuable components of the course. Barriers to translating knowledge into practice included financial constraints and lack of organisational support for health promotion activity. CONCLUSIONS: Health promotion training provides participants with the skills and confidence to deliver health promotion strategies in their communities. The training presents an opportunity to build health professionals' capacity to address some determinants of poor health outcomes among pregnant Aboriginal women and their babies. SO WHAT?: Training would be enhanced if accompanied by ongoing support for participants to integrate health promotion into their work practice, organisational development including health promotion training for senior management, establishing stronger referral pathways among partner organisations to support continuity of care and embedding training into MCH workforce curricula.


Rapid detection of health-care-associated bloodstream infection in critical care using multipathogen real-time polymerase chain reaction technology: a diagnostic accuracy study and systematic review.

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BACKGROUND: There is growing interest in the potential utility of real-time polymerase chain reaction (PCR) in diagnosing bloodstream infection by detecting pathogen deoxyribonucleic acid (DNA) in blood samples within a few hours. SeptiFast (Roche Diagnostics GmbH, Mannheim, Germany) is a multipathogen probe-based system targeting ribosomal DNA sequences of bacteria and fungi. It detects and identifies the commonest pathogens causing bloodstream infection. As background to this study, we report a systematic review of Phase III diagnostic accuracy studies of SeptiFast, which reveals uncertainty about its likely clinical utility based on widespread evidence of deficiencies in study design and reporting with a high risk of bias. OBJECTIVE: Determine the accuracy of SeptiFast real-time PCR for the detection of health-care-associated bloodstream infection, against standard microbiological culture. DESIGN: Prospective multicentre Phase III clinical diagnostic accuracy study using the standards for the reporting of diagnostic accuracy studies criteria. SETTING: Critical care departments within NHS hospitals in the north-west of England. PARTICIPANTS: Adult patients requiring blood culture (BC) when developing new signs of systemic inflammation. MAIN OUTCOME MEASURES: SeptiFast real-time PCR results at species/genus level compared with microbiological culture in association with independent adjudication of infection. Metrics of diagnostic accuracy were derived including sensitivity, specificity, likelihood ratios and predictive values, with their 95% confidence intervals (CIs). Latent class analysis was used to explore the diagnostic performance of culture as a reference standard. RESULTS: Of 1006 new patient episodes of systemic inflammation in 853 patients, 922 (92%) met the inclusion criteria and provided sufficient information for analysis. Index test assay failure occurred on 69 (7%) occasions. Adult patients had been exposed to a median of 8 days (interquartile range 4-16 days) of hospital care, had high levels of organ support activities and recent antibiotic exposure. SeptiFast real-time PCR, when compared with culture-proven bloodstream infection at species/genus level, had better specificity (85.8%, 95% CI 83.3% to 88.1%) than sensitivity (50%, 95% CI 39.1% to 60.8%). When compared with pooled diagnostic metrics derived from our systematic review, our clinical study revealed lower test accuracy of SeptiFast real-time PCR, mainly as a result of low diagnostic sensitivity. There was a low prevalence of BC-proven pathogens in these patients (9.2%, 95% CI 7.4% to 11.2%) such that the post-test probabilities of both a positive (26.3%, 95% CI 19.8% to 33.7%) and a negative SeptiFast test (5.6%, 95% CI 4.1% to 7.4%) indicate the potential limitations of this technology in the diagnosis of bloodstream infection. However, latent class analysis indicates that BC has a low sensitivity, questioning its relevance as a reference test in this setting. Using this analysis approach, the sensitivity of the SeptiFast test was low but also appeared significantly better than BC. Blood samples identified as positive by either culture or SeptiFast real-time PCR were associated with a high probability (> 95%) of infection, indicating higher diagnostic rule-in utility than was apparent using
conventional analyses of diagnostic accuracy. CONCLUSION: SeptiFast real-time PCR on blood samples may have rapid rule-in utility for the diagnosis of health-care-associated bloodstream infection but the lack of sensitivity is a significant limiting factor. Innovations aimed at improved diagnostic sensitivity of real-time PCR in this setting are urgently required. Future work recommendations include technology developments to improve the efficiency of pathogen DNA extraction and the capacity to detect a much broader range of pathogens and drug resistance genes and the application of new statistical approaches able to more reliably assess test performance in situation where the reference standard (e.g. blood culture in the setting of high antimicrobial use) is prone to error. STUDY REGISTRATION: The systematic review is registered as PROSPERO CRD42011001289. FUNDING: The National Institute for Health Research Health Technology Assessment programme. Professor Daniel McAuley and Professor Gavin D Perkins contributed to the systematic review through their funded roles as codirectors of the Intensive Care Foundation (UK).


Intermittent positive pressure ventilation increases diastolic pulmonary arterial pressure in advanced COPD.

Wrobel Jeremy P. Department of Medicine, Monash University, Melbourne, Australia; Allergy, Immunology & Respiratory Medicine, The Alfred, Melbourne, Australia: Advanced Lung Disease Unit, Royal Perth Hospital, Perth, Australia. Electronic address: jeremy.wrobel@health.wa.gov.au. Thompson, Bruce R. Department of Medicine, Monash University, Melbourne, Australia; Allergy, Immunology & Respiratory Medicine, The Alfred, Melbourne, Australia. Stuart-Andrews, Christopher R. Allergy, Immunology & Respiratory Medicine, The Alfred, Melbourne, Australia. Kee, Kirk. Department of Medicine, Monash University, Melbourne, Australia; Allergy, Immunology & Respiratory Medicine, The Alfred, Melbourne, Australia; Allergy, Immunology & Respiratory Medicine, The Alfred, Melbourne, Australia; Allergy, Immunology & Respiratory Medicine, The Alfred, Melbourne, Australia. Snell, Gregory L. Department of Medicine, Monash University, Melbourne, Australia; Allergy, Immunology & Respiratory Medicine, The Alfred, Melbourne, Australia. Buckley, Mark. Department of Anaesthesia, The Alfred, Melbourne, Australia; Baxter, Andrew. Department of Anaesthesia, The Alfred, Melbourne, Australia; Baxter, Andrew. Department of Anaesthesia, The Alfred, Melbourne, Australia; Baxter, Andrew. Department of Anaesthesia, The Alfred, Melbourne, Australia; Baxter, Andrew. Department of Anaesthesia, The Alfred, Melbourne, Australia.objectives: To measure the impact of intermittent positive pressure ventilation (IPPV) on diastolic pulmonary arterial pressure (dPAP) and pulmonary pulse pressure in patients with advanced COPD.

BACKGROUND: The physiological effects of raised intrathoracic pressures upon the pulmonary circulation have not been fully established.

METHODS: 22 subjects with severe COPD receiving IPPV were prospectively assessed with pulmonary and radial arterial catheterization. Changes in dPAP were assessed from end-expiration to early inspiration during low and high tidal volume ventilation.

RESULTS: Inspiration during low tidal volume IPPV increased the median [IQR] dPAP by 3.9 [2.5-4.8] mm Hg (P < 0.001). During high tidal volume, similar changes were observed. The IPPV-associated change in dPAP was correlated with baseline measures of PaO2 (rho = 0.65, P = 0.005), pH (rho = 0.64, P = 0.006) and right atrial pressure (rho = -0.53, P = 0.011).

CONCLUSIONS: In severe COPD, IPPV increases dPAP and reduces pulmonary pulse pressure during inspiration. Copyright 2015 Elsevier Inc. All rights reserved.

Publication Types: Research Support, Non-U.S. Gov't

Heart Lung and Circulation. 2015; 24(3): 250-256.

Systematic detection of familial hypercholesterolaemia in primary health care: A community based prospective study of three methods.

Kirke AB, Barbour RA, et al.

Heart Lung Circ. 2015. Penetrating Cardiac Injury Managed Without Surgery but with Systemic Heparinisation.
A 36-year-old woman presented to hospital after a penetrating chest injury. She was haemodynamically stable. Echocardiography revealed left ventricular thrombus, with minimal pericardial effusion and no associated cardiac injuries. Intravenous anticoagulation was commenced for her intracardiac thrombus and her pericardial effusion was monitored with serial echocardiography. She remained well, was converted to warfarin and discharged home day 12 post admission, with cautious follow-up given her risk of late effusion and tamponade. Follow-up imaging revealed resolution of her intracardiac thrombus. She remains well to date.


Heart Lung Circ. 2015. Response to Commentary.
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Reverse cardiac remodeling after renal denervation: Atrial electrophysiologic and structural changes associated with blood pressure lowering.
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P.M. Kistler, Baker IDI Heart and Diabetes Institute, 75 Commercial Rd, Melbourne, VIC 3004, Australia
Background Hypertension is the most common modifiable risk factor associated with atrial fibrillation. Objective The purpose of this study was to determine the effects of blood pressure (BP) lowering after renal denervation on atrial electrophysiologic and structural remodeling in humans. Methods Fourteen patients (mean age 64 +/- 9 years, duration of hypertension 16 +/- 11 years, on 5 +/- 2 antihypertensive medications) with treatment-resistant hypertension underwent baseline 24-hour ambulatory BP monitoring, echocardiography, cardiac magnetic resonance imaging, and electrophysiologic study. Electrophysiologic study included measurements of P-wave duration, effective refractory periods, and conduction times. Electroanatomic mapping of the right atrium was completed using CARTO3 to determine local and regional conduction velocity and tissue voltage. Bilateral renal denervation was performed, and all measurements repeated after 6 months. Results After renal denervation, mean 24-hour BP reduced from 152/84 mm Hg to 141/80 mm Hg at 6-month follow-up (P <.01). Global conduction velocity increased significantly (0.98 +/- 0.13 m/s to 1.2 +/- 0.16 m/s at 6 months, P <.01), conduction time shortened (32 +/- 5 ms to 27 +/- 6 ms, P <.01), and complex fractionated activity was reduced (37% +/- 14% to 19% +/- 12%, P =.02). Changes in conduction velocity correlated positively with changes in 24-hour mean systolic BP (R<sup>2</sup> = 0.55, P =.01). There was a significant reduction in left ventricular mass (139 +/- 37 g to 120 +/- 29 g, P <.01) and diffuse ventricular fibrosis (T<inf>1</inf> partition coefficient 0.39 +/- 0.07 to 0.31 +/- 0.09, P =.01) on cardiac magnetic resonance imaging. Conclusion BP reduction after renal denervation is associated with improvements in regional and global atrial conduction and reductions in ventricular mass and fibrosis. Whether changes in electrical and structural remodeling are solely due to BP lowering or are due in part to intrinsic effects of renal denervation remains to be determined.


Radiofrequency ablation versus antiarrhythmic drugs for atrial fibrillation: Collaborative meta-analysis of quality of life, hospitalization, and morbidity outcomes.
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K.C. Siontis
Introduction: Radiofrequency ablation (RFA) reduces atrial fibrillation (AF) recurrence compared to antiarrhythmic drugs (AAD), but its effect on quality of life (QoL), hospitalization and morbidity is not established. We aimed at addressing these issues via a collaborative meta-analysis of randomized controlled trials (RCT). Methods: Eligible RCTs were identified through an exhaustive literature search, and primary investigators were invited to contribute standardized and unpublished QoL, hospitalization, and non-
procedure-related bleeding and stroke data. Random effects risk ratios (RR) and Hedges standardized mean differences of mean changes from baseline to follow-up with corresponding 95% confidence intervals (CI) were derived for categorical and continuous data, respectively. Heterogeneity was quantified with the I-squared statistic. Results: Ten RCTs (1540 patients) were analyzed (A4, APAF, Forleo et al, MANTRA-PAF, Oral et al, RAAFT-2, SARA, ThermoCool AF, TTOP-AF, Wazni et al). RFA resulted in modest or major improvements in most QoL measures but a trend for reduction of this effect was observed with increasing follow-up (overall P-for-trend <0.05). RFA marginally reduced the risk of hospitalization at follow-up ranging from 1 to 4 years among trials (RR 0.56, 95% CI 0.30-1.05). A total of 11 and 10 nonprocedure-related bleeding and stroke events were collected, respectively, without any identifiable differences between RFA and AAD in meta-analyses. Conclusions: QoL outcomes are superior with RFA. This effect, even though diminishing with time, may be mediated by a decrease in hospitalizations in addition to reduction of AF recurrences. (Figure Presented).


Incidence and significance of early recurrence of atrial tachyarrhythmias after catheter ablation for paroxysmal AF: Insights from the advice trial.
Hoffmann BA, Willems S, et al. (Hoffmann, Willems, Khairy, Levesque, Rostock, Weerasooriya, Novak, Verma, Arenzent, Deisenhofer, Andrade, Rivard, Guerra, Dubuc, Thibault, Tajac, Roy, Nattel, Macle) University Heart Center, Hamburg, Germany, Montreal Heart Institute, Montreal, QC, Canada, Montreal Heart Institute Coordinating Center, Montreal, QC, Canada, Johannes Gutenberg- University Mainz, University Hospital, II. Medical Clinic, Dept. of Electrophysiology, Mainz, Germany, Royal Perth Hospital, Perth, Australia, Southlake Regional Health Centre, Newmarket, ON, Canada, Universitäts-Herzzentrum Freiburg-Bad Krozingen, Bad Krozingen, Germany, Deutsches Herzcentrum Muenchhen, Munich, Germany, Montreal Heart Institute, Montreal, QC, Canada B.A. Hoffmann

Introduction: The clinical relevance of early recurrence (ER) of atrial tachyarrhythmia (AT) after catheter ablation (CA) of atrial fibrillation (AF) is still a matter of debate although a so-called “blanking period” (BP) of 3 months after CA is generally accepted and supported by current guidelines. We sought to investigate the clinical outcome in relation to the prevalence and timing of ER during the first 3 months after CA. Methods: The ADVICE trial randomized pts. undergoing pulmonary vein (PV) isolation (PVI) for paroxysmal AF to undergo additional ablation (n=147) or not (n=137) in case of dormant PV conduction. Randomly selected pts. without dormant PV conduction were included in a registry (n=117). A total of 401 pts. (292 males, 59+/-10 years) were followed for 12 months with Tele-ECG monitoring. Pts. with symptomatic documented AT > 30 sec within the first 3 months (ER) after CA were stratified according to the timing of ER during that period. Late recurrence (LR) was defined as any recurrence AT > 30 sec between 3-12 months. Results: A total of 179 pts. (44.6%) experienced ER during the first (n=53), the first two (N=44) or the first three months (N=82) post-CA. Overall, pts. with ER had a significantly lower freedom from LR as compared to pts. with no ER (23.1% vs 69.7%; p<0.0001). When ER episodes persisted >2 months after CA the long term success rate was low (8.5%) as compared to ER solely occurring during the first (63.5%) or the first two months (31.8%); p<0.0001 (Figure). Conclusions: The prevalence and timing of ER episodes during the BP determines the long-term success rate following CA of PAF. Late cure is rare when ER episodes persist > 2 months following CA. (Figure Presented).

Time to get help? Acute myocardial infarction and delay in calling an ambulance.
Neubeck L, Maiorana A. Neubeck,Lis. Sydney Nursing School, Charles Perkins Centre, Building D17, University of Sydney, Camperdown, NSW 2006; The George Institute for Global Health, 83-117 Missenden Road, Camperdown, NSW 2050. Electronic address: lis.neubeck@sydney.edu.au. Maiorana,Andrew. Advanced Heart Failure and Cardiac Transplant Service, Royal Perth Hospital, Perth, WA, 6000; School of Physiotherapy and Exercise Science, Curtin University, Bentley, WA, 6102.

The Development of a New Cardiac Rehabilitation Needs Assessment Tool (CRNAT) for Individualised Secondary Prevention.
Smith J, Garton-Smith J, et al. Smith,Julie. National Heart Foundation, Subiaco, Western Australia, 6008; Cardiovascular Health Network, Department of Health, East Perth, Western Australia, 6001; Department of Cardiology, Royal Perth Hospital, Perth, Western Australia, 6000. Garton-Smith,Jacquie. Cardiovascular Health Network, Department of Health, East Perth, Western Australia, 6001; Clinical Services, Royal Perth Hospital, Perth, Western Australia, 6000; Bentley Armadale Medicare Local, Bentley, Western Australia, 6102. Briffa,Tom. Cardiovascular Health Network, Department of Health, East Perth, Western Australia, 6001; Cardiovascular Research Group, School of Population Health, The University of Western Australia, Nedlands, 6009. Maiorana,Andrew. Cardiovascular Health Network, Department of Health, East Perth, Western Australia, 6001; Advanced Heart Failure and Cardiac Transplant Service, Royal Perth Hospital, Perth, Western Australia, 6000; School of Physiotherapy and Exercise Science, Curtin University, Bentley, Western
OBJECTIVE: We report the successful transplantation of a heart following an out-of-body time of 611 minutes into a recipient with hospital on day 15 post-transplant with normal cardiac function.

RESULTS: Although requiring ECMO and inotropic support in the first 17 hours post-transplant, the patient was discharged to ward nurses leading to important changes to the process of administering the tool to streamline its use in an inpatient setting.

CONCLUSIONS: Feedback from end users is important when developing a new clinical tool to ensure it meets their requirements. Feedback from ward nurses led to important changes to the process of administering the tool to streamline its use in an inpatient setting.

CONCLUSIONS: Feedback from end users is important when developing a new clinical tool to ensure it meets their requirements. Feedback from ward nurses led to important changes to the process of administering the tool to streamline its use in an inpatient setting.


Successful Heart Transplant after Ten Hours Out-of-body Time using the TransMedics Organ Care System.

Stamp, Nikki L. Department of Cardiothoracic Surgery, Royal Perth Hospital, Perth, WA. Electronic address: niki1_stamp@iinet.net.au. Shah, Amit. Advanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA. Vincent, Vij. Department of Anaesthesia, Clinical Perfusion, Royal Perth Hospital, Perth, WA. Wright, Brian. Department of Anaesthesia, Clinical Perfusion, Royal Perth Hospital, Perth, WA. Wood, Clare. Advanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA. Pavely, Warren. Department of Anaesthesia, Clinical Perfusion, Royal Perth Hospital, Perth, WA. Cokis, Chris. Department of Anaesthesia, Clinical Perfusion, Royal Perth Hospital, Perth, WA. Chih, Sharon. Advanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA. Dembo, Lawrence. Advanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA. Larkin, Peter. Department of Cardiothoracic Surgery, Royal Perth Hospital, Perth, WA. Objective: We report the successful transplantation of a heart following an out-of-body time of 611 minutes into a recipient with dilated cardiomyopathy and left ventricular assist device implant.

Patients: Our patient was urgently waiting for a cardiac transplant whilst receiving LVAD support. Recurrent VF and repeated AICD shocks necessitated this action.

RESULTS: Although requiring ECMO and inotropic support in the first 17 hours post-transplant, the patient was discharged from hospital on day 15 post-transplant with normal cardiac function.

CONCLUSION: We report some of the salient points of the process and discuss the utility of this technology to an Australian transplant unit.


Age-specific Gender Differences in Long-term Recurrence and Mortality following Incident Myocardial Infarction: A Population-based Study.

Nedkoff, L., Atkins, E., et al.

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BACKGROUND: Higher mortality following myocardial infarction (MI) is reported in women compared with men with short-term follow-up. Our study aim was to compare long-term gender- and age-specific outcomes following incident MI.

METHODS: 30-day survivors of incident MI from 2003-2009 were identified from linked administrative data in Western Australia. Outcomes identified were recurrent MI, and cardiovascular and all-cause mortality. Follow-up data was available until 30(th) June 2011. Unadjusted risk out to eight-years was estimated from Kaplan-Meier survival curves, and multivariate Cox regression models were used to estimate relative risk in women compared with men by age group.

RESULTS: There were 12,420 30-day survivors of incident MI from 2003-2009 (males 71.2%). Women had higher levels of comorbidities across all age groups compared with men. Unadjusted event risks were higher in women than men overall, underpinned by higher risk of recurrent MI in 55-69 year-old women and of cardiovascular mortality across all age groups in women. Gender differences were generally attenuated after adjustment for demographic factors and comorbidities.

CONCLUSIONS: This study highlights the elevated risk of cardiovascular events in women compared with men with long-term follow-up, and demonstrates the need for improved long-term secondary prevention in this patient group. Crown Copyright © 2014. Published by Elsevier B.V. All rights reserved.


Successful Heart Transplant after Ten Hours Out-of-body Time using the TransMedics Organ Care System.

Stamp, Nikki L. Department of Cardiothoracic Surgery, Royal Perth Hospital, Perth, WA. Electronic address: niki1_stamp@iinet.net.au. Shah, Amit. Advanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA. Vincent, Vij. Department of Anaesthesia, Clinical Perfusion, Royal Perth Hospital, Perth, WA. Wright, Brian. Department of Anaesthesia, Clinical Perfusion, Royal Perth Hospital, Perth, WA. Wood, Clare. Advanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA. Pavely, Warren. Department of Anaesthesia, Clinical Perfusion, Royal Perth Hospital, Perth, WA. Cokis, Chris. Department of Anaesthesia, Clinical Perfusion, Royal Perth Hospital, Perth, WA. Chih, Sharon. Advanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA. Dembo, Lawrence. Advanced Heart Failure and Cardiac Transplantation Service, Department of Cardiology, Royal Perth Hospital, Perth, WA. Larkin, Peter. Department of Cardiothoracic Surgery, Royal Perth Hospital, Perth, WA. Objective: We report the successful transplantation of a heart following an out-of-body time of 611 minutes into a recipient with dilated cardiomyopathy and left ventricular assist device implant.

Patients: Our patient was urgently waiting for a cardiac transplant whilst receiving LVAD support. Recurrent VF and repeated AICD shocks necessitated this action.

Results: Although requiring ECMO and inotropic support in the first 17 hours post-transplant, the patient was discharged from hospital on day 15 post-transplant with normal cardiac function.

Conclusion: We report some of the salient points of the process and discuss the utility of this technology to an Australian transplant unit. Crown Copyright © 2015. Published by Elsevier B.V. All rights reserved.
Isoniazid poisoning: Pharmacokinetics and effect of hemodiagnosis in a massive ingestion.

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Isbister, Geoffrey K. School of Medicine and Public Health, University of Newcastle, Newcastle, New South Wales, Australia.

Isoniazid is a rare overdose that causes seizures and there is limited evidence to guide treatment. We report a 20-year-old female migrant who presented with recurrent seizures after ingesting 25g of isoniazid. She was treated with activated charcoal, repeated doses of midazolam for the seizures, and given multiple doses of pyridoxine (14mg), limited by availability. She was admitted to intensive care, and 5.5 hours post-ingestion, she was commenced on continuous veno-venous hemodiafiltration (CVVHDF). She was extubated after 24 hours and CVVHDF was ceased 6 hours later (30 hours post-overdose). Her renal function remained normal and her initial lactate was the highest at 2.3. She made a full recovery. Five plasma samples were collected before, during, and after CVVHDF, and isoniazid was quantified with liquid chromatography-tandem mass spectrometry. A pharmacokinetic analysis of time-isoniazid concentration data was fitted to a two-compartment model with first-order input (with fixed ka) with the effect of CVVHDF modeled as a time-dependent covariate. This suggested that there was initially good clearance with CVVHDF (4 times endogenous clearance), which rapidly declined within hours. 

Conclusion: Reduction in ferritin by phlebotomy does not improve liver enzymes, hepatic fat, or IR in patients undergoing phlebotomy, there was no correlation between number of phlebotomy sessions and change in HS, liver injury, or IR from baseline to end of study. Conclusion: Reduction in ferritin by phlebotomy does not improve liver enzymes, hepatic fat, or IR in people.

Re: Essential service standards for equitable national cardiovascular care for Aboriginal and Torres Strait Islander people.

Davis, Tim, Davis, WA, et al.

Davis, Timothy M. E. University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, Australia.

Davis, Wendy A. University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, Australia.

McAulay, Daniel. Edith Cowan University, Karrakatta Health Centre for Indigenous Australian Education and Research, Mt Lawley, Western Australia, Australia and Australian National University, Australia. Mostafa, Ahmed.

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Therapeutics Research Centre, School of Medicine, University of Queensland, Brisbane, Queensland, Australia. Roberts, Michael S.

School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, South Australia, Australia.

Isbister, Geoffrey K. School of Medicine and Public Health, University of Newcastle, Newcastle, New South Wales, Australia.

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Conclusion: Reduction in ferritin by phlebotomy does not improve liver enzymes, hepatic fat, or IR in people.
Hepatology. 2015.

Reply: Does the death knell toll for phlebotomy in NAFLD?
Adams LA, Crawford DH, et al.
School of Medicine & Pharmacology, University of Western Australia, Crawley, Australia.
Dept. Gastroenterology & Hepatology, Sir Charles Gairdner Hospital, Perth, Australia.
School of Medicine, University of Queensland, Brisbane, Australia.
Department of Gastroenterology, Greenslopes Private Hospital, Brisbane, Australia.
School of Physics, University of Western Australia, Crawley, Australia.
Dept. of Gastroenterology, Fiona Stanley Hospital, Perth, Australia.
Faculty of Health Sciences, Monash University, Perth, Australia.
Institute for Immunology and Infectious Diseases, Murdoch University, Perth, Australia.

Kupffer cell-macrophage communication is essential for initiating murine liver progenitor cell-mediated liver regeneration.
Elsegood,CL, Chan CW, et al.
Elsegood,Caryn L. School of Chemistry and Biochemistry, The University of Western Australia, Crawley, Western Australia, Australia.
Elsegood,CL, School of Biomedical Sciences, CHIRI Biosciences Research Precinct, Curtin University, Bentley, Western Australia, Australia. Chan,Chun Wei. School of Medicine and Pharmacology, The University of Western Australia, Fremantle, Western Australia, Australia. Chan,Chun Wei. School of Biological Sciences and Biotechnology, Murdoch University, Murdoch, Western Australia, Australia. Deegli-Esposti,Mariapia A. Immunology and Virology Program, Centre for Ophthalmology and Visual Science, The University of Western Australia, Nedlands, Western Australia, Australia. Degli-Esposti,Mariapia A. Centre for Experimental Immunology, Lions Eye Institute, Nedlands, Western Australia, Australia. Wikstrom,Matthew E. Immunology and Virology Program, Centre for Ophthalmology and Visual Science, The University of Western Australia, Nedlands, Western Australia, Australia. Wikstrom,Matthew E. Centre for Experimental Immunology, Lions Eye Institute, Nedlands, Western Australia, Australia. Domenichini,Alice. School of Biomedical Sciences, CHIRI Biosciences Research Precinct, Curtin University, Bentley, Western Australia, Australia. Lazarus,Kyren. School of Biomedical Sciences, CHIRI Biosciences Research Precinct, Curtin University, Bentley, Western Australia, Australia. Lazarus,Kyren. Harry Perkins Institute of Medical Research, QEII Medical Centre, Nedlands and Centre for Medical Research, The University of Western Australia, Crawley, Western Australia, Australia. van Rooijen,Nico. Department of Molecular Cell Biology, VU Medisch Centrum, Amsterdam, The Netherlands. Ganss,Ruth. Harry Perkins Institute of Medical Research, QEII Medical Centre, Nedlands and Centre for Medical Research, The University of Western Australia, Crawley, Western Australia, Australia. Olynyk,John K. School of Biomedical Sciences, CHIRI Biosciences Research Precinct, Curtin University, Bentley, Western Australia, Australia. Olynyk,John K. Department of Gastroenterology and Hepatology, Fiona Stanley and Fremantle Hospitals, South Metropolitan Health Service, Western Australia, Australia. Olynyk,John K. Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, Western Australia, Australia. Yeoh,George C T. School of Chemistry and Biochemistry, The University of Western Australia, Crawley, Western Australia, Australia. Yeoh,George C T. Harry Perkins Institute of Medical Research, QEII Medical Centre, Nedlands and Centre for Medical Research, The University of Western Australia, Crawley, Western Australia, Australia. Wikstrom,Matthew E. Centre for Experimental Immunology, Lions Eye Institute, Nedlands, Western Australia, Australia. Wikstrom,Matthew E. School of Medicine and Pharmacology, The University of Western Australia, Fremantle, Western Australia, Australia. Elsegood CL, Chan CW, et al.

UNLABELLED: Liver progenitor cells (LPCs) are necessary for repair in chronic liver disease because the remaining hepatocytes cannot replicate. However, LPC numbers also correlate with disease severity and hepatocellular carcinoma risk. Thus, the progenitor cell response in diseased liver may be regulated to optimize liver regeneration and minimize the likelihood of tumorigenesis. How this is achieved is currently unknown. Human and mouse diseased liver contain two subpopulations of macrophages with different ontogenetic origins: prenatal yolk sac-derived Kupffer cells and peripheral blood monocyte-derived macrophages. We examined the individual role(s) of Kupffer cells and monocyte-derived macrophages in the induction of LPC proliferation using clodronate liposome depletion of Kupffer cells and adoptive transfer of monocytes, respectively, in the choline-deficient, ethionine-supplemented diet model of liver injury and regeneration. Clodronate liposome treatment reduced initial liver monocyte numbers together with the induction of injury and LPC proliferation. Adoptive transfer of monocytes increased the induction of liver injury, LPC proliferation, and tumor necrosis factor-alpha production.

CONCLUSION: Kupffer cells control the initial accumulation of monocyte-derived macrophages. These infiltrating monocytes are in turn responsible for the induction of liver injury, the increase in tumor necrosis factor-alpha, and the subsequent proliferation of LPCs. (Hepatology 2015;62:1272-1284). Copyright © 2015 by the American Association for the Study of Liver Diseases.


All oral fixed dose combination therapy with daclatasvir asunaprevir beclabuvir for patients with chronic HCV genotype 1 infection without cirrhosis unity 1 phase 3 results.
Poordad F, Sievert W, et al.
(Poordad) University of Texas, Health Science Center, Texas Liver Institute, San Antonio, United States (Sievert) Monash Health and Monash University, Melbourne, Australia (Mollison) Fremantle Hospital, Hepatitis Services, Fremantle, Australia (Brau) James J Peters Veterans Affairs Medical Center, New York, United States (Levin) Foundation, Madison, United States (Sepe) University Gastroenterology, Providence, United States (Lee) University of Calgary, Calgary, United States (Boyer) Hospital Beaujon, Service D

Geographic barriers and complex therapies for patients with hepatitis C can be overcome by innovative and effective strategy utilizing telehealth.

Nazareth S, Kontorinis N, et al.

Background: The well-established Royal Perth Hospital Hepatitis C Telehealth (TH) Service has received increasing referrals for rural HCV patients with comorbidities requiring complex treatment. Aims: To compare (1) patient profiles and treatment outcomes of TH with face to face (FTF) clinics (2) regional notification with treatment uptake. Retrospective analysis of TH (2005-2014) and all HCV patients with comorbidities requiring complex treatment. Aims: To compare (1) patient profiles and treatment outcomes of TH (n = 93) and FTF patients (n = 1094): mean age 45 years; weight 83.7kgs; 58.1 % male; 52.7 % genotype 1; 84.0 % patients treated FTF. Statistical analysis was performed using the Chi Square test. Results: Baseline characteristics were similar for TH and FTF patients. interferon alpha-2a (68.8 %) compared to FTF(44.9 %) (P<0.05). Conclusions: Patients with comorbidities and cirrhosis in remote areas were analyzed for impact of antiviral treatment on fasting lipid profile. Methods: 570 subjects with fasting baseline and week 24 total cholesterol, LDL, HDL, and triglyceride were included. Regression analyses of on-treatment changes in lipid profile were examined, adjusted for baseline lipid values, age, sex, race, and BMI. Results: Comparing baseline and week 24 results, TDF monotherapy was significantly associated with reductions in total cholesterol, LDL, and HDL (-25.6 mg/dL, -16.4 mg/dL, and, -9.6 mg/dL, respectively, P<0.05) with no significant change in triglyceride or total cholesterol/HDL ratio (p-values > 0.05). Moreover,
TDF + PEG x 48 weeks combination therapy was significantly associated with an even greater reductions in total cholesterol, LDL, and HDL, and a moderate triglyceride increase (-42.5 mg/dL, -29.0 mg/dL, and -18.1 mg/dL, +18.8 mg/dL, respectively, p-values<0.05) compared to baseline. The changes were also significant relative to either monotherapy. In patients who were on TDF + PEG x 16 weeks then continuing on TDF, the lipid impact of PEG lessened after its discontinuation. Only minor, cardiovascular events, mostly palpitations, occurred up to Week 72. Conclusion: TDF monotherapy was associated with significant improvements in total cholesterol and LDL in CHB patients. PEG + TDF x 48 weeks was associated with greater changes in lipid profile than either monotherapy.

Publication Types: Conference Abstract

A review of surgical repair methods and patient outcomes for gluteal tendon tears.
Ebert JR, Bucher TA, et al.
(Ebert) School of Sport Science, Exercise and Health and the School of Surgery, University of Western Australia, Perth, Australia (Bucher) Royal Perth Hospital, Perth, Australia (Bail, Janes) Perth Orthopaedic and Sports Medicine Centre, Perth, Australia J.R. Ebert, School of Sport Science, Exercise and Health and the School of Surgery, University of Western Australia, 35 Stirling Highway, Crawley, Perth, WA 6009, Australia

Advanced hip imaging and surgical findings have demonstrated that a common cause of greater trochanteric pain syndrome (GTPS) is gluteal tendon tears. Conservative measures are initially employed to treat GTPS and manage gluteal tears, though patients frequently undergo multiple courses of non-operative treatment with only temporary pain relief. Therefore, a number of surgical treatment options for recalcitrant GTPS associated with gluteal tears have been reported. These have included open trans-osseous or bone anchored suture techniques, endoscopic methods and the use of tendon augmentation for repair reinforcement. This review describes the anatomy, pathophysiology and clinical presentation of gluteal tendon tears. Surgical techniques and patient reported outcomes are presented. This review demonstrates that surgical repair can result in improved patient outcomes, irrespective of tear aetiology, and suggests that the patient with "trochanteric bursitis" should be carefully assessed as newer surgical techniques show promise for a condition that historically has been managed conservatively.

Publication Types: Review

HIV and aging: Insights from the Asia Pacific HIV Observational Database (APHOD).
Han N, Wright ST, et al.
(Han, Zhao, Zhang) Beijing Ditan Hospital, Capital Medical University, Beijing, China (Wright, O'Connor, Law, Petoumenos, McManus, Bendall, Boyd) The Kirby Institute, University of New South Wales, Sydney, NSW, Australia (O'Connor, Templeton, Dijanosic) RPA Sexual Health, Sydney Local Health District, Camperdown, NSW, Australia (O'Connor) Central Clinical School, Sydney University, Camperdown, NSW, Australia (Hoy) Department of Infectious Diseases, The Alfred Hospital and Monash University, Melbourne, VIC, Australia (Ponnampalavanar, Kamarulzaman, Syed Omar, Azwa) University of Malaya Medical Centre, Kuala Lumpur, Malaysia (Grotowski) Hunter New England Area Health Service - Clinic 468, Tamworth, NSW, Australia (Ellis) General Medical Practice, Coffs Harbour, NSW, Australia (Bloch, Franic, Agrawal, McCann, Cunningham, Vincent) Holdsworth House General Practice, Darklinghurst, NSW, Australia (Allen, Little) Holden Street Clinic, Gosford, NSW, Australia (Smith, Gray) Lismore Sexual Health and AIDDS Services, Lismore, NSW, Australia (Baker, Vale) East Sydney Doctors, Surry Hills, NSW, Australia (Jackson, McCallum) Blue Mountains Sexual Health and HIV Clinic, Katoomba, NSW, Australia (Taylor) Tamworth Sexual Health Service, Tamworth, NSW, Australia (Coope, Lee, Hesse, Sinn, Norris) St Vincent's Hospital, Darlinghurst, NSW, Australia (Finlayson, Prone) Taylor Square Private Clinic, Darlinghurst, NSW, Australia (Jackson, Shakeshaft) Nepean Sexual Health and HIV Clinic, Penrith, NSW, Australia (Brown, McGrath, McGrath, Halligan) Illawarra Sexual Health Service, Warrawong, NSW, Australia (Wray, Read, Lu) Sydney Sexual Health Centre, Sydney, NSW, Australia (Coulidwell) Parramatta Sexual Health Clinic, Sydney, NSW, Australia (Smith, Furner) Albion Street Centre, Dubbo Sexual Health Centre, Dubbo, NSW, Australia (Watson) National Association of People Living with HIV/AIDS, Newtown, NSW, Australia (Lawrence) National Aboriginal Community Controlled Health Organisation, Canberra City, ACT, Australia (Muhall) Department of Public Health and Community Medicine, University of Sydney, NSW, Australia (Kulatunga, Knibbs) Communicable Disease Centre, Royal Darwin Hospital, Darwin, NT, Australia (Chua, Ngieng, Dickson) Gold Coast Sexual Health Clinic, Miami, QLD, Australia (Russell, Downing) Cairns Sexual Health Service, Cairns, QLD, Australia (Sowden, Broom, Taing, Johnston, McGill) Clinic 87, Sunshine Coast-Wide Bay Health Service District, Nambour, QLD, Australia (Orth, Youlds) Gladstone Road Medical Centre, Highgate Hill, QLD, Australia (Kelly, Gibson, Magon) Brisbane Sexual Health and HIV Service, Brisbane, QLD, Australia (Donohue) O'Brien Street General Practice, Adelaide, SA, Australia (Moore, Edwards, Liddle, Locke) Northside Clinic, North Fitzroy, VIC, Australia (Roth, Nicolson, Lau) Prahran Market Clinic, South Yarra, VIC, Australia (Read, Silvers, Zeng) Melbourne Sexual Health Centre, Melbourne, VIC, Australia (Watson, Bryant, Price) The Alfred Hospital, Melbourne, VIC, Australia (Wooley, Giles, Korman, Williams) Monash Medical Centre, Clayton, VIC, Australia (Nolan, Skett, Robinson) Department of Clinical Immunology, Royal Perth Hospital, Perth, WA, Australia (Mean, Saphonn, Vohith) National Center for HIV/AIDS, Dermatology and STDs, Phnom Penh, Cambodia (Li, Lee) Queen Elizabeth Hospital, Hong Kong (Kumarasamy, Saghayam, Ezharali) YRG Centre for AIDS Research and Education, Chennai, India (Pujari, Joshi, Makane) Institute of Infectious Diseases, Pune, India (Merati, Wirawan, Yulianta) Faculty of Medicine Udayana University and Sanglah Hospital, Bali, Indonesia (Yunihastuti, Imran, Widhan) Working Group on AIDS Faculty of Medicine, University of Indonesia/Ciptomangunkusumo Hospital, Jakarta, Indonesia (Oka, Tanuma, Nishijima) National Center for Global Health and Medicine, Tokyo, Japan (Choi, Na, Kim) Division of Infectious Diseases, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea (Lee, Sim, David) Hospital Sungai Buloh, Sungai Buloh, Malaysia (Ditangco, Uy, Bantique) Research Institute for Tropical Medicine, Manila,
2.27; 95% confidence interval (CI) 1.34-3.83; HR for >60 years: 4.28; 95% CI 2.42-7.55]. The effect of older age on CD4 count 
appear to be similar in statistically significant differences in outcomes between AHOD and TAHOD participants for all endpoints examined. Conclusions: The 
trend=<0.0001). The effect of older age on time to first treatment modification was insignificant (p-trend=0.21). We found no 
analyses, those aged >50 years were at least twice as likely to die as those aged 30-39 years [hazard ratio (HR) for 50-59 years: 2.27; 95% confidence interval (CI) 1.34-3.83; HR for >60 years: 4.28; 95% CI 2.42-7.55]. The effect of older age on CD4 count changes was insignificant (p-trend=0.06). The odds of detectable viral load after CART initiation decreased with age (p-
trend=0.0001). The effect of older age on time to first treatment modification was insignificant (p-trend=0.21). We found no statistically significant differences in outcomes between AHOD and TAHOD participants for all endpoints examined. Conclusions: The associations between older age and typical patient outcomes in HIV-positive patients from the Asia Pacific region are similar in 
AHOD and TAHOD. Our data indicate that 'age effects' traverse the resource-rich and resource-limited divide and that future ageing-related findings might be applicable to each setting.

Horn Behav. 2015.
The impact of luteinizing hormone and testosterone on beta amyloid (Abeta) accumulation: Animal and human 
clinical studies.
Verdile G, Ash PR, et al.
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Centre of Excellence for Alzheimer's Disease Research and Care, School of Medical Sciences, Edith Cowan University, Joondalup, Western Australia 6027, Australia; Sir James McCusker Alzheimer's disease Research Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Crawley, Western Australia 6009, Australia; School of Biomedical Sciences, CHIRI Biosciences, Curtin University, Bentley, Western Australia 6102, Australia.
This article is part of a Special Issue "SBN 2014". Hormonal changes associated with ageing have been implicated in the pathogenesis of Alzheimer's disease (AD), the most common form of dementia. Reductions in serum testosterone and increases in luteinizing hormone (LH) are established AD risk factors for dementia in men and have important roles in modulating AD pathogenesis. One of the defining features of AD is the accumulation of amyloid-beta (Abeta) in the brain, which has a key role in the neurodegenerative cascade. Both testosterone and LH have been shown to modulate CNS Abeta accumulation in animal studies, and associations with cerebral amyloid load in human studies have supported this. The underlying mechanisms by which these hormones modulate Abeta accumulation and contribute to neurodegeneration are not completely understood, however they have been shown to regulate Abeta metabolism, enhance its clearance and alter the processing of its parent molecule, the amyloid precursor protein. This review will discuss underlying mechanisms by which testosterone and LH modulate Abeta and provide an update on therapeutic approaches targeting these hormones.

Muscle weakness in TPM3-myopathy is due to reduced Ca2+-sensitivity and impaired acto-myosin cross-bridge 
cycling in slow fibres.
Yuen M, Cooper ST, et al.
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Dominant mutations in TPM3, encoding alpha-tropomyosin slow, cause a congenital myopathy characterised by generalised muscle weakness. Here, we used a multidisciplinary approach to investigate the mechanism of muscle dysfunction in twelve TPM3-myopathy patients. We confirm that slow myofibre hypotrophy is a diagnostic hallmark of TPM3-myopathy, and is commonly accompanied by skewing of fibre-type ratios (either slow or fast fibre predominance). Patient muscle contained normal ratios of the three tropomyosin isoforms and normal fibre-type expression of myosins and troponins. Using 2D-PAGE, we demonstrate that mutant alpha-tropomyosin slow was expressed, suggesting muscle dysfunction is due to a dominant-negative effect of mutant protein on muscle contraction. Molecular modelling suggested mutant alpha-tropomyosin slow likely impacts acto-tropomyosin interactions and, indeed, co-sedimentation assays showed reduced binding of mutant alpha-tropomyosin slow (R168C) to filamentous actin. Single fibre contractility studies of patient myofibres revealed marked slow myofibre specific abnormalities. At saturating [Ca2+] (pCa 4.5), patient slow fibres produced only 63% of the contractile force produced in control slow fibres and had reduced acto-myosin cross-bridge cycling kinetics. Importantly, due to reduced Ca2+-sensitivity at sub-saturating [Ca2+] (pCa 6, levels typically released during in vivo contraction) patient slow fibres produced only 26% of the force generated by control slow fibres. Thus, weakness in TPM3-myopathy patients can be directly attributed to reduced slow fibre force at physiological [Ca2+] and impaired acto-myosin cross-bridge cycling kinetics. Fast myofibres are spared; however, they appear to be unable to compensate for slow fibre dysfunction. Abnormal Ca2+-sensitivity in TPM3-myopathy patients suggests Ca2+-sensitising drugs may represent a useful treatment for this condition. 


Hypertension. 2015; 65(4): 766-74. First Report of the Global SYMPLICITY Registry on the Effect of Renal Artery Denervation in Patients With Uncontrolled Hypertension. Bohm M, Mahfoud F, et al. Bohm,Michael. From the Kardiologie, Angiologie und Internistische Intensivmedizin, Universitätskliniken des Saarlandes, Klinik fur Innere Medizin III, Homburg/Saar, Germany (M.B., F.M, C.U.); Department of Internal Medicine II, Paracelsus University Salzburg, Salzburg, Austria (U.C.H.); Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, Poland (K.N.); Global Clinical Research, Coronary and Structural Heart Disease Management, Medtronic Inc, Santa Rosa, CA (M.N.); Institute of Research & Hypertension Unit, Department of Nephrology, Hospital 12 de Octubre, Madrid, Spain (L.R.); School of Medicine and Pharmacology-Royal Perth Hospital Unit, The University of Western Australia, Perth, Australia (M.P.S.); Department of Nephrology and Hypertension, University Hospital Erlangen, Erlangen, Germany (R.E.S.); Cardiovascular Research Centre, Interventional Cardiology, St. Vincent's Hospital, Melbourne, Australia (R.W.); Institute of Cardiovascular Sciences, University College London (UCL), National Institute for Health Research UCL Hospitals Biomedical Research Centre, London, United Kingdom (B.W.); Klinikum der Stadt Ludwigshafen am Rhein, Ludwigshafen am Rhein, Germany (U.Z.); Department of Cardiology and Angiology I, Universitäts-Herzzentrum Freiburg, Bad Krozingen, Freiburg, Germany (A.Z.); and IRCCS Istituto Auxologico Italiano, Center of Epidemiology and Clinical Trials, University of Milano-Bicocca, Milan, Italy (G.M.). michael.boehm@uks.eu. Mahfoud,Felix. From the Kardiologie, Angiologie und Internistische Intensivmedizin, Universitätskliniken des Saarlandes, Klinik fur Innere Medizin III, Homburg/Saar, Germany (M.B., F.M, C.U.); Department of Internal Medicine II, Paracelsus University Salzburg, Salzburg, Austria (U.C.H.); Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, Poland (K.N.); Global Clinical Research, Coronary and Structural Heart Disease Management, Medtronic Inc, Santa Rosa, CA (M.N.); Institute of Research & Hypertension Unit, Department of Nephrology, Hospital 12 de Octubre, Madrid, Spain (L.R.); School of Medicine and Pharmacology-Royal Perth Hospital Unit, The University of Western Australia, Perth, Australia (M.P.S.); Department of Nephrology and Hypertension, University Hospital Erlangen, Erlangen, Germany (R.E.S.); Cardiovascular Research Centre, Interventional Cardiology, St. Vincent's Hospital, Melbourne, Australia (R.W.); Institute of Cardiovascular Sciences, University College London (UCL), National Institute for Health Research UCL Hospitals Biomedical Research Centre, London, United Kingdom (B.W.); Klinikum der Stadt Ludwigshafen am Rhein, Ludwigshafen am Rhein, Germany (U.Z.); Department of Cardiology and Angiology I, Universitäts-Herzzentrum Freiburg, Bad Krozingen, Freiburg, Germany (A.Z.); and IRCCS Istituto Auxologico Italiano, Center of Epidemiology and Clinical Trials, University of Milano-Bicocca, Milan, Italy (G.M.). Ukena,Christian. From the Kardiologie, Angiologie und Internistische Intensivmedizin, Universitätskliniken des Saarlandes, Klinik fur Innere Medizin III, Homburg/Saar, Germany (M.B., F.M, C.U.); Department of Internal Medicine II, Paracelsus University Salzburg, Salzburg, Austria (U.C.H.); Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, Poland (K.N.); Global Clinical Research, Coronary and

Randomized Controlled Intervention of the Effects of Alcohol on Blood Pressure in Premenopausal Women.
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Alcohol has been consistently demonstrated to elevate blood pressure (BP) in intervention studies in men. There are uncertainties, however, as to the nature of the relationship in women. We, therefore, determined in healthy premenopausal women the dose-dependent effects of alcohol on ambulatory BP. Twenty-four participants aged 25 to 49 years, with a mean alcohol intake of 202+/−159.0 mmHg. At 6 months, the changes in office and 24-hour systolic BPs were -11.6+/−25.3 and -6.6+/−18.0 mmHg for all patients (P<0.001 for both) and -20.3+/−22.8 and -8.9+/−16.9 mmHg for those with severe hypertension (P<0.001 for both). Renal denervation was associated with low rates of adverse events. After the procedure through 6 months, there was 1 new renal artery stenosis >70% and 5 cases of hospitalization for a hypertensive emergency. In clinical practice, renal denervation resulted in significant reductions in office and 24-hour BPs with a favorable safety profile. Greater BP-lowering effects occurred in patients with higher baseline pressures.


Outcome of combined autologous chondrocyte implantation and anterior cruciate ligament reconstruction.
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BACKGROUND: Instability of the knee joint, after anterior cruciate ligament (ACL) injury, is contraindication to osteochondral defect repair. This prospective study is to investigate the role of combined autologous chondrocyte implantation (ACI) with ACL reconstruction. MATERIALS AND METHODS: Three independent groups of patients with previous ACL injuries undergoing ACI were identified and prospectively followed up. The first group had ACI in combination with ACL reconstruction (combined group); the 2(nd) group consisted of individuals who had an ACI procedure having had a previously successful ACL reconstruction (ACL first group); and the third group included patients who had an ACI procedure to a clinically stable knee with documented nonreconstructed ACL disruption (No ACL group). Their outcomes were assessed using the modified Cincinnati rating system, the Bentley functional (BF) rating system (BF) and a visual analog scale (VAS). RESULTS: At a mean follow-up of 64.24 months for the ACL first group, 63 months for combined group and 78.33 months for the No ACL group; 60% of ACL first patients, 72.73% of combined group and 83.33% of the No ACL group felt their outcome was better following surgery. There was no significant difference demonstrated in BF and VAS between the combined and ACL first groups. Results revealed a significant affect of osteochondral defect size on outcome measures. CONCLUSION: The study confirms that ACI in combination with ACL reconstruction is a viable option with similar outcomes as those patients who have had the procedures staged.
Biomechanical properties of a posterior fully threaded positioning screw for cannulated screw fixation of displaced neck of femur fractures.

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OBJECTIVES: Displaced intracapsular neck of femur fractures (NOF) in younger patients are usually fixed with partially-threaded cannulated screws. However posterior comminution may lead to construct failure. We hypothesised that a posterior fully threaded positioning screw would enhance stability. METHODS: A total of 16 left composite femora (Sawbone) were used for testing. To mimic a subcapital fracture with posterior comminution, a subcapital osteotomy was performed and a posterior wedge was resected from the neck. Group A (n=8) was fixed using 3 partially threaded cancellous screws. In Group B (n=8), a fully threaded positioning screw instead of a partially threaded was used posteriorly. The specimens were tested for bending (antero-posterior=A-P) and axial stiffness. Finally, they were axially loaded up to failure or up to 10,000 cycles and the final displacement was measured at the site of the resected neck. More than 5mm of displacement was considered as a failure of the construct. RESULTS: Group B showed significantly higher average A-P stiffness (665 +/- 17N/mm compared to 414 +/- 41N/mm, p=0.0004); whereas axial stiffness did not significantly differ between the two groups (p=0.301). In Group B, the mean final displacement after cyclic axial loading was 0.51 +/- 0.13mm and none of the specimens failed, whereas 7 of 8 constructs failed in Group A (p=0.001). CONCLUSIONS: This biomechanical study points out a potential benefit of replacing the posterior partially threaded cancellous screw with a fully threaded positioning screw in subcapital NOF with posterior comminution. The construct with the fully threaded screw significantly improved the A-P stiffness and reduced the collapse of the fracture.


RESPOND-a patient-centred programme to prevent secondary falls in older people presenting to the emergency department with a fall: protocol for a multicentre randomised controlled trial.

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Lp(a), hypertension and renal insufficiency are independent risk factors beyond elevated pretreatment LDL-cholesterol which predict independent predictors of CAD (P<0.05 for all) in FH after adjusting for other modifiable risk factors. CONCLUSIONS: Elevated LDL-cholesterol, raised Lp(a), hypertension and reduced eGFR remained significant elevated plasma Lp(a) and pre-treatment LDL-cholesterol and triglyceride (or low HDL-cholesterol) than FH patients without CAD other CAD risk factors remains unclear. In this study, we examined the association between Lp(a) and other cardiovascular risk factors and prevalent CAD in patients with FH. METHODS: A cross-sectional study of 390 patients with genetically confirmed FH were studied. Clinical and biochemical parameters of FH patients with and without CAD were compared. RESULTS: FH patients with CAD were older and more often male and had a higher prevalence of hypertension, smoking, diabetes, obesity, reduced eGFR, and elevated plasma Lp(a) and pre-treatment LDL-cholesterol and triglyceride (or low HDL-cholesterol) than FH patients without CAD (P<0.05 for all). In univariate analyses, age, male gender, smoking, hypertension, reduced eGFR, diabetes, obesity, plasma creatinine, Lp(a) and pretreatment LDL-cholesterol, triglycerides and HDL-cholesterol levels were significant predictors of CAD in the FH patients (P<0.05 for all). Elevated LDL-cholesterol, raised Lp(a), hypertension and reduced eGFR remained significant independent predictors of CAD (P<0.05 for all) in FH after adjusting for other modifiable risk factors. CONCLUSIONS: Elevated Lp(a), hypertension and renal insufficiency are independent risk factors beyond elevated pretreatment LDL-cholesterol which predict CAD in patients with FH. In spite of the cross-sectional design of our study, we propose the need for identifying and managing these abnormalities to reduce excess CAD risk in FH patients. However, this proposal remains to be formally tested in a prospective study.
Statins do not increase the risk of developing type 2 diabetes in familial hypercholesterolemia: The SAFEHEART study.
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BACKGROUND: Familial Hypercholesterolemia (FH) is the most common monogenic disorder that causes premature coronary artery disease (CAD). Our objective was to examine the risk of new onset type 2 diabetes mellitus (T2DM) among FH patients and unaffected relatives in relation to treatment with different statins in the SAFEHEART cohort study.

METHODS: This is a cross-sectional and prospective cohort study in 2558 FH and 1265 unaffected relatives with a mean follow-up of 5.9 years. Several pertinent data, such as age, gender, metabolic syndrome, lipid profile, body mass index (BMI), waist circumference, HOMA-IR, dose, duration and type of statins, were obtained and examined as predictors of incident diabetes.

RESULTS: The new onset diabetes was 1.7% in FH and 0.2% in non FH patients (p=0.001). In multivariate logistic regression, age (OR 1.02, CI 95%: 1.02-1.08), HOMA-IR (OR 1.17, CI 95%: 1.03-1.33), metabolic syndrome (OR 3.3, CI 95%: 1.32-8.28) and specifically plasma glucose, as a component of metabolic syndrome (OR 15.7, CI 95%: 4.70-52.53) were significant predictors of new onset T2DM in the FH group alone. In the adjusted Cox regression model in FH group, age (HR 1.03, CI 95% 1.00-1.06, p=0.031) and metabolic syndrome (HR 4.16, CI 95% 1.58-10.92, p=0.004) remained significant predictors of new onset T2DM.

CONCLUSIONS: Our data do not support the postulated diabetogenic effect associated with high-dose statins use in our cohort of FH patients.


The role of heparin in a warfarinized patient with mesenteric venous thrombosis.
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BACKGROUND: Heparin is commonly used in conjunction with warfarin; however, there are limited data on the role of heparin in patients on warfarin who present with mesenteric venous thrombosis.

METHODS: We present a case report of a 50-year-old man with a history of diabetes, hypertension, and chronic kidney disease who presented with abdominal pain and was found to have mesenteric venous thrombosis on imaging. He had been taking warfarin for atrial fibrillation for several years. A venous thromboembolism was ruled out. Heparin was started concurrently with warfarin and discontinued when the INR was adequate. The patient had an uneventful recovery.

RESULTS: This case highlights the potential role of heparin in the management of mesenteric venous thrombosis in patients on warfarin.

CONCLUSIONS: Further research is needed to determine the optimal management of mesenteric venous thrombosis in patients on warfarin.


Depression as a risk factor for cognitive impairment in later life: the Health in Men cohort study.
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BACKGROUND: Depression is an established risk factor for dementia in later life, but it is unclear if this relationship is causal. This study aimed to determine if clinically significant depressive symptoms are likely to be causally related to cognitive impairment in later life.

METHODS: Observational cohort study of 4568 men aged 70-89 years living in Perth, Western Australia, who were free of cognitive impairment at the beginning of follow-up. Current clinically significant depressive symptoms were defined by a score of 7 or more on the Geriatric Depression Scale 15 items. Past depression was ascertained via electronic medical records, by self-report.
or use of antidepressants. A score of 27 or less on the Telephone Interview for Cognitive Status modified or a recorded diagnosis of dementia in electronic medical records established the presence of cognitive impairment. RESULTS: During the 5-year follow-up, 534 men developed cognitive impairment; 811 died and 1455 were lost. The presence of clinically significant depressive symptoms at study entry was associated with increased risk rate (RR) of cognitive impairment (RR = 2.59, 95% confidence interval: 95% CI = 1.57-4.27), death (RR = 5.07, 95% CI = 3.32-7.75) and loss to follow-up (RR = 2.03, 95% CI = 1.32-3.13). These associations remained statistically significant after adjustment for age, country of birth, education, smoking history, and prevalence hypertension, diabetes, coronary heart disease and stroke. History of past clinically significant depressive symptoms was not associated with incident cognitive impairment (RR = 1.09, 95% CI = 0.78-1.52). CONCLUSIONS: The lack of association between past depression and cognitive impairment suggests that the link between depression and cognitive impairment is not causal and that the presence of clinically significant depressive symptoms in later life may herald the onset of cognitive impairment in at least some people. Copyright (c) 2015 John Wiley & Sons, Ltd.

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Prevalence, associated factors, mood and cognitive outcomes of traumatic brain injury in later life: the health in men study (HI MS).
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BACKGROUND: The incidence of traumatic brain injury (TBI) is rising, as are its neuropsychiatric complications. This study aims to determine (1) the prevalence of TBI, (2) the association between history of past TBI and sociodemographic, lifestyle and clinical factors, and (3) the risk of depression and cognitive impairment in later life associated with exposure to TBI. METHODS: Cross-sectional study of a community-derived sample of 5486 Australian men aged 70-89 years. Information on TBI was retrieved from the Western Australian Data Linkage System (WADLS) and via self-report. We used the WADLS and self-report to ascertain history of past depression, and the Geriatric Depression Scale 15-items to assess current clinically significant symptoms of depression, defined by score >/=7. We defined cognitive impairment by a mini-mental state examination score <24 or a WADLS diagnosis of dementia. RESULTS: Nine hundred fifty-three men had history of TBI (17.4%). Factors associated with TBI included coronary heart disease, stroke, poor self-perceived physical health and falls. TBI increased the odds ratio of past (odds ratio (OR) = 1.55, 95% confidence interval (CI) = 1.21, 1.99) and current depression (OR = 1.77, 95% CI = 1.36, 2.32), as well as of cognitive impairment (OR = 1.23, 95% CI = 1.00, 1.51). The population fractions of depression and cognitive impairment attributable to TBI were 6.9% (95% CI = 3.3%, 10.3%) and 3.4% (95% CI = 0.0%, 6.9%). CONCLUSIONS: History of TBI is common in older men, and is associated with increased risk of depression and cognitive impairment. If this association is truly causal, then the effective reduction of events leading to TBI (e.g., motor vehicle accidents and falls) may also decrease the prevalence of depression and cognitive impairment in later life. Copyright (c) 2015 John Wiley & Sons, Ltd.

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Changes in mental health outcomes with the intensive in-home child and adolescent psychiatric service: a multi-informant, latent consensus approach.
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This study investigates the Intensive In-home Child and Adolescent Psychiatric Service (IICAPS), a large-scale home-based intervention that collaboratively engages the family, school, and various other service providers (e.g. health practitioners or judicial systems) to prevent the hospitalization, institutionalization or out-of-home placement of children and adolescents with serious emotional disturbance. Multi-informant data (youth, parents and clinician) on the level of youth problem severity and functioning was gathered from 7169 youth and their families served by the IICAPS network, pre- and post-intervention. A newly developed “Multi-informant Latent Consensus” (MILC) approach was employed to measure mental health “baseline levels” and change, within a Structural Equation Modeling framework. The MILC approach demonstrated promise integrating information from multiple informants involved in the therapeutic process to yield a more accurate and systemic view of a child's level of functioning and problem severity than each report taken individually. Results indicated that the IICAPS family and community based intervention model led to a reduction of problem severity and improved functioning in children and adolescents with severe emotional disturbance. Copyright (c) 2015 John Wiley & Sons, Ltd.

Survey of Australasian oral and maxillofacial surgeons 2011-scope and workforce issues.
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This study examined the qualifications, training, and practice patterns of oral and maxillofacial surgeons in Australia in 2011. This information was compared to similar studies performed in 1986 and 1995. It was found that dentoalveolar surgery comprised the greatest proportion of practice. There had been major growth in dental implantology, orthognathic surgery, and management of pathology. These increases were directly related to the standardization and increase in qualifications and training. The workforce had increased at the highest rate predicted, but was only just keeping up with the increases in population and the number of general health practitioners.


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Anti-embolic stockings for the prevention of VTE in orthopaedic patients: A practice update.
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Complementary medicine use by people living with HIV in Australia - a national survey.
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Little is known about the use of complementary medicines by people living with HIV in Australia since the advent of more effective combination antiretroviral therapy. We conducted an anonymous survey of 1211 adult patients receiving combination antiretroviral therapy from one of eight specialist HIV clinics across Australia, aiming to identify the current patterns of use of ingestible complementary medicines. Data collected included reasons for use, information sources and rates of disclosure of use of complementary medicines to medical practitioners and pharmacists. Ingestible complementary medicine was used by up to 53% of the 1037 patients returning a survey. Complementary medicine was commonly used for general health, to boost immune function and, to a lesser extent, to address co-morbidities. Disclosure of complementary medicines use to doctors was far higher than to pharmacists. Given the potential for interactions, pharmacists should be more aware of patients' complementary medicines use.


Intensive versus conventional glucose control in critically ill patients with traumatic brain injury: long-term follow-up of a subgroup of patients from the NI CE-SUGAR study.
(Chittock, Dhingra, Foster, Cook, Dodek, Hebert, Henderson, Heyland, McDonald, Ronco) Irwin Schweitzer, Canadian Institutes for Health Research, Canada (Li, Li, Bompoin, Billot, Li, Crampton, Darcy, Jayne, Kumarasinghe, Little, McEvoy, MacMahon, Pandey, Ryan, Shukla, Vijayan) The George Institute for International Health, University of Sydney, NSW, Australia (Robinson) University of Sydney, Kolling Institute and Department of Endocrinology, Royal North Shore Hospital, Sydney, Australia (Atherton, Bell, Hadfield,
Purpose: To compare the effect of intensive versus conventional blood glucose control in patients with traumatic brain injury.

Methods: In a large international randomized trial patients were randomly assigned to a target blood glucose (BG) range of either 4.5-6.0 mmol/L (intensive control) or <10 mmol/L (conventional control). Patients with traumatic brain injury (TBI) were identified at randomization and data were collected to examine the extended Glasgow outcome score (includes mortality) at 24 months.

Results: Of the 6104 randomized patients, 391 satisfied diagnostic criteria for TBI; 203 (51.9 %) were assigned to intensive and 188 (48.1 %) to conventional control; the primary outcome was available for 166 (81.8 %) and 149 (79.3 %) patients, respectively. The two groups had similar baseline characteristics. At 2 years 98 (58.7 %) patients in the intensive group and 79 (53.0 %) in the conventional group had a favorable neurological outcome (odds ratio [OR] 1.26, 95 % CI 0.81-1.97; P = 0.3); 35 patients (20.9 %) in the intensive group and 29 (18.9 %) in the conventional group had a poor neurological outcome (OR 1.58, 95 % CI 0.93-2.69; P = 0.09); 24 patients (14.5 %) in the intensive group and 19 (12.1 %) in the conventional group died (OR 1.22, 95 % CI 0.72-2.08; P = 0.48).

Conclusion: Intensive blood glucose control was not associated with a significant reduction in the primary outcome compared to conventional blood glucose control in patients with traumatic brain injury.

A systematic review and meta-analysis of early goal-directed therapy for septic shock: the ARISE, ProCESS and ProMISe Investigators.

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Purpose: To determine whether early goal-directed therapy (EGDT) reduces mortality compared with other resuscitation strategies for patients presenting to the emergency department (ED) with septic shock. Methods: Using a search strategy of PubMed, EmBase and CENTRAL, we selected all relevant randomised clinical trials published from January 2000 to January 2015. We translated non-English papers and contacted authors as necessary. Our primary analysis generated a pooled odds ratio (OR) from a fixed-effect model. Sensitivity analyses explored the effect of including non-ED studies, adjusting for study quality, and conducting a random-effects model. Secondary outcomes included organ support and hospital and ICU length of stay. Results: From 2395 initially eligible abstracts, five randomised clinical trials (n = 4735 patients) met all criteria and generally scored high for quality except for lack of blinding. There was no effect on the primary mortality outcome (EGDT: 23.2 % [495/2134] versus control: 22.4 % [582/2601]; p = 0.81). The pooled estimate of 90-day mortality from the three recent multicentre studies (n = 4063) also showed no difference (pooled OR 0.99 [95 % CI 0.86-1.15]; P = 0.93) with no heterogeneity (I^2 = 0.0 %; P = 0.97). EGDT increased vasopressor use (OR 1.25 [95 % CI 1.10-1.41]; P < 0.001) and ICU admission [OR 2.19 (95 % CI 1.82-2.65); P < 0.001]. Including six non-ED randomised trials...
increased heterogeneity ($I^2 = 71\%$; $P < 0.001$) but did not change overall results [pooled OR 0.94 (95% CI 0.82 to 1.07); $P = 0.33$]. Conclusion: EGDT is not superior to usual care for ED patients with septic shock but is associated with increased utilisation of ICU resources.


**Red cell and platelet transfusion burden following myeloablative allogeneic haematopoietic stem cell transplantation.**

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**BACKGROUND:** Adult allogeneic haemopoietic stem cell transplant (HSCT) usually requires blood transfusion support of red cells and platelets. There are few studies describing transfusion burden after allogeneic HSCT.

**OBJECTIVES:** To quantify and identify determinants of transfusion burden after allogeneic HSCT to improve planning, inventory management and patient counselling.

**METHODS:** A retrospective audit of blood use (red cells and platelets) of all adult HSCT ($n = 169$) was performed over an 8 year period extracted from pathology and hospital databases. ABO compatibility, graft type, conditioning regimes and recipient factors were analysed for up to 12 months post transplant.

**RESULTS:** Transfusion burden was lower than expected and lower than reported by other groups. The median number of units transfused was 4 red cells and 4 platelets by day 30, and 6/6 by day 365. The median time to transfusion independence was 12 days for red cells and 16 days for platelets. Factors associated with increased red cell use included sex, disease stage, graft type (cord blood) and ABO compatibility. Disease stage and graft type (cord blood) were associated with increased platelet transfusion.

**CONCLUSIONS:** Donor and recipient characteristics are associated with transfusion burden after allogeneic HSCT. Determining transfusion burden in HSCT and identifying determinants of increased transfusion use assists in inventory planning and patient information.


**Cost savings with a new screening algorithm for pulmonary arterial hypertension in systemic sclerosis.**

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**INTRODUCTION:** Screening for pulmonary arterial hypertension (PAH) in systemic sclerosis (SSc) is now standard care in this disease. The existing Australian Scleroderma Interest Group algorithm (ASIGSTANDARD) is based on transthoracic echocardiography (TTE) and pulmonary function tests (PFTs). Recently, ASIG has derived and validated a new screening algorithm (ASIGPROPOSED) that incorporates N-terminal pro-B-type natriuretic peptide level together with PFTs in order to decrease reliance on TTE, which has some limitations. Right heart catheterisation (RHC) remains the gold standard for the diagnosis of PAH in patients who screen ‘positive’.

**METHODS:** We applied both ASIGSTANDARD and ASIGPROPOSED algorithms to 643 screen-naive SSc patients from the Australian Scleroderma Cohort Study (ASCs), assuming a PAH prevalence of 10%. We compared the costs of screening, the number of TTEs required and both the total number of RHCs required as well as the number of RHCs needed to diagnose one case of PAH, and costs, according to each algorithm. We then extrapolated the costs to the estimated total Australian SSc population.

**RESULTS:** In screen-naive patients from the ASCs, ASIGPROPOSED resulted in 64% fewer TTEs and 10% fewer RHC compared with ASIGSTANDARD, with $\$1,936 (15\%)$ saved for each case of PAH diagnosed. When the costs were extrapolated to the entire Australian SSc population, there was an estimated screening cost saving of $\$946,000 per annum with ASIGPROPOSED, with a cost saving of $\$851,400 in each subsequent year of screening.

**CONCLUSIONS:** ASIGPROPOSED substantially reduces the number of TTE and RHC required and results in substantial cost savings in SSc-PAH screening compared with ASIGSTANDARD.


**Ulcerative colitis outpatient management: Development and evaluation of tools to support primary care practitioners.**

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Dose tailoring of anti-tumour necrosis factor-alpha therapy delivers useful clinical efficacy in Crohn disease patients experiencing loss of response.


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BACKGROUND: ‘Dose tailoring’ of anti-tumour necrosis factor alpha (TNF-alpha) therapy in Crohn disease (CD), by dose escalation, or shortening of dosing intervals, has been suggested to regain clinical response following a flare in a proportion of patients.

However, reported outcome data are sparse and none exists from Australia.

METHOD: In an observational multicentre, retrospective study, the impact of anti-TNF-alpha dose tailoring on corticosteroid use, the need for surgery and physician perception of clinical efficacy was examined in a real-world setting at six Australian adult teaching hospitals. Demographics, disease characteristics, medications, indication for and duration of dose tailoring were documented.

RESULTS: Fifty-five CD patients were identified as requiring dose tailoring and secondary loss of response was the indication in 96%. Either adalimumab (64%) or infliximab (36%) was dose escalated for a median of 5 months (range 1-47), with a median of 20 months follow up (range 3-65). At 3 months, dose tailoring reduced the mean number of days on high-dose corticosteroids (45 vs 23, P = 0.01). Most (78%) patients remained resection free, and 73% of physicians reported good clinical efficacy of dose tailoring. Of those who de-escalated therapy due to induction of remission, long-term (>12 months) follow up is recommended to regain clinical response following a flare in a proportion of patients.

CONCLUSION: Short-term dose tailoring regains disease response in the majority of patients with CD. Of these, most will remain steroid free at 1 year. The concept and end product have been well received by all stakeholder groups. These tools should support non-specialist clinicians to optimise UC management and empower patients by facilitating them to safely self-manage and identify when medical support is needed.

Systemic lupus erythematosus patients and tertiary specialist care - simple considerations dropping through the cracks: osteoporosis monitoring as an example.

Hew M, McKinnon EJ, et al.

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Systemic lupus erythematosus (SLE) is a potentially life-threatening autoimmune disease that can affect multiple organ systems and has been associated with osteoporosis. The importance of timely and appropriate management of osteoporosis in patients with SLE has been highlighted. However, osteoporosis monitoring is often overlooked in clinical practice. This is likely due to a number of factors, including the complexity of SLE care, the need for ongoing education of specialist and non-specialist clinicians, and the lack of specific guidelines for osteoporosis monitoring in this patient population. The aim of this study was to evaluate the current practice of osteoporosis monitoring in SLE patients attending a tertiary referral centre. A retrospective audit was conducted of all SLE patients attending our clinic over a 5-year period. The data were collected using a comprehensive audit tool that included demographics, disease characteristics, medications, indication for and duration of osteoporosis monitoring. The results showed that osteoporosis monitoring was not consistently performed, with only 50% of patients receiving regular bone density scans. This indicates a need for improved education and awareness of the importance of osteoporosis monitoring in SLE patients. Furthermore, the results highlight the importance of developing specific guidelines for osteoporosis monitoring in SLE patients, as well as the need for ongoing education and support for both specialist and non-specialist clinicians.

Familial pulmonary arterial hypertension at a tertiary referral unit: Patterns in presentation and prognosis.

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Publication Types: Letter


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Familial pulmonary arterial hypertension at a tertiary referral unit: Patterns in presentation and prognosis.

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Systemic lupus erythematosus patients and tertiary specialist care - simple considerations dropping through the cracks: osteoporosis monitoring as an example.

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Encephalitis is a complex neurological syndrome caused by inflammation of the brain parenchyma. The management of encephalitis is challenging because: the differential diagnosis of encephalopathy is broad; there is often rapid disease progression; it often possible based on clinical features, risk factors and radiological features?; When to consider empiric antimicrobials and immune modulatory therapies?; and What is the role of brain biopsy? Copyright © 2015 Royal Australasian College of Physicians. http://www.ncbi.nlm.nih.gov/pubmed?tool=iaufhhslib&term=25955477

Consensus guidelines for the investigation and management of encephalitis in adults and children in Australia and New Zealand.

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Physical activity and sedentary behaviour: applying lessons to chronic obstructive pulmonary disease.

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Glycogenic hepatopathy (GH) is an under-recognised complication of type 1 diabetes mellitus (T1DM) not controlled to target.

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Glycogenic hepatopathy (GH) is an under-recognised cause of hepatomegaly and elevated liver transaminases in type 1 diabetes mellitus.

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Glycogenic hepatopathy (GH) is an under-recognised complication of type 1 diabetes mellitus (T1DM) not controlled to target resulting in hepatomegaly and elevated liver transaminases. We report the case of a 19-year-old man with T1DM not controlled to target who presented with abdominal pain, hepatomegaly and deranged liver transaminases. He was subsequently diagnosed with GH on liver biopsy, with the mainstay of treatment being reduction in caloric intake and insulin.

Decompressive hemicraniectomy in the management of extensive middle cerebral artery stroke: Increased survival, at a price.

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A binational registry of adults with pulmonary arterial hypertension complicating congenital heart disease.

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BACKGROUND: The management of children with congenital heart disease (CHD) has improved over recent decades and several patients surviving with CHD into adulthood are increasing. In developed countries, there are now as many adults as there are children living with CHD. Pulmonary arterial hypertension (PAH) occurs in ~5% of patients with CHD.

AIM: We aimed to understand the characteristics and outcomes of this emerging population.

METHODS: We collected data retrospectively and prospectively from 12 contributing centres across Australia and New Zealand.
Population; the fluoroquinolone-susceptible H41 subclone comprised 4.5% and the H30 subclone comprised 3.5%. The H30 resistant isolates, including 40 (45%) ST131 isolates. Population estimates indicate that ST131 comprises 8% of all E. coli within our isolates differed, with six MLST clusters amongst susceptible isolates (median 7 isolates/cluster) and three clusters amongst the H30 subclone comprised 39% of all ESC-R-EC and 41% of all fluoroquinolone-resistant E. coli within our population. Patients with ST131 were also more likely than those with non-ST131 isolates to present with an upper than lower urinary tract infection (RR = 1.8, 95% CI 1.01-3.1). ST131 and the H30 subclone were predominant amongst ESC-R-EC but were infrequent amongst susceptible mechanisms, clonality by DiversiLab (rep-PCR) and multilocus sequence typing (MLST), and subtyping of ST131 by identification of clones. Drivers for the spread of these clones and risks for their acquisition have been difficult to define. In this study, molecular}


Emergence of blaKPC carbapenemase genes in Australia.
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bla<sub>KPC</sub> genes encoding resistance to carbapenem are increasingly widely reported and are now endemic in parts of several countries, but only one Klebsiella pneumoniae isolate carrying bla<sub>KPC-2</sub> had previously been reported in Australia, in 2010. Here we characterised this isolate, six additional K. pneumoniae and one Escherichia coli carrying bla<sub>KPC</sub>, and another K. pneumoniae lacking bla<sub>KPC</sub>, all isolated in Australia in 2012. Seven K. pneumoniae belonged to clonal complex (CC) 292, associated with bla<sub>KPC</sub> in several countries. Five with bla<sub>KPC-2</sub> plus the isolate lacking a bla<sub>KPC</sub> gene were sequence type 258 (ST258) and the seventh was the closely related ST512 with bla<sub>KPC-3</sub>. The eighth K. pneumoniae isolate, novel ST1048, and the E. coli (ST131) also carried bla<sub>KPC-2</sub>. bla<sub>KPC-2</sub> genes were associated with the most common Tn4401a variant, which gives the highest levels of expression, in all isolates. The ST258 isolates appeared to share a similar set of plasmids, with IncFII and CoE-type plasmid identified in most isolates. All K. pneumoniae isolates had a characteristic insertion in the ompK35 gene resulting in a frameshift and early termination, but only the ST512 isolate had a GlyAsp insertion in loop 3 of OmpK36 that may contribute to increased resistance. The clinical epidemiology of bla<sub>KPC</sub> emergence in Australia thus appears to reflect the global dominance of K. pneumoniae CC292 (and perhaps E. coli ST131). Some, but not all, patients carrying these isolates had previously been hospitalised outside Australia, suggesting multiple discrete importation events of closely related strains, as well as undetected nosocomial spread.


Sequence type 131 fimH30 and fimH41 subclones amongst Escherichia coli isolates in Australia and New Zealand.
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The clonal composition of Escherichia coli causing extra-intestinal infections includes ST131 and other common uropathogenic clones. Drivers for the spread of these clones and risks for their acquisition have been difficult to define. In this study, molecular epidemiology was combined with clinical data from 182 patients enrolled in a case-control study of community-onset expanded-spectrum cephalosporin-resistant E. coli (ESC-R-EC) in Australia and New Zealand. Genetic analysis included antimicrobial resistance mechanisms, clonality by DiversiLab (rep-PCR) and multilocus sequence typing (MLST), and subtyping of ST131 by identification of polymorphisms in the fimH gene. The clonal composition of expanded-spectrum cephalosporin-susceptible E. coli and ESC-R-EC isolates differed, with six MLST clusters amongst susceptible isolates (median 7 isolates/cluster) and three clusters amongst resistant isolates, including 40 (45%) ST131 isolates. Population estimates indicate that ST131 comprises 8% of all E. coli within our population; the fluoroquinolone-susceptible H41 subclone comprised 4.5% and the H30 subclone comprised 3.5%. The H30 subclone comprised 39% of all ESC-R-EC and 41% of all fluoroquinolone-resistant E. coli within our population. Patients with ST131 were also more likely than those with non-ST131 isolates to present with an upper than lower urinary tract infection (RR = 1.8, 95% CI 1.01-3.1). ST131 and the H30 subclone were predominant amongst ESC-R-EC but were infrequent amongst susceptible
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INTRODUCTION: Vitamin D (vit D) deficiency may be associated with an increased risk of statin-related symptomatic myalgia in patients. Background: Familial hypercholesterolemia (FH) is a serious genetic disorder affecting approximately 1 in every 300 to 500 individuals and is characterised by excessively high low-density lipoprotein (LDL) cholesterol levels, substantially increased risk of early-onset coronary heart disease (CHD) and premature mortality. If FH is untreated, it leads to a greater than 50 % risk of CHD in men by the age of 50 and at least 30 % in women by the age of 60. FH can be diagnosed through genetic screening and effectively managed through pharmacological treatment and lifestyle changes. Purpose: Familial hypercholesterolemia (FH) is a genetic health condition that increases the risk of cardiovascular disease. Although FH can be effectively managed with appropriate pharmacological and dietary interventions, FH detection rate through genetic screening remains low. The present study explored perceptions and experiences of FH patients (N = 18) involved in a genetic cascade screening programme. Methods: Face-to-face interviews were conducted to assess patients' knowledge and understanding of FH, explore factors linked to adherence to health-protective behaviours and examine perceptions of genetic screening. Results: Thematic analysis of interviews revealed four themes: disease knowledge, severity of FH, lifestyle behavioural change and barriers to cascade screening and treatment. Participants recognised FH as a permanent, genetic condition that increased their risk of CHD and premature mortality. Many participants dismissed the seriousness of FH and the importance of lifestyle changes because they perceived it to be effectively managed through medication. Despite positive attitudes toward screening, many participants reported that relatives were reluctant to attend screening due to their relatives' 'fatalistic' outlook or low motivation. Participants believed that they had insufficient authority or control to persuade family members to attend screening and welcomed greater hospital assistance for contact with relatives. Conclusions: Findings support the adoption of direct methods of recruitment to cascade screening led by medical professionals, who were perceived as having greater authority. Other implications included the need for clinicians to provide clear information, particularly to those who are asymptomatic, related to the seriousness of FH and the necessity for adherence to medication and lifestyle changes. (PsycINFO Database Record (c) 2015 APA, all rights reserved) (journal abstract). Publication Types: Empirical Study; Interview; Qualitative Study


Patients' perceptions and experiences of familial hypercholesterolemia, cascade genetic screening and treatment.

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INTRODUCTION: Vitamin D (vit D) deficiency may be associated with an increased risk of statin-related symptomatic myalgia in statin-treated patients. The aim of this meta-analysis was to substantiate the role of serum vitamin D levels in statin-associated myalgia.


Analysis of vitamin D levels in patients with and without statin-associated myalgia - a systematic review and meta-analysis of 7 studies with 2420 patients.


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METHODS: The search included PUBMED, Cochrane Library, Scopus, and EMBASE from January 1, 1987 to April 1, 2014 to identify studies that investigated the impact of vit D levels in statin-treated subjects with and without myalgia. Two independent reviewers extracted data on study characteristics, methods and outcomes. Quantitative data synthesis was performed using a fixed-effect model.

RESULTS: The electronic search yielded 437 articles; of those 20 were scrutinized as full texts and 13 studies were considered unsuitable. The final analysis included 7 studies with 2420 statin-treated patients divided into subgroups of patients with (n=666 [27.5%]) or without (n=1754) myalgia. Plasma vit D concentrations in the symptomatic and asymptomatic subgroups were 28.4+/-.36.89ng/mL and 31.38+/-.11.63ng/mL, respectively. The combination of data from individual observational studies showed that vit D plasma concentrations were significantly lower in patients with statin-associated myalgia compared with patients not manifesting this side effect (weighted mean difference -9.41ng/mL; 95% confidence interval: -10.17 to -8.64; p<0.00001).

CONCLUSIONS: This meta-analysis provides evidence that low vit D levels are associated with myalgia in patients on statin therapy. Randomized controlled trials are necessary to establish whether vitamin D supplementation reduces the risk for statin-associated myalgia.


Prevalence and treatment of familial hypercholesterolaemia in Australian communities.
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International Journal of Cardiology. 2015; 189: 47-55.

Lack of efficacy of resveratrol on C-reactive protein and selected cardiovascular risk factors - Results from a systematic review and meta-analysis of randomized controlled trials.
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METHODS: The search included PUBMED, Cochrane Library, Web of Science, Scopus, and EMBASE (up to August 31, 2014) to identify RCTs investigating the efficacy of resveratrol supplementation on selected CV risk factors. Quantitative data synthesis was performed using a random-effects model, with weighted mean difference (WMD) and 95% confidence intervals (CI) as summary statistics.

RESULTS: Meta-analysis of data from 10 RCTs (11 treatment arms) did not support a significant effect of resveratrol supplementation in altering plasma CRP concentrations (WMD: -0.144mg/L, 95% CI: -0.968-0.680, p=0.731). Resveratrol supplementation was not found to alter plasma levels of total cholesterol (WMD: 1.49mg/dL, 95% CI: -14.96-17.93, p=0.859), low density lipoprotein cholesterol (WMD: -0.31mg/dL, 95% CI: -9.57-8.95, p=0.948), triglycerides (WMD: 2.67mg/dL, 95% CI: -28.34-33.67, p=0.866), and glucose (WMD: 1.28mg/dL, 95% CI: -5.28-7.84, p=0.703). It also slightly reduced high density lipoprotein cholesterol concentrations (WMD: -4.18mg/dL, 95% CI: -6.54 to -1.82, p=0.001). Likewise, no significant effect was observed on systolic (WMD: 0.82mmHg, 95% CI: -8.86-10.50, p=0.868) and diastolic blood pressure (WMD: 1.72mmHg, 95% CI: -6.29-9.73, p=0.674).

CONCLUSIONS: This meta-analysis of available RCTs does not suggest any benefit of resveratrol supplementation on CV risk factors. Larger, well-designed trials are necessary to confirm these results.

Rectal adenocarcinoma in prolapsed rectal stump following Hartmann's procedure.

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Publication Types: Letter


Rectal adenocarcinoma in prolapsed rectal stump following Hartmann's procedure.

Nabi H.

India, New Zealand (Crofts) Nossal Institute, VIC, Australia (Spelman)
Alavi M, Spelman T, et al.

Rectal adenocarcinoma in prolapsed rectal stump following Hartmann's procedure.

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Publication Types: Letter


Injecting risk behaviours following treatment for hepatitis C virus infection among people who inject drugs: The Australian Trial in Acute Hepatitis C.

Alavi M, Spelman T, et al.

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Background: A barrier to hepatitis C virus (HCV) treatment among people who inject drugs (PWID) has been a concern that interferon-based HCV treatment may increase injecting risk behaviours. This study evaluated recent (past month) injecting risk behaviours during follow-up among PWID that did and did not receive HCV treatment. Methods: The Australian Trial in Acute Hepatitis C (ATAHC) was a prospective study of natural history and treatment of recent HCV infection. Analyses were performed using generalized estimating equations. Results: Among 124 participants with a history of injecting drug use (median age 32 years), 69% were male and 68% were treated for HCV infection. HCV treatment was not associated with an increase in recent injecting drug use (adjusted odds ratio (aOR) 1.06, 95% CI 0.93, 1.21) or recent used needle and syringe borrowing during follow-up (aOR 0.99, 95% CI 0.89, 1.08). HCV treatment was associated with a decrease in recent ancillary injecting equipment sharing during follow-up (aOR 0.85, 95% CI 0.74, 0.99). Further, among treated participants who remained in follow-up (n= 24), ancillary injecting equipment sharing significantly decreased from 54% at enrolment to 17% during follow-up (P= 0.012). Conclusions: HCV treatment was not associated with drug use or used needle and syringe borrowing during follow-up, but was associated with decreased ancillary injecting equipment sharing during follow-up. Programs to enhance HCV assessment and treatment among PWID should be expanded, given that HCV treatment does not lead to increases in injecting risk behaviours and has previously
Aim: The aim of this qualitative study was to describe the post-discharge experience of elderly patients following primary total hip replacement (THR).

Methods: Ten patients, six women and four men, provided descriptions of their experience. Data were collected by face-to-face interviews and the analysis process was based on Giorgi's phenomenological scientific methodology (Giorgi, 1994, 1997, 2000).

Results: The analysis of the data resulted in four themes, namely: an inadequate assessment of suitable adaptive aids and personal needs; personal frustration; coping with the physical and mobility and limited social interaction.

Conclusion: Findings from this study demonstrated a need to review the discharge process and implement strategies to prepare patients for the stressors that the participants in this study encountered as a result of their early discharge. Copyright © 2015 Elsevier Ltd. All rights reserved.

A pilot study investigating basic fibroblast growth factor for the repair of chronic tympanic membrane perforations in pediatric patients.

Acharya AN, Coates H, et al.

Aim: Objective: A pilot study to investigate the utility of basic Fibroblast Growth Factor (bFGF) in tympanic membrane perforation (TMP) closure in a small cohort of pediatric patients.

Methods: Prospective cohort study. Suitability for inclusion in the study was confirmed by the application of defined inclusion and exclusion criteria, and informed parental consent obtained. The technique used was a modification of the bFGF-technique by Kanemaru et al. Response to treatment was monitored with serial otoscopy and audiometric outcomes were determined. Statistical analysis of the outcomes was carried out.

Results: TMPs were successfully closed in 7/12 children at the first attempt (58%) and in 10/12 children overall (83%). Hearing improvement was observed in 8/10 successfully treated cases (80%). There were no complications or adverse outcomes.
Australian and New Zealand recommendations for the diagnosis and management of gout: Integrating systematic literature review and expert opinion in the 3e Initiative.
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Aim: To develop evidence-based recommendations for the diagnosis and management of gout in Australia and New Zealand as part of the multi-national 3e Initiative. Method: Using a formal voting process, a panel of 78 international rheumatologists selected 10 key clinical questions pertinent to the diagnosis and management of gout. An additional question was also developed by participating Australian and New Zealand rheumatologists. Each question was investigated with a systematic literature review. MEDLINE, EMBASE, Cochrane CENTRAL and abstracts from 2010 to 2011 European League Against Rheumatism and American College of Rheumatology meetings were searched in each review. Relevant studies were independently reviewed by two individuals for data extraction and synthesis and risk of bias assessment. Using this evidence, 47 Australian and New Zealand rheumatologists developed national recommendations. For each recommendation the level of agreement was assessed and the level of evidence graded. Result: Eleven recommendations were produced relating to the diagnosis of gout, different aspects of the management of gout, cardiovascular and renal comorbidities and the management of asymptomatic hyperuricemia. The mean level of agreement with the recommendations was 9.1 on a 1-10 scale, with 10 representing full agreement. Conclusion: Eleven Australian and New Zealand recommendations on the diagnosis and management of gout were developed combining systematically reviewed evidence with local expertise, enhancing their utility in clinical practice.


Ankylosing spondylitis(self-management education program-6 month follow-up results.
Inderjeeth CA, Raymond W, et al. (Inderjeeth, Raymond) Rehabilitation and Aged Care, Sir Charles Gairdner Hospital, Perth, Australia (Connor, Mcquade) Arthritis WA, Health Services, Perth, Australia (Edelman) Sir Charles Gairdner Hospital, Rheumatology, Perth, Australia (Cook) Royal Perth Hospital, Rheumatology, Perth, Australia (Briffa) Curtin University, School of Physiotherapy, Perth, Australia C.A. Inderjeeth, Rehabilitation and Aged Care, Sir Charles Gairdner Hospital, Perth, Australia

Background: Disease specific self-management interventions are rare. After a needs assessment, focus group discussions, and Plan, Do, Study, Act (PDSA) model a Self-Management for Ankylosing Spondylitis (SMAS) program was developed for Ankylosing Spondylitis (AS) participants. Objectives: Examine the changes to health status, quality of life, and disease activity for AS participants receiving the SMAS program. Methods: 134 people were recruited in this case-cohort intervention. Exclusion criteria: <18yo; non-English speaking; comorbid inflammatory disease; visual/auditory/cognitive impairment. Participants attended six, 2.5 hour SMAS sessions, weekly. Scripted content, from the same two professionals, included multidimensional strategies and stretches. With an optional supervised exercise class in week seven. Demographic, AS disease management characteristics, medication patterns, and outcomes were measured using repeated measures ANOVA at baseline, 6 weeks, 3 and 6 months for: back pain (VAS), fatigue (MF), anxiety and depression (HAD), health distress (Hq), fatigue severity scale (FSS), pain self-efficacy (PSEQ), quality of life (SF-36) and Evaluating Ankylosing Spondylitis Qol (EASIqol), global perceived health (GPH), patients disease global assessment (PDGA). AS outcomes were analysed using repeated measures ANOVA for: Bath Ankylosing Spondylitis - Global, Disease Activity Index, and Functional Index (BAS-G, BASDAI, & BASFI), and Ankylosing Spondylitis Qol (ASQol). Results: At baseline, 43.3% were male, and the mean age was 47.2 +/- 15.1 years. The median time to AS diagnosis from the index symptom was 3 years, IQR (1-6). The BAS-G improved between baseline and 3 months (P = 0.011) and were sustained at 6 months (P = 0.039). The BASDAI improved between baseline, 3 months (P = 0.01), and 6 months (P = 0.009). The ASQol improved between baseline and 6 months (P = 0.051). The MAFs GFI, back pain (i.e. nocturnal and total), and the PDGA over the 6 months had positive trends despite statistical insignificance. No improvement in SF-36, HADs, Hq, FSS, Easiqol, and PSEQ. Medication usage didn't change over the study. (Table Presented).

**First diagnosis of polycythemia rubra vera in a general hospital stroke unit.**

Bates TR, Boudville AC, et al. (Bates, Boudville, Kho) Comprehensive Stroke Unit, Swan District Hospital, Perth, Australia (P'Ng) Haemostasis and Thrombosis, Royal Perth Hospital, Perth, Australia

**Introduction:** Identifying the cause of ischemic stroke (IS) guides management. Polycythemia rubra vera (PRV) is a well described although, uncommon cause of stroke that may be easily overlooked. Aim: In this study we aim to report the clinical and radiological characteristics of patients who presented to a general hospital stroke unit who were subsequently diagnosed with PRV. Methods: all 165 patients with confirmed stroke who presented to our hospital in 2014 were included; 3 patients with PRV were identified. Stroke was confirmed on neuroimaging. PRV was diagnosed by the presence of an elevated hemoglobin, low serum erythropoietin level and/or the presence of a JAK-2 mutation. Results: Of the 3 patients who were identified, 2 were male and mean age was 69 years (range 60-79). None were hypoxic on room air at presentation. Mean hemoglobin at presentation was 194.7 g/L (range 177-210, normal 135-180 g/L), hematocrit 0.56 (range 0.51-0.58, normal 0.4-0.54), EPO level 2.3 U/L (range 1.7-26, normal 4.3-29.4 U/L). 2 of 3 patients were JAK-2 mutation positive. 2 of 3 patients had multiple territory cerebral infarctions, with one patient presenting with small vessel disease. All patients made a good recovery with venescence, hydration and antithrombotic medication.

**Conclusion:** PRV may be a not uncommon cause of stroke. Multiple territory infarction was more common, although small vessel occlusive stroke may also occur. Clinicians should be aware of the possibility of PRV being the cause of stroke.

**Publication Types:** Conference Abstract


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**Spinal radicular artery pseudoaneurysms presenting with spontaneous spinal subarachnoid hemorrhage—an unconsidered diagnosis with a benign course?**

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T.J. Singh, NIISwa, Perth, Australia

**Spinal subarachnoid hemorrhage is rare, representing <1% of all subarachnoid hemorrhage (SAH). Underlying etiologies are trauma (including lumbar puncture), vascular lesions (arteriovenous malformations, arteriovenous fistula, aneurysm), neoplastic lesions, coagulopathy, vasculitis (polymyositis nodosa, systemic lupus erythematosus, Behcet's disease), hypertension, and coarctation of the aorta. Spontaneous subarachnoid hemorrhage of unknown pathogenesis is diagnosed after underlying causes are ruled out with selective spinal angiography, computed tomography (CT), magnetic resonance (MR) imaging or autopsy. We present two cases of radicular artery pseudoaneurysms, one arising from the radicular medullary artery (supply to the Anterior Spinal Artery) and the other, the radiculopial artery (supply to the Posterolateral Spinal Artery). Each case presented with spontaneous spinal subarachnoid hemorrhage. Early spinal angiography disclosed the underlying etiology in both cases. Both patients were treated conservatively with good outcome. Follow up spinal angiography showed not only resolution of the pseudoaneurysm, but loss of the radicular arteries. Without the prior spinal angiogram, follow up angiography would have been reported as normal due to the significant variations in supply of radicular arteries to the spinal cord. These patients would then have been mischaracterized as "Spontaneous SAH of unknown pathogenesis". Literature review discloses many cases of spontaneous spinal SAH of unknown etiology either have no or delayed angiography potentially missing this diagnosis. This suggests that spinal radicular artery pseudoaneurysm causing spinal SAH may be more common than thought. These two cases suggest that this disease is self-limiting with good prognosis. The clinical and imaging features of these two cases are presented.

**Publication Types:** Conference Abstract


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**Long-term efficacy, safety, and patient acceptability of ibandronate in the treatment of postmenopausal osteoporosis.**

Inderjeeth CA, Glendenning P, et al. (Inderjeeth, Charles A. Department of Geriatric Medicine and Rheumatology, North Metropolitan Health Service, WA, Australia : Department of Geriatric Medicine and Pharmacology, University of Western Australia, WA, Australia ; Department of Clinical Biochemistry, PathWest Royal Perth Hospital, Perth, WA, Australia ; Department of Geriatric Medicine and Rheumatology, North Metropolitan Health Service, WA, Australia. Inderjeeth, Diren Che. Department of Geriatric Medicine and Rheumatology, North Metropolitan Health Service, WA, Australia. Ondhia, Chandni. Department of Geriatric Medicine and Rheumatology, North Metropolitan Health Service, WA, Australia)

**Several second-generation bisphosphonates (BPs) are approved in osteoporosis treatment. Efficacy and safety depends on potency of farnesyl pyrophosphate synthase (FPPS) inhibition, hydroxyapatite affinity, compliance and adherence. The latter may be influenced by frequency and route of administration. A literature search using "ibandronate", "postmenopausal osteoporosis", "fracture", and "bone mineral density" (BMD) revealed 168 publications. The Phase III BONE study, using low dose 2.5 mg daily oral ibandronate demonstrated 49% relative risk reduction (RRR) in clinical vertebral fracture after 3 years. Non-vertebral fracture (NVF) reduction was demonstrated in a subgroup (pretreatment T-score < -3.0; RRR 38%). Hip fracture reduction was not demonstrated. Long-term treatment efficacy has been confirmed over 5 years. Long term safety is comparable to placebo over 3 years apart from flu-like symptoms which are more common with oral monthly and intravenous treatments. No cases of atypical femoral fracture or...**

**Publication Types:**


osteonecrosis of the jaw have been reported in randomized controlled trial studies. Ibandronate inhibits FPPS more than alendronate but less than other BPs which could explain rate of action onset. Ibandronate has a higher affinity for hydroxyapatite compared with risedronate but less than other BPs which could affect skeletal distribution and rate of action offset. High doses (150 mg oral monthly or intravenous equivalent) were superior to low doses (oral 2.5 mg daily) according to 1 year BMD change. Data are limited by patient selection, statistical power, under-dosing, and absence of placebo groups in high dose studies. Ibandronate treatment offers different doses and modalities of administration which could translate into higher adherence rates, an important factor when the two main limitations of BP treatment are initiation and adherence rates. However, lack of consistency in NVF reduction and absence of hip fracture data limits more generalized use of this agent.

Publication Types: Review

Systematic review and meta-analysis of randomized placebo-controlled trials of folate and vitamin B12 for depression.
Almeida OP, Ford AH, et al.
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(Almeida, Ford) School of Psychiatry and Clinical Neurosciences, University of Western Australia, Crawley, WA, Australia
(Almeida, Ford) Department of Psychiatry, Royal Perth Hospital, Perth, WA, Australia
(Flicker) School of Medicine and Pharmacology, University of Western Australia, Crawley, WA, Australia

Background: Folate and vitamin B12 insufficiencies have been associated with increased risk of depression. This systematic review aimed to clarify if, compared with placebo, treatment with folate and/or vitamin B12 reduces depression scale scores, increases remission, and prevents the onset of clinically significant symptoms of depression in people at risk. Methods: This systematic review searched the PubMed, PsychInfo, Embase, and Cochrane databases from inception to 6 June 2014, using the following terms and strategy: (vitamin B12 or vitamin B9 or folate or folic acid or cobalamin or cyanocobalamin) and (depression or depressive disorder or depressive symptoms) and (randomized controlled trial or RCT). The electronic search was supplemented by manual search. Two independent reviewers assessed all papers retrieved for eligibility and bias, and extracted crude data. Review Manager 5 was used to manage and analyze the data. Results: Two hundred and sixty-nine manuscripts were identified, of which 52 were RCTs and 11 fulfilled criteria for review. We found that the short-term use of vitamins (days to a few weeks) does not contribute to improve depressive symptoms in adults with major depression treated with antidepressants (5 studies, standardized mean difference = -0.12, 95% confidence interval-95% CI = -0.45, 0.22), but more prolonged consumption (several weeks to years) may decrease the risk of relapse (1 study, odds ratio (OR) = 0.33, 95% CI = 0.12, 0.94) and the onset of clinically significant symptoms in people at risk (2 studies, risk ratio = 0.65, 95% CI = 0.43, 0.98). Conclusions: The number of available trials remains small and heterogeneity between studies high. The results of these meta-analyses suggest that treatment with folate and vitamin B12 does not decrease the severity of depressive symptoms over a short period of time, but may be helpful in the long-term management of special populations.
Publication Types: Review

Poisoning among older people with dementia: a wake up call.
Etherton-Beer CD.
Etherton-Beer,Christopher D. Western Australian Centre for Health & Ageing,Centre for Medical Research and School of Medicine and Pharmacology,Royal Perth Hospital and University of Western Australia,Perth,Australia.
Medical care can be both "a blessing and a curse". The contributions of medicines to increased human lifespan and falling mortality from the major cardiovascular diseases are undisputed. However, in lockstep with remarkable extension of human lifespan has been increase in the numbers of people living with chronic age related neurodegenerative conditions and frailty. In frail, multi-morbid populations, with limited homeostatic reserve and life expectancy, the balance between the risk and harms of medicines can be in equipoise. In this context the number of older people living with dementia is increasing, and understanding threats to the quality of life of people with dementia is of growing significance. Among the myriad potential causes of harm to older people with dementia, in this issue of the journal Mitchell and colleagues present new Australian data reminding us of the importance of admissions due to both intentional and unintentional poisoning.

Independent effect of type 2 diabetes beyond characteristic comorbidities and medications on immediate but not continued knee extensor exercise hyperemia.
Poitras VJ, Bentley RF, et al.
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Cardiac Rehabilitation Centre, Hotel Dieu Hospital, Kingston, Ontario, Canada; and School of Rehabilitation Therapy, Queen's University, Kingston, Ontario, Canada.
Cardiac Rehabilitation Centre, Hotel Dieu Hospital, Kingston, Ontario, Canada; and
School of Kinesiology and Health Studies, Queen's University, Kingston, Ontario, Canada; mt29@queensu.ca.
We tested the hypothesis that type 2 diabetes (T2D), when present in the characteristic constellation of comorbidities (obesity, hypertension, dyslipidemia) and medications, slows the dynamic adjustment of exercising muscle perfusion and blunts the steady state relative to that of controls matched for age, body mass index, fitness, comorbidities, and non-T2D medications. Thirteen persons with T2D and 11 who served as controls performed rhythmic single-leg isometric quadriceps exercise (rest-to-6 kg and 6-to-12 kg transitions, 5 min at each intensity). Measurements included leg blood flow (LBF, femoral artery ultrasound), mean arterial pressure (MAP, finger photoplethysmography), and leg vascular conductance (LVK, calculated). Dynamics were quantified using mean response time (MRT). Measures of amplitude were also used to compare response adjustment: the change from baseline to 1) the peak initial response (greatest 1-s average in the first 10 s; DeltaLBFPIR, DeltaLVKPIR) and 2) the on-transient (average from curve fit at 15, 45, and 75 s; DeltaLBFON, DeltaLVKON). DeltaLBFPIR was significantly blunted in T2D vs. control individuals ($P = 0.037$); this was due to a tendency for reduced DeltaLVKPIR ($P = 0.063$). In contrast, the overall response speed was not different between groups (MRT $P = 0.856$, DeltaLBFON $P = 0.150$) nor was the change from baseline to steady state ($P = 0.204$). DeltaLBFPIR, DeltaLVKON, and LBF MRT did not differ between rest-to-6 kg and 6-to-12 kg workload transitions (all $P > 0.05$).

Despite a transient amplitude impairment at the onset of exercise, there is no robust or consistent effect of T2D on top of the comorbidities and medications typical of this population on the overall dynamic adjustment of LBF, or the steady-state levels achieved during low- or moderate-intensity exercise.

J Arthroplasty. 2015.  
**Better Axial Stiffness of a Bicortical Screw Construct Compared to a Cable Construct for Comminuted Vancouver B1 Proximal Femoral Fractures.**  
Griffiths J T, Taheri A, et al.  
Fremantle Hospital, Fremantle, Western Australia.  
Medical Engineering and Physics Department, Royal Perth Hospital, Perth, Western Australia, Australia.  
The aim of this study was to biomechanically evaluate the Locking attachment plate (LAP) construct in comparison to a Cable plate construct, for the fixation of periprosthetic femoral fractures after cemented total hip arthroplasty. Each construct incorporated a locking compression plate with bicortical locking screws for distal fixation. In the Cable construct, 2 cables and 2 uni-cortical locking screws were used for proximal fixation. In the LAP construct, the cables were replaced by a LAP with 4 bi-cortical locking screws. The LAP construct was significantly stiffer than the cable construct under axial load with a bone gap ($P=0.01$). The LAP construct offers better axial stiffness compared to the cable construct in the fixation of comminuted Vancouver B1 proximal femoral fractures.

**Oxidation of Second Generation Sequentially Irradiated and Annealed Highly Cross-Linked X3 Polyethylene Tibial Bearings.**  
Kop AM, Pabbruwe MB, et al.  
Centre for Implant Technology and Retrieval Analysis, Department of Medical Engineering and Physics, Royal Perth Hospital, Perth, WA, Australia.  
Since the first use of ultra-high-molecular-weight polyethylene as a bearing material, research and development efforts have sought to improve wear resistance, increase longevity and lessen the potential for debris mediated adverse tissue responses. A series of second generation sequentially cross-linked and annealed tibial bearings were analysed after several bearings sent for routine retrieval analysis showed oxidative degradation including subsurface whitening, cracking and gross material loss. Evaluation incorporated visual and white banding assessment, mechanical testing and spectroscopy analysis. Whilst visual observation and white banding assessment confirmed oxidative changes, a decrease in mechanical properties and increasing ketone oxidation index as a function of time in vivo suggest time dependent oxidative degradation. Clinically relevant degradation of the sequentially cross-linked and annealed tibial bearings was observed.

**A comparison of multivariate and univariate time series approaches to modelling and forecasting emergency department demand in Western Australia.**  
Aboagye-Sarfo P, Mai Q, et al.  
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Emergency Medicine, Royal Perth Hospital, The University of Western Australia, Australia.  
**OBJECTIVE:** To develop multivariate vector-ARIMA (VARMA) forecast models for predicting emergency department (ED) demand in Western Australia (WA) and compare them to the benchmark univariate autoregressive moving average (ARMA) and Winter models. **METHODS:** Seven-year monthly WA state-wide public hospital ED presentation data from 2006/07 to 2012/13 were modelled. Graphical and VARMA modelling methods were used for descriptive analysis and model fitting. The VARMA models were
Optical coherence tomography for longitudinal monitoring of vasculature in scars treated with laser fractionation.

Gong P, Es'haghian S, et al.
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Optical+Biomedical Engineering Laboratory, School of Electrical, Electronic & Computer Engineering, The University of Western Australia, 35 Stirling Highway, Crawley WA, 6009, Australia.
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Centre for Microscopy, Characterisation & Analysis, The University of Western Australia, 35 Stirling Highway, Crawley WA, 6009, Australia.

This study presents the first in vivo longitudinal assessment of scar vasculature in ablative fractional laser treatment using optical coherence tomography (OCT). A method based on OCT speckle decorrelation was developed to visualize and quantify the scar vasculature over the treatment period. Through reliable co-location of the imaging field of view across multiple imaging sessions, and compensation for motion artifact, the study was able to track the same scar tissue over a period of several months, and quantify changes in the vasculature area density. The results show incidences of occlusion of individual vessels 3 days after the first treatment. The subsequent responses 20 weeks after the initial treatment show differences between immature and mature scars. Image analysis showed a distinct decrease (25 +/- 13%, mean +/- standard deviation) and increase (19 +/- 5%) of vasculature area density for the immature and mature scars, respectively. This study establishes the feasibility of OCT imaging for quantitative longitudinal monitoring of vasculature in scar treatment. En face optical coherence tomography vasculature images pre-treatment (top) and 20 weeks after the first laser treatment (bottom) of a mature burn scar. Arrows mark the same vessel pattern.


J Burn Care Res. 2015.

Is Real-Time Feedback of Burn-Specific Patient-Reported Outcome Measures in Clinical Settings Practical and Useful? A Pilot Study Implementing the Young Adult Burn Outcome Questionnaire.

Ryan CM, Lee AF, et al.
From the *Massachusetts General Hospital/Harvard Medical School/Shriners Hospitals for Children-Boston, Massachusetts; daggerCenter for Medical Statistics and Actuarial Science, School of Statistics, Xi’an University of Finance and Economics, China; double daggerDepartment of Mathematical Sciences, Bentley University, Waltham, Massachusetts; section signMassachusetts General Hospital, Boston; ||Department of Health Policy and Management, Center for the Assessment of Pharmaceutical Practices (CAPP), Boston University School of Public Health, Massachusetts; paragraph signSainte-Justine University Health Centre and University of Montreal, Canada; #Spaulding Rehabilitation Hospital, Harvard Medical School, Boston, Massachusetts; "*Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; daggerspauldingBoston University School of Public Health, Massachusetts; and double daggerspauldingBoston University School of Public Health, Massachusetts.

Long-term follow-up care of survivors after burn injuries can potentially be improved by the application of patient-reported outcome measures (PROMs). PROMs can inform clinical decision-making and foster communication between the patient and provider. There are no previous reports using real-time, burn-specific PROMs in clinical practice to track and benchmark burn recovery over time. This study examines the feasibility of a computerized, burn-specific PROM, the Young Adult Burn Outcome Questionnaire (YABOQ), with real-time benchmarking feedback in a burn outpatient practice. The YABOQ was redesigned for formatting and presentation purposes using images and transcribed to a computerized format. The redesigned questionnaire was administered to young adult burn survivors (ages 19-30 years, 1-24 months from injury) via an ipad platform in the office before outpatient visits. A report including recovery curves benchmarked to a nonburned relatively healthy age-matched population and to patients with similar injuries was produced for the domains of physical function and social function limited by appearance. A copy of the domain reports as well as a complete copy of the patient’s responses to all domain questions was provided for use during the clinical visit. Patients and clinicians completed satisfaction surveys at the conclusion of the visit. Free-text responses, included in the satisfaction surveys, were treated as qualitative data adding contextual information about the assessment of feasibility. Eleven patients and their providers completed the study for 12 clinical visits. All patients found the ipad survey and report “easy” or “very easy” to use. In nine instances, patients “agreed” or “strongly agreed” that it helped them communicate their situation to their doctor/nurse practitioner. Patients “agreed” or “strongly agreed” that the report helped them understand their course of recovery in 10 visits. In 11 visits, the patients “agreed” or “strongly agreed” that they would recommend this feedback to others. Qualitative comments included: “it helped organize my thoughts of recovery,” “it opened lines of communication with the doctor,” “it showed me how far I have come, and how far I need to go,” and “it raised questions I would not have thought of.” Only four of 12 provider surveys agreed that it helped them understand a patient’s condition; however, in two visits, the providers stated that it helped identify a pertinent clinical issue. During two visits, providers stated that a treatment plan was discussed or recommended based on the


J Biophotonics. 2015.
survey results. Separately, qualitative comments from the providers included "survey was not sensitive enough to identify that this patient needed surgery for their scars." This is the first report describing clinical use of a burn-specific patient reported outcome measure. Real-time feedback using the ipad YABOQ was well received for the most part by the clinicians and burn survivors in the outpatient clinical setting. The information provided by the reports can be tested in a future randomized controlled clinical study evaluating impacts on physician decisions.


Recovery trajectories after burn injury in young adults: does burn size matter?
From the *Massachusetts General Hospital, Boston; daggerHarvard Medical School, Boston, Massachusetts; double daggerShriners Hospitals for Children, Boston, Massachusetts; section signCenter for the Assessment of Pharmaceutical Practice (CAPP), Department of Health Policy and Management, Boston University School of Public Health, Massachusetts; |Spaulding Rehabilitation Hospital, Boston, Massachusetts; paragraph signSainte-Justine University Health Centre, Montreal, Canada; #University of Montreal, Canada; **Shriners Hospital for Children, Galveston, Texas; daggerspauldingUniversity of Texas Medical Branch, Galveston; double daggerspauldingShriners Hospital for Children, Sacramento, California; section sign section signUniversity of California at Davis, Los Angeles; | |Kennedy Krieger Institute, Baltimore, Maryland; paragraph sign paragraph signUniversity of Nebraska, Omaha; and 
#Xi'an University for Finance and Economics, Research Center for Medical Statistics and Actuarial Science, China, and Bentley University, Department of Mathematical Sciences, Waltham, Massachusetts.

The impact of burn size on mortality is well known, but the association of burn size with the trajectories of long-term functional outcomes remains poorly studied. This prospective multi-center study included burned adults ages 19 to 30 years who completed the Young Adult Burn Outcome Questionnaire at initial baseline contact, 2 weeks, and at 6 and 12 months after initial questionnaire administration. Non-burned adults of comparable ages also completed the questionnaire as a reference group. The association between functional recovery and TBSA burned was analyzed longitudinally using a linearized model with the generalized estimation equation technique. Functional status was characterized in 15 domains: physical function, fine motor function, pain, itch, social function limited by physical function, perceived appearance, social function limited by appearance, sexual function, emotion, family function, family concern, satisfaction with symptom relief, satisfaction with role, work reintegration, and religion. Scores were standardized to a mean of 50 and a SD of 10 based on non-burned controls. There were 153 burned and 112 non-burned subjects with a total of 620 questionnaires. TBSA burned was 11 +/- 14% (mean +/- SD); 31% had face involvement and 57% had hand involvement. The lag time from burn injury to questionnaire administration was on average 7 +/- 7.7 months, with a maximum of 36 months. Lower recovery levels were associated with increasing burn size for physical function, pain, itch, work reintegration, emotion, satisfaction with symptom relief, satisfaction with role, family function, and family concern (P value ranged from .04-<.0001). No significant differences in recovery levels were found with increasing burn size for fine motor function, social function limited by physical function, sexual function, and religion. These areas tracked toward the age-matched non-burned group regardless of burn size. Perceived appearance and social function limited by appearance remained below the non-burn levels throughout the 3-year period regardless of burn size. Three-year recovery trajectories of survivors with larger burn size showed improvements in most areas, but these improvements lagged behind those with smaller burns. Poor perceived appearance was persistent and prevalent regardless of burn size and was found to limit social function in these young adult burn survivors. Expectations for multidimensional recovery from burns in young adults can be benchmarked based on burn size with important implications for patient monitoring and intervening in clinical care.


J Clin Endocrinol Metab. 2015; jc20152731.

Lipoprotein metabolism in APOB L343V familial hypobetalipoproteinemia.
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CONTEXT: Familial hypobetalipoproteinemia (FHLB) is a co-dominant disorder of lipoprotein metabolism characterized by decreased plasma concentrations of low density lipoprotein (LDL)-cholesterol and apolipoprotein B (apo B). OBJECTIVE: To examine the effect of heterozygous APOB L343V FHLB on postprandial triglyceride-rich lipoprotein (TRL) and fasting lipoprotein metabolism. METHODS: Plasma incremental area under the curve (IAUC) apoB-48 and apoB-48 kinetics were determined after ingestion of a standardized oral fat load using compartmental modeling. Very low density lipoprotein (VLDL)-, intermediate density lipoprotein (IDL)-, and LDL-apoB kinetics were determined in the fasting state using stable isotope methods and compartmental modeling. RESULTS: The postprandial IAUC (0-10 h) in FHLB subjects (n=3) was lower for large TRL-triglyceride (-77%; P<0.0001), small TRL-cholesterol (-83%; P<0.001), small TRL-triglyceride (-88%; P<0.001), and plasma triglyceride (-70%; P<0.01) and apoB (-63%, P<0.0001) compared with controls. Compartmental analysis showed that apoB-48 production was lower (-91%; P<0.05) compared with controls. VLDL-apoB concentrations in FHLB subjects (n=2) were lower by more than 75% compared with healthy, normolipidemic control subjects (P<0.01). VLDL-apoB fractional catabolic rate (FCR) was more than 9-fold higher in the FHLB subjects (P<0.07). ApoB production rates and IDL- and LDL-apoB FC rates were not different between FHLB subjects and controls. CONCLUSIONS: We conclude that when compared to controls, APOB L343V FHLB heterozygotes show lower TRL production with normal postprandial TRL particle clearance. In contrast, VLDL-apoB production was normal, while the FCR was higher in heterozygotes compared with lean control subjects. These mechanisms account for the marked hypolipidemic state observed in these FHLB subjects.
Answer to October 2015 Photo Quiz.
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Photo Quiz: A 66-Year-Old Man With Severe Sepsis.
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Genomics Reveals the Worldwide Distribution of Multidrug-Resistant Serotype 6E Pneumococci.
Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom.
Department of Zoology, University of Oxford, Oxford, United Kingdom.
Institute of Child Health, University College London, London, United Kingdom.
University of Iceland, Reykjavik, Iceland Landspital University Hospital, Reykjavik, Iceland.
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Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom angela.brueggemann@ndm.ox.ac.uk.
The pneumococcus is a leading pathogen infecting children and adults. Safe, effective vaccines exist, and they work by inducing antibodies to the polysaccharide capsule (unique for each serotype) that surrounds the cell; however, current vaccines are limited by the fact that only a few of the nearly 100 antigenically distinct serotypes are included in the formulations. Within the serotypes, serogroup 6 pneumococci are a frequent cause of serious disease and common colonizers of the nasopharynx in children. Serotype 6E was first reported in 2004 but was thought to be rare; however, we and others have detected serotype 6E among recent pneumococcal collections. Therefore, we analyzed a diverse data set of approximately 1,000 serogroup 6 genomes, assessed the prevalence and distribution of serotype 6E, analyzed the genetic diversity among serogroup 6 pneumococci, and investigated whether pneumococcal conjugate vaccine-induced serotype 6B antibodies were able to elicit killing of serotype 6E pneumococci. We found that 43% of all genomes were of serotype 6E, and they were recovered worldwide from healthy children and patients of all ages with pneumococcal disease. Four genetic lineages, three of which were multidrug resistant, described approximately 90% of the serotype 6E pneumococci. Serological assays demonstrated that vaccine-induced serotype 6B antibodies were able to elicit killing of serotype 6E pneumococci. We also revealed three major genetic clusters of serotype 6A capsular sequences, discovered a new hybrid 6C/6E serotype, and identified 44 examples of serotype switching. Therefore, while vaccines appear to offer protection against serotype 6E, genetic variants may reduce vaccine efficacy in the longer term because of the emergence of serotypes that can evade vaccine-induced immunity.

Finding privacy from a public death: a qualitative exploration of how a dedicated space for end-of-life care in an acute hospital impacts on dying patients and their families.
Slatyer S, Pienaar C, et al.
School of Nursing and Midwifery, Curtin University, Bentley, WA, Australia.
Centre for Nursing Research, Sir Charles Gairdner Hospital, Nedlands, WA, Australia.
School of Nursing and Midwifery, Edith Cowan University, Joondalup, WA, Australia.
Health Research, School of Health Professions, Murdoch University, Murdoch, WA, Australia.
Palliative Care Service, Sir Charles Gairdner Hospital, Nedlands, WA, Australia.
AIMS AND OBJECTIVES: To explore the experiences and perceptions of hospital staff caring for dying patients in a dedicated patient/family room (named Lotus Room). BACKGROUND: Dying in hospital is a common outcome for people across the world. However, noise and activity in acute environments present barriers to quality end-of-life care. This is of concern because care provided to dying patients has been shown to affect both the patients and the bereaved families. DESIGN: A qualitative descriptive approach was used. METHODS: Semi-structured interviews were conducted with 17 multidisciplinary staff and seven families provided information through an investigator-developed instrument. RESULTS: Qualitative data analysis generated three categories
of biennial review. Serum 25-hydroxyvitamin D (25(OH)D) concentrations were measured in 358 patients. Those with positive
660 Fremantle Diabetes Study Phase II patients (mean+/-SD age 65.1+/-11.5years, 53.1% males) had nasal/axillary swabs as part
729 Hospitalizations with S. aureus infections were ascertained from validated data linkage.

AIMS: To determine the prevalence and associates of Staphylococcus aureus and methicillin-resistant S. aureus (MRSA) carriage in
137 patients (53.1% of those with an initially positive swab) grew

J Diabetes Complications. 2015.
Changes in characteristics and management of Asian and Anglo-Celts with type 2 diabetes over a 15-year period in
an urban Australian community: The Fremantle Diabetes Study.
Tan ED, Davis WA, et al.
School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia, Fremantle, Western Australia, Australia.
BACKGROUND: The aim of the present study was to determine temporal changes in characteristics and management of Asians with
type 2 diabetes (T2D) compared with those of the majority Anglo-Celt (AC) patients in an urban Australian community. METHODS:
Cross-sectional data from the observational Fremantle Diabetes Study (FDS) collected in 1993-96 (Phase I; FDS1) and 2008-11
(Phase II; FDS2) were analyzed for patients classified as Asian (n = 44 and 65 in FDS1 and FDS2, respectively) or AC (n = 796 and
793, respectively). Between-group differences in changes in key variables between FDS phases were analyzed by generalized linear
modeling with adjustment for age and gender. RESULTS: Asians patients were significantly younger at diagnosis and recruitment
and had a lower body mass index and smaller waist circumference than the AC participants in both FDS phases. They were also less
likely to be treated for hypertension. Cardiovascular risk factors and their management and macrovascular complications were
similar in the two groups over time. A greater propensity to retinopathy with Asian ethnicity in FDS1 (27.3% vs 13.5%; P = 0.23)
was attenuated in FDS2 (23.3% vs 19.0%; P = 0.39). Asians had a significantly lower prevalence of peripheral sensory neuropathy in
FDS2 (33.8% vs 63.3%; P < 0.001; adjusted P = 0.011 for between-group temporal change). CONCLUSIONS: There were persistent
differences between the phenotypic features of Asian migrants with T2D versus AC patients in an Australian urban
community over 15 years of follow-up, but management of diabetes and non-glycemic risk factors remained comparable. Ethnicity-
specific differences in susceptibility to microvascular complications should be considered in clinical management.

J Diabetes. 2015.

Changes in characteristics and management of Asian and Anglo-Celts with type 2 diabetes over a 15-year period in
an urban Australian community: The Fremantle Diabetes Study.
Tan ED, Davis WA, et al.
School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia, Fremantle, Western Australia, Australia.

The interactive effects of type 2 diabetes mellitus and schizophrenia on all-cause mortality: The Fremantle Diabetes Study.
Davis WA, Starkstein SE, et al.
School of Medicine and Pharmacology, the University of Western Australia, Fremantle Hospital, Western Australia.

In a study of the effects of type 2 diabetes and schizophrenia on mortality in 1296 community-based diabetic patients followed for a
mean+/-SD 12.9+/-6.1years and in 5159 matched non-diabetic residents, 0.4% of each group had schizophrenia. Patients with
both conditions had a six-fold adjusted increased risk of death.

J Diabetes Complications. 2015.
Prevalence, risk factors and sequelae of Staphylococcus aureus carriage in diabetes: the Fremantle Diabetes Study Phase II.
Hart J, Hamilton EJ, et al.
Infectious Diseases Department, Fremantle Hospital, Fremantle, Western Australia, Australia.

AIMS: To determine the prevalence and associates of Staphylococcus aureus and methicillin-resistant S. aureus (MRSA) carriage in
community-based diabetes, and their relationship to hospitalization with S. aureus infection. METHODS: A cross-sectional subset of
660 Fremantle Diabetes Study Phase II patients (mean+/-SD age 65.1+/-11.5years, 53.1% males) had nasal/axillary swabs as part of
biennial review. Serum 25-hydroxyvitamin D (25(OH)D) concentrations were measured in 358 patients. Those with positive
swabs were invited back for a repeat swab. Hospitalizations with S. aureus infections were ascertained from validated data linkage.
Multiple logistic regression was used to identify associates of carriage, and Cox proportional hazards modelling was used to
determine predictors of subsequent hospitalization. RESULTS: 258 patients (39.1%) were positive for S. aureus and eight (3.1%)
carried MRSA. S. aureus carriage was independently associated with being married/in a de facto relationship and inversely with
older age and being born overseas (P<0.043). Repeat swabs in 137 patients (53.1% of those with an initially positive swab) grew
OBJECTIVE: To demonstrate a novel and effective surgical technique for the treatment of refractory cerebrospinal fluid rhinorrhea after skull base surgery. The novel surgical technique is described and the findings of a review of relevant world English-language publications are reported. CASE REPORT: A 44-year-old woman, otherwise fit and well, presented with more than a 2-year history of right-sided facial pain. A diagnosis of classical trigeminal neuralgia was made. Surgical treatment was undertaken with a retromastoid suboccipital craniotomy. Post-operatively, the patient showed signs of right-sided cerebrospinal fluid rhinorrhea which was recalcitrant. In light of a continuous leak and several hospital admissions, a novel technique was performed whereby the eustachian tube orifice was obliterated using an endonasal endoscopic approach. The technique proved to be successful, with no further leakage. CONCLUSION: Endoscopic obliteration of the eustachian tube using a double seal technique is a simple, safe and effective procedure in the treatment of refractory cerebrospinal fluid leak.


J Laryngol Otol. 2015; 1-4.

Double seal technique to obliterate the eustachian tube orifice: a novel method for the treatment of recalcitrant cerebrospinal fluid leak.

Taghi AS, Bentley M, et al.
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BACKGROUND: Prenatal androgen exposure has been hypothesized to be linked to autism spectrum disorder (ASD). While previous studies have found a link between testosterone levels in amniotic fluid and autistic-like traits, a similar relationship has not been found for testosterone in umbilical cord blood. However, it may be the net biological activity of multiple androgens and estrogens that influences postnatal effects of prenatal sex steroids. Accordingly, composite levels of androgens (A) and estrogens (E) were investigated, along with their ratio, in relation to autistic-like traits in young adulthood. METHODS: Sex steroid data in umbilical cord blood were available from 860 individuals at delivery. Samples were analyzed for androgens (testosterone, androstenedione, and dehydroepiandrosterone) and estrogens (estrone, estradiol, estriol, and estetrol). Levels of bioavailable testosterone, estradiol, and estrone were measured and used to calculate A and E composites and the A to E ratio. Participants were approached in early adulthood to complete the autism-spectrum quotient (AQ) as a self-report measure of autistic-like traits, with 183 males (M = 20.10 years, SD = 0.65 years) and 189 females (M = 19.92 years, SD = 0.68 years) providing data. RESULTS: Males exhibited significantly higher androgen composites and A to E composite ratios than females. Males also scored significantly higher on the details/patterns subscale of the AQ. Subsequent categorical and continuous analyses, which accounted for covariates, revealed no substantial relationships between the A/E composites or the A to E ratio and the AQ total or subscale scores. CONCLUSIONS: The current study found no link between the A/E composites or the A to E ratio in cord blood and autistic-like traits in the population as measured by the AQ. These outcomes do not exclude the possibility that these sex steroid variables may predict other neurodevelopmental traits in early development.


J Neurol Neurosurg Psychiatry. 2015.

The perinatal androgen to estrogen ratio and autistic-like traits in the general population: a longitudinal pregnancy cohort study.

Jammadass ES, Keelan JA, et al.
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School of Women’s and Infant’s Health, University of Western Australia, Perth, Australia.
Faculty of Health Sciences, Curtin University, Kent Street, Bentley, Western Australia 6102 Australia.
Department of Otolaryngology and Gynaecology, University of Melbourne and the Royal Women’s Hospital, Victoria, Australia.
School of Psychology, University of Western Australia, 35 Stirling Hwy, Crawley, WA 6009 Australia.
Telethon Kids Institute, Centre for Child Health Research, University of Western Australia, 100 Roberts Road, Subiaco, WA 6008 Australia.

BACKGROUND: Prenatal androgen exposure has been hypothesized to be linked to autism spectrum disorder (ASD). While previous studies have found a link between testosterone levels in amniotic fluid and autistic-like traits, a similar relationship has not been found for testosterone in umbilical cord blood. However, it may be the net biological activity of multiple androgens and estrogens that influences postnatal effects of prenatal sex steroids. Accordingly, composite levels of androgens (A) and estrogens (E) were investigated, along with their ratio, in relation to autistic-like traits in young adulthood. METHODS: Sex steroid data in umbilical cord blood were available from 860 individuals at delivery. Samples were analyzed for androgens (testosterone, androstenedione, and dehydroepiandrosterone) and estrogens (estrone, estradiol, estriol, and estetrol). Levels of bioavailable testosterone, estradiol, and estrone were measured and used to calculate A and E composites and the A to E ratio. Participants were approached in early adulthood to complete the autism-spectrum quotient (AQ) as a self-report measure of autistic-like traits, with 183 males (M = 20.10 years, SD = 0.65 years) and 189 females (M = 19.92 years, SD = 0.68 years) providing data. RESULTS: Males exhibited significantly higher androgen composites and A to E composite ratios than females. Males also scored significantly higher on the details/patterns subscale of the AQ. Subsequent categorical and continuous analyses, which accounted for covariates, revealed no substantial relationships between the A/E composites or the A to E ratio and the AQ total or subscale scores. CONCLUSIONS: The current study found no link between the A/E composites or the A to E ratio in cord blood and autistic-like traits in the population as measured by the AQ. These outcomes do not exclude the possibility that these sex steroid variables may predict other neurodevelopmental traits in early development.


J Neurol Neurosurg Psychiatry. 2015.

Candidate-gene analysis of white matter hyperintensities on neuroimaging.

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Department of Neurology, John Hunter Hospital, Hunter Medical Research Institute, Newcastle, New South Wales, Australia.
Departments of Neurology and Public Health Sciences, University of Virginia Health System, Charlottesville, Virginia, USA.
were also differences between the CM-I and control groups: a more acute clivus-canal angle was associated with CM-I in the adult population. These CCJ findings could have an influence on presurgical planning.

**Odontoid process inclination in normal adults and in an adult population with Chiari malformation Type I.**

Besachio DA, Khaleel Z, et al.
Department of Radiology, University of Utah, Salt Lake City, Utah; US Naval Medical Center Portsmouth, Virginia; Royal Perth Hospital, Perth; and, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia.

**OBJECT** Posterior odontoid process inclination has been demonstrated as a factor associated with Chiari malformation Type I (CM-I) in the pediatric population; however, no studies to date have examined this measurement in the adult CM-I population. The purpose of this study was to evaluate cranio cervical junction (CCJ) measurements in adult CM-I versus a control group. METHODS The odontoid retroflexion, odontoid retroversion, odontoid height, posterior basion to C-2 line measured to the dural margin (pB-C2 line), posterior basion to C-2 line measured to the dorsal odontoid cortical margin (pB-C2* line), and clivus-canal angle measurements were retrospectively analyzed in adult patients with CM-I using MRI. These measurements were compared with normative values established from CT scans of the cervical spine in adults without CM-I. RESULTS A statistically significant difference was found between 55 adults with CM-I and 150 sex-matched controls (125 used for analysis) in the mean clivus-canal angle and the mean pB-C2 line. CONCLUSIONS These data suggest that there are sex-specific differences with respect to measurements at the CCJ between men and women, with women showing a more posteriorly inclined odontoid process. There were also differences between the CM-I and control groups: a more acute clivus-canal angle was associated with CM-I in the adult population. These CCJ findings could have an influence on presurgical planning.

**Professional practice models for nursing: a review of the literature and synthesis of key components.**

Slatyer S, Coventry LL, et al.
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Centre for Nursing Research, Sir Charles Gairdner Hospital, Nedlands, Perth, WA, Australia.
School of Nursing and Midwifery, Edith Cowan University, Joondalup, WA, Australia.
Corporate Nursing, Research and Education, Sir Charles Gairdner Hospital, Nedlands, Perth, WA, Australia.

**AIM:** This review aimed to synthesise literature describing the development and/or implementation and/or evaluation of a professional practice model to determine the key model components. **BACKGROUND:** A professional practice model depicts nursing values and defines the structures and processes that support nurses to control their own practice and to deliver quality care. **EVALUATION:** A review of English language papers published up to August 2014 identified 51 articles that described 38 professional practice models. Articles were subjected to qualitative analysis to identify the concepts common to all professional practice models. **KEY ISSUE:** Key elements of professional practice models were theoretical foundation and six common components: leadership; nurses' independent and collaborative practice; environment; nurse development and reward; research/innovation; and patient outcomes. **CONCLUSIONS:** A professional practice model provides the foundations for quality nursing practice. This review is an important resource for nurse leaders who seek to advance their organisation in a journey for excellence through the implementation of a professional practice model. **IMPLICATIONS FOR NURSING MANAGEMENT:** This summary of published professional practice models provides a guide for nurse leaders who seek to develop a professional practice model. The essential elements of a professional practice model; theoretical foundation and six common components, are clearly described. These elements can provide the starting point for nurse leaders' discussions with staff to shape a professional practice model that is meaningful to direct care nurses.
Late Reactivation of Cherubism in a Patient With New-Onset Polycystic Ovary Syndrome.
Lenouve1 D, Chapireau D, et al.


Cyclic mechanical stimulation rescues achilles tendon from degeneration in a bioreactor system.

Randomized Controlled Trial of Shared Care for Patients With Cancer Involving General Practitioners and Cancer Specialists.
Johnson CE, Saunders CM, et al.

PURPOSE: We aimed to determine whether a shared care model (SCM) during chemotherapy treatment improved emotional well-being, empowerment, and prevalence of symptoms for people being treated for cancer.

METHODS: People receiving chemotherapy for hematologic, breast, ovarian, or colorectal malignancies at two cancer centers were randomly assigned to receive SCM or standard care. The SCM involved a patient-held record, a project coordinator, routine contact between the patient and general practitioner/primary care physician, and primary care physician education. Participants completed the Hospital Anxiety and Depression Scale, the Mini-Mental Adjustment to Cancer, and an empowerment questionnaire before, in the middle of, and on completion of chemotherapy. The presence and severity of adverse effects of chemotherapy were recorded by patients in a symptom diary.

RESULTS: Ninety-seven eligible participants were randomly allocated, less than half the intended recruitment. There were no significant differences between the groups for empowerment, symptom prevalence, or Mini-Mental Adjustment to Cancer scores. The proportion with clinical anxiety (Hospital Anxiety and Depression Scale anxiety score of >/= 11) decreased over time in both groups (P = .013) but decreased more in the intervention group (P = .002). Depression was unchanged over time.

CONCLUSION: Our study was limited by low recruitment and predominance of patients with breast cancer, and was underpowered for the main analyses. Results should therefore be interpreted with caution. Little benefit was seen for SCM in the majority of domains including empowerment, symptom prevalence, and psychological adjustment to cancer. The SCM showed efficacy in clinically anxious patients. Such interventions may be better implemented by using a targeted approach to identify at-need subgroups.

model of progressive tendinopathy-like degeneration in the rabbit Achilles. Following ex vivo loading deprivation culture in a bioreactor system for 6 and 12 days, tendons exhibited progressive degenerative changes, abnormal collagen type I production, increased cell apoptosis, and weakened mechanical properties. When intervention was applied at day 7 for another 6 days by using cyclic tensile mechanical stimulation (6% strain, 0.25 Hz, 8 h/day) in a bioreactor, the pathological changes and mechanical properties were almost restored to levels seen in healthy tendon. Our results indicated that a proper biomechanical environment was able to rescue early-stage pathological changes by increased collagen type I production, decreased collagen degradation and cell apoptosis. The ex vivo model developed in this study allows systematic study on the effect of mechanical stimulation on tendon biology. (c) 2015 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res. http://www.ncbi.nlm.nih.gov/pubmed?tool=iaufhhslib&term=26123799

J Rheumatol. 2015. **Ultrasound as an Outcome Measure in Gout. A Validation Process by the OMERACT Ultrasound Working Group.**

Terslev L, Gutierrez M, et al.

From the Centre for Rheumatology and Spine Diseases, Rigshospitalet-Glostrup, Copenhagen, Denmark; Clinica Reumatologica, Universita Politecnica delle Marche, Jesi, Italy; Medical Centre for Rheumatology, Immanuel Krankenhaus, Berlin, Germany; Department of Rheumatology, Royal Perth Hospital, Perth, Australia; Department of Rheumatology, Trinity College, Dublin, Ireland; Department of Medicine, Allergy/Immunology and Rheumatology Division, University of Rochester, Rochester, NY, USA; College of Medicine, University of Florida, Jacksonville, FL, USA; National Institute of Rheumatology and Physiotherapy, Budapest, Hungary; Medical University of Vienna, Vienna, Austria; U.O. Reumatologia, Azienda Ospedaliero-Universitaria Pisana (AOUP), Pisa, Italy; Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway; The Parker Institute, Department of Rheumatology, Bispebjerg and Frederiksberg Hospital, The Capital Region of Copenhagen, Denmark; Instituto Poal de Reumatologia, Barcelona, Spain; Instituto Nacional de Rehabilitacion, Mexico City, Mexico; Boston University Medical Center, Boston, MA, USA; Department of Rheumatology, MC Groep Hospitals, Leestad, the Netherlands; Rheumatology Unit, Sapienza Universita di Roma, Rome, Italy; Hospital Gu Gregorio Maranon and Universidad Complutense, Madrid, Spain; APHP, Hospital Ambroise Pare, Rheumatology Department, 92100 Boujogne-Billancourt; INSERM U1173, Laboratoire d'Excellence INFLAMEX, UFR Simone Veil, Versailles-Saint-Quentin University, Saint-Quentin en Yvelines, France. Dr. Christensen is supported and acknowledges unrestricted grants from the Oak Foundation. Dr. Terslev is supported by the Danish Rheumatism Association. L. Terslev, MD, PhD, Centre for Rheumatology and Spine Diseases, Rigshospitalet-Glostrup; M. Gutierrez, MD, Clinica Reumatologica, Universita Politecnica delle Marche; W.A. Schmidt, MD, PhD, Medical Centre for Rheumatology, Immanuel Krankenhaus; H.I. Keen, MD, Department of Rheumatology, Royal Perth Hospital; E. Filippucci, Clinica Reumatologica, Universita Politecnica delle Marche; D. Kane, MD, PhD, Department of Rheumatology, Trinity College; R. Thiele, MD, PhD, Department of Medicine, Allergy/Immunology and Rheumatology Division, University of Rochester; G. Kaelay, MD, College of Medicine, University of Florida; P. Balint, MD, PhD, National Institute of Rheumatology and Physiotherapy; P. Mandl, MD, PhD, Medical University of Vienna; A. Delle Sedie, MD, U.O. Reumatologia, AOUP; H.B. Hamroun, MD, PhD, Department of Rheumatology, Diakonhjemmet Hospital; R. Christensen, PhD, The Parker Institute, Department of Rheumatology, Bispebjerg and Frederiksberg Hospital; E. Naredo, MD, Hospital Gu Gregorio Maranon and Universidad Complutense; I. Moller, MD, Instituto Poal de Reumatologia; C. Pineda, MD, Instituto Nacional de Rehabilitacion; E. Kissin, MD, Boston University Medical Center; G.A. Bruyn, MD, PhD, Department of Rheumatology, MC Groep Hospitals; A. Iagnocco, MD, Rheumatology Unit, Sapienza Universita di Roma; M-A. D'Agostino, MD, PhD, APHP, Hopital Ambroise Pare, Rheumatology Department; INSERM U1173, Laboratoire d'Excellence INFLAMEX, UFR Simone Veil, Versailles-Saint-Quentin University. Address correspondence to Prof. D'Agostino, Rheumatology Department, Ambroise Pare Hospital, APHP, 9 avenue Charles de Gaulle, 92100 Boujogne-Billancourt, France. E-mail: maria-antonietta.dagostino@apr.aphp.fr.

Objective: To summarize the work performed by the Outcome Measures in Rheumatology (OMERACT) Ultrasound (US) Working Group on the validation of US as a potential outcome measure in gout. METHODS: Based on the lack of definitions, highlighted in a recent literature review on US as an outcome tool in gout, a series of iterative exercises were carried out to obtain consensus-based definitions on US elementary components in gout using a Delphi exercise and subsequently testing these definitions in static images and in patients with proven gout. Cohen's kappa was used to test agreement, and values of 0-0.20 were considered poor, 0.20-0.40 fair, 0.40-0.60 moderate, 0.60-0.80 good, and 0.80-1 excellent. RESULTS: With an agreement of > 80%, consensus-based definitions were obtained for the 4 elementary lesions highlighted in the literature review: tophi, aggregates, erosions, and double contour (DC). In static images interobserver reliability ranged from moderate to almost perfect, and similar results were found for the intrareader reliability. In patients the intraobserver agreement was good for all lesions except DC (moderate). The interobserver agreement was poor for aggregates and DC but moderate for the other components. CONCLUSION: These first steps in evaluating the validity of US as an outcome measure for gout show that the reliability of the definitions ranged from moderate to excellent in static images and somewhat lower in patients, indicating that a standardized scanning technique may be needed, before testing the responsiveness of those definitions in a composite US score. http://www.ncbi.nlm.nih.gov/pubmed?tool=iaufhhslib&term=26329333

J Stroke Cerebrovasc Dis. 2015; 24(4): 874-80. **Quality of referrals and guideline compliance for time to consultation at an acute neurovascular clinic.**

Sales M, Quain D, et al.

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BACKGROUND: The Age, Blood pressure, Clinical features, Duration of symptoms, Diabetes (ABCD2) score can be used to predict early recurrent stroke risk following Transient ischemic attack (TIA). Given that recurrent stroke risk can be as high as 20% in the first week, international guidelines recommend “high-risk” TIA (ABCD2 >3) be seen by specialist services such as dedicated acute neurovascular clinics within 24 hours. The goal of this study was to examine the associations of both quality of referrals to a specialist acute clinic and of “guideline congruence” of time-to-clinic consultation after TIA/minor stroke. We hypothesized high-quality referrals containing key clinical elements would be associated with greater guideline congruence. METHODS: A retrospective analysis of referrals to an acute neurovascular clinic within a tertiary care hospital of consecutive patients with TIA/minor stroke. Quality of general practitioner and emergency department referrals was defined on the basis of information content enabling ABCD2-based risk stratification by the clinic triage service. Time-to-clinic consultation was used to define "guideline congruence."

RESULTS: Referrals of 148 consecutive eligible patients were reviewed. Sixty-six percent of cases were subsequently neurologist-diagnosed as TIA or minor stroke. Seventy-nine percent were referred by general practitioners. Fifty-three percent of referrals were of high quality, but quality was not associated with guideline congruence. Of the high-risk patients, only 3.6% were seen at the clinic within 24 hours of index event and 31.3% within 24 hours of referral. CONCLUSIONS: Current guidelines are pathophysiologically logical and evidence based, but are difficult to implement. Improving quality of primary-secondary communication by improved referral quality is unlikely to improve guideline compliance. Alternative strategies are needed to reduce recurrent stroke risk after TIA/minor stroke.


Fixed-dose combination therapy with daclatasvir, asunaprevir, and beclabuvir for noncirrhotic patients with HCV genotype 1 infection.

Poordad F, Sievert W, et al.

A key secondary outcome was SVR12 in the treatment-experienced cohort. A key secondary outcome was SVR12 in the treatment-experienced cohort. RESULTS: Baseline characteristics were comparable between the treatment-naïve and treatment-experienced cohorts. Patients were 58% male, 26% had IL28B (rs12979860) CC genotype, 73% were infected with genotype 1a, and 27% were infected with genotype 1b. Overall, SVR12 was observed in 379 of 415 patients (91.3%; 95% CI, 88.6%-94.0%): 287 of 312 treatment-naïve patients (92.0%; 95% CI, 89.0%-95.0%) and 92 of 103 treatment-experienced patients (89.3%; 95% CI, 83.4%-95.3%). Virologic failure occurred in 34 patients (8%) overall. One patient died at posttreatment week 3; this was not considered related to study medication. There were 7 serious adverse events, all considered unrelated to study treatment, and 3 adverse events (<1%) leading to treatment discontinuation, including 2 grade 4 alanine aminotransferase elevations. The most common adverse events (in >10% of patients) were headache, fatigue, diarrhea, and nausea.

IMPORTANCE: The antiviral activity of all-oral, ribavirin-free, direct-acting antiviral regimens requires evaluation in patients with chronic hepatitis C virus (HCV) infection.

OBJECTIVE: To determine the rates of sustained virologic response (SVR) in patients receiving the 3-drug combination of daclatasvir (a pan-genotypic NSSA inhibitor), asunaprevir (an NS3 protease inhibitor), and beclabuvir (a nonnucleoside NS5B inhibitor).

DESIGN, SETTING, AND PARTICIPANTS: This was an open-label, single-group, uncontrolled international study (UNITY-1) conducted at 66 sites in the United States, Canada, France, and Australia between December 2013 and August 2014. Patients without cirrhosis who were either treatment-naïve (n=312) or treatment-experienced (n=103) and had chronic HCV genotype 1 infection were included.

INTERVENTIONS: Patients received a twice-daily fixed-dose combination of daclatasvir, 30 mg; asunaprevir, 200 mg; and beclabuvir, 75 mg.

MAIN OUTCOMES AND MEASURES: The primary study outcome was SVR12 (HCV-RNA <25 IU/mL at posttreatment week 12) in patients naive to treatment. A key secondary outcome was SVR12 in the treatment-experienced cohort.

RESULTS: Baseline characteristics were comparable between the treatment-naïve and treatment-experienced cohorts. Patients were 58% male, 26% had IL28B (rs12979860) CC genotype, 73% were infected with genotype 1a, and 27% were infected with genotype 1b. Overall, SVR12 was observed in 379 of 415 patients (91.3%; 95% CI, 88.6%-94.0%): 287 of 312 treatment-naïve patients (92.0%; 95% CI, 89.0%-95.0%) and 92 of 103 treatment-experienced patients (89.3%; 95% CI, 83.4%-95.3%). Virologic failure occurred in 34 patients (8%) overall. One patient died at posttreatment week 3; this was not considered related to study medication. There were 7 serious adverse events, all considered unrelated to study treatment, and 3 adverse events (<1%) leading to treatment discontinuation, including 2 grade 4 alanine aminotransferase elevations. The most common adverse events (in >10% of patients) were headache, fatigue, diarrhea, and nausea.

CONCLUSIONS AND RELEVANCE: In this open-label, nonrandomized, uncontrolled study, a high rate of SVR12 was achieved.
The Tobacco, Exercise and Diet Messages (TEXT ME) trial was a parallel-group, single-blind, randomized clinical trial that recruited patients to usual care. Text messages provided advice, motivational reminders, and support to change lifestyle behaviors. Patients in the intervention group (n = 352) received 4 text messages per week for 6 months in addition to usual care. Messages for each participant were selected from a bank of messages according to baseline characteristics (eg, smoking) and delivered via an automated computerized message management system. The program was not interactive. MAIN OUTCOMES AND MEASURES: The primary end point was low-density lipoprotein cholesterol (LDL-C) level at 6 months. Secondary end points included systolic blood pressure, body mass index (BMI), physical activity, and smoking status. RESULTS: At 6 months, levels of LDL-C were significantly lower in intervention participants, with concurrent reductions in systolic blood pressure and BMI, significant increases in physical activity, and a significant reduction in smoking. The majority reported the text messages to be useful (91%), easy to understand (97%), and appropriate in frequency (86%). CONCLUSIONS AND RELEVANCE: Among patients with coronary heart disease, the use of a lifestyle-focused text messaging service compared with usual care resulted in a modest improvement in LDL-C level and greater improvement in other cardiovascular disease risk factors. The duration of these effects and hence whether they result in improved clinical outcomes remain to be determined.


Effect of lifestyle-focused text messaging on risk factor modification in patients with coronary heart disease: A randomized clinical trial.

Chow CK, Redfern J, et al.

(Chow, Redfern, Hillis, Thakkar, Santo, Hackett, Jan, De Keizer, Bompoint, Stepien, Rodgers, Thiagalingam) George Institute for Global Health, Sydney Medical School, University of Sydney, Cardiovascular Division, PO Box M201, Missenden Road, Sydney, Camperdown, NSW 2050, Australia (Chow, Thakkar, Barry, Thiagalingam) Westmead Hospital, Sydney, Australia (Hillis) Royal Perth Hospital, Perth, Australia (Hillis) University of Western Australia, Perth, United States (Graves) Queensland University of Technology, QLD, Australia (Whitaker) University of Auckland, Auckland, New Zealand

IMPORTANCE: Cardiovascular disease prevention, including lifestyle modification, is important but underutilized. Mobile health strategies could address this gap but lack evidence of therapeutic benefit. OBJECTIVE: To examine the effect of a lifestyle-focused semipersonalized support program delivered by mobile phone text message on cardiovascular risk factors. DESIGN AND SETTING: The Tobacco, Exercise and Diet Messages (TEXT ME) trial was a parallel-group, single-blind, randomized clinical trial that recruited 710 patients (mean age, 58 [SD, 9.2] years; 82% men; 53% current smokers) with proven coronary heart disease (prior myocardial infarction or proven angiographically) between September 2011 and November 2013 from a large tertiary hospital in Sydney, Australia. INTERVENTIONS: Patients in the intervention group (n = 352) received 4 text messages per week for 6 months in addition to usual care. Text messages provided advice, motivational reminders, and support to change lifestyle behaviors. Patients in the control group (n = 358) received usual care. Messages for each participant were selected from a bank of messages according to baseline characteristics (eg, smoking) and delivered via an automated computerized message management system. The program was not interactive.

RESULTS: At 6 months, levels of LDL-C were significantly lower in intervention participants, with concurrent reductions in systolic blood pressure and BMI, significant increases in physical activity, and a significant reduction in smoking. The majority reported the text messages to be useful (91%), easy to understand (97%), and appropriate in frequency (86%). CONCLUSIONS AND RELEVANCE: Among patients with coronary heart disease, the use of a lifestyle-focused text messaging service compared with usual care resulted in a modest improvement in LDL-C level and greater improvement in other cardiovascular disease risk factors. The duration of these effects and hence whether they result in improved clinical outcomes remain to be determined.

TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT01979939.
studies evaluated different interventions provided by organizations to improve coping and resilience. Evidence for the effectiveness of interventions was limited to three studies. The results are discussed under four headings: (i) preventative measures (ii) control measures (iii) unburdening and 'letting go', and (iv) growing and thriving. Conclusion: This review identified a number of strategies to better prepare nurses for practice and maintain their psychological wellbeing. Although no firm conclusions can be drawn in respect to the most effective interventions, strategies with merit included those that: a) foster connections within the team; b) provide education and training to develop behaviors that assist in controlling or limiting the intensity of stress, or aiding recovery; and c) assist in processing emotion and experiences. Although individuals must take responsibility for developing personal strategies to assist coping and resilience, organizational support is integral to equipping individuals to deal with work related challenges.

Publication Types: Review

JBI Library of Systematic Reviews. 2015; 13(3): 111-123

**Effectiveness of daily fluid balance charting in comparison to the measurement of body weight when used in guiding fluid therapy for critically ill adult patients: A systematic review protocol.**


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H. Davies, Royal Perth Hospital Evidence Synthesis Group, Australia

Review objective The objective of this review is to determine the effectiveness of daily fluid balance charting in comparison to the measurement of body weight when used in guiding fluid therapy for critically ill adult patients. More specifically, the objectives are to identify: The accuracy and utility of estimating body fluid status by charting daily fluid balance totals; The accuracy and utility of estimating body fluid status by daily body weight measurements; The utility of both approaches for estimation of changes in body fluid status; Any special considerations required for patients who are oliguric and at risk of fluid overload; Inclusion criteria Types of participants This review will consider studies involving critically ill adult patients (18 years and over) that have body fluid status evaluated according to fluid balance and measurement of body weight. Of particular interest will be studies which include patients who are susceptible to the consequences of fluid overload. The studies may include patients with severe acute kidney injury requiring renal replacement therapy, patients with cardiogenic shock who develop significant heart failure and patients with acute lung injury who require mechanical ventilation. Studies that focus on the intensive care unit pediatric or neonatal population will be excluded from the review process. Anatomical, physiological and biochemical differences in pediatric and neonatal studies make comparisons of findings difficult to extrapolate when making recommendations on clinical practice to the adult population for this particular issue. Types of intervention Only non-invasive methods of estimating body fluid status will be reviewed. The primary focus will be on studies that have evaluated the charting of inputs and outputs and daily fluid balance totals to estimate body fluid status. Types of comparator The comparator will be the alternative non-invasive method of measuring daily body weight for the estimation of body fluid status. Types of outcome measures The review will consider studies that include, but are not restricted to, the following outcome measures: Duration of hospitalization, as defined by number of day's in intensive care unit and as a ward patient Number of hour's patient intubated and required mechanical ventilation Patient survival post transfer from TRUNCATED AT 350 WORDS.

Publication Types: Review


**Improving the Effectiveness of Penicillin Allergy De-labeling.**


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BACKGROUND: Approximately 10-20% of hospitalized patients are labeled as penicillin allergic, and this is associated with significant health and economic costs.

OBJECTIVES: We looked at the effectiveness of penicillin allergy de-labeling in clinical practice with the aim of deriving risk stratification models to guide testing strategies.

METHODS: Consecutive patients aged 15 years or more, referred to a Western Australian public hospital drug allergy service between 2008 and 2013 for beta-lactam allergy, were included. Follow-up surveys were conducted. Results of skin prick testing and intradermal testing (SPT/IDT) and oral challenge (OC), and follow-up of post testing antibiotic usage were the main outcomes.

RESULTS: SPT/IDT was performed in 401 consecutive patients with immediate (IMM) (<1 hour) (n = 151) and nonimmediate (NIM) (>1 hour) (n = 250) reactions. Of 341 patients, 42 (12.3%) were SPT/IDT+ to >1 penicillin reagents, including 35/114 (30.4%) in the IMM group and 7/227 (3.1%) in the NIM group (P < .0001). Of 355 SPT/IDT patients, 3 (0.8%), all in the IMM group, had nonserious positive OC reactions to single dose penicillin VK (SPT/IDT negative predictive value [NPV] 99.2%). Selective or unrestricted beta-lactam was recommended in 118/151 (78.4%) in the IMM group and 126/151 (83.4%) in the NIM group (P = .0001). Of 182 patients, 137 (75.3%) were following the allergy label modifications (ALM) at the
time of follow-up.

CONCLUSIONS: Penicillin SPT/IDT/OC safely de-labels penicillin-allergic patients and identifies selective beta-lactam allergies; however, incomplete adherence to ALM recommendations impairs effectiveness. Infrequent SPT/IDT+ and absent OC reactions in patients with penicillin allergy de-labeling in lower risk populations.


Journal of Allergy and Clinical Immunology. 2015; 1: AB141.

A multicentre cross-sectional survey of allergic sensitisation to subtropical and temperate grass pollens. Davies JM, Solley GO, et al. (Davies, Timbrell, Upham) University of Queensland, Brisbane, Australia (Solley) Watkins Medical Centre, Brisbane, Australia (Smith) Royal Adelaide Hospital, Adelaide, Australia (McLean-Tookey) Fremantle Hospital, Fremantle, Australia (Van Nunen) Royal North Shore Hospital, Sydney, Australia (Smith) Department of Clinical Medicine, Griffith University, Southport, QLD, Australia (Langguth) Sullivan Nicolaides Pathology, Brisbane, Australia

J.M. Davies, University of Queensland, Brisbane, Australia

RATIONALE: Grass pollens (GP) are major triggers of allergic rhinitis and asthma but allergic sensitisation to pollen of subtropical (Panicoideae and Chloridoideae) and temperate (Pooidaeae) species in patients from diverse biogeographical regions is not well understood. METHODS: Subjects (non-atopic, n = 31, other allergies; n = 42) and patients with allergic rhinitis (n = 321) were recruited at specialist centres in Queensland (subtropical), Adelaide, Perth and Sydney (temperate). Clinical history and skin prick test (SPT) to GP extracts were assessed. Serum total and specific IgE to GP extracts and biotinylated allergen component-streptavidin ImmunoCAPs, were measured. Subjects with prior GP immunotherapy were excluded. Data was analysed by nonparametric tests. RESULTS: GP-allergic patients from Queensland showed higher SPT and IgE to Bahia and Bermuda GP as well as Pas n 1 and Cyn d 1, than Ryegrass pollen and Lol p 1. In contrast, patients from Adelaide and Sydney showed higher SPT and IgE to Ryegrass than Bermuda and Johnson GP. In Perth, SPT to Ryegrass was higher than Johnson GP but IgE with Ryegrass was higher than both Johnson and Bermuda GP. Sensitivity to Bahia GP did not differ from Ryegrass in patients from Adelaide, Sydney or Perth. However, IgE to Lol p 1 was higher than IgE to subtropical group 1 allergens in patients from Adelaide, Sydney and Perth.

CONCLUSIONS: Patients with GP allergy show significant differences in levels of allergic sensitivity with subtropical and temperate GP depending on biogeographical region. Primary sensitisation to different types of grasses should be considered in choice of GP immunotherapy.

Publication Types: Conference Abstract


Journal of Allergy and Clinical Immunology. 2015; 136(4): 993-1006e1.

Monogenic mutations differentially affect the quantity and quality of T follicular helper cells in patients with human primary immunodeficiencies. Ma CS, Wong N, et al. (Ma, Wong, Rao, Avery, Torpy, Hambridge, Deenick, Pelham, Payne, Phan, Tangye) Immunology Research Program, Garvan Institute of Medical Research, Darlinghurst, Australia (Ma, Deenick, Pelham, Phan, Roscioli, Tangye) St Vincent’s Clinical School, UNSW Australia, Melbourne, Australia (Bustamante, Boisson-Dupuis, Puel, Picard, Casanova) Laboratory of Human Genetics of Infectious Diseases, Necker Branch, University Paris Descartes, Paris, France (Bustamante, Picard) Study Center for Primary Immunodeficiencies, Assistance Publique-Hopitaux de Paris (AP-HP), Necker Hospital for Sick Children, Paris, France (Okada, Kohno) Department of Pediatrics, Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan (Stoddard) Clinical Center, National Institutes of Health, Bethesda, MD, United States (Boisson-Dupuis, Casanova) St Giles Laboratory of Human Genetics of Infectious Diseases, Rockefeller Branch, Rockefeller University, New York, NY, United States (Arkwright) University of Manchester, Royal Manchester Children's Hospital, Manchester, United Kingdom (Killic) Department of Pediatric Immunology, Uldaq University Medical Faculty, Gurnike, Bursa, Turkey (El Baghdadi) Genetics Unit, Military Hospital Mohamed v Hay Riad, Rabat, Morocco (Nonoyama) Department of Pediatrics, National Defense Medical College, Tokorozawa, Saitama, Japan (Minegishi) Division of Molecular Medicine, Institute for Genome Research, University of Tokushima, Tokushima, Japan (Mahdaviani, Mansouri) Pediatric Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran, Islamic Republic of (Bousfiha) Clinical Immunology Unit, Pediatric Infectious Diseases Department, Averroes University Hospital, King Hasan II University, Casablanca, Morocco (Blincoe) Starship Children's Hospital, Auckland, New Zealand (French) Department of Clinical Immunology, Royal Perth Hospital, Perth, Australia (French) School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Australia (Hsu, Campbell, Stormon, Wong) Children's Hospital at Westmead, Westmead, Australia (Adelestein) Clinical Immunology, Royal Prince Alfred Hospital, Sydney, Australia (Smart) Department of Allergy and Immunology, Royal Children's Hospital Melbourne, Melbourne, Australia (Fulcher) Department of Immunology, Westmead Hospital, Sydney, Australia (Cook) Australian National University Medical School, Australian National University, Acton, Australia (Cook) John Curtin School of Medical Research, Australian National University, Acton, Australia (Cook) Department of Immunology, Canberra Hospital, Canberra, Australia (Stepensky) Pediatric Hematology-Oncology and Bone Marrow Transplantation Hadassah, Hebrew University Medical Center, Jerusalem, Israel (Boztug) CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria (Boztug) Department of Paediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria (Kansu) Department of Pediatric Gastroenterology, A&N University Medical School, Ankara, Turkey (Ikinciotullari) Department of Pediatric Immunology and Allergy, Ankara University Medical School, Ankara, Turkey (Baumann) Paediatric Pulmonology, Allergy and Neonatology, Hannover Medical School, Hannover, Germany (Beier) Pediatric Haematology and Oncology, University Hospital Essen, Essen,
Phenomenology of depression in Alzheimer's disease.

Novais F, Starkstein S.


Depression is among the most frequent psychiatric comorbid conditions in dementia. There is no strong consensus as to what criteria should be used to diagnose depression in AD. This is at least partially explained by the overlap between symptoms of depression and symptoms of AD. Recent studies using latent class analysis provided clarification to this diagnostic dilemma. All nine DSM-IV symptoms of major depression were found to characterize a class with a high chance (96%) of having a clinical diagnosis of major depression, and symptoms of anxiety were also frequent. Other psychiatric symptoms may also be included under the construct of depression in AD, since both apathy and anxiety are among the most frequent comorbid conditions for major depression in AD. Subtypes of depression should also be validated in this condition. For instance, increased awareness of cognitive and functional deficits is significantly associated with dysthymia but not with major depression, suggesting that different depressive syndromes in AD may have different etiology.

Publication Types: Review


Staphylococcus aureus plasmids without mobilization genes are mobilized by a novel conjugative plasmid from community isolates.


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OBJECTIVES: To describe a family of conjugative plasmids isolated from colonizing community Staphylococcus aureus and determine their ability to mobilize unrelated antimicrobial resistance/virulence plasmids, not encoding mobilization functions.

METHODS: Plasmid pWBG749 was labelled with Tn551 (pWBG749e) to enable laboratory manipulation. Plasmid pWBG749e was conjugated into S. aureus of seven different lineages that harboured unrelated plasmids and mobilization experiments were performed. Plasmids were screened by EcoRI restriction and hybridization with probes prepared from unique pWBG749 conjugation genes.

RESULTS: Conjugal plasmids pWBG745, pWBG748 and pWBG749 belong to the same conjugative-plasmid family as the vancomycin resistance plasmid pBR210. Plasmid pWBG749e mobilized five unrelated plasmids. Mobilized plasmid pWBG744 is a pB485-family plasmid that was also found in international S. aureus.

CONCLUSIONS: Plasmid pWBG749e can mobilize unrelated S. aureus plasmids whose means of dissemination have not previously been understood. Copyright The Author 2014. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.


Association of microparticles and neutrophil activation with decompression sickness.

Thom SR, Bennett M, et al.

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Does the ingrowth surface make a difference? A retrieval study of 423 cementless acetabular components.

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The effect of factors such as bone, alloy and coating on porous or fibrous tissue ingrowth was evaluated in a study of 423 retrieved cementless acetabular shells representing 16 shell designs. Small-beaded (250 mum) porous coatings, either with or without hydroxyapatite (HA) coatings, proved to be the superior porous surface for bone ingrowth. Small-beaded shells that were Duofix coated had predominantly fibrous tissue ingrowth. In addition to bead size, alloy type and surface type have significant effect on bone ingrowth. In contrast, there is no significant association between bone ingrowth and time in situ, with most bone ingrowth occurring early. Although roughened, press-fit shells have acceptable clinical and Registry data, they showed some of the lowest ingrowth/ongrowth scores of all the shells tested.


**TKR without tourniquet: A laboratory study investigating the quality of the tibial cement mantle when using metaphyseal suction and cement gun.**


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Purpose: The majority of cemented replacements worldwide are performed with a tourniquet. The benefits of surgery in TKR without a tourniquet have been well described but questions have been raised about the ability to prepare the bone for cementation, and take up of a tourniquet-less technique has been slow. A laboratory based model was constructed to directly compare the quality of cementing between tourniquet and tourniquet-less knee replacement supplemented by metaphyseal suction and a cement gun. Methods: A Sawbone model to represent the metaphyseal proximal tibia was constructed. The model allowed the inflow of simulated blood and the use of metaphyseal suction. The study compared four different techniques; the use of a tourniquet, no tourniquet, no tourniquet with cancellous suction and no tourniquet with cancellous suction and a cement gun. Each subtype of experiment was repeated 5 times. Quality of cementation was assessed using a calibrated engineering planimeter. Results: This model has shown that combining the use of metaphyseal suction and a cement gun but without the use of a tourniquet offers significantly better cement penetration (p. < 0.0001) than cementing using a tourniquet alone. Conclusions: This study offers further in vitro evidence to the argument that tourniquet-less surgery when supplemented by appropriate techniques can achieve a good cement-bone interface, whilst avoiding the additional risk of using a tourniquet to perform the procedure.


**Renal denervation and pulmonary vein isolation in patients with drug resistant hypertension and symptomatic atrial fibrillation.**


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Systemic hypertension is the most consistent modifiable risk factor for atrial fibrillation (AF) in adults with consistent data from both animal models and human studies suggesting a consistent pattern of autonomic imbalance underlying both conditions. Relative sympathetic nervous system activation is a demonstrably common attendant to the local mechanisms in pulmonary veins that sustain persistent or recurrent AF and may represent a new objective for adjunctive treatment. Established management of AF aims to achieve durable control through either pharmacologic or catheter-based interventions. The introduction of catheter-based renal denervation as a safe, alternate approach to target the sympathetic nervous system therapeutically represents a potential opportunity to treat the shared pathophysiological mechanisms with minimal additional treatment burden when added in this context. Preliminary investigations have demonstrated both proof-of-concept and the technical feasibility of combined renal denervation and AF ablation procedures with the suggestion of benefit in terms of freedom from AF recurrence. The available data is promising but absolute confirmation of efficacy remains unconfirmed in the absence of more definitive evidence. This paper reviews the role of autonomic imbalance in the initiation and maintenance of AF by summarizing the observations from both experimental models and clinical studies from the perspective of potential therapeutic overlap between catheter-based treatments.

Publication Types: Review


**Evaluation of an established pericardium patch for delivery of mesenchymal stem cells to cardiac tissue.**
The hip beyond the intertrochanteric line may compromise neurovascular structures supplying the quadriceps muscle.

Distal extension of the direct anterior approach to the hip is challenging to accomplish without neurovascular injury to nerve branches to the vastus lateralis, lateral parts of the vastus intermedius, and branches of the lateral femoral circumflex artery. Introduction of a cerclage cable passer through the anterior approach also jeopardizes to the anterolateral portions of the quadriceps. The distal extension of the anterior approach, sometimes needed intraoperatively, potentially endangers neurovascular structures to the quadriceps. The aim of this study was to determine the anatomical structures placed at risk by distal extension of the anterior approach to the hip.

Methods: Seventeen cadaveric hemipelves from twelve human specimens were dissected. The femoral nerve and its branches and the vessels arising from the lateral femoral circumflex artery were assessed in relation to the distal extension of the anterior approach. The damage caused by the introduction of a cerclage cable passer was also investigated. Results: The area immediately distal to the intertrochanteric line is a common entry point for several nerve branches and is a useful distal landmark for surgeons to use to protect important neurovascular structures. The distal extension of the anterior approach compromises the nerve supply to the anterolateral portions of the quadriceps. Introduction of a cerclage cable passer through the anterior access also jeopardizes nerve branches to the vastus lateralis, lateral parts of the vastus intermedius, and branches of the lateral femoral circumflex artery. Conclusions: Distal extension of the direct anterior approach to the hip is challenging to accomplish without neurovascular injury to anterolateral parts of the quadriceps muscle group. In addition, important neurovascular structures are endangered with the introduction of a cable passer through the anterior approach. Clinical Relevance: Distal extension of the direct anterior approach to the hip beyond the intertrochanteric line may compromise neurovascular structures supplying the quadriceps muscle.

The present study has evaluated a commercial pericardial material for its capacity to assist as a natural extracellular matrix (ECM) patch for the delivery and retention of mesenchymal stem cells for cardiac repair. The repair of cardiac tissue with cells delivered by an appropriate bioscaffold is expected to offer a superior, long-lasting treatment strategy. The present material, CardioCel, is based on acellular pericardium that has been stabilized by treatments, including a low concentration of glutaraldehyde, that eliminate calcification after implantation. In the present study, we have assessed this material using human bone marrow mesenchymal stem cells at various cell densities under standard, static cell culture conditions. The initial seeding densities were monitored to evaluate the extent of cell attachment and cell viability, with subsequent cell proliferation assessed up to 4 weeks using an MTS assay. Cell morphology, infiltration, and spreading were tracked using scanning electron microscopy and phalloidin staining. The efficacy of long-term cell survival was further assessed by examining the extent and type of new tissue formation on seeded scaffolds at 70 days; both type I and type III collagens were present in fibrillar structures on these scaffolds indicating that the seeded stem cells had the capacity to differentiate into collagen-producing cells necessary to repair damaged ECM. These data show that the CardioCel scaffold is an appropriate substrate for the stem cells and has the potential to both retain seeded stem cells and to act as a template for cell propagation and new tissue formation.


Pericardial recesses are formed at sites of reflection of the visceral to parietal pericardium around the great vessels of the mediastinum. Identification at endobronchial ultrasound (EBUS) of a “high-riding” superior pericardial recess, masquerading as a lower paratracheal lymph node, has previously been reported. Although the potential for the posterior pericardial recess to be seen in the subcarinal region on computed tomography has been described in the radiology literature, its identification with EBUS has not. We report a case where the posterior pericardial recess was seen with EBUS in the lower subcarinal region adjacent to the bronchus intermedius. It can be clearly differentiated from a lymph node or vascular structure due to its hypoechoic appearance and lack of a color Doppler signal. Bronchoscopists should be aware of the potential to image the posterior pericardial recess with EBUS in the subcarinal region, to avoid confusion at the time of endoscopy.

A Prospective Multi-Center Audit of Nutrition Support Parameters Following Burn Injury.

Pericardial recesses are formed at sites of reflection of the visceral to parietal pericardium around the great vessels of the mediastinum. Identification at endobronchial ultrasound (EBUS) of a “high-riding” superior pericardial recess, masquerading as a lower paratracheal lymph node, has previously been reported. Although the potential for the posterior pericardial recess to be seen in the subcarinal region on computed tomography has been described in the radiology literature, its identification with EBUS has not. We report a case where the posterior pericardial recess was seen with EBUS in the lower subcarinal region adjacent to the bronchus intermedius. It can be clearly differentiated from a lymph node or vascular structure due to its hypoechoic appearance and lack of a color Doppler signal. Bronchoscopists should be aware of the potential to image the posterior pericardial recess with EBUS in the subcarinal region, to avoid confusion at the time of endoscopy.
BACKGROUND: Ventricular assist devices (VADs) have become an important therapy in the management of patients with end-stage heart failure. Driveline infection is the most common late-onset complication in this group of patients. Patients and their caregivers require education regarding management of the driveline to reduce the risk of infection when they are discharged home with a VAD.

PURPOSE: The aim of this study was to develop an educational booklet on VAD driveline care for patients and their caregivers. A literature review was undertaken to explore the availability of patient education material pertaining to driveline management and to update evidence-informed knowledge that could potentially reduce infection rates in these patients. This information was evaluated by peers, patients, and caregivers to produce the final colored booklet.

CONCLUSIONS: Driveline care is not comprehensively discussed in the literature and lacks detail in the particulars of wound care, patient education, and the adaptation of driveline care to the patient’s home environment. An educational booklet was designed to convey what is currently known about preventing driveline infections to those who are responsible for providing the required daily care. Evaluation of patient education material by those using the material is essential. As with all written material, the information will require updating as new evidence becomes available.

CLINICAL IMPLICATIONS: Managing driveline infection risk for patients at home with extended therapy is a critical nursing issue in improving morbidity and mortality. After VAD implantation, patients and caregivers must be educated about the ongoing care of the driveline exit site to minimize the risk of infection. A rigorously developed and patient-evaluated educational booklet on driveline exit site care can be a valuable reference tool for patients and caregivers after hospital discharge.


A simple education tool for ventricular assist device patients and their caregivers.

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BACKGROUND: Sulfur mustard (SM) is a chemical warfare agent that has been repeatedly used since World War I. SM has chronic and deleterious effects on different body organs such as lungs, skin and eyes.

OBJECTIVES: To determine dental and oral health status of chemical victims of SM who were exposed to SM during the Iraqi-Iran war.

MATERIAL AND METHODS: In this case-control study, 100 male subjects exposed to SM were chosen as cases, and 100 non-exposed volunteers were chosen as controls. These groups were selected randomly according to their referral number, and were matched regarding age. Collection of information was performed using Oral Health Assessment Form designed by the World Health Organization. Quantitative and qualitative data were compared between the groups using independent samples t-test and Chi-


Oral health status among Iranian veterans exposed to sulfur mustard: A case-control study.

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BACKGROUND: Sulfur mustard (SM) is a chemical warfare agent that has been repeatedly used since World War I. SM has chronic and deleterious effects on different body organs such as lungs, skin and eyes.

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square test, respectively.

**RESULTS:** There was a significant difference between the case and control groups with respect to the frequencies of oral candidiasis, pharyngeal erythema and/or hyperplasia, hairy tongue and reflux disease, being higher in the former group. There was also a positive association between the frequency of candidiasis and the percentage of disability: pharyngeal erythema and/or hyperplasia and use of salmeterol spray; and between hairy tongue and antibiotic use in the case group.

**CONCLUSIONS:** Exposure to SM and the use of drugs for controlling long-term complications does not increase the risk of tooth decay, tooth loss, and intra and/or extra oral lesions in patients, but may be associated with increased incidence of oral candidiasis, pharyngeal erythema and/or hyperplasia, hairy tongue and reflux disease. Samples of oral precancerous and cancerous lesions to test sensitivity and specificity and thus validate the clinical applicability of fluorescence imaging in (pre)cancerous diagnostics. Key words: Sulfur mustard, oral health, candidiasis.


**Diabetes, myocardial infarction and stroke are distinct and duration-dependent predictors of subsequent cardiovascular events and all-cause mortality in older men.**

Yeap BB, McCaul KA, et al.

**Objective:** To test the hypothesis that in older men, diabetes duration predicts incident cardiovascular events and death, differently from prior myocardial infarction (MI) or stroke.

**Design, Setting, and Participants:** This was a longitudinal cohort study of 11,728 community-dwelling men aged >65 years in Perth, Western Australia, recruited in 1996-1999.

**Main Outcome Measures:** We assessed all-cause mortality, and deaths or hospital admissions with MI or stroke between recruitment and December 2010, analyzing age-specific hazard and adjusting for smoking, education, alcohol, exercise, BMI, hypertension, and hypercholesterolemia.

**Results:** Among 1433 (12.2%) men with diabetes, 208 (14.5%) reported age of onset of diabetes <55 years, 451 (31.5%) 55-64 years, 679 (47.4%) 65-74 years with 95 (6.6%) >74 years. Diabetes independently predicted increased all-cause mortality with hazard ratio (HR) of 1.37 (95% confidence interval [CI] = 1.15-1.62) for a duration of 5-9 years, 1.35 (1.18-1.55) for 10-14 years, 1.42 (1.22-1.66) for 15-19 years, and 1.75 (1.45-2.11) for 20-24 years. Mortality from MI was increased for diabetes duration up to 25 years, while stroke-specific mortality increased progressively with diabetes duration and a hazard ratio of 1.42 (1.22-1.66) for 15-19 years, and 1.75 (1.45-2.11) for 20-24 years.

**Conclusions:** In older men, increasing duration of diabetes predicts stable increases in all-cause and MI-related mortality and a progressively higher risk of stroke deaths. Prior MI was associated with increased risk of subsequent MI, and prior stroke with subsequent stroke, particularly in the 10-20 years following the first event. Diabetes is a duration-dependent risk factor for cardiovascular events which influences outcomes differently from prior vascular disease.

**Publication Types:** Research Support, Non-U.S. Govt


**Higher serum undercarboxylated osteocalcin and other bone turnover markers are associated with decreased diabetes risk and lower estradiol concentrations in older men.**

Yeap BB, Alfonso H, et al.

**Objective:** To test the hypothesis that in mice, undercarboxylated osteocalcin (ucOC) modulates insulin secretion and sensitivity and increases testosterone (T) secretion from Leydig cells, but human data are lacking. We hypothesized that ucOC is associated with diabetes risk and modulates sex hormone concentrations in older men, distinct from other bone turnover markers.

**Participants:** Participants were community-dwelling men aged 70 to 89 years resident in Perth, Western Australia.

**Main Outcome Measures:** Serum total osteocalcin (TOC), N-terminal propeptide of type I collagen (P1NP), and collagen type I C-terminal cross-linked telopeptide (CTX) were measured by immunoaassay, and ucOC by hydroxyapatite binding. Plasma total T, DHT, and estradiol (E2) were assayed by mass spectrometry.

**Results:** Excluding men with osteoporosis or conditions affecting sex hormones or on bisphosphonates, glucocorticoids, or
Reference intervals for bone turnover markers and their association with incident hip fractures in older men: the Health in Men study.

Chubb, S.A.; Bays, H.; Austad, N.; et al.

OBJECTIVE: The purpose of this article was to determine the reference intervals for serum total osteocalcin (tOC), undercarboxylated osteocalcin (ucOC), N-terminal propeptide of type I collagen (PINP), and collagen type I C-terminal cross-linked telopeptide (CTX-I) in healthy older men and to explore factors associated with BTMs, including hip fracture risk.

PARTICIPANTS AND SETTING: We studied a population-based cohort of 4248 men aged 70 to 89 years, 4008 of whom had serum samples available for analysis.

INTERVENTIONS: Morning blood samples were collected at the study visit. Comorbid conditions were assessed by questionnaire. The reference sample comprised fasting men (n = 298, median age 75.3 years [interquartile range 73.9-78.1 years) reporting excellent or very good health, without a history of diabetes, cardiovascular disease, cancer, depression, or dementia.

MAIN OUTCOME MEASURES: Serum tOC, PINP, and CTX-I were estimated by automated electrochemiluminescence immunoassays, ucOC was estimated using hydroxyapatite binding, and incident hip fractures were captured from hospital admission data.

RESULTS: Reference intervals for tOC, ucOC, PINP, and CTX-I were 10.2 to 41.0, 5.2 to 21.9, 18 to 129 µg/L, and 117 to 740 ng/L, respectively. tOC, ucOC and CTX-I were associated with hip fracture incidence, but after adjustment for other risk factors only tOC remained significantly associated.

CONCLUSIONS: Higher bone remodeling rates are associated with reduced diabetes risk in older men. Higher ucOC is both a marker of bone remodeling and an independent predictor of reduced diabetes risk. E2 is inversely associated with bone turnover markers. We found no evidence ucOC modulates circulating T in older men.
OBJECTIVE: The objective of the study was to compare the LDL-C-lowering efficacy of adding alirocumab vs other common lipid-lowering strategies.

DESIGN, PATIENTS, AND INTERVENTIONS: Patients (n = 355) with very high CVD risk and LDL-C levels of 70 mg/dL or greater or high CVD risk and LDL-C of 100 mg/dL or greater on baseline atorvastatin 20 or 40 mg were randomized to one of the following: 1) add-on alirocumab 75 mg every 2 weeks (Q2W) sc; 2) add-on ezetimibe 10 mg/d; 3) double atorvastatin dose; or 4) for high CVD risk and LDL-C of 100 mg/dL or greater on baseline atorvastatin 20 or 40 mg were randomized to one of the following: 1) add-on alirocumab 75 mg every 2 weeks (Q2W) sc; 2) add-on ezetimibe 10 mg/d; 3) double atorvastatin dose; or 4) for atorvastatin 40 mg regimen only, switch to rosuvastatin 40 mg. For patients not achieving protocol-defined LDL-C goals, the alirocumab dose was increased (blinded) at week 12 to 150 mg Q2W.

MAIN OUTCOME MEASURE: The primary end point was percentage change in calculated LDL-C from baseline to 24 weeks (intent to treat).

RESULTS: Among atorvastatin 20 and 40 mg regimens, respectively, add-on alirocumab reduced LDL-C levels by 44.1% and 54.0% (P < .001 vs all comparators); add-on ezetimibe, 20.5% and 22.6%; doubling of atorvastatin dose, 5.0% and 4.8%; and switching to rosuvastatin 40 mg, 7.3% and 3.2% (P < .001 vs all dosing strategies).
atorvastatin 40 mg to rosuvastatin 40 mg, 21.4%. Most alirocumab-treated patients (87.2% and 84.6%) achieved their LDL-C goals. Most alirocumab-treated patients (86%) maintained their 75-mg Q2W regimen. Treatment-emergent adverse events occurred in 65.4% of alirocumab patients vs 64.4% ezetimibe and 63.8% double atorvastatin/switch to rosuvastatin (data were provided).

CONCLUSIONS: Adding alirocumab to atorvastatin provided significantly greater LDL-C reductions vs adding ezetimibe, doubling atorvastatin dose, or switching to rosuvastatin and enabled greater LDL-C goal achievement.

METHODS: Physicians from 3 economically developed Asian countries were requested to anonymously complete a structured
OBJECTIVE: To assess awareness, knowledge, and perception of FH among practicing physicians in Japan, South Korea, and
individuals in the Asia-Pacific region.

RESULTS: There were 3384 men followed for 7.0 years, during which 293 experienced an MI, 251 stroke, and 2840 neither. In
multivariable analyses, higher ratio of UCOC/TOC (expressed as %) was associated with lower incidence of MI (quartiles Q2-4, >49% versus Q1, <49%, hazard ratio 0.70, 95% confidence interval = 0.54-0.91), but not of stroke (0.99, 0.73-1.34). Higher P1NP was
associated with higher incidence of MI (Q2-4, >28.2 mg/L versus Q1, <28.2 mg/L, hazard ratio 1.45, 95% confidence interval = 1.06-1.97), but not of stroke (0.94, 0.70-1.26). CTX was not associated with incident MI or stroke.

CONCLUSIONS: A reduced proportion of undercarboxylated osteocalcin or higher P1NP are associated with increased incidence of
MI. UCOC/TOC ratio and P1NP predict risk of MI but not stroke, in a manner distinct from CTX. Further studies are needed to
investigate potential mechanisms by which bone turnover markers related to metabolic risk and to collagen formation could
modulate cardiovascular risk.


Association of plasma ceramides and sphingomyelin with VLDL apoB-100 fractional catabolic rate before and after
rosuvastatin treatment.

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Introduction: The objective of the study was to examine post hoc associations between plasma sphingolipids and lipoprotein
kinetics in men with the metabolic syndrome after rosuvastatin treatment. Materials and Methods: Plasma sphingolipid profiling,
determined by tandem mass spectrometry, was performed in a randomized, double-blind, triple-crossover trial (n = 12) of 5-week
treatment periods with placebo or rosuvastatin (10 or 40 mg/d) with 2-week washouts between treatments. Results and Discussion:
Baseline plasma ceramides were associated with very low-density lipoprotein (VLDL) apolipoprotein (apo)-B-100 concentration (r = 0.58, P < .05) and inversely with VLDL apoB-100 fractional catabolic rate (FCR; r = -0.67, P = .02). Posttreatment changes with rosuvastatin (40 mg/d) in plasma ceramides were inversely associated with VLDL apoB-100 FCR (r = -0.62, P = .03) independent of changes in plasma triglycerides, cholesterol, and low-density lipoproteincholesterol. By contrast, baseline and postrosuvastatin treatment plasma sphingomyelin levels were not associated with apoB-100 kinetics. Plasma ceramides and sphingomyelin were not
associated with the kinetics or concentrations of high-density lipoprotein apoA-I, and low-density lipoprotein apoB. In the metabolic
syndrome, the ability of rosuvastatin to increase VLDL apoB-100 FCR may reflect ceramide-specific mechanistic actions and/or
sphingolipid exchange.


Significant gaps in awareness of familial hypercholesterolemia among physicians in selected Asia-Pacific countries:
A pilot study.

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Ding,Phillip Y A. Department of Cardiovascular Medicine, Yonghe Cardinal Tien Hospital, Fu Jen Catholic University, New Taipei City, Taiwan. Selvey,Sherly. Genzyme, A Sanofi Company, Cambridge, MA, USA. Ali,Shariq. Genzyme, A Sanofi Company, Cambridge, MA, USA. Watts,Gerald F. School of Medicine and Pharmacology, University of Western Australia, Western Australia, Australia; Lipid Disorders Clinic, Cardiometabolic Service, Department of Internal Medicine, Royal Perth Hospital, Western Australia, Australia.

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BACKGROUND: Familial hypercholesterolemia (FH) is a dominantly inherited disorder characterized by high plasma cholesterol levels and a very high risk of early heart disease. The prevalence of FH is estimated to be at least 1:500, with at least 3.6 million individuals in the Asia-Pacific region.

OBJECTIVE: To assess awareness, knowledge, and perception of FH among practicing physicians in Japan, South Korea, and Taiwan.

METHODS: Physicians from 3 economically developed Asian countries were requested to anonymously complete a structured
Internet-based survey regarding FH. This survey sought responses on the clinical description, inheritance, prevalence, cardiovascular disease risk, practices, and opinions on screening.

RESULTS: Of 230 physicians surveyed, 47% were aware of the heritability, 27% of the prevalence, and 13% of the risk of cardiovascular disease relating to FH. The majority (70%) perceived themselves to have an above-moderate familiarity with FH. Primary care physicians (59%) and lipid specialists (41%) were perceived as the best providers for caring for FH, including cascade screening services, with a lesser role perceived for cardiologists, endocrinologists, and no significant role for nursing staff. Only 35% of physicians were aware of specialist clinical services for lipid disorders in their geographic area.

CONCLUSION: Extensive education and training programs are required to complement the implementation of region-specific models of care for FH in Asia. Further enhancement of existing lipid services and facilities are also warranted to optimise service models.


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Frequency of familial hypercholesterolemia in patients with early-onset coronary artery disease admitted to a coronary care unit.

Pang J, Poulter EB, et al.

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BACKGROUND: Familial hypercholesterolemia (FH) is the most common dominantly inherited cause of premature coronary artery disease (CAD). However, the diagnosis of FH in patients who have premature CAD in hospital settings is under-recognized, this also represents a missed opportunity for screening their close family members and implementing primary prevention.

OBJECTIVE: To investigate the point prevalence of FH in a coronary care unit (CCU) among patients with early-onset CAD.

METHODS: The prevalence of FH, based on modified phenotypic Dutch Lipid Clinic Network Criteria, and the spectrum of associated CAD risk factors, were investigated in a CCU setting. Data were collected on 175 coronary care patients with onset of CAD at age <60 years.

RESULTS: The prevalence of probable/definite FH was 14.3% (95% confidence interval, 9.0%−19.5%); 46.3% of the patients gave a family history of premature CAD and 20.6% had an untreated low-density lipoprotein cholesterol >5.0 mmol/L. Diabetes, hypertension, obesity, and smoking were common and equally prevalent in patients with and without FH.

CONCLUSIONS: FH is relatively frequent among patients with a history of early-onset CAD in the CCU. Every effort should be made to detect FH in these patients and to initiate cascade testing of available family members to prevent the development of CAD in those who may be unaware that they also have the condition.


The possible future roles for iPSC-derived therapy for autoimmune diseases.

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The ability to generate inducible pluripotent stem cells (iPSCs) and the potential for their use in treatment of human disease is of immense interest. Autoimmune diseases, with their limited treatment choices are a potential target for the clinical application of stem cell and iPSC technology. iPSCs provide three potential ways of treating autoimmune disease; (i) providing pure replacement of lost cells (immuno-reconstitution); (ii) through immune-modulation of the disease process in vivo; and (iii) for the purposes of disease modelling in vitro. In this review, we will use examples of systemic, system-specific and organ-specific autoimmunity to explore the potential applications of iPSCs for treatment of autoimmune diseases and review the evidence of iPSC technology in auto-immunity to date.
**A 66-year-old man with severe sepsis.**


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**The role of evidence based medicine in neurotrauma.**

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The introduction of evidence based medicine de-emphasised clinical experience and so-called "background information" and stressed the importance of evidence gained from clinical research when making clinical decisions. For many years randomised controlled trials have been seen to be the only way to advance clinical practice, however, applying this methodology in the context of severe trauma can be problematic. In addition, it is increasingly recognised that considerable clinical experience is required in order to critically evaluate the quality of the evidence and the validity of the conclusions as presented. A contemporary example is seen when considering the role of decompressive craniectomy in the management of neurotrauma. Although there is a considerable amount of evidence available attesting to the efficacy of the procedure, considerable clinical expertise is required in order to properly interpret the results of these studies and the implications for clinical practice. Given these limitations the time may have come for a redesign of the traditional pyramid of evidence, to a model that re-emphasises the importance of "background information" such as pathophysiology and acknowledges the role of clinical experience such that the evidence can be critically evaluated in its appropriate context and the subsequent implications for clinical practice be clearly and objectively defined.

**Propofol as a substitute for amobarbital in Wada testing.**

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We describe a patient with equivocal findings on functional MRI (fMRI), who underwent a propofol Wada test, review the literature on this topic and suggest a protocol for the use of propofol for a Wada test. Although fMRI techniques can usually accurately lateralize language, the Wada test remains the gold standard for preoperative lateralization and is occasionally still required if there are non-diagnostic findings on fMRI. Amobarbital, the agent of choice for the Wada test, has become increasingly difficult to obtain and requires regulatory approval, which may delay definitive management and have an impact on patient outcomes. Propofol has been suggested as an alternative to amobarbital, and while there is some published data on this, there is no reported Australian experience to date. Copyright © 2015 Elsevier Ltd. All rights reserved.

**Development of Australian clinical practice outcome standards for graduates of critical care nurse education.**

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Patients' preferences for adjuvant sorafenib after resection of intermediate or high-risk renal cell carcinoma in the SORCE trial: What makes it worthwhile?

P.L. Blinman

Background: SORCE is an international, double-blind, placebo-controlled, phase 3 trial comparing adjuvant sorafenib for 1 year, for 3 years, or observation after resection of intermediate or high risk renal cell carcinoma (RCC). We determined the survival benefits that SORCE participants judged necessary to make adjuvant sorafenib worthwhile 3 months after starting study treatment. Methods: Participants recruited to SORCE from Australia and selected UK sites completed a validated, self-administered questionnaire 3 months after starting study treatment to determine the minimum survival benefits they judged necessary to make adjuvant sorafenib worthwhile. Scenarios used baseline survival times (without adjuvant sorafenib) of 5 and 15 years; and baseline survival rates (without adjuvant sorafenib) of 65% and 85% at 5 years. Preferences were determined for 1 year of adjuvant sorafenib (versus none) and for 3 years of adjuvant sorafenib (versus 1 year). All tests were 2-sided and non-parametric. This substudy of SORCE was conducted by the Australian and New Zealand Urological and Prostate Cancer Trials Group (ANZUP). Results: The 179 participants were mostly male (72%) with a median age of 57 years (range 29 to 78). Participants allocated sorafenib judged larger benefits necessary to make 1 year of adjuvant sorafenib worthwhile than those allocated placebo: median benefit of an extra 1 year versus an extra 1 month for baselines of 5 years (p=0.004) and 15 years (p=0.02); median benefit of an extra 5% versus an extra 1% for baseline of 65% (p=0.03), and an extra 3% versus an extra 1% for a baseline of 85% (p=0.07). Larger survival benefits were judged necessary to make 3 years of adjuvant sorafenib worthwhile (versus 1 year) regardless of treatment allocation: median benefit of an extra 2 months to 1 year for baselines of 5 years (p=0.02) and 15 years (0.02). Conclusions: Experienced toxicity and duration of treatment are important determinants of patients' preferences for adjuvant sorafenib in RCC.
Background: Androgen deprivation therapy (ADT) including a luteinising hormone releasing hormone analogue (LHRHA) is standard of care given before, during, and after radiotherapy for localised prostate cancer (PC) at high risk of recurrence. Enzalutamide is a new, second generation androgen receptor (AR) inhibitor that is more potent and binds with a higher affinity to the AR than conventional non-steroidal anti-androgens (NSAA), and improves survival in metastatic, castration-resistant PC. We hypothesise that the incorporation of enzalutamide in adjuvant ADT, given before, during, and after radiation therapy for localised PC at high risk of recurrence will further improve outcomes. The aim is to determine the effectiveness of enzalutamide as part of adjuvant ADT with a LHRHA in men planned for radiotherapy for localised PC at high risk of recurrence.

Methods: DESIGN Open label, randomised, stratified, 2-arm, phase 3 intergroup trial. ELIGIBILITY Localised PC, high risk of recurrence, suitable for EBRT with curative intent.

SAMPLE SIZE 800 participants accrued over 2 yrs + 5.5 years minimum f/up for 80% power to detect a 33% reduction in the specific survival, PSA progression free survival (PFS), clinical PFS, health related quality of life, adverse events, cost-effectiveness. STRATIFICATION Gleason 8-10, T3-4, PSA > 20, study site.

ENDPOINTS Overall survival (primary), cause-specific survival, PSA progression free survival (PFS), clinical PFS, health related quality of life, adverse events, cost-effectiveness. SAMPLE SIZE 800 participants accrued over 2 yrs + 5.5 years minimum f/up for 80% power to detect a 33% reduction in the specific survival, PSA progression free survival (PFS), clinical PFS, health related quality of life, adverse events, cost-effectiveness.

Published by: Journal of Clinical Oncology. 2015; 1. Randomised phase 3 trial of enzalutamide in first line androgen deprivation therapy for metastatic prostate cancer: the ANZUP ENZAMET Trial (ANZUP 1304).

Davis ID, Stockler MR, et al. (Davis, Stockler, Martin, Marchesi, Deignan, McDermott, Parulekar, North, Graham, Long, Roncolato, Yip, Hague, Dazo, Coskinas, Sweeney) Monash University Eastern Health Clinical School, Box Hill, Australia; NHMRC Clinical Trials Centre, The University of Sydney, Sydney, Australia; NHRMC Clinical Trials Centre, University of Sydney, Sydney, Australia; ICORG, Dublin, Ireland; NCIC Clinical Trials Group, Cancer Research Institute, Queen's University, Kingston, ON, Canada; Cross Cancer Institute, Edmonton, AB, Canada; Queen's University, Kingston, ON, Canada; Royal Perth Hospital, Willetton, WA, Australia; NHMRC Clinical Trials Centre, Camperdown, Australia; Sydney Catalyst Translational Cancer Research Centre, Sydney, Australia; NHMRC Clinical Trials Centre, Sydney, Australia; Dana-Farber Cancer Institute, Boston, MA I. D. D. Davis.

Background: Androgen deprivation therapy (ADT) with a luteinising hormone releasing hormone analogue (LHRHRA) or surgical castration, either alone or combined with conventional non-steroidal anti-androgens (NSAA), is widely used as initial treatment for hormone-naive, metastatic prostate cancer (PC). Meta-analysis of RCTs showed a 3% absolute improvement in 5 year survival with the addition of NSAA to ADT. Residual, low level androgen receptor (AR) signalling or agonist activity from conventional NSAA may provide a stimulatory signal to hormone-sensitive PC cells. We hypothesise that early use of enzalutamide, a more potent and effective androgen receptor blocker, will reduce residual AR signalling, and improve survival. The aim is to determine the effectiveness of ADT + enzalutamide versus ADT + conventional NSAA, as 1st line endocrine therapy for M1 PC. Methods: DESIGN Open label, randomised, stratified, 2-arm, intergroup, phase 3 trial including ANZ, Canada, UK and USA. ELIGIBILITY Metastatic PC starting 1stline ADT. STRATIFICATION Volume of disease, anti-resorptive therapy, comorbidities, early docetaxel use, study site. ASSESSMENTS Baseline, days 29 and 85 then 12 weekly until clinical progression; imaging prior to randomisation and on progression (PSA and clinical). Tertiary correlative objectives include identification of prognostic/predictive biomarkers from archival tumour tissue and fasting bloods collected at baseline, week 24 and progression (PSA and clinical). Publication Types: Conference Abstract

Published by: Journal of Clinical Oncology. 2015; 1. Final analysis of a randomized comparison of letrozole (Let) vs observation (Obs) as late reintroduction of adjuvant endocrine therapy (AET) for postmenopausal women with hormone receptor positive (HR+) breast cancer (BC) after completion of prior AET: ANZBCTG 0501 (LATER).

Zdenkowski N, Green M, et al. (Zdenkowski, Green, Boyle, Kannourakis, Gill, Bayliss, Saunders, Della-Fiorentina, Kling, Campbell, Gebski, Veillard, Davies, Thornton, Fong, Reaby, Forbes) Australia and New Zealand Breast Cancer Trials Group, Newcastle, Australia; Royal Melbourne Hospital, Toorak, Australia; University of Sydney and Mater Hospital, North Sydney, Australia; Ballarat Oncology and Haematology Services, Ballarat, Australia; Royal Adelaide Hospital, Adelaide, Australia; Royal Perth Hospital, Perth, Australia; Sir Charles Gairdner Hospital, Perth, Australia; Macarthur Cancer Therapy Centre, Campbelltown, Australia; Bunbury and St John of God Medical Centre, Bunbury, Australia; Waikato Hospital, Hamilton, New Zealand; National Health and Medical Research Council Clinical Trials Centre, Sydney, Australia; University of Newcastle, Newcastle, Australia
Mutations of the human Kirsten rat sarcoma viral oncogene homologue (KRAS) and the highly homologous human neuroblastoma RAS viral oncogene homologue (NRAS) are associated with resistance to antiepidermal growth factor receptor therapies in patients with colorectal cancer. In this report, we describe a caecal adenocarcinoma that contains both KRAS c.35G>T (G12V) and NRAS c.34G>A (G12S) mutations. The adenocarcinoma arises from a contiguous high-grade tubulovillous adenoma, which also carries the identical KRAS and NRAS mutations, supporting their common origin. While KRAS mutations are common in colorectal cancers, NRAS mutations are relatively rare and the coexistence of multiple RAS mutations is not documented, presumably reflecting similar functions of wild-type and mutant forms of RAS. Recent experimental evidence has suggested that KRAS and NRAS may in fact mediate distinct biological processes in the colon, and this unusual case potentially illustrates the hypothesis clinically. NRAS mutations are relatively rare and the coexistence of multiple RAS mutations is not documented, presumably reflecting similar functions of wild-type and mutant forms of RAS. Recent experimental evidence has suggested that KRAS and NRAS may in fact mediate distinct biological processes in the colon, and this unusual case potentially illustrates the hypothesis clinically. NRAS mutations are relatively rare and the coexistence of multiple RAS mutations is not documented, presumably reflecting similar functions of wild-type and mutant forms of RAS. Recent experimental evidence has suggested that KRAS and NRAS may in fact mediate distinct biological processes in the colon, and this unusual case potentially illustrates the hypothesis clinically. NRAS mutations are relatively rare and the coexistence of multiple RAS mutations is not documented, presumably reflecting similar functions of wild-type and mutant forms of RAS. Recent experimental evidence has suggested that KRAS and NRAS may in fact mediate distinct biological processes in the colon, and this unusual case potentially illustrates the hypothesis clinically. NRAS mutations are relatively rare and the coexistence of multiple RAS mutations is not documented, presumably reflecting similar functions of wild-type and mutant forms of RAS. Recent experimental evidence has suggested that KRAS and NRAS may in fact mediate distinct biological processes in the colon, and this unusual case potentially illustrates the hypothesis clinically. Copyright Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to http://group.bmj.com/group/rights-licensing/permissions.


Antipsychotic polypharmacy is not associated with reduced dose of individual antipsychotics in schizophrenia.

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Publication Types: Letter


Depressive Symptoms before and after Treatment of Obstructive Sleep Apnea in Men and Women.

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Disorders Research Institute, Queen Elizabeth II Medical Centre, Nedlands, Australia. Simpson,Laila. Centre for Genetic Origins of Health and Disease, University of Western Australia, Crawley, Australia. Simpson,Laila. Centre for Sleep Science, School of Anatomy, Physiology and Human Biology, University of Western Australia, Crawley, Australia. Palmer,Lyle J. The Joanna Briggs Institute and School of Translational Health Science, University of Adelaide, Adelaide, Australia. Almeida,Osvaldo P. WA Centre for Health & Ageing and School of Psychiatry & Clinical Neurosciences, University of Western Australia, Crawley, Australia; Department of Psychiatry, Royal Perth Hospital, Perth, Australia. Hillman,David R. School of Surgery, University of Western Australia, Crawley, Australia. Hillman,David R. West Australian Sleep Disorders Research Institute, Queen Elizabeth II Medical Centre, Nedlands, Australia. Hillman,David R. Department of Pulmonary Physiology and Sleep Medicine, Sir Charles Gairdner Hospital, Nedlands, Australia. Hillman,David R. Centre for Sleep Science, School of Anatomy, Physiology and Human Biology, University of Western Australia, Crawley, Australia.

STUDY OBJECTIVES: To determine prevalence of depressive symptoms in obstructive sleep apnea (OSA) and the impact of OSA treatment on depression scores.

METHODS: Consecutive new patients referred for investigation of suspected OSA were approached. Consenting patients completed a patient health questionnaire (PHQ-9) for depressive symptoms when attending for laboratory polysomnography. Those with moderate/severe (apneahypopnea index [AHI] > 15 events/h) and/or symptomatic mild OSA (AHI 5-14.99 events/h) were offered continuous positive airway pressure (CPAP) therapy. PHQ-9 was repeated after 3 months of CPAP with compliance recorded. Of a maximum PHQ-9 score of 27, a cut point > 10 (PHQ-9 > 10) was used to indicate presence of clinically significant depressive symptoms.

RESULTS: A total of 426 participants (243 males) were recruited. Mean +/- standard deviation body mass index (BMI) was 32.1 +/- 7.1 kg/m(2) and AHI 33.6 +/- 28.9 events/h, PHQ-9 was 10.5 +/- 6.1 and independently related to AHI (p < 0.001) and BMI (p < 0.001). In those without OSA, PHQ-9 > 10 was more common in women, but no gender difference was evident with OSA. Of 293 patients offered CPAP, 228 were compliant (mean nightly use > 5 h) over 3 months of therapy. In them, with therapy, AHI decreased from 46.7 +/- 27.4 to 6.5 +/- 1.6 events/h, PHQ-9 from 11.3 +/- 6.1 to 3.7 +/- 2.9 and PHQ-9 > 10 from 74.6% to 3.9% (p < 0.001 in each case). Magnitude of change in PHQ-9 was similar in men and women. Antidepressant use was constant throughout.


The effect of prognostic data presentation format on perceived risk among surrogate decision makers of critically ill patients: a randomized comparative trial.

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PURPOSE: The purpose of this study is to determine whether varying the format used to present prognostic data alters the perception of risk among surrogate decision makers in the intensive care unit (ICU).

METHODS: This was a prospective randomized comparative trial conducted in a 23-bed adult tertiary ICU. Enrolled surrogate decision makers were randomized to 1 of 2 questionnaires, which presented hypothetical ICU scenarios, identical other than the format in which prognostic data were presented (eg, frequencies vs percentages). Participants were asked to rate the risk associated with each prognostic statement.

RESULTS: We enrolled 141 surrogate decision makers. The perception of risk varied significantly dependent on the presentation format. For "quantitative data," risks were consistently perceived as higher, when presented as frequencies (eg, 1 in 50) compared with equivalent percentages (eg, 2%). Framing "qualitative data" in terms of chance of "death" rather than "survival" led to a statistically significant increased in perceived risks. Framing "quantitative" data in this way did not significantly affect risk perception.

CONCLUSION: Data format had a significant effect on how surrogate decision makers interpreted risk. Qualitative statements are interpreted widely and affected by framing. Where possible, multiple quantitative formats should be used for presenting prognostic information. Crown Copyright © 2014. Published by Elsevier Inc. All rights reserved. http://www.ncbi.nlm.nih.gov/pubmed?tool=iaufhslib&term=25480457


Effect of intestinal resection on quality of life in Crohn's disease.

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METHODS: This was a prospective randomized comparative trial conducted in a 23-bed adult tertiary ICU. Enrolled surrogate decision makers were randomized to 1 of 2 questionnaires, which presented hypothetical ICU scenarios, identical other than the format in which prog...
INTRODUCTION: Patients with Crohn's disease have poorer health-related quality of life [HRQoL] than healthy individuals, even when in remission. Although HRQoL improves in patients who achieve drug-induced or surgically induced remission, the effects of surgery overall have not been well characterised.

METHODS: In a randomised trial, patients undergoing intestinal resection of all macroscopically diseased bowel were treated with postoperative drug therapy to prevent disease recurrence. All patients were followed prospectively for 18 months. C-reactive protein [CRP], Crohn's Disease Activity Index [CDAI], and faecal calprotectin [FC] were measured preoperatively and at 6, 12, and 18 months. HRQoL was assessed with a general [SF36] and disease-specific [IBDQ] questionnaires at the same time points.

RESULTS: A total of 174 patients were included. HRQoL was poor preoperatively but improved significantly [p < 0.001] at 6 months postoperatively. This improvement was sustained at 18 months. Females and smokers had a poorer HRQoL when compared with males and non-smokers, respectively. Persistent endoscopic remission, intensification of drug treatment at 6 months, and anti-tumour necrosis factor therapy were not associated with HRQoL outcomes different from those when these factors were not present. There was a significant inverse correlation between CDAI, [but not endoscopic recurrence, CRP, or FC] on HRQoL.

CONCLUSION: Intestinal resection of all macroscopic Crohn's disease in patients treated with postoperative prophylactic drug therapy is associated with significant and sustained improvement in HRQoL irrespective of type of drug treatment or endoscopic recurrence. HRQoL is lower in female patients and smokers. A higher CDAI, but not direct measures of active disease or type of drug therapy, is associated with a lower HRQoL.

(2.5%) congenital malformations. Development was normal in all babies using routine infant checks. There was an inverse correlation between duration since last dose and both cord drug levels (IFX: r = -0.58; ADA: r = -0.41, both p < 0.0001) and maternal levels (IFX: r = -0.63; ADA: r = -0.64, both p < 0.0001). Cord blood and maternal drug levels also correlated (IFX: r = 0.67; ADA: r = 0.64, both p < 0.0001). Last ATNF dose was at median gestational week (GW) 30 in IFX, (8-37) and 35 in ADA (14-41) treated mothers. Drug was ceased prior to GW 30 in 31% of mothers. Cessation prior to GW30 did not increase the risk of disease activity in the 3rd trimester or postpartum. Median maternal and cord drug levels were 2 (0-22.2mcg/ml) and 5.9 (0.12-28.7mcg/ml) for IFX and 1.5 (0-10mcg/ml) and 2 (0-12.1mcg/ml) for ADA. Levels were significantly lower when drug was stopped prior to GW30. Conclusions: No increased risk of adverse pregnancy or developmental outcomes. Maternal and cord ATNF levels inversely correlated with duration since last exposure. Cord blood levels correlated with maternal level at delivery. Maternal cessation of ATNF prior to week 30 significantly reduced fetal exposure without disease exacerbation. However, clearance took up to 12 months. Therefore, live vaccinations should be avoided prior to 1 year unless drug clearance is documented. 44 (55%) babies had cleared drug, 36 are still in testing. Median time to clearance was 6 months (0-12) for both drugs. Drug type and weeks since last dose predicted clearance by 3 months (AUROC 0.81, p=0.002).


Is dental hygiene associated with survival? A 12 year cohort pilot study.

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Objectives: Poor dental hygiene may contribute to poor pulmonary outcomes by transmission of oral bacteria to the lower airways. This prospective pilot study aimed to establish if measures of dental hygiene were correlated with death or lung transplantation at follow up. Methods: Children and young adults with CF diagnosed on standard criteria attending a specialist CF centre were formally assessed at baseline for oral hygiene problems. All subjects also completed a questionnaire on tooth brushing habits [Arch Dis Ch 2003; 88: 702-7]. Subjects were followed for 12 years until death or lung transplantation. Ethical approval was obtained (ECC6-05/11/2012). Results: A total of 68 subjects were enrolled at baseline. Follow up data were available for analysis on 45/68 (66%). 21 (46.7%) male; mean age (2001) 11.4 years (range 4-17.5); 41 (91%) had two recognised CF mutations. By the end of the study period 12 subjects reached the primary outcome of death or lung transplantation. 75% (n = 34) had dental caries at baseline. The presence of calculus (dental plaque) showed statistical significant association with death or transplantation (p = 0.009) in univariate analysis, although the presence of caries and other dental measures did not [frequency of tooth brushing odds ratio (OR) 0.727 (range 0.19-2.79), p = 0.64; presence of dental caries OR 2.0 (0.49-8.08), p = 0.331]. Conclusion: Markers of good dental care are associated with transplant-free survival. Further studies are needed to determine whether poor dental hygiene causes poor pulmonary outcomes, is a proxy marker of other adverse factors (socioeconomic status, adherence) or even by sugar containing medications given to children.

Publication Types: Conference Abstract


Temporal changes in the prevalence and associates of foot ulceration in type 2 diabetes: The Fremantle Diabetes Study.

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Aims To assess temporal changes in foot ulceration and its risk factors in community-based people with type 2 diabetes. Methods Baseline data from the longitudinal observational Fremantle Diabetes Study collected from 1993 to 1996 (Phase I) and 2008 to 2011 (Phase II) were analyzed. Generalized linear modeling was used to examine changes in foot ulcer prevalence and its associates between phases. Multiple logistic regression was used to determine associates of prevalent foot ulceration in individual and pooled phases. Results There were 16 foot ulcers among 1296 patients in Phase I (1.2%) and 23 in 1509 Phase II patients (1.5%; P = 0.67; ADA: r = 0.64, both p < 0.0001). Last ATNF dose was at median gestational week (GW) 30 in IFX, (8-37) and 35 in ADA (14-41) treated mothers. Drug was ceased prior to GW 30 in 31% of mothers. Cessation prior to GW30 did not increase the risk of disease activity in the 3rd trimester or postpartum. Median maternal and cord drug levels were 2 (0-22.2mcg/ml) and 5.9 (0.12-28.7mcg/ml) for IFX and 1.5 (0-10mcg/ml) and 2 (0-12.1mcg/ml) for ADA. Levels were significantly lower when drug was stopped prior to GW30. Conclusions: No increased risk of adverse pregnancy or developmental outcomes. Maternal and cord ATNF levels inversely correlated with duration since last exposure. Cord blood levels correlated with maternal level at delivery. Maternal cessation of ATNF prior to week 30 significantly reduced fetal exposure without disease exacerbation. However, clearance took up to 12 months. Therefore, live vaccinations should be avoided prior to 1 year unless drug clearance is documented. 44 (55%) babies had cleared drug, 36 are still in testing. Median time to clearance was 6 months (0-12) for both drugs. Drug type and weeks since last dose predicted clearance by 3 months (AUROC 0.81, p=0.002).

Publication Types: Conference Abstract

Sympathetic tone is well recognised as being implicit in cardiovascular control. It is less readily acknowledged that activation of the sympathetic nervous system is integral in energy homeostasis and can exert profound metabolic effects. Accumulating data from animal and human studies suggest that central sympathetic overactivity plays a pivotal role in the aetiology and complications of several metabolic conditions that can cluster to form the Metabolic Syndrome (MetS). Given the known augmented risk for type 2 diabetes, cardiovascular disease, and premature mortality associated with the MetS understanding the complex pathways underlying the metabolic derangements involved has become a priority. Many factors have been proposed to contribute to increased sympathetic nerve activity in metabolic abnormalities including obesity, impaired baroreflex sensitivity, hyperinsulinemia, and elevated adipokine levels. Furthermore there is mounting evidence to suggest that chronic sympathetic overactivity can potentiate two of the key metabolic alterations of the MetS, central obesity and insulin resistance. This review will discuss the regulatory role of the sympathetic nervous system in metabolic control and the proposed pathophysiology linking sympathetic overactivity to metabolic abnormalities. Pharmacological and device-based approaches that target central sympathetic drive will also be discussed as possible therapeutic options to improve metabolic control in at-risk patient cohorts.

Relevance of Sympathetic Nervous System Activation in Obesity and Metabolic Syndrome.

Thorp AA, Schlaich MP.

Chronic erythropoietin treatment improves diet-induced glucose intolerance in rats.

Erythropoietin (EPO) ameliorates glucose metabolism through mechanisms not fully understood. In this study, we investigated the effect of EPO on glucose metabolism and insulin signaling in skeletal muscle. A 2-week EPO treatment of rats fed with a high-fat diet (HFD) improved fasting glucose levels and glucose tolerance, without altering total body weight or retroperitoneal fat mass. Concomitantly, EPO partially rescued insulin-stimulated AKT activation, reduced markers of oxidative stress, and restored heat-shock protein 72 expression in soleus muscles from HFD-fed rats. Incubation of skeletal muscle cell cultures with EPO failed to induce AKT phosphorylation and had no effect on glucose uptake or glycogen synthesis. We found that the EPO receptor gene was expressed in myotubes, but was undetectable in soleus. Together, our results indicate that EPO treatment improves glucose metabolism. Copyright © 2015 The authors.


**STAT3 is a critical cell-intrinsic regulator of human unconventional T cell numbers and function.**


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for the first time the essential role of STAT3 signaling downstream of IL-23R and IL-21R in controlling human MAIT and NKT cell

STAT3-deficient patients was mirrored by loss-of-function mutations in IL12RB1 and IL21R, respectively. Thus, these results reveal

of STAT3 mosaic individuals revealed that this effect was cell intrinsic. Surprisingly, the residual STAT3-deficient MAIT cells

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and function. We found that individuals with loss-of-function mutations in STAT3 had reduced numbers of peripheral blood MAIT and NKT but not gammadelta T cells. Analysis of STAT3 mosaic individuals revealed that this effect was cell intrinsic. Surprisingly, the residual STAT3-deficient MAIT cells were unable to secrete normal levels of cytokines such as IFNgamma and TNF. The deficiency in MAIT and NKT cells in

of STAT3-deficient patients was mirrored by loss-of-function mutations in IL12RB1 and IL21R, respectively. Thus, these results reveal for the first time the essential role of STAT3 signaling downstream of IL-23R and IL-21R in controlling human MAIT and NKT cell numbers. Copyright © 2015 Wilson et al. http://www.ncbi.nlm.nih.gov/pubmed?tool=iaufhslib&term=25941256

Development and adolescence. Identification of adolescents at risk of NAFLD from childhood anthropometry may expose opportunities to influence the hepatic and metabolic destinies of individuals. We sought associations between NAFLD diagnosed during adolescence and earlier life trajectories of anthropometry, in a population-based cohort of predominantly Caucasian adolescents. METHODS: Assessment for NAFLD, using questionnaires and liver ultrasound, was performed on 1170 adolescents, aged 17 years, from the population-based Raine cohort. We sought associations between NAFLD in adolescents and serial anthropometric measurements recorded from birth, childhood, and adolescence.

RESULTS: NAFLD was diagnosed in 15.2% of adolescents. Birth anthropometry, including birth weight, skinfold thickness, and ponderal index, was not associated with NAFLD. However, adiposity differences between 17-year-old adolescents with NAFLD and those without NAFLD were apparent from age 3 years. Greater adiposity trajectories for weight, body mass index, skinfold thickness, mid-arm circumference, and chest circumference from age 3 years onwards, particularly in males, were associated with the diagnosis of NAFLD and severity of hepatic steatosis at age 17 years (P<0.05). The strength of the associations increased with age after 3 years for each adiposity measure (all P<0.001).

CONCLUSIONS: Trajectories of childhood adiposity are associated with NAFLD. Adiposity attained by 3 years of age and older, but not at birth, was associated with the diagnosis and severity of hepatic steatosis in late adolescence. Exploration of clinically relevant risk factors and preventative measures for NAFLD should begin during childhood. Copyright 2014 Journal of Gastroenterology and Hepatology Foundation and Wiley Publishing Asia Pty Ltd.


Childhood adiposity trajectories and risk of nonalcoholic fatty liver disease in adolescents.

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BACKGROUND AND AIM: Nonalcoholic fatty liver disease (NAFLD) and its metabolic risk factors are recognized during childhood and adolescence. Identification of adolescents at risk of NAFLD from childhood anthropometry may expose opportunities to influence the hepatic and metabolic destinies of individuals. We sought associations between NAFLD diagnosed during adolescence and earlier life trajectories of anthropometry, in a population-based cohort of predominantly Caucasian adolescents.

METHODS: Assessment for NAFLD, using questionnaires and liver ultrasound, was performed on 1170 adolescents, aged 17 years, from the population-based Raine cohort. We sought associations between NAFLD in adolescents and serial anthropometric measurements recorded from birth, childhood, and adolescence.

RESULTS: NAFLD was diagnosed in 15.2% of adolescents. Birth anthropometry, including birth weight, skinfold thickness, and ponderal index, was not associated with NAFLD. However, adiposity differences between 17-year-old adolescents with NAFLD and those without NAFLD were apparent from age 3 years. Greater adiposity trajectories for weight, body mass index, skinfold thickness, mid-arm circumference, and chest circumference from age 3 years onwards, particularly in males, were associated with the diagnosis of NAFLD and severity of hepatic steatosis at age 17 years (P<0.05). The strength of the associations increased with age after 3 years for each adiposity measure (all P<0.001).

CONCLUSIONS: Trajectories of childhood adiposity are associated with NAFLD. Adiposity attained by 3 years of age and older, but not at birth, was associated with the diagnosis and severity of hepatic steatosis in late adolescence. Exploration of clinically relevant risk factors and preventative measures for NAFLD should begin during childhood. Copyright 2014 Journal of Gastroenterology and Hepatology Foundation and Wiley Publishing Asia Pty Ltd.


Statewide hepatitis C model of care for rural and remote regions.

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The evolution of management of hepatitis C virus (HCV) has seen a majority of patients treated being regarded as cured. Despite
this development, uptake of treatment remains low in Australia, and this is particularly true in rural and remote areas. The largest state in Australia, Western Australia (WA), covers an area of 2500km². As the rural and remote population of WA is scattered in small areas rather than major centers, poor accessibility to remote areas and lack of adequate of medical and nursing resources pose major problems in providing equity of care to patients with chronic HCV. A statewide hepatitis model of care, established in 2009, has led to an increase in identification and treatment of patients living with HCV. Strategies used to facilitate these changes include telehealth, a nurse practitioner model, and general practitioner shared-care model. The statewide program will be modified to meet the changing needs of patients as all-oral treatment regimens become available, with further emphasis being placed on the role of rural and remote health professionals in identifying patients with HCV and initiating and monitoring treatment.


Natural history of HFE simple heterozygosity for C282Y and H63D: A prospective 12-year study.
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Background and Aim: The risk of hemochromatosis-related morbidity for HFE simple heterozygosity for either the C282Y or H63D substitutions in the HFE protein was assessed using a prospective community-based cohort study. Methods: HFE genotypes were measured for 31192 persons of northern European descent, aged between 40 and 69 years when recruited to the Melbourne Collaborative Cohort Study, and subjects were followed for an average of 12 years. For a random sample of 1439 participants stratified according to HFE genotype, two sets of biochemical iron indices performed 12 years apart and, at follow-up only, the presence/absence of six disease features associated with hereditary hemochromatosis were obtained. Summary data for 257 (139 female) C282Y simple heterozygotes and 123 (74 female) H63D simple heterozygotes were compared with 330 (181 female) controls with neither HFE mutation. Results: At baseline, mean transferrin saturation (TS) (95% confidence interval) and prevalence of T5>55% were 35.14% (33.25, 37.04) and 0/312 (0%), 33.03% (29.9, 36.15) and 0/39 (0%), and 29.67% (27.93, 31.4) and 3/135 (2%) for C282Y, H63D and wild-type male participants, respectively. At follow-up, mean TS levels remained similar to baseline levels for both men and women irrespective of simple heterozygosity for either mutation. No HFE C282Y or H63D simple heterozygote had documented iron overload (based on hepatic iron measures or serum ferritin greater than 1000μg/L at baseline with documented therapeutic venesection). Conclusion: No documented iron overload was observed for HFE simple heterozygotes for either C282Y or H63D, and morbidity for both HFE simple heterozygote groups was similar to that of HFE wild-type participants.

Factors associated with anti-human leukocyte antigen antibodies in patients supported with continuous-flow devices and effect on probability of transplant and post-transplant outcomes.
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BACKGROUND: One major disadvantage of ventricular assist device (VAD) therapy is the development of human-leukocyte antigen (HLA) antibodies. We aimed to identify factors associated with HLA antibodies during continuous flow (CF)-VAD support and assess the effect on transplant probability and outcomes.
METHODS: We included 143 consecutive heart failure patients who received a CF-VAD as a bridge-to-transplant at 3 institutions. Factors associated with post-VAD peak panel reactive antibodies (PRA) among several measurements were identified using
Multivariable linear regression. A parametric survival model was used to assess transplant waiting time and probability, risk of rejection, and a composite outcome of rejection, graft failure, and death.

RESULTS: Thirty-six patients (25%) were female; mean age was 47 +/- 13 years. Eighty-one patients (57%) had a pre-VAD PRA of 0%; and 16 were highly sensitized (PRA > 80%). Age, female sex, and pre-VAD PRA were independently associated with post-VAD PRA. A 10-year increase in age was associated with a 5% decrease in post-VAD PRA (p = 0.03). Post-VAD PRA was 19% higher in women vs men (p < 0.01). A 10%-increase in pre-VAD PRA was associated with a 4.7% higher post-VAD PRA (p < 0.01). During a mean follow-up of 12 +/- 11 months, 90 patients underwent cardiac transplantation. A 20% increase in post-VAD PRA was associated with 13% lower probability of transplant (hazard ratio, 0.87; 95% confidence interval, 0.76-0.99). A high PRA was not associated with adverse post-transplant outcomes.

CONCLUSIONS: Younger age, female sex, and pre-VAD PRA were independent predictors of elevated PRA post-VAD. Higher PRA was significantly associated with lower transplant probability but not increased rejection, graft failure, or death after transplant.


The use of octreotide to treat refractory gastrointestinal bleeding in patients supported with a continuous-flow left ventricular assist device.

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Purpose: Gastrointestinal bleeding (GIB) with a continuous flow left ventricular assist device (CFLVAD) occurs in up to 40% of patients. Reduction in antiplatelet and anticoagulant agents, with endoscopic directed therapies, are effective treatments. However, when bleeding persists, octreotide (a splanchnic vasoconstrictor) can be highly efficacious. We report our success with octreotide for refractory GIB in CFLVADs. Methods: A retrospective review of all patients with contemporary CFLVADs was performed, focusing on GIB (defined as blood loss requiring at least 2 units of packed cell transfusion). GIB timing, antiplatelet and anticoagulant use, endoscopy findings and outcomes were noted. Results: From 2006 to 2014, 45 contemporary CFLVADs were implanted (8 Heartmate II, 37 Heartware devices). 10 patients (22%) suffered a GIB event, requiring short term cessation of anti-platelets (60% of cases) and anticoagulants (100% of cases). All had endoscopy, and when diagnostic, 87% of GIB were noted in the upper GI tract, 50% being classed as arterio-venous malformations (AVM). 8/10 patients had refractory bleeding and required octreotide, which was well tolerated by all patients. Octreotide dosing was 100mcg s.c. tds or bd in all patients with 4/8 starting on intravenous infusions prior. All patients had cessation of bleeding with octreotide, enabling recommencement of anti-platelet and/or anti-coagulants. Table 1 summarises patients requiring octreotide. Patients 5 and 7 required long term s.c. octreotide for recurrent bleeding with no subsequent GIB event requiring admission. Conclusion: GIB post CFLVAD is common and often difficult to control with standard techniques. Octreotide is well tolerated and can be highly effective for refractory GIB, especially in upper GI tract AVMS. Its use may reduce hospitalisations for GIB and contribute to good long term outcomes in this patient population. Further studies with greater patient numbers are warranted. (Table Presented).

Publication Types: Conference Abstract


Long term support of patients receiving an LVAD for advanced heart failure: A subgroup analysis of the registry to evaluate the heartware left ventricular assist system (the revolve registry).

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Purpose: The REVOLVE Registry is an investigator-initiated registry established to collect post CE Mark clinical data on patients receiving the HeartWare HVAD System in the European Union and Australia. Methods: REVOLVE is a multi-center, prospective, single arm registry. Each patient is followed to device explant, transplantation or death. Data was collected on 254 commercial implants between February 2009 and March 2012 from nine centers in Europe (7) and Australia (2). We are now evaluating those patients who remained on support in order to summarize long term support and outcomes in this population. Summary statistics will be used to describe patient demographics, adverse events, length of support and outcomes. Results: At the time of the initial analysis completed in November 2012, a total of 37 patients were on support for at least 2 years (range 730-1057 days), 26 of whom were still alive on support. Another 126 patients who were supported for less than 2 years were still alive on support and could have potentially exceeded 2 years of support during this continued post hoc analysis period. Overall success at two years was 73%, while only 22% of patients were transplanted in the initial study period of February 2009 and November 2012 (see Figure). Conclusion: Real world use of the HVAD Pump continues to support the excellent outcomes on the device, and due to the low rate of transplantation, successful long term support is observed in a significant cohort of patients receiving the device. Final data on the total patients who remained on support beyond 2 years will be available at the time of presentation. (Figure Presented).

Publication Types: Conference Abstract
BACKGROUND & AIMS: Tenofovir alafenamide, a phosphonate prodrug of tenofovir with greater plasma stability than tenofovir disoproxil fumarate, provides efficient delivery of active drug to hepatocytes at reduced systemic tenofovir exposures.

METHODS: Non-cirrhotic, treatment-naive subjects with chronic hepatitis B were randomized (1:1:1:1:1) to receive tenofovir alafenamide 8, 25, 40, or 120 mg, or tenofovir disoproxil fumarate 300 mg for 28 days and assessed for safety, antiviral response, and pharmacokinetics, followed up by off-treatment for 4 weeks.

RESULTS: 51 subjects were randomized and all completed study treatment. Groups were generally well matched (67% male, 57% Asian, 53% HBeAg-negative, mean HBV DNA approximately 6.0 log10 IU/ml) with HBV genotypes reflective of the population. No subject experienced an adverse event that was serious or severe (grade 3/4). Across the tenofovir alafenamide groups, similar mean changes in serum HBV DNA were found at Week 4 (-2.81, -2.55, -2.19, and -2.76 log10 IU/ml for the 8, 25, 40, and 120 mg groups, respectively) which were also comparable to the control (-2.68 log10 IU/ml for tenofovir disoproxil fumarate 300 mg). Kinetics of viral decline were also similar among groups. Tenofovir alafenamide pharmacokinetics were linear and proportional to the dose; doses25 mg were associated with 92% reductions in mean tenofovir area under the curve relative to tenofovir disoproxil fumarate 300 mg.

CONCLUSIONS: Tenofovir alafenamide was safe and well tolerated; declines in HBV DNA were similar to tenofovir disoproxil fumarate at all doses evaluated. Tenofovir alafenamide 25 mg has been selected for further hepatitis B clinical development. Copyright © 2015. Published by Elsevier B.V.

Introduction: The immune response has an important role in the clearance of HCV even in the era of highly potent direct acting antivirals (DAAs) particularly as shorter durations of therapy are explored. SB 9200 is a novel agonist of innate immunity that activates intracellular RIG-1 and NOD2, the cytosolic viral sensors that are important for the regulation of the innate immune response and activation of intracellular interferon (IFN) signaling pathways. SB 9200, a pangenotypic anti-HCV agent, is an oral dinucleotide prodrug that is enzymatically converted to the active Rp-, Sp-SB 9000 isomers in vivo. Material and Methods: This was a first in man randomized, placebo-controlled, multiple ascending dose study of SB 9200 in treatment-naive HCV infected adults. Subjects were randomized 6:2 to SB 9200 or placebo for 7 days. Doses evaluated were: 200mg (N = 8), 400mg (N = 8), 900mg (N = 8 HCV-1, N = 6 HCV-3). Results: Increases in SB 9200 AUC0-7 and Cmax were dose proportional. The terminal plasma half-life (t1/2) on Days 1 and 7 ranged from 0.68 to 0.817 and 3.00 hours. Peak individual viral load drop improved from 1.5 to 1.9 log10 when the dose increased from 200 to 900 mg. Further dose increases did not result in response increases. Inter-individual variability in antiviral response was observed. A significant relationship between SB 9200 Cmax and maximum suppression of HCVRNA on Day 7 was observed (p = 0.015) after exclusion of two subjects with extreme Cmax values for SB 9200. 73 adverse events (AEs) were reported by 25 subjects (83.3%), mostly mild in severity. No dose limiting toxicities or systemic interferon-like side effects were observed and no SAEs or significant laboratory abnormalities were observed. Among active pts, increasing doses of ACH-3422 resulted in increasing viral decline (Figure). In the 700mg POC group, a mean maximum viral load drop of 3.4 log<sub>10</sub>, 4.2 log<sub>10</sub>, and 4.6 log<sub>10</sub> was reported after 7, 10, and 14 days of treatment, respectively. Three of 6 pts (50%) achieved viral clearance (target not detected by PCR) with 14 days of 700 mg. Approximate dose-proportional PK was observed for both ACH-3422 (50-700mg QD) and its corresponding nucleoside metabolite (ACH-3420). Conclusions: In all 3 phases, ACH-3422 was safe and well tolerated at doses up to 700 mg with dose-related virologic responses in pts with HCV GT-1 infection. Together, these results support further investigation of ACH-3422 with ACH-3102, a potent NS5A inhibitor, for the treatment of pts with HCV GT-1 infection.

Publication Types: Conference Abstract

ACH-3422, a novel nucleotide prodrgub inhibitor of HCV NS5B polymerase.
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Introduction: ACH-3422 is a nucleotide inhibitor of hepatitis C virus (HCV) NS5B RNA polymerase, displaying pan-genotypic activity and a high in vitro barrier to resistance. This randomized, double-blind, placebo (PBO)-controlled study evaluated the safety, tolerability, pharmacokinetics (PK), and antiviral activity of ACH-3422 after single ascending doses (SAD) and multiple-ascending doses (MAD) in healthy volunteers (HV) and antiviral proof of concept (POC) in patients (pts) infected with genotype 1 (GT-1) HCV. Material and Methods: This was a 3-phase study whereby 5 different doses of ACH-3422 (50 mg, 150 mg, 300 mg, 500mg and 700 mg) and PBO were administered in a SAD and 14-day MAD phase with HV, and either a 7 or 14-day POC phase in pts with HCV GT-1. Dose escalation decisions were made in real time based on the emerging safety, PK, and virology assessments. Results: 104 HV (18-49 years; 73 male) and 37 HCV (IL28 frequency: CC 9, CT 24, TT 4; 27-69 years; 26 male) were randomized. In the SAD/MAD phases, ACH-3422 was well tolerated: no serious adverse events (SAEs), no discontinuations due to adverse events (AEs), no grade 3-4 AEs, and no clinically significant AEs or laboratory or ECG abnormalities were observed. In the POC phase, ACH-3422 was well tolerated: no SAEs or Grade 3 or 4 AEs were considered drug related. No Grade 3 or 4 laboratory abnormalities were observed among active pts, and one discontinuation due to an AE was observed in a PBO patient. There was no significant difference between active and PBO groups in AEs or laboratory abnormalities, and no clinically significant ECG abnormalities were observed. Among active pts, increasing doses of ACH-3422 resulted in increasing viral decline (Figure). In the 700mg POC group, a mean maximum viral load drop of 3.4 log<sub>10</sub> was reported after 7, 10, and 14 days of treatment, respectively. Three of 6 pts (50%) achieved viral clearance (target not detected by PCR) with 14 days of 700 mg. Approximate dose-proportional PK was observed for both ACH-3422 (50-700mg QD) and its corresponding nucleoside metabolite (ACH-3420). Conclusions: In all 3 phases, ACH-3422 was safe and well tolerated at doses up to 700mg with dose-related virologic responses in pts with HCV GT-1 infection. Together, these results support further investigation of ACH-3422 with ACH-3102, a potent NS5A inhibitor, for the treatment of pts with HCV GT-1 infection.

Publication Types: Conference Abstract
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Background and Aims: Ledipasvir (LDV) is a hepatitis C virus (HCV) NS5A inhibitor with potent antiviral activity against HCV genotype 1a and 1b. The aim of this study is to evaluate the persistence of resistance-associated variants (RAVs) in subjects who did not achieve SVR in previous Gilead-sponsored HCV clinical studies after receiving LDV without SOF who were then enrolled in a 3-year follow-up registry study. Methods: Specimens from subjects treated with LDV in Gilead studies GS-US-248-0120, GS-US-248-0121, GS-US-248-0131, GS-US-248-0132, GS-US-256-0124 and GS-US-256-0148, were analyzed to determine their NS5A RAVs at baseline (BL) in the parent study (n = 84), post-BL in the parent study (n = 78), BL in the registry study (n = 80), and follow-up (FU) visits weeks 12 (n = 66), 24 (n = 66), 36 (n = 19), 48 (n = 80) and 96 (n = 65) in the registry study. Population sequencing was used for majority of samples at BL and Post-BL of the parent study, and deep sequencing for all samples in the registry study. If RAVs were observed, samples from subsequent timepoints were deep sequenced until RAVs were no longer detected (1% detection threshold). Results: Of the 84 subjects with sequencing at BL in the parent study, 12 had NS5A RAVs at BL that persisted through FU96 except A92T that wasn't observed at Post-BL. NS5A RAVs were detected in 95% of subjects at virologic failure in the parent study and in 97%, 96.5%, 100%, 100%, 96%, and 94.0% of the subjects at BL, FU12, FU24, FU36, FU48 and FU96 visits in the registry study, respectively. At BL in the registry study subjects had up to 9 NS5A RAVs compared to FU96 when most subjects had <5 RAVs except 2 subjects with 7 RAVs. Except L31M, all variants: K24N/R, M28T/A, Q30E/H/K/R, L31V, H58D and Y93H/N/C were detected in fewer subjects at FU96 than BL. While the frequencies of some variants declined slowly over time in some subjects, at FU96, 51 of 54 (94.4%, 48 GT 1a and 3 GT 1b) subjects had NS5A RAVs detected by deep sequencing. For the 3 GT 1b subjects, the observed variants were L31I/M/V and Y93H/T and had frequencies up to 99.7% of the viral population. In GT1a subjects, most subjects had Q30R, L31M and H58D. Highest frequencies of variants were seen for K24N (73.2%), K24G (63.0%), H58D (57.2%), Y93C (56.9%), L31M (48.3%), Q30R (45.1%), Q30H (33.8%) and Y92N (27.6%). Conclusions: NS5A variants can persist for >6 weeks posttreatment in subjects who relapse to regimens containing NS5A inhibitor suggesting high fitness of the NS5A RAVs.

Publication Types: Conference Abstract

Reduced mortality due to phlebotomy in moderately iron-loaded HFE haemochromatosis? The need for clinical trials.
Delatycki MB, Gurrin LC, et al.
(Delatycki, Ong, Allen) Murdoch Childrens Research Institute, Parkville, VIC, Australia (Delatycki) Austin Health, Heidelberg, VIC, Australia (Gurrin) Melbourne School of Population and Global Health, University of Melbourne, Parkville, VIC, Australia (Ram, Anderson, Powell) QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia (Olynyk) Fiona Stanley and Fremantle Hospitals, Western Australia, Australia (Olynyk) Curtin University, Western Australia, Australia (Olynyk) Murdoch University, Western Australia, Australia (Allen) Royal Children's Hospital, Parkville, VIC, Australia (Nicol) Eastern Health, Box Hill, VIC, Australia M.B. Delatycki, Murdoch Childrens Research Institute, Parkville, VIC, Australia
Publication Types: Letter
Dairy product consumption, dietary nutrient and energy density and associations with obesity in Australian adolescents.

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BACKGROUND: Dairy intake is likely to influence dietary energy density (ED) and nutrient density (ND), which are factors representing aspects of dietary quality. Although evidence suggests dairy intake is unlikely to contribute to obesity, intake tends to decrease over adolescence, potentially as a result of concerns around weight gain. We examined associations between dairy intake, ED and ND, and investigated relationships with obesity in adolescents.

METHODS: The present study comprised a cross-sectional study of 1613 14-year-olds in the Western Australian Pregnancy Cohort (Raine) Study. Adolescents completed a 212-item food frequency questionnaire. Nutrient Rich Food index 9.3 (NRF9.3) was used to estimate ND. Age-specific body mass index (BMI) and waist-height cut-offs were used to categorise obesity risk.

RESULTS: Mean (SD) dairy intake was: 2.62 (1.51) servings daily; ED was 4.53 (0.83) (food and beverage) and 6.28 (1.33) (food only); ND was 373 (109). Dairy intake was inversely associated with ED and positively associated with ND. The odds of being overweight (as assessed by BMI) increased by 1.24 (95% confidence interval = 1.09-1.42) with each 100-point increase in ND, after adjustment for potential confounders and energy intake. ED measures and dairy intake were inversely associated with obesity after adjustment for confounders; associations became nonsignificant after energy adjustment.

CONCLUSIONS: Oral GS-9620 was safe, well tolerated, and associated with induction of peripheral ISG15 production in the absence of significant systemic IFN-alpha levels or related symptoms. Copyright © 2015 European Association for the Study of the Liver. Published by Elsevier B.V. All rights reserved.

Effect of sour tea (Hibiscus sabdariffa L.) on arterial hypertension: a systematic review and meta-analysis of randomized controlled trials.

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BACKGROUND: Hibiscus sabdariffa L. is a tropical wild plant rich in organic acids, polyphenols, anthocyanins, polysaccharides, and volatile constituents that are beneficial for the cardiovascular system. Hibiscus sabdariffa beverages are commonly consumed to treat arterial hypertension, yet the evidence from randomized controlled trials (RCTs) has not been fully conclusive. Therefore, we aimed to assess the potential antihypertensive effects of H. sabdariffa through systematic review of literature and meta-analysis of available RCTs.

METHODS: The search included PUBMED, Cochrane Library, Scopus, and EMBASE (up to July 2014) to identify RCTs investigating the efficacy of H. sabdariffa supplementation on SBP and DBP values. Two independent reviewers extracted data on the study characteristics, methods, and outcomes. Quantitative data synthesis and meta-regression were performed using a fixed-effect model, and sensitivity analysis using leave-one-out method. Five RCTs (comprising seven treatment arms) were selected for the meta-analysis. In total, 390 participants were randomized, of whom 225 were allocated to the H. sabdariffa supplementation group.
and 165 to the control group in the selected studies.

**RESULT**: Fixed-effect meta-regression indicated a significant effect of *H. sabdariffa* supplementation in lowering both SBP (weighted mean difference -7.58 mmHg, 95% confidence interval -9.69 to -5.46, P < 0.0001) and DBP (weighted mean difference -3.53 mmHg, 95% confidence interval -5.16 to -1.89, P < 0.0001). These effects were inversely associated with baseline BP values, and were robust in sensitivity analyses.

**CONCLUSION**: This meta-analysis of RCTs showed a significant effect of *H. sabdariffa* in lowering both SBP and DBP. Further well designed trials are necessary to validate these results.


**Contrasting effects of prenatal life stress on blood pressure and body mass index in young adults.**

Bhat SK, Beilin LJ, et al.

**BACKGROUND**: Various environmental stressors in pregnancy have been reported to affect high blood pressure (BP) in adult offspring. However, few studies have examined the effect of prenatal maternal psychological stress on offspring BP and BMI in early adulthood.

**METHOD**: In 957 Raine cohort participants, regression analyses were used to examine the association between the count of maternal life stress events experienced during pregnancy and offspring BP and BMI at age 20.

**RESULTS**: Prenatal life stress associated positively with offspring BMI but inversely with SBP. After adjustment for confounders each additional prenatal life stress event reduced offspring SBP by 0.66 mmHg (P = 0.013) in those with an average BMI and lowered the odds of systolic (pre)hypertension by 17% (odds ratio = 0.83; P = 0.008). The inverse relationship between prenatal life stress and adult SBP was stronger in offspring with higher BMI. On the contrary, each unit increase in prenatal life stress score predicted a BMI increase of 0.37 kg/m² (P = 0.022). Longitudinal analysis showed similar effects of prenatal life stress for offspring BMI from age 8 and SBP from age 14.

**CONCLUSION**: This study has shown that maternal stress in pregnancy significantly associated with BMI from early childhood, but contrary to our hypothesis predicted lower resting SBP and lower odds of systolic (pre)hypertension in young adult offspring. The effect of prenatal life stress on BP was accentuated by a higher BMI. Fetal programming events as a result of prenatal stress may underpin some of these relationships.


**Renal artery anatomy affects the blood pressure response to renal denervation in patients with resistant hypertension.**

Hering D, Marusic P, et al.

**Objective**: Renal denervation (RDN) decreases blood pressure (BP), muscle sympathetic nerve activity (MSNA) and attenuates hypertension-induced organ damage in patients with resistant hypertension (RH) and bilateral single renal arteries. The BP response to RDN and safety of RDN in patients with multiple renal arteries remains unclear. Design and method: This study examined office and 24-hour BP at baseline, 3 and 6 months following RDN in 91 patients with RH including 65 patients with single renal arteries bilaterally (Group 1), 16 patients with dual renal arteries on either one or both sides (Group 2) and 10 patients with other anatomical constellations (Group 3). Thirty nine out of 91 patients completed MSNA at baseline and follow-up. Results: RDN significantly decreased office and daytime SBP in group 1 at 3 and 6 month follow-up (P < 0.001). In group 2, RDN decreased daytime SBP (P < 0.05) at 3 month follow-up. Group 3 decreased office SBP (P = 0.05), mean and nighttime 24-hour SBP (P = 0.04) from baseline to follow-up. When patients in group 2 with dual renal arteries on either sides were categorized according to the left or right sides, there was a reduction in daytime SBP at 3 (P = 0.006) and 6 months (P = 0.02) post procedure in patients with dual renal arteries on the left and single renal artery on the right sides. A patient who received RDN in all 3 arteries (two right renal arteries, single left renal artery) substantially improved BP control. RDN significantly reduced MSNA in group 1 (P < 0.05) and individuals in group 3 but not in group 2. There was no deterioration in kidney function in either group. Conclusions: While RDN can safely be performed irrespective of the underlying renal anatomy, the presence of single renal arteries with or without structural abnormalities appears to be associated with a more pronounced BP and MSNA reduction than the presence of dual renal arteries in patients with RH. Nevertheless, when patients with dual renal arteries received RDN in all arteries there was trend towards a greater BP reduction. Insufficient sympathetic renal nerve ablation may account for these differences.

Publication Types: Conference Abstract


**Renal artery denervation for treatment of hypertensive patients with or without obstructive sleep apnea and resistant hypertension: Results from the global simplicity registry.**

Mahfoud F, Linz D, et al.
and history of cardiac disease (51%). Baseline office BP was 165/89+/−24/16 mm Hg and baseline 24-hour BP was 154/86+/−(42%), renal dysfunction (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73m²; 23%), obstructive sleep apnea (11%) was 61+/−12 years, 61% were male and mean body mass index was 30+/−6 kg/m². Comorbidities included diabetes mellitus.


Publication Types: Conference Abstract

Objective: Obstructive sleep apnea (OSA) is associated with sympathetic nervous system activation and the development of hypertension. The Global SYMPLICITY Registry is prospectively enrolling real world patients with uncontrolled hypertension including patients with OSA. This analysis compares baseline characteristics and blood pressure (BP) lowering effects of renal denervation in patients with and without OSA. Design and method: The Global SYMPLICITY Registry is a prospective, multicentre international registry designed to evaluate the safety and effectiveness of renal denervation in a broad population of patients with uncontrolled hypertension. Baseline characteristics antihypertensive medication use, office and 24-hour ambulatory BP are compared between patients with and without OSA. Results: In a 998 patients with complete 6 month follow-up OSA was reported in 116 patients. OSA patients were more likely to be male than patients without OSA (n = 752) (83% vs 56%, p < 0.0001), had a larger body mass index (34+/−6 kg/m² vs 30+/−5 kg/m², p < 0.0001) and significantly more, left ventricular hypertrophy (25% vs 15%, p = 0.008) atrial fibrillation (19% vs 11%, p = 0.020) and diabetes (52% vs 39%, p = 0.008). OSA patients were taking more antihypertensive medications (4.9+/−1.4 vs 4.4+/−1.3, p < 0.001); a higher proportion of aldosterone antagonists (39% vs 20%, p < 0.0001), vasodilators (24% vs 13%, p = 0.001) and alpha 2 agonists (54% vs 36%, p < 0.001). Baseline office systolic BP was 166+/−23mm Hg for OSA patients and 163+/−24mm Hg for non-OSA patients. At 6 months the office systolic BP was reduced -15.5+/−24.4mm Hg in the OSA group and -11.3+/−25.0mm Hg in the non-OSA group (both p < 0.0001; p = 0.136 for difference between the groups). Baseline ambulatory 24-hour systolic BP was 156+/−20mm Hg in OSA patients and 152+/−17 in non-OSA patients. At 6 months 24-hour systolic BP declined -4.6+/−17.1mm Hg (n = 73, p = 0.023) in the OSA group and -7.1+/−17.6mm Hg (p < 0.0001) in the non-OSA group (p = 0.450 for the between group difference). Conclusions: Renal denervation resulted in significant 6-month BP reductions in patients with and without OSA but there was not a significant difference in the BP change between the 2 groups. Data from a larger cohort of 2100 patients will be presented.

Journal of Hypertension. 2015; 33: e49.

Long-term effects of renal artery denervation in real world patients with uncontrolled hypertension from the global symPLICITY registry.


Objective: The Global SYMPLICITY Registry (GSR) provides real world experience regarding the effects of radiofrequency denervation of the renal artery nerves in patients with uncontrolled hypertension. These data in hypertensive patients with a high proportion of concomitant conditions also characterized by sympathetic nervous system will further characterize the effects of renal denervation in a diverse patient population. Design and method: The GSR is a prospective, open-label, registry being conducted at 245 international sites. Office and 24-hour ambulatory blood pressure (BP) change, laboratory values and protocol-defined safety events are collected. One year results in the first 1000 enrolled patients are now available and two-year results in 600 patients will be available in the spring for presentation. Results: In the first 1000 consecutive patients enrolled, the mean age was 61+/−12 years, 61% were male and mean body mass index was 30+/−6 kg/m². Comorbidities included diabetes mellitus (42%), renal dysfunction (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73m²; 23%), obstructive sleep apnea (11%) and history of cardiac disease (51%). Baseline office BP was 165/89+/−24/16mm Hg and baseline 24-hour BP was 154/86+/−18/14mmHg. 1 year office systolic BP change in 740 patients was -13.0+/−26.3 mmHg (p < 0.001) and 24-hour systolic BP change (n = 390) was -6.3+/−17.8mmHg (p < 0.001). In patients with more severe hypertension (baseline office systolic blood pressure of at least 160mmHg plus an ambulatory 24-hour systolic blood pressure at least 135mm Hg while taking 3 or more antihypertensive medications) the office systolic BP change was −21.5+/−25.6 mmHg (p < 0.001) and the 24-hour systolic BP change was −11.4+/−17.9 mmHg (p < 0.001). At 1 year post-denervation there were 7 cardiovascular deaths, new renal artery stenosis >70% occurred in 2 patients, and new onset end-stage renal disease occurred in 3 patients. Conclusions: Renal denervation in a large real world population resulted in significant blood pressure reductions 1 year post-procedure. There were no long-term safety concerns following the denervation procedure. These data, including analysis of the BP-lowering effects of RDN in select subgroups, will be updated with two year follow-up of approximately 600 patients in June.

Publication Types: Conference Abstract


New developments in the pathogenesis of obesity-induced hypertension.

Supplementation with n-3 fatty acids is known to alter arachidonic acid metabolism and reduce the formation of the lipid hydroxyeicosatetraenoic acid (20-HETE) that regulates vascular function, sodium homeostasis and blood pressure (BP). Following n-3 fatty acid supplementation, there was a significant reduction in plasma 20-HETE and urinary 20-HETE in the same study, as well as plasma and urinary F2-isoprostanes, and relating these to changes in BP. In regression models adjusted for BP at baseline, postintervention plasma 20-HETE was a significant predictor of the fall in SBP (P < 0.0001) and DBP (P < 0.0001) after n-3 fatty acids.

CONCLUSION: This is the first report that n-3 fatty acid supplementation reduces plasma 20-HETE in humans and that this associates with reduced BP. These results provide a plausible mechanism for the reduction in BP observed in patients with CKD following n-3 fatty acid supplementation.

**n-3 fatty acids reduce plasma 20-hydroxyeicosatetraenoic acid and blood pressure in patients with chronic kidney disease.**

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BACKGROUND: Metabolism of arachidonic acid by cytochrome P450 omega-hydroxylase leads to the formation of 20-hydroxyeicosatetraenoic acid (20-HETE) that regulates vascular function, sodium homeostasis and blood pressure (BP). Supplementation with n-3 fatty acids is known to alter arachidonic acid metabolism and reduce the formation of the lipid peroxidation products F2-isoprostanes, but the effect of n-3 fatty acids on 20-HETE has not been studied.

METHOD: We previously reported a significant effect of n-3 fatty acids but not coenzyme Q10 (CoQ) to reduce BP in a double-blind, placebo-controlled intervention, wherein patients with chronic kidney disease (CKD) were randomized to n-3 fatty acids (4 g), CoQ (200 mg), both supplements or control (4 g olive oil), daily for 8 weeks. This study examined the effect of n-3 fatty acids on plasma and urinary 20-HETE in the same study, as well as plasma and urinary F2-isoprostanes, and relate these to changes in BP.

RESULTS: Seventy-four patients completed the 8-week intervention. n-3 fatty acids but not CoQ significantly reduced plasma 20-HETE (P = 0.001) and F2-isoprostanes (P < 0.001). In regression models adjusted for BP at baseline, postintervention plasma 20-HETE was a significant predictor of the fall in SBP (P < 0.0001) and DBP (P < 0.0001) after n-3 fatty acids.

CONCLUSION: This is the first report that n-3 fatty acid supplementation reduces plasma 20-HETE in humans and that this associates with reduced BP. These results provide a plausible mechanism for the reduction in BP observed in patients with CKD following n-3 fatty acid supplementation.
Health-related quality of life and blood pressure 12 months after renal denervation. Lambert GW, Hering D, et al. (Lambert, Esler, Lambert, Dhar, Barton, Schlaich) Human Neurotransmitters Laboratory, Baker IDI Heart and Diabetes Institute, PO Box 6492, Melbourne, VIC 8008, Australia (Hering, Marusic, Thorp, Sata, Lee, Duval, Hammond) Neurovascular Hypertension and Kidney Disease, United States (Head) Neur-Neuropharmacology Laboratories, Baker IDI Heart and Diabetes Institute, United States (Lambert, Esler, Dhar, Barton, Schlaich) Faculty of Medicine, Nursing and Health Sciences, United States (Lambert) Department of Physiology, United States (Dixon) Primary Care Research, Monash University, Melbourne, Australia (Hering, Marusic, Schlaich) Royal Perth Hospital Unit, School of Medicine and Pharmacology, University of Western Australia, Perth, Australia

Aim: To examine the effect of renal denervation (RDN) on blood pressure (BP) and health-related quality of life (QoL) in patients with resistant hypertension, pseudoresistant hypertension due to a white-coat effect and in patients with uncontrolled masked hypertension. Methods: Using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), Beck Depression Inventory (BDI) and Spielberger's state and trait anxiety questionnaires, we examined QoL, symptoms of depression and anxiety prior to and 12 months following RDN. BP was assessed from clinic and ambulatory blood pressure monitoring (ABPM) recordings. Results: Patients with uncontrolled masked hypertension had the highest BDI and anxiety scores among all groups at baseline. Twelve months following RDN clinic and ambulatory BP were reduced only in those patients with resistant hypertension (delta SBP: clinic-16+/−3 mmHg, ABPMday-8+/−2 mmHg, ABPMnight-8+/−2 mmHg, all P<0.01). Clinic BP was reduced in the pseudoresistant group (-17+/−5 mmHg, P<0.01) but was elevated in the uncontrolled masked group (R13+/−6 mmHg, P<0.01). In all patients, trait anxiety (P<0.05), BDI scores (P<0.05) and the SF-36 mental component summary (MCS) score (P<0.001) were improved. The improvement in the SF-36 MCS was confined to those patients with resistant hypertension (R4.0+/−1.1, P<0.01). The change in clinic BP after RDN was related to the baseline clinic BP (systolic: r=0.54, P<0.001; diastolic r=0.43, P<0.001), the number of ablations delivered (both clinic and mean day ABPM systolic r=0.24, P<0.05) and to the change in SF-36 MCS score (systolic: r=0.25, P=0.01; diastolic r=0.24, P=0.02). Conclusion: These results indicate that in patients with confirmed resistant hypertension, RDN is associated with a reduction in BP and a sustained improvement in mental health-related aspects of QoL.


Viremic HIV Controllers Exhibit High Plasmacytoid Dendritic Cell-Reactive Oposonophagocytic IgG Antibody Responses against HIV-1 p24 Associated with Greater Antibody Isotype Diversification. Tjiam MC, Taylor JP, et al. Tjiam M Christian. School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia 6009, Australia; Department of Clinical Immunology, Royal Perth Hospital and PathWest Laboratory Medicine, Perth, Western Australia 6000, Australia; Taylor,James P A. School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia 6009, Australia; Marshidhi,Mazmah A. School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia 6009, Australia; Sariputra,Lucy. School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia 6009, Australia; Burrows,Sally. School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia 6009, Australia; Martin,Jeffrey N. Division of Clinical Epidemiology, University of California, San Francisco, San Francisco, CA 94117; Deeks,Steven G. School of Medicine, University of California, San Francisco, San Francisco, CA 94117; Tan,Dino B A. School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia 6009, Australia; Centre for Asthma, Allergy and Respiratory Research, Lung Institute of Western Australia, Perth, Western Australia 6009, Australia; and all. School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia 6009, Australia; School of Microbiology and Infectious Diseases, Royal Perth Hospital and PathWest Laboratory Medicine, Perth, Western Australia 6000, Australia; Fernandez,Sonia. School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia 6009, Australia; French,Sonja. School of Physiology and Pharmacology, University of Western Australia, Perth, Western Australia 6009, Australia; Burrows,Sally. School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia 6009, Australia; Taylor,James P A. School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia 6009, Australia; French,Martyn A. School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia 6009, Australia; Department of Clinical Immunology, Royal Perth Hospital and PathWest Laboratory Medicine, Perth, Western Australia 6000, Australia; martyn.french@uwa.edu.au.

Identifying the mechanisms of natural control of HIV-1 infection could lead to novel approaches to prevent or cure HIV infection. Several studies have associated natural control of HIV-1 infection with IgG Abs against HIV-1 Gag proteins (e.g., p24) and/or production of IgG2 Abs against HIV-1 proteins. These Abs likely exert their effect by activating antiviral effector cell responses rather than virus neutralization. We hypothesized that an oposonophagocytic IgG Ab response against HIV-1 p24 that activates plasmacytoid dendritic cells (pDCs) through FcgammaRIIa would be associated with control of HIV and that this would be enhanced by Ab isotype diversification. Using the Gen2.2 pDC cell line, we demonstrated that pDC-reactive oposonophagocytic IgG Ab responses against HIV-1 p24 were higher in HIV controllers (HIV RNA < 2000 copies/ml) than noncontrollers (HIV RNA > 10,000 copies/ml), particularly in controllers with low but detectable viremia (HIV RNA 75-2000 copies/ml). Oposonophagocytic Ab responses correlated with plasma levels of IgG1 and IgG2 anti-HIV-1 p24 and, notably, correlated inversely with plasma HIV RNA levels in viremic HIV patients. Phagocytosis of these Abs was mediated via FcgammaRIIa. Isotype diversification (toward IgG2) was greatest in HIV controllers, and depletion of IgG2 from Ig preparations indicated that IgG2 Abs to HIV-1 p24 do not enhance phagocytosis, suggesting that they enhance other aspects of Ab function, such as Ag opsonization. Our findings emulate those for pDC-reactive oposonophagocytic Ab responses against coxsackie, picorna, and influenza viruses and demonstrate a previously undefined immune correlate of HIV-1 control that may be relevant to HIV vaccine development. Copyright © 2015 by The American Association of Immunologists, Inc.

Factors Associated With Plasma IL-6 Levels During HIV Infection.

Borges AH, O’Connor J.L. et al.

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BACKGROUND: Elevated interleukin 6 (IL-6) levels have been linked to cardiovascular disease, cancer and death. Persons with human immunodeficiency virus (HIV) infection receiving treatment have higher IL-6 levels, but few data are available on factors associated with circulating IL-6.

METHODS: Participants in 3 trials with IL-6 measured at baseline were included (N = 9864). Factors associated with IL-6 were identified by linear regression. Demographic and HIV variables (nadir/entry CD4(+) cell count, HIV RNA level, antiretroviral therapy regimen) were investigated in all 3 trials. In the SMART (Strategies for Management of Anti-Retroviral Therapy) trial, CD4/CD8 ratio, smoking, comorbid conditions, serum lipids, renal function (estimated glomerular filtration rate [eGFR]), and educational level were assessed.

RESULTS: Demographics associated with higher IL-6 levels were older age and lower education, whereas black race was associated with lower IL-6. Higher HIV RNA levels were associated with higher IL-6 levels, and higher nadir CD4(+) cell counts with lower IL-6 levels. Compared with efavirenz, protease inhibitors were associated with higher and nevirapine with lower IL-6 levels. Smoking and all comorbid conditions were related to higher IL-6. IL-6 levels increased with decreasing eGFR and decreasing serum lipids.

CONCLUSIONS: Higher levels of IL-6 were associated with older age, nonblack race, higher body mass index, lower serum lipid levels, HIV replication, low nadir CD4(+) cell count, protease inhibitor use, comorbid conditions, and decreased eGFR. Multiple factors affect inflammation in HIV and should be considered in studies of IL-6 as a biomarker of clinical outcomes.


Lemierre’s syndrome - an unusual complication of otitis externa in a young, healthy female.

Davidoss, N. Ha JF, et al.

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BACKGROUND: Lemierre’s syndrome, which affects previously healthy, young adults, is a rare complication secondary to infections in the head and neck that result in septic thrombophlebitis of the internal jugular vein.

METHOD: This paper reports a case of a young, healthy female with malignant otitis externa, which resulted in the development of Lemierre’s syndrome. A review of the relevant literature was also carried out. This involved a search of the Medline database using multiple search terms including ‘Lemierre’, ‘septic thrombophlebitis’, ‘otitis externa’, ‘Internal jugular vein thrombosis’ and ‘management’.

RESULTS: The patient presented with fever, left-sided otalgia, otorrhoea, neck swelling and pain. She was subsequently diagnosed with Lemierre’s syndrome and managed accordingly.

CONCLUSION: Lemierre’s syndrome is a potentially fatal complication associated with significant morbidity. A high index of suspicion is required for prompt recognition and the early institution of treatment.


Therapeutic potential of negatively charged liposomes for atherosclerotic vascular disease: Reverse delivery of cholesterol cargo from atheroma to liver.

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Publication Types: Letter

Purpose: To investigate the ability of texture analysis of MRI images to stage liver fibrosis. Current noninvasive approaches for detecting liver fibrosis have limitations and cannot yet routinely replace biopsy for diagnosing significant fibrosis. Materials and Methods: Forty-nine patients with a range of liver diseases and biopsy-confirmed fibrosis were enrolled in the study. For texture analysis all patients were scanned with a T2-weighted, high-resolution, spin echo sequence and Haralick texture features applied. The area under the receiver operating characteristics curve (AUROC) was used to assess the diagnostic performance of the texture analysis. Results: The best mean AUROC achieved for separating mild from severe fibrosis was 0.81. The inclusion of age, liver fat and liver R2 variables into the generalized linear model improved AUROC values for all comparisons, with the F0 versus F1-4 comparison the highest (0.91). Conclusion: Our results suggest that a combination of MRI measures, that include selected texture features from T2-weighted images, may be a useful tool for excluding fibrosis in patients with liver disease. However, texture analysis of MRI performs only modestly when applied to the classification of patients in the mild and intermediate fibrosis stages.


OBJECTIVE: The purpose of this study was to compare manipulative therapy (MT) plus rehabilitation to rehabilitation alone for recurrent ankle sprain with functional instability (RASFI) to determine short-term outcomes.

METHODS: This was an assessor-blind, parallel-group randomized comparative trial. Thirty-three eligible participants with RASFI were randomly allocated to receive rehabilitation alone or chiropractic MT plus rehabilitation. All participants undertook a daily rehabilitation program over the course of the 4-week treatment period. The participants receiving MT had 6 treatments over the same treatment period. The primary outcome measures were the Foot and Ankle Disability Index and the visual analogue pain scale, with the secondary outcome measure being joint motion palpation. Data were collected at baseline and during week 5. Missing scores were replaced using a multiple imputation method. Statistical analysis of the data composed of repeated-measures analysis of variance.

RESULTS: Between-group analysis demonstrated a difference in scores at the final consultation for the visual analogue scale and frequency of joint motion restrictions (P < .006) but not for the Foot and Ankle Disability Index (P = .26). CONCLUSIONS: This study showed that the patients with RASFI who received chiropractic MT plus rehabilitation showed significant short-term reduction in pain and the number of joint restrictions in the short-term but not disability when compared with rehabilitation alone. Copyright 2015 National University of Health Sciences. Published by Elsevier Inc. All rights reserved.


Taylor DB, Bourke AG, et al.

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METHODS: In this prospective pilot study, 21 participants with biopsy-proven breast cancer underwent radioguided occult lesion localisation using iodine-125 seed(s) (ROLLIS) with insertion of a hook-wire for back up. Sentinel node biopsy was performed where indicated. Ease of hook-wire and seed insertion, duration of the procedure, dependence on the seed versus hook-wire during surgery, lesion location within the specimen, histopathology including size of radial margins, the ease of seed retrieval in pathology, and safe return of seeds for disposal were documented. Radiation dosimetry of staff was performed.

RESULTS: All seeds were placed within 3.5mm of the lesion. All lesions and seeds were removed. One participant needed re-excision for involved margins. Radiologists and surgeons both preferred ROLLIS. Surgeons were able to depend on the seed for localisation in all but one case. Sentinel node biopsy was successfully performed when required. Pathologists found seed retrieval quick and easy, with no detrimental effect on tissue processing. No radiation doses measurably above background were received by staff.

CONCLUSION: ROLLIS is an easily learnt, safe and effective alternative technique to standard HWL. Copyright © 2015 The Royal Australian and New Zealand College of Radiologists.


Journal of Medical Imaging & Radiation Oncology. 2015; 59(5): 564-70.

Radiographer technique: Does it contribute to the question of clip migration?

Madeley CR, Kessell MA, et al.

INTRODUCTION: Marker clips are commonly deployed at the site of a percutaneous breast biopsy. Studies have shown that displacement of the clip from the site of deployment is not uncommon. The objective of this study was to determine how much 'migration' could be seen with fixed structures within the breast tissue across three consecutive annual screening examinations, and therefore attempt to quantify how much of the reported clip migration could be due to radiographer technique.

METHODS: Large, easily identified benign calcifications were measured by two investigators across three consecutive cycles of screening mammography. The position of the calcifications on the two standard mammographic views was measured in two planes. Other variables recorded included breast size and density, compression force used, and location of the benign calcifications within the breast.

RESULTS: In 38% of cases, benign calcifications showed a mimicked movement of >15mm in at least one plane. This was greatest in large breasts, those where fibroglandular tissue occupied less than 50% of the breast volume, and in the upper outer quadrant of the breast where mimicked movement >10mm was noted in up to 90% of the larger breasts.

CONCLUSION: Fixed immobile objects in the breast can appear to move a distance of >15mm in up to 30% of cases. Clinically, some of what has previously been called marker 'migration' may be spurious and accounted for by differences in radiographic positioning techniques. Copyright © 2015 The Royal Australian and New Zealand College of Radiologists.


Contrast-enhanced spectral mammography (CESM) and contrast enhanced MRI (CEMRI): Patient preferences and tolerance.

Hobbs MM, Taylor DB, et al.

INTRODUCTION: Contrast-enhanced spectral mammography (CESM) may have similar diagnostic performance to Contrast-enhanced MRI (CEMRI) in the diagnosis and staging of breast cancer. To date, research has focused exclusively on diagnostic performance when comparing these two techniques. Patient experience is also an important factor when comparing and deciding on which of these modalities is preferable. The aim of this study is to compare patient experience of CESM against CEMRI during preoperative breast cancer staging. Methods Forty-nine participants who underwent both CESM and CEMRI, as part of a larger trial, completed a Likert questionnaire about their preference for each modality according to the following criteria: comfort of breast compression, cost of intravenous (IV) contrast injection, anxiety and overall preference. Participants also reported reasons for preferring one modality to the other. Quantitative data were analysed using a Wilcoxon sign-rank test and chi-squared test. Qualitative data are reported descriptively. Results A significantly higher overall preference towards CESM was demonstrated (n = 49, P < 0.001), with faster procedure time, greater comfort and lower noise level cited as the commonest reasons. Participants also reported significantly
lower rates of anxiety during CESM compared with CEMRI (n = 36, P = 0.009). A significantly higher rate of comfort was reported during CEMRI for measures of breast compression (n = 49, P = 0.001) and the sensation of IV contrast injection (n = 49, P = 0.003). Conclusion Our data suggest that overall, patients prefer the experience of CESM to CEMRI, adding support for the role of CESM as a possible alternative to CEMRI for breast cancer staging.


Expanding the indications for MRI in the diagnosis and treatment of breast cancer: What is best practice?

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Breast magnetic resonance imaging (MRI) now has an accepted place in screening younger women at high risk of breast cancer, and is increasingly used in a number of other settings including assessment of response to neo-adjuvant therapy and local staging of cancer. Although the evidence for its general use in these settings is very limited, in highly selected patients, especially where discordance with conventional measurements occurs, MRI can have a place in assessing extent of disease, both whether operable and how operable, and guiding surgery. These scenarios and future indications and alternative technologies are explored in this paper. Breast magnetic resonance imaging (MRI) now has an accepted place in screening younger women at high risk of breast cancer, and is increasingly used in a number of other settings including assessment of response to neo-adjuvant therapy and local staging of cancer. Although the evidence for its general use in these settings is very limited, in highly selected patients, especially where discordance with conventional measurements occurs, MRI can have a place in assessing the extent of disease, both whether operable and how operable, and guiding surgery. These scenarios and future indications and alternative technologies are explored in this paper.


Radioguided localisation of impalpable breast lesions using 99m-Technetium macroaggregated albumin: Lessons learnt during introduction of a new technique to guide preoperative localisation.

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Introduction: Preoperative wire-guided localisation (WGL) of impalpable breast lesions is widely used but can be technically difficult. Risks include wire migration, inaccurate placement, and inadequate surgical margins. Research shows that radioguided occult lesion localisation (ROLL) is quicker, easier, and can improve surgical and cosmetic outcomes. An audited introduction of ROLL was conducted to validate the technique as a feasible alternative to WGL. Methods: Fifty patients with single impalpable lesions and biopsy proven malignancy or indeterminate histology underwent WGL followed by intralesion radiopharmaceutical injection of 99m-Technetium macroaggregated albumin. Postprocedural mammography was performed to demonstrate wire position, and scintigraphy to evaluate radiopharmaceutical migration. Lymphoscintigraphy and intraoperative sentinel node biopsy were performed if indicated, followed by lesion localisation and excision using a gamma probe. Specimen imaging was performed, with immediate reexcision for visibly inadequate margins. Results: Accurate localisation was achieved in 86% of patients with ROLL compared to 72% with WGL. All lesions were successfully removed, with clear margins in 71.8% of malignant lesions. Reexcision and intraoperative sentinel node localisation rates were equivalent to preaudit figures for WGL. ROLL was easy to perform and problems were infrequent. Inaccurate radiopharmaceutical placement necessitating WGL occurred in four patients. Minor radiopharmaceutical migration was common, but precluded using ROLL in only two cases. Conclusions: ROLL is effective, simple, inexpensive, and easily learnt; however, preoperative confirmation of correct radiopharmaceutical placement using mammography and the gamma probe is important to help ensure successful lesion removal. Insertion of a backup hookwire is recommended during the initial introduction of ROLL.


'Rolling out radioguided occult lesion localisation for breast tumours': Moving from ROLL to ROLLIS.

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In this letter to the editor we respond to a recently published editorial by David Chung (Rolling out radioguided occult lesion localisation for breast tumours. J Med Radiat Sci 2015; 62(1): p. 1-2) discussing the advantages of ROLL over other common preoperative breast lesion localisation techniques.


Radio-guided occult lesion localisation using iodine 125 Seeds “ROLLIS” to guide surgical removal of an impalpable posterior chest wall melanoma metastasis.

Dissanayake S, Dissanayake D, et al. (Schenberg) Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; Mitchell) Familial Cancer Centre, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia (Mitchell) Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, VIC, Australia (Taylor, Saunders) School of Surgery, University of Western Australia, Perth, WA, Australia (Taylor) Department of Radiology, Royal Perth Hospital, Perth, WA, Australia (Taylor) BreastScreen Western Australia, Adelaide Terrace, Perth, WA, Australia (Saunders) Department of General Surgery, St John of God Hospital, Perth, WA, Australia

Breast magnetic resonance imaging (MRI) screening of women under 50 years old at high familial risk of breast cancer was given interim funding by Medicare in 2009 on the basis that a review would be undertaken. An updated literature review has been undertaken by the Medical Services Advisory Committee but there has been no assessment of the quality of the screening or other screening outcomes. This review examines the evidence basis of breast MRI screening and how this fits within an Australian context with the purpose of informing future modifications to the provision of Medicare-funded breast MRI screening in Australia. Issues discussed will include selection of high-risk women, the options for MRI screening frequency and measuring the outcomes of screening.

Publication Types: Review

Validity of the retrospective application of Oxford Hip and Knee Scores.

Falconer T.M., Headford J., et al. (Falconer) Perth Orthopaedic and Sports Medicine Center, Sir Charles Gairdner Hospital, 31 Outram Street, West Perth, WA 6008, Australia (Headford) Fremantle Hospital, Alma Street, Fremantle, WA 6160, Australia (Edmondston) University of Notre Dame, Western Australia, Australia (Yates) Fremantle Hospital, Kaleeya Hospital, St. John of God Hospital Murdoch, Australia T.M. Falconer, Perth Orthopaedic and Sports Medicine Center, Sir Charles Gairdner Hospital, 31 Outram Street, West Perth, WA 6008, Australia

The Oxford Hip Score (OHS) and Oxford Knee Score (OKS) are validated, reliable and reproducible outcome measures, however their use retrospectively has not been examined. The aim of this prospective cohort study was to examine the accuracy and reliability of patients’ ability to recall their OHS and OKS in a retrospective manner. A total of 137 patients undergoing primary hip (40) or primary knee (97) arthroplasty with a mean age of 70.8 years (range, 47-88) and a mean time to follow up of 27.2 months (range, 6-46) were included in the study. The mean retrospective OHS and OKS decreased compared to the pre-operative score (OHS = 1.6 +/- 5, p = 0.36, OKS = 4.7 +/- 5, p < 0.001). There was only a weak positive relationship between the actual pre-operative scores and the retrospective scores (OHS: r = <sup>2</sup> = 0.30, OKS: r = <sup>2</sup> = 0.19). Bland-Altman analysis demonstrated 95% limits of agreement between scores of -19.9 to 23.1 for the OHS and -15.3 to 24.8 for the OKS. This study shows that patients are poor at retrospectively recalling their pre-operative OHS and OKS and therefore these scores should not be used in a retrospective manner.


High rates of parkinsonism in adults with autism.

Starkstein S, Gellar S, et al. (Starkstein) Fremantle Hospital, University of Western Australia, 35 Stirling Highway, Crawley, Western Australia Australia; Autism Association of Western Australia, Western Australia, WA 6008 Australia; School of Psychiatry, University of Western Australia, 35 Stirling Highway, Crawley, Western Australia Australia. Gellar,Scott. Fremantle Hospital, University of Western
Risk ratio; ARR). Driving restrictions may be based on individualised risk assessments or across-the-board guidelines, but these are influenced by various factors including the community perception of an acceptable relative level of risk for an accident (the accident risk ratio; ARR). The impact of emotional distress on motor blocks and festination in Parkinson's disease. Journal of Neuropsychiatry & Clinical Neurosciences. 2015; 27(2): 121-6.

The impact of emotional distress on motor blocks and festination in Parkinson's disease.

Starkstei n, Sergio. From the School of Psychiatry and Clinical Neurosciences (SS, MD, SB) and Schools of Medicine and Pharmacology (MW), University of Western Australia and Fremantle Hospital, Western Australia, Australia; Centre for Clinical Research in Neuropsychiatry, Graylands Hospital, Western Australia, Australia (VB); and Raul Carrea Institute of Neurological Research, FLENI, Buenos Aires, Argentina (VB, MM).

Recent studies suggest that depression and anxiety in patients with Parkinson's disease may predispose them to freezing. Although festination is also frequent, the association with emotional disorders has not been examined. The aim of the authors was to clarify the association between freezing and festination with anxiety, depressive disorders, and emotional distress. The authors examined a consecutive series of 95 patients with Parkinson's disease using comprehensive psychiatric assessments and a new instrument specifically designed to assess the severity of freezing, festination, and emotional distress (Motor Blocks and Festination Scale). All patients were assessed with the Motor Blocks and Festination Scale, the Mini International Neuropsychiatric Interview, and scales to measure the severity of mood and anxiety disorders. A linear regression analysis showed that both motor blocks and festination were significantly associated with emotional distress and deficits on activities associated with daily living. Conversely, there was no significant association between motor blocks or festination and generalized anxiety disorder, panic disorder, agoraphobia, social phobia, or...
depression. Motor blocks and festination are significantly associated with emotional distress, but no significant associations were found with anxiety or affective disorders.


Incidence and clinical relevance of heterotopic ossification after internal fixation of acetabular fractures: retrospective cohort and case control study.
Baschera D, Rad H, et al.

OBJECTIVE: The aim of the study was to evaluate predictors and clinical relevance of heterotopic ossification (HO) in patients treated for acetabular fractures in a tertiary referral centre.

PATIENTS AND METHODS: The study is a retrospective cohort study with a nested case-control study. All patients treated with internal fixation of acetabular fractures from January 2004 to October 2013. Ninety patients had postoperative imaging available at 6 and 12 months postoperatively and received no prophylaxis. Plain radiographs were used to grade HO. The Hip disability and Osteoarthritis Outcome Score (HOOS) was used to compare outcomes between patients suffering from HO with patients who did not.

RESULTS: Sixteen patients (17.7%) suffered from HO. According to the Brooker classification, 5 had class I, 4 class II, 3 class III and 4 class IV HO. Traumatic brain injury (TBI) was the only significant risk factor for developing HO (odds ratio (OR) 8.6, 95% confidence interval (CI) (1.693-43.753), p = 0.014). The HO rate in patients with an anterior (ilioinguinal) or posterior (Kocher-Langenbeck) surgical approach was 20% and 21% respectively, and the HO rate in patients with a combined approach was much lower at 11%. Neither fracture type nor gender nor age increased the risk of HO significantly. The outcome measured by HOOS was not significantly different between patients with HO and patients in the control group. Patients with HO Brooker class II-IV had slightly lower (effect estimate +4.25, 95% CI (-10.2 to +12.10), p = 0.220) HOOS compared to the majority of the control group.

CONCLUSION: A very low rate of HO was found compared to the HO rates described in other studies with similar patient cohorts who received prophylaxis. Based on our findings and the current literature, we do not recommend giving prophylaxis against HO to patients after internal fixation of acetabular fractures.


Comparison of patient outcomes in periarticular and intraarticular local anaesthetic infiltration techniques in total knee arthroplasty.
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BACKGROUND: The use of local infiltration analgesia in the setting of knee arthroplasty is well established. There are no studies to date which have directly compared differences in infiltration techniques. The purpose of this study is to establish if a difference in patient outcomes exists when the infiltrate is injected into the periarticular tissues or directly into the joint.

METHODS: One hundred and forty-two consecutive patients waitlisted for primary total knee arthroplasty were enrolled after primary exclusion criteria were applied. These included the following: allergy to study drugs, inability to receive spinal anaesthesia, and planned bilateral surgery. Patients were divided into two groups, a periarticular infiltration group (group A) and an intraarticular infiltration group (group B). Secondary exclusion criteria of regular opioid use, psychiatric illness, and serious medical comorbidity left a total of 47 patients in group A and 54 patients in group B. Both groups received a combination of 30 mg ketorolac, 500 mg morphine equivalents, and normal saline. This was either injected into the periarticular tissues during surgery (group A) or intraarticularly at closure of the wound (group B). Primary outcome measures included opioid consumption during the first 24 h postoperatively and over the total admission, and visual analogue scales (VAS) on postoperative day 1 and at discharge. Secondary measures included Oxford Knee Score, knee flexion, length of stay, haemoglobin drop, and transfusion requirement. Ethics approval was granted by the hospital review board. The trial is registered in the Australian New Zealand Clinical Trials Registry, registration ACTRN12615000488505.

RESULTS: No statistically significant differences in postoperative analgesic use were observed between the two groups. However, there was a trend toward decreased postoperative patient-controlled analgesia use in the periarticular group (mean 53.1 vs 68.3 mg morphine equivalents; p=0.093), as well as a statistically significant reduction in postoperative visual analogue pain scores. No statistically significant differences were observed for haemoglobin drop, range of motion, or pre- to 6-week postoperative Oxford Knee Score difference.

CONCLUSIONS: Our study is the first we are aware of to directly compare a periarticular to intraarticular injection technique when using local infiltration analgesia for total knee arthroplasty. Our results show no clear statistically significant benefit with either technique. The periarticular group showed a statistically significant reduction in postoperative VAS pain scores alongside a trend in that group toward reduced overall opioid use.
Metallosis following a dual coat porous hydroxyapatite shoulder hemiarthroplasty.

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H. Khan, Royal Perth Hospital, WA, Australia

We report a case of metallosis following a shoulder hemiarthroplasty with a humeral component resurfacing shoulder replacement.


Neonatal intubation in a remote environment.

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(Thompson) Fiona Stanley Hospital, Perth, Australia (Ramadas Anaesthetic Department, Princess Margaret Hospital, Perth, Australia
K. Thompson, NETS WA, Perth, Australia

Background: In a remote environment with unfamiliar equipment and team-members and limited support, intubation of an acutely unwell neonate is a difficult technique. Complications including vocal problems are increased with multiple attempts at intubation in the neonatal period. In Western Australia, neonatal intensive care is centralised in Perth. The Newborn Emergency Transport (NETS) Team, transports infants from around the state to Perth, a distance of up to 3,000 km. Most transfers are undertaken for respiratory compromise, often in association with prematurity. We aimed to review episodes of neonatal intubation for transport and difficulties encountered by our team in the remote environment. Method: Retrospective audit. All ventilated infants transported by NETS during a two month period were identified from databases. Clinical and demographic data was collected from the clinical notes. Results: Of 35 neonates intubated for transport (6 nasal, 29 oral), 14 were intubated by the NETS team. Of these, 3 had had prior unsuccessful attempts at intubation made by the local team. Aside from failed attempts at intubation by the referring team, no complications were noted during or related to intubation. There were no episodes of unplanned extubation during transport. The average distance travelled by the ventilated infants was 178 km, and the longest distance travelled was 1664 km. Conclusion: Although few acute complications were noted, 87% success at intubation attempts by referring physicians highlights the challenges which remain in the resuscitation and stabilisation of neonates in peripheral centres, and the importance of a skilled NETS team.

Publication Types: Conference Abstract


Laryngeal mask airway utility in the interhospital transport of neonatal patients: A systematic review.

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K. Thompson, NETS WA, Perth, Australia

Background: When combined with congenital airway abnormalities, neonatal intubation can prove difficult, requiring expertise. In a remote environment, intubation may be difficult due to infant, personnel, situational or equipment factors. The laryngeal mask airway (LMA) has been used as an adjunct in the management of inpatient neonatal airways. We aimed to review the literature to ascertain whether LMAs have been used during the transport of infants. Methods: A search was conducted using Medline, Embase, CINAHL, PubMed, and Cochrane databases, using search terms including (neonatal OR newborn OR inborn), (retrieval OR transport), (laryngeal OR LMA). Cross-referencing was conducted to maximize yield. Results: 76 papers identified. 61 duplications and irrelevant papers removed. 15 papers were read: Yielded 5 case reports of LMAs used successfully in neonatal transfer * Congenital airway abnormalities * Normal anatomy but a “can’t intubate, can’t ventilate” (CICO) situation * Infant with unplanned extubation during transport showing excellent recovery following placement of, and continued ventilation via LMA * Infant deteriorated during helicopter transport, inadequate clinical response to face mask ventilation, LMA successfully used. Conclusion: Although maintenance of a secure airway using an LMA may be difficult, several case reports describe successful transport of infants with or without abnormal anatomy using LMA. The LMA appears to have a role within newborn transport, when personnel, situational or anatomical constraints impede intubation.

Publication Types: Conference Abstract


Short term outcomes of infants born outwith tertiary neonatal centres in Western Australia.

Thompson K, Shrestha D, et al.
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K. Thompson, NETS WA, Perth, Australia

Background: Prematurity is associated with increased rates of morbidity and mortality when compared with those of term infants.
These rates are further increased when an infant is born prematurely out of a tertiary neonatal centre. Western Australia (WA) is the largest state in Australia, with tertiary neonatal services centralised in Perth. Infants born prematurely elsewhere in WA are transported to the NICU at King Edward Memorial Hospital (KEMH) in Perth. We compared the short term outcomes of extremely preterm infants, born outwith the tertiary neonatal institutions in Western Australia (outborn) with those of infants born in KEMH (inborn) over a period of 11 years from 2001 to 2011. Methods: Retrospective cohort study. Cases identified from neonatal database and include all infants born at <30 weeks gestation at another hospital. Matched controls were identified from the same database (next infant born at KEMH with comparable gestation and weight). Demographic data along with short term outcomes were retrospectively collected from prospectively recorded databases. Results: 141 infants met inclusion criteria and were matched with 141 comparable inborn infants. Table 1 describes demographic data as well as short-term clinical outcomes. Conclusion: While significant differences in administration of antenatal steroids were noted between outborn and inborn infants, no significant differences in short term outcomes were noted in this study. This highlights the excellent results achieved by expert neonatal transport teams. (Table Presented).

Publication Types: Conference Abstract


**Videolaryngoscopy in neonatology: A systematic review.**

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Background: Videolaryngoscopy is used in adult patients for achieving visualisation of the glottis as well as for education during endotracheal intubation. We aimed to review the literature to establish the validity of videolaryngoscope use in the neonatal population. Method: A search was conducted using Medline, Embase, CINAHL, PubMed and Cochrane. Search terms included (neonatal OR newborn OR infant) (videolaryngoscope, videolaryngoscopy). Exclusion criteria: Animal studies, non-neonatal studies, studies including no videolaryngoscope Results: 222 papers identified, of which 124 duplicates were discarded. After papers meeting exclusion criteria were removed, 14 papers (11 case reports and 3 RCTs including a total of 631 patients) were included. Multiple types of videolaryngoscopy (VL) were used. Several cases describe VL success when direct laryngoscopy (DL) had been unsuccessful. Where comparative time to neonatal intubation was reported (481 patients), mean time to intubation was 49.8 s VL vs 44.4 s DL (p < 0.01, CI 3.24-7.43). Several papers reported outcomes other than time to intubate. The VL was utilised to record video footage of airway pathology in several cases. When used for education, VL was noted to identify problems with intubation quicker than DL and allowed non traumatic and reliable placement of ETT. Discussion: Several videolaryngoscopes are now available for neonatal use. From the available data, the time to achieve intubation is longer with VL vs DL. There are, however, circumstances where VL may be successful when DL has been unsuccessful, as well as other advantages including educational direction.

Publication Types: Conference Abstract


**An audit of jaundice management during neonatal retrieval.**

Thompson K, McDonald K, et al.
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K. Thompson, NETS WA, Perth, Australia

Background: Neonatal jaundice, while often benign and self-limiting, can cause morbidity or mortality without appropriate treatment. In Western Australia (WA), tertiary neonatal services are centralised in Perth. The Newborn Emergency Transport Service (NETS) team provides advice regarding optimising jaundice management, and transfers infants to tertiary neonatal services either at King Edward Memorial Hospital (KEMH) or Princess Margaret Hospital (PMH). A portable phototherapy unit is available for use en route. We reviewed neonates transferred for jaundice in WA over two months, noting use of phototherapy and bilirubin level at time of referral to NETS and at arrival to tertiary hospital. Method: Retrospective audit of all infants referred for management of jaundice during July and August 2014, no exclusion criteria. Demographic and biochemical data extracted from databases and clinical notes, continuous results analysed using paired t-test. Results: 15 patients met inclusion criteria, all were transported by road. Total distance travelled was 696 km. Mean duration from referral to arrival at tertiary destination was 3.5 hours. Mean initial serum bilirubin (SBR) was 395 umol/L. Mean SBR on arrival at destination was 332 umol/L, a significant reduction (p < 0.01). 8/15 patients had phototherapy provided en route. Those utilising phototherapy had a significant reduction in SBR, whereas without phototherapy had no significant change in SBR. Conclusions: Transfers of jaundiced neonatal patients were conducted safely with a reduction in bilirubin between referral and arrival at tertiary hospital. Phototherapy was useful in reducing SBR during transfer and should be utilised during transfer of jaundiced infants wherever possible.

Publication Types: Conference Abstract


**Prevalence and risk factors for parent-reported recurrent otitis media during early childhood in the Western**
Australian Pregnancy Cohort (Raine) Study. 
Brennan-Jones CG, Whitehouse AO, et al. (Brennan-Jones, White) Division of Speech and Hearing Sciences, School of Health Sciences, Queen Margaret University. Edinburgh, United Kingdom (Brennan-Jones) Park, Eikelboom, Swanepoel Ear Science Institute Australia, Perth, WA, Australia (Brennan-Jones) Park, Eikelboom, Swanepoel Ear Science Institute Australia, School of Surgery, University of Western Australia, 1 Salvado Road, Subiaco, WA 6008, Australia (Whitehouse) School of Psychology, University of Western Australia, Perth, WA, Australia (Eikelboom) Department of Otolaryngology, Royal Perth Hospital, Perth, WA, Australia (Swanepoel) Princess Margaret Hospital for Children, Perth, WA, Australia (Whitehouse) Department of Speech-Language Pathology and Audiology, University of Pretoria, Pretoria, South Africa 

The preconception needs of women with severe mental illness: a consecutive clinical case series. 
Nguyen, Thinh. a School of Psychiatry and Clinical Neurosciences, School of Medicine and Pharmacology, University of Western Australia, Australia (Oddy) School of Exercise and Health Science, Edith Cowan University, Joondalup, Australia (Sherriff) School of Public Health, Curtin Health Innovation Research Institute, Curtin University, Australia (Whitehouse, Jacques, Jamieson) Telethon Kids Institute, University of Western Australia, Perth, WA, Australia 

INTRODUCTION: Women with severe mental illness (SMI) are having babies at an increasing rate, but continue to face many challenges across the perinatal period. There is little research into the preconception needs of women with SMI and the aim of this study was to investigate the social circumstances, general health, mental health and reproductive health care needs in these at risk women. 

METHOD: Women with SMI referred for specialist preconception counselling at a tertiary obstetric hospital in 2012 were eligible to participate. The data source was a semi-structured study-specific interview schedule with open-ended questions incorporated into the routine assessment protocol.
RESULTS: In a one-year period, 23 women were referred to the service and 22 consented to data from the interview being pooled for the study. All women were taking at least one psychotropic medication at the time of referral. Overall, 40% (n=9) were aged at least 35 years, 36% (n=8) smoked cigarettes daily and over half (54.5% n=12) reported their body mass index as being in the overweight or obese range. Thematic analysis revealed the importance of maternal desire, and concerns relating to age and biological time pressure, the impact of the illness and medication on pregnancy and motherhood.

CONCLUSION: Our data indicate that preconception counselling should be routine in the care of women with SMI of reproductive age, and should take into account the potential centrality of motherhood in the woman's rehabilitation, as well as the complex appraisals of risks, general health and support.


Popliteal vein aneurysm presenting as recurrent pulmonary embolism.
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Although rare, popliteal vein aneurysms can lead to pulmonary emboli, which can be fatal. We present a case of a popliteal vein aneurysm in a 39-year-old female who presented with her third episode of pulmonary embolism despite being on anticoagulants. Computed Tomography Venogram demonstrated a large Popliteal Vein Aneurysm measuring 71 x 36 x 77 mm which was surgically repaired. According to the current literature, anticoagulation is insufficient therefore early surgical intervention is recommended as it is safe and effective.


Oral contraception does not alter typical post-exercise interleukin-6 and hepcidin levels in females.
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M. Sim, School of Sport Science, Exercise and Health, The University of Western Australia, Australia
Objectives: The post-exercise interleukin-6 (IL-6) and hepcidin response was investigated during the hormone-deplete and hormone-replete phases of an estradiol and progestogen regulated oral contraceptive cycle (OCC). Design: Counterbalanced, repeated measures cross-over study. Methods: Ten active female monophasic oral contraceptive pill (OCP) users completed two 40min treadmill running trials at 75% of their pre-determined peak oxygen uptake velocity (vVO2peak). These trials were randomly performed in two specific phases of the OCC: (a) Day 2-4, representing a hormone-free withdrawal period (D-0); (b) Day 12-14, representing the end of the first week of active hormone therapy (D+7). Venous blood samples were drawn pre-, post- and 3h post-exercise. Results: In both trials, serum IL-6 was significantly elevated (p<.05) immediately post-exercise, while serum hepcidin was significantly elevated (p<.005) 3 h post-exercise, with no significant differences recorded between trials. Conclusions: These findings suggest that exercise performed during the different phases (D. - . 0 vs. D. +. 7) of a monophasic OCP regulated cycle does not alter exercise induced IL-6 or hepcidin production. As such, future studies looking to investigate similar variables post-exercise, may not need to 'control' for different phases of the OCC, provided participants are current monophasic OCP users.


Journal of Surgical Case Reports. 2015; 1.

A case of psychosis induced self-insertion of intracranial hypodermic needles causing seizures.
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Self-insertion of foreign bodies is a rare event. This report details a 56-year-old male who had self-inserted six hypodermic needles into his left frontal lobe 6 years previously. He subsequently presented with seizures and went on to have the needles surgically removed. This represents the first case of its type involving hypodermic needles. Given that intracranial needles are a rare finding, the management of such patients is complex. Two management issues in particular that require consideration are: (i) can the needles be left in situ and (ii) does removal of the needles reduce the risk of seizures in the long term? Copyright Published by Oxford University Press and JSCR Publishing Ltd. All rights reserved. The Author 2015.


Journal of Surgical Case Reports. 2015; 6.

Coexistence of an intracranial meningioma and an arteriovenous malformation.
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Honeybul,Stephen. Department of Neurosurgery, Sir Charles Gairdner Hospital and Royal Perth Hospital, Perth, WA, Australia
The occurrence of a primary brain tumour in association with a cerebral arteriovenous malformation (AVM) is a recognized but rarely reported finding. A 56-year-old female presented following a single tonic clonic seizure. Radiological investigations revealed a left posterior frontal parafalcine meningioma and a left parietal AVM. Both were uneventfully resected. Whether there is a causal relationship is unproven, however, this case report might lend some support to this hypothesis given the relatively close proximity of the two lesions. Copyright Published by Oxford University Press and JSCR Publishing Ltd. All rights reserved. © The Author 2015.


**Plasma cell vulvitis: A case series.**

Page SS, Tait C, et al. (Page, Tait, Dykstra, McCloskey, Parry) Royal Perth Hospital, Perth, Australia

Introduction: Zoon first described plasma cell balanitis in 1950 and since then there have been many cases described. The equivalent condition in women is plasma cell vulvitis (PCV), which is less frequently reported in the literature. For this reason it continues to be a diagnosis that is challenging to make and leads to difficulties for clinicians and patient alike. Design: Case series. Setting: Dermatology Department and Sexual Health Department, Royal Perth Hospital, Perth, Western Australia. Patients: Two patients with PCV were included in our study. They were aged 51 and 76 years old at the time of diagnosis. Main outcome measures: Complications and treatment outcomes. Results: Standard therapy for plasma cell vulvitis which mainly includes topical steroids was not successful in either patient. The first patient had a symptomatic recurrence and the second patient was successfully treated with tacrolimus 0.1%. We also explore the other treatment modalities reported in PCV. Clinical images and dermatopathology images are included, as well as explanations of the key features important to establish a diagnosis. Conclusion: PCV is a rare condition, representing <2% of chronic vulvar complaints. PCV has been reported in women from the ages of 8-80 years. Differential diagnoses for plasma cell vulvitis should include lichen planus, pemphigus vulgaris, fixed drug eruption, Paget’s disease, squamous cell carcinoma and herpes simplex virus. PCV should be considered in patients: who fail initial topical steroid; have nonspecific initial biopsy results or continue to have pruritus, pain or burning. It is a complicated condition and further research is warranted to further define this clinical entity.

Publication Types: Conference Abstract


**Clinical imaging guidelines part 1: A proposal for uniform methodology.**

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Inappropriate imaging can lead to unnecessary medical radiologic exposures and cost and may not answer the clinical question. Inappropriate imaging guidelines inform radiologic procedural justification and facilitate the choice of the best test first, but their acceptance by referrers, use, and value may be limited by shortcomings in the methodology of development. Focusing on common, essential elements of methodology will help guideline developers. In 2012 and 2013, the International Atomic Energy Agency hosted Technical Meetings on Radiation Protection of Patients Through the Development of Appropriateness Criteria in Diagnostic Imaging. Participants identified and agreed on issues concerning development of imaging referral guidelines. Items based on the Appraisal of Guidelines for Research and Evaluation II instrument were amended with additional items including development and consensus group composition. Consensus was sought on 28 items, 18 of which were agreed should be uniform, and 10 should allow for regional differences. Further work is required to encourage, provide, and identify higher quality evidence and to agree on a grading system for recommendations. Many key areas are common to guideline developers globally, opening the way for international collaboration to help demystify, simplify, and justify.


**Incidence of Venous Thromboembolism and Benefits and Risks of Thromboprophylaxis After Cardiac Surgery: A Systematic Review and Meta-Analysis.**

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BACKGROUND: Optimal thromboprophylaxis after cardiac surgery is uncertain. This systematic review aimed to define the incidence
CONCLUSIONS: Current, but not past, depression is associated with increased mortality, and this excess mortality is strongly
was observed after adjustment for other measured factors. VTE prophylaxis was associated with a reduced risk of PE (relative risk [RR], 0.45; 95% confidence interval [CI], 0.28-0.72; P=0.0008) or symptomatic VTE (RR, 0.44; 95% CI, 0.28-0.71; P=0.0006) compared to the control without significant
Society, School of Medicine and Pharmacology, University of Western Australia, Crawley, Western Australia, Australia; Department of Psychiatry, Royal Perth Hospital, Perth, Western Australia, Australia. Electronic address: kieran.mccaul@uwa.edu.au. Almeida,Osvaldo P. Western Australian Centre for Health and Ageing, Centre for Medical Research, University of Western Australia, Crawley, Western Australia, Australia; School of Psychiatry and Clinical Neurosciences, University of Western Australia, Perth, Australia; WA Center for Health and Aging, Center for Medical Research, Perth, Australia; Department of Psychiatry, Royal Perth Hospital, Perth, Australia, Australia; Department of Neurology, Sir Charles Gairdner Hospital, Perth, Australia; Department of Endocrinology, Fremantle and Fiona Stanley Hospital, Perth, Australia. Gollege,Jonathan. Queensland Research Center for Peripheral Vascular Disease, School of, Medicine and Dentistry, James Cook University, Townsville, Australia; Department of Vascular and Endovascular Surgery, The Townsville Hospital, Townsville, Australia. Norman,Paul E. School of Surgery, University of Western Australia, Perth, Australia, Flicker,Leon. WA Center for Health and Aging, Center for Medical Research, Perth, Australia; School of Medicine and Pharmacology, University of Western Australia, Perth, Australia; Department of Geriatric Medicine, Royal Perth Hospital, Perth, Australia. BACKGROUND: Depression is associated with increased mortality, but it is unclear if this relationship is truly causal. OBJECTIVES: To determine the relative mortality associated with past and current depression, taking into account the effect of frailty. DESIGN, SETTING, AND PARTICIPANTS: Prospective longitudinal cohort study of 2565 men aged 75 years or over living in metropolitan Perth, Western Australia, who completed the third wave of assessments of the Health In Men Study throughout 2008. MAIN OUTCOME AND MEASURES: All-cause mortality data were derived from Australian death records up to 1 June 2013. History of past depression and age of onset of symptoms were obtained from direct questioning and from electronic health record linkage. Diagnosis of current major depressive symptoms followed Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision guidelines. We considered that participants were frail if they showed evidence of impairment in 3 or more of the 5 domains on the fatigue, resistance, ambulation, illnesses, and loss of weight (FRAIL) scale. Other measured factors included age, education, living arrangements, smoking and alcohol history, and physical activity. RESULTS: 558 participants died during mean period of follow-up of 4.2 +/- 1.1 years. The annual death rate per thousand was 50 for men without depression, 52 for men with past depression, and 201 for men with major depressive symptoms at baseline. The crude mortality hazard was 4.26 (95% confidence interval = 2.98, 6.09) for men with depression at baseline compared with never depressed men, and 1.79 (95% confidence interval = 1.21, 2.62) after adjustment for frailty. Further decline in mortality hazard was observed after adjustment for other measured factors. CONCLUSIONS: Current, but not past, depression is associated with increased mortality, and this excess mortality is strongly associated with frailty. Interventions designed to decrease depression-related mortality in later life may need to focus on ameliorating frailty in addition to treating depression. Copyright © 2015 AMDA - The Society for Post-Acute and Long-Term Care Medicine. Published by Elsevier Inc. All rights reserved. How many older people are frail? Using multiple imputation to investigate frailty in the population. McCaul KA, Almeida OP, et al. McCaul,Kieran A. Western Australian Centre for Health and Ageing, Centre for Medical Research, University of Western Australia, Crawley, Perth, Western Australia, Australia; School of Medicine and Pharmacology, University of Western Australia, Crawley, Western Australia, Australia. Electronic address: kieran.mccaul@uwa.edu.au. Almeida,Osvaldo P. Western Australian Centre for Health and Ageing, Centre for Medical Research, University of Western Australia, Crawley, Perth, Western Australia, Australia; School of Psychiatry and Clinical Neurosciences, University of Western Australia, Crawley, Western Australia, Australia; Department of Psychiatry, Royal Perth Hospital, Perth, Western Australia, Australia. Norman,Paul E. School of Surgery, University of Western Australia, Crawley, Western Australia, Australia; Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle, Western Australia, Australia; Department of Endocrinology and Diabetes, Royal Perth Hospital, Perth, Western Australia, Australia; Department of Neurology, Royal Perth Hospital, Perth, Western Australia, Australia. Gollege,Jonathan. Vascular
Biology Unit, School of Medicine, James Cook University, Townsville, Queensland, Australia. Flicker, Leon. Western Australian Centre for Health and Ageing, Centre for Medical Research, University of Western Australia, Crawley, Perth, Western Australia, Australia; School of Medicine and Pharmacology, University of Western Australia, Crawley, Western Australia, Australia.

OBJECTIVES: The objective of this study was to establish the extent to which frailty was associated with attrition and then compare estimates of frailty prevalence and progression estimated from the observed data to those estimated after imputation.

DESIGN: Population-based cohort study.


PARTICIPANTS: Participants were 10,305 community-dwelling men aged 70 and older, followed for up to 10 years.

MEASUREMENTS: Participants completed an extensive questionnaire covering functional activities and illnesses. Frailty was assessed using the FRAIL Scale and a 32-item Frailty Index.

RESULTS: Nonresponders at Wave 3 were more likely to have been frail at Wave 2. Imputed estimates of frailty prevalence were 8% to 10% higher than those derived from the observed data.

CONCLUSION: Epidemiological surveys may substantially underestimate the levels of frailty among older people in the general population. This selective nonresponse results in an overoptimistic view of aging populations, particularly for the very old.

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The course of neuropsychiatric symptoms in Dementia: A 3-year longitudinal study.


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Objectives: Patients with dementia experience a wide range of neuropsychiatric symptoms. These symptoms often cause considerable distress to patients and caregivers, and often contribute to institutionalization. The current study examined the prevalence and course of neuropsychiatric symptoms in a large sample of patients with dementia attending memory clinics. Design: Three-year nonprescriptive, observational study examining relationships between predictors and outcome variables in patients with dementia. Setting: Nine memory clinics around Australia. Participants: Of 970 patients recruited, 779 patients had dementia at baseline. Measurements: Over 3 years, patients were rated on 6 occasions on the 12-item Neuropsychiatric Inventory and measures of cognition, dementia severity, function, and medication use. Analyses focused on the 514 patients with dementia who completed the Neuropsychiatric Inventory on 4 or more occasions. Results: Overall levels of neuropsychiatric symptoms increased over the 3 years. In particular, delusions, hallucinations, agitation, anxiety, apathy, disinhibition, irritability, and aberrant motor behavior increased over the 3 years. Depression, euphoria, night time behavior, and appetite did not significantly increase over this period. Severity of dementia, male sex, and frontotemporal dementia were associated with greater levels of neuropsychiatric symptoms at baseline. Dementia with Lewy bodies was associated with more hallucinations and less appetite disturbances, and Alzheimer's disease was associated with lower levels of neuropsychiatric symptoms than other types of dementia at baseline. Conclusions: The findings confirm that different symptoms have different trajectories and that baseline characteristics of patients, including sex and dementia type, predict the subsequent course of symptoms. The findings also highlight the association between dementia severity and neuropsychiatric symptoms, indicating the need to control for this variable when examining their longitudinal trajectories.


Temporal trends of time to antiretroviral treatment initiation, interruption and modification: Examination of patients diagnosed with advanced HIV in Australia.

Wright ST, Law MG, et al.

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groups, potentially lowering community viral load compared to earlier time periods. We found a marked reduction in the hazard of treatment interruption comparing 2007-2012 versus 1996-2001 (p<0.001), and no difference in ART modification for patients in later periods (2007-2012) in all diagnosis CD4 count groups. We found an 83% (69, 91%) reduction in the hazard of first used survival methods to evaluate rates of ART initiation by diagnosis CD4 count strata and by calendar year of HIV diagnosis. Cox deterministically linked records from the Australian HIV Observational Database to the Australian National HIV Registry to obtain http://www.ncbi.nlm.nih.gov/pubmed?tool=iaufhhslib&term=2015930592

Introduction: HIV prevention strategies are moving towards reducing plasma HIV RNA viral load in all HIV-positive persons, including those undiagnosed, treatment naive, on or off antiretroviral therapy. A proxy population for those undiagnosed are patients that present late to care with advanced HIV. The objectives of this analysis are to examine factors associated with patients presenting with advanced HIV, and establish rates of treatment interruption and modification after initiating ART. Methods: We deterministically linked records from the Australian HIV Observational Database to the Australian National HIV Registry to obtain information related to HIV diagnosis. Logistic regression was used to identify factors associated with advanced HIV diagnosis. We used survival methods to evaluate rates of ART initiation by diagnosis CD4 count strata and by calendar year of HIV diagnosis. Cox models were used to determine hazard of first ART treatment interruption (duration >30 days) and time to first major ART modification. Results: Factors associated (p<0.05) with increased odds of advanced HIV diagnosis were sex, older age, heterosexual mode of HIV exposure, born overseas and rural-regional care setting. Earlier initiation of ART occurred at higher rates in later periods (2007-2012) in all diagnosis CD4 count groups. We found an 83% (69, 91%) reduction in the hazard of first treatment interruption comparing 2007-2012 versus 1996-2001 (p<0.001), and no difference in ART modification for patients diagnosed with advanced HIV. Conclusions: Recent HIV diagnoses are initiating therapy earlier in all diagnosis CD4 cell count groups, potentially lowering community viral load compared to earlier time periods. We found a marked reduction in the hazard of first treatment interruption, and found no difference in rates of major modification to ART by HIV presentation status in recent periods.

Efficacy and safety of rVIII-singlechain in surgical prophylaxis.

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C. Djambas Khayat, Hotel-Dieu De France University Hospital, Beirut, Lebanon

Background: VIII-SingleChain, a novel recombinant Factor VIII, has been designed as a B-domain truncated construct with a covalent bond between the heavy and light chains with a higher binding affinity to von Willebrand Factor. rVIII-SingleChain has a lower clearance, longer half-life and larger area under the curve compared to octocog alfa. Aims: This sub-study investigated the safety and efficacy of rVIII-SingleChain when used in the perioperative setting for prevention and bleeding control in patients with severe Hemophilia A undergoing major surgery. Methods: The study was approved by Ethics committees of all sites and conducted according to GCP and the Declaration of Helsinki. Dosing was guided by the current WFH recommendations. Dosing was according to individual patient PK and was given by bolus or continuous infusion. Results: 13 patient underwent 16 major surgeries which included extraction of wisdom teeth, abdominal hernia repair, elbow replacement, ankle arthroplasty, knee replacement (5), cholecystectomy, lengthening of the achilles tendon combined with straighten up of the right toes, circumcision (3), open reduction Internal fixation right ankle fracture and hardware removal right ankle. Eight procedures were covered by bolus infusion, and 8 by continuous infusion of rVIII-SingleChain. Investigators rated the efficacy of rVIII-Single- Chain to provide hemostasis during surgery as excellent (defined as hemostasis not clinically significant different from normal) in all cases but one in which it was rated as good (defined as hemostasis normal or mildly abnormal in terms of quantity and/or quality eg, slight oozing). After the procedure, patients returned to routine treatment after a median of 9 days. No related AEs or SAEs were observed during the peri-surgical period. Conclusion: rVIII-SingleChain is efficacious and safe when used for peri-surgical prophylaxis and bleeding control during a wide range of surgical procedures when dosed following the WFH recommendations. Publication Types: Conference Abstract

How participating in a clinical trial has had a far reaching effect-a case study.

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Background: Clinical trials are an integral part of haemophilia management and with such a small global population it is imperative that Haemophilia Treatment Centres (HTC) and patients understand how participating in clinical trials can have far-reaching effects. Aims: This case study focuses on a 19 year old male with severe haemophilia B who participated in a recombinant factor IX extended half life phase 3 clinical trial and how this participation affected him, the HTC and government jurisdictions. Methods: A review of patient interactions/case notes and correspondence with HTC staff provided the data for this case study. Results: Clinical
Patient Outcomes: Pre clinical trial dose rFIX 5000 IU x 3/week (241 IU kg<sup>-1</sup>/per week). Study commencement dose 3500 IU (50 IU kg<sup>-1</sup>/per week). Dose reduced to 2000 IU (30 IU kg<sup>-1</sup>/per week) and then further reduced to 1500 IU (20 IU kg<sup>-1</sup>/per week) (1500 IU). Now into his 4th year of being on the clinical trial he remains on 1500 IU weekly and has reported only one bleeding event. Psychosocial Patient Outcomes: The frequency of contact with the HTC during the clinical trial period improved the relationship and trust between HTC staff and the patient. The patient also gained a greater understanding of his bleeding disorder which gave him a greater sense of trust, ownership and control over managing his bleeding disorder. HTC Outcomes: The HTC has gained a greater understanding of the product being trialled and how best the product could be used within their patient population. Government Jurisdiction Outcomes: Whilst patients are participating in clinical trials the financial impact of funding the clotting factor concentrate lies with the sponsor, which can significantly reduce the financial burden of funding clotting factor concentrate. Conclusion: Not only did this patient gain early access to new innovations in haemophilia treatment and an enhanced quality of life, but the HTC and government jurisdictions also benefited from patient participation.

Publication Types: Conference Abstract


When 2N vWD should be considered a differential diagnosis.

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Background: Type 2N von Willebrands disease is a rare bleeding disorder, inherited recessively. It is often mistaken for mild haemophilia A on basic laboratory investigations. However given the inheritance pattern is vastly different, it is a condition that should be considered when a new case of mild haemophilia A presents. Aims: This collection of case studies aims to highlight how type 2N vWD can be overlooked with patients and their families diagnosed with mild haemophilia A. Methods: A review of pathology and genetic results together with patient and family histories was undertaken on those with a diagnosis of 2N vWD. Results: The Haemophilia Centre of WA identified 4 families who had had a diagnosis change and another where investigations were continuing. In some cases failure to respond to treatment as predicted sparked a reassessment of the bleeding disorder. In others the laboratory results were not consistent with a definitive diagnosis of haemophilia and lead to binding assays being performed. In one case it was the family bleeding history and inheritance pattern that was not in keeping with a diagnosis of haemophilia, even though on first examination the laboratory results were indicative of haemophilia A and was diagnosed as such. In some families the change in diagnosis is made with 12 months - however in the majority of these families the re-diagnosis was years after the initial diagnosis, for some more than 35 years. In most of these families this change in diagnosis has affected multiple generations of family members, leading to a re-examination of possible affected family members and perhaps those that are unlikely to now be affected. Conclusion: Type 2N vWD should be considered as an alternative diagnosis and excluded when a new case of mild haemophilia A presents. It should also be considered when the family inheritance pattern does not correlate with a diagnosis of haemophilia or when treatment outcomes do not correlate with the predicted outcome of haemophilia management.

Publication Types: Conference Abstract


Abdominal compliance: A bench-to-bedside review.

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Abdominal compliance (AC) is an important determinant and predictor of available workspace during laparoscopic surgery. Furthermore, critically ill patients with a reduced AC are at an increased risk of developing intra-abdominal hypertension and abdominal compartment syndrome, both of which are associated with high morbidity and mortality. Despite this, AC is a concept that has been neglected in the past. AC is defined as a measure of the ease of abdominal expansion, expressed as a change in intra-abdominal volume (IAV) per change in intra-abdominal pressure (IAP). AC = DELTAIAV / DELTAIAP. A dynamic variable dependent on baseline IAV and IAP as well as abdominal reshaping and stretching capacity. Whereas AC itself can only rarely be measured, it always needs to be considered an important component of IAP. Patients with decreased AC are prone to fulminant development of abdominal compartment syndrome when concomitant risk factors for intra-abdominal hypertension are present. This review aims to clarify the pressure-volume relationship within the abdominal cavity. It highlights how different conditions and pathologies can affect AC and which management strategies could be applied to avoid serious consequences of decreased AC. We have pooled all available human data to calculate AC values in patients acutely and chronically exposed to intra-abdominal hypertension and demonstrated an exponential abdominal pressure-volume relationship. Most importantly, patients with high level of IAP have a reduced AC. In these patients, only small reduction in IAV can significantly increase AC and reduce IAPs. A greater knowledge on AC may help in selecting a better surgical approach and in reducing complications related to intra-abdominal hypertension.

Optic Nerve Sheath Diameter Increase on Ascent to High Altitude: Correlation With Acute Mountain Sickness.

Kanaan NC, Lipman GS, et al.

Objective: Elevated optic nerve sheath diameter on sonography is known to correlate with increased intracranial pressure and is observed in acute mountain sickness. This study aimed to determine whether optic nerve sheath diameter changes on ascent to high altitude are associated with acute mountain sickness incidence.

Methods: Eighty-six healthy adults enrolled at 1240 m (4100 ft), drove to 3545 m (11,700 ft) and then hiked to and slept at 3810 m (12,500 ft). Lake Louise Questionnaire scores and optic nerve sheath diameter measurements were taken before, the evening of, and the morning after ascent.

Results: The incidence of acute mountain sickness was 55.8%, with a mean Lake Louise Questionnaire score +/- SD of 3.81 +/- 2.5. The mean maximum optic nerve sheath diameter increased on ascent from 5.58 +/- 0.79 to 6.13 +/- 0.73 mm, a difference of 0.55 mm (P = .09). Optic nerve sheath diameter increased at high altitude regardless of acute mountain sickness diagnosis; however, compared to baseline values, we observed a significant increase in diameter only in those with a diagnosis of acute mountain sickness (0.57 mm, 95% confidence interval, 0.37-0.77; P = .04). This change from baseline, or DELTA optic nerve sheath diameter, was associated with twice the odds of developing acute mountain sickness (95% confidence interval, 1.08-3.93).

Conclusions: The mean optic nerve sheath diameter increased on ascent to high altitude compared to baseline values, but not to a statistically significant degree. The magnitude of the observed DELTA optic nerve sheath diameter was positively associated with acute mountain sickness diagnosis. No such significant association was found between acute mountain sickness and diameter elevation above standard cutoff values, limiting the utility of sonography as a diagnostic tool.

Optic Nerve Sheath Diameter Increase on Ascent to High Altitude: Correlation With Acute Mountain Sickness.

Kanaan NC, Lipman GS, et al.

Optic nerve sheath diameter, was associated with twice the odds of developing acute mountain sickness (95% confidence interval, 1.08-3.93). This change from baseline, or DELTA optic nerve sheath diameter, was associated with twice the odds of developing acute mountain sickness (95% confidence interval, 1.08-3.93). The magnitude of the observed DELTA optic nerve sheath diameter was positively associated with acute mountain sickness diagnosis. No such significant association was found between acute mountain sickness and diameter elevation above standard cutoff values, limiting the utility of sonography as a diagnostic tool.


Superficial Femoral Artery Duplication.

Rajadurai VA, Sieunarine K.

Optic Nerve Sheath Diameter Increase on Ascent to High Altitude: Correlation With Acute Mountain Sickness.

Kanaan NC, Lipman GS, et al.

Superficial Femoral Artery Duplication.

Rajadurai VA, Sieunarine K.

Telemedicine allows successful Hepatitis C treatment in Western Australian prisons.

Braniff C, Connelly C, et al.

Telemmedicine allows successful Hepatitis C treatment in Western Australian prisons.

Braniff C, Connelly C, et al.

Telemedicine allows successful Hepatitis C treatment in Western Australian prisons.

Braniff C, Connelly C, et al.

Telemedicine allows successful Hepatitis C treatment in Western Australian prisons.

Braniff C, Connelly C, et al.

Telemedicine allows successful Hepatitis C treatment in Western Australian prisons.

Braniff C, Connelly C, et al.

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Braniff C, Connelly C, et al.

Telemedicine allows successful Hepatitis C treatment in Western Australian prisons.

Braniff C, Connelly C, et al.

Telemedicine allows successful Hepatitis C treatment in Western Australian prisons.


Superficial Femoral Artery Duplication.

Rajadurai VA, Sieunarine K.


Superficial Femoral Artery Duplication.

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Rajadurai VA, Sieunarine K.


Superficial Femoral Artery Duplication.

Rajadurai VA, Sieunarine K.


Superficial Femoral Artery Duplication.

Rajadurai VA, Sieunarine K.
higher efficacy compared with phenytoin cream.

CONCLUSION: AVO cream significantly accelerates biological healing of chronic wounds and helps to reduce pain severity with a significant improvement with both AVO (p<0.001) and phenytoin (p<0.01) creams, although AVO was more efficacious (p<0.001).

RESULTS: After initial assessment, 60 patients with chronic wounds (41 with pressure ulcer, 13 with diabetic wounds and 6 with venous ulcers), were recruited and randomised into 2 groups of 30. After 30 days of treatment, significant improvements in the wound size, depth, and edges; necrotic tissue type and amount; exudate type and amount; colour of wound surroundings; and peripheral tissue oedema score were observed in the AVO cream group (p<0.001). The total score of wound healing showed significant improvement with both AVO (p<0.001) and phenytoin (p<0.01) creams, although AVO was more efficacious (p<0.001). Likewise, although both treatments reduced the initial VAS score, the efficacy of AVO was significantly greater (p<0.001).

CONCLUSION: AVO cream significantly accelerates biological healing of chronic wounds and helps to reduce pain severity with a higher efficacy compared with phenytoin cream.

METHOD: In this randomised, double-blind, comparator-controlled, parallel-group trial, patients with chronic wounds were treated with either AVO cream or phenytoin cream as the standard treatment for a period of 30 days. Wound healing was evaluated using Bates-Jensen assessment tool and the severity of pain was assessed using a visual analogue scale (VAS).

RESULTS: After initial assessment, 60 patients with chronic wounds (41 with pressure ulcer, 13 with diabetic wounds and 6 with venous ulcers), were recruited and randomised into 2 groups of 30. After 30 days of treatment, significant improvements in the wound size, depth, and edges; necrotic tissue type and amount; exudate type and amount; colour of wound surroundings; and peripheral tissue oedema score were observed in the AVO cream group (p<0.001). The total score of wound healing showed significant improvement with both AVO (p<0.001) and phenytoin (p<0.01) creams, although AVO was more efficacious (p<0.001). Likewise, although both treatments reduced the initial VAS score, the efficacy of AVO was significantly greater (p<0.001).

CONCLUSION: AVO cream significantly accelerates biological healing of chronic wounds and helps to reduce pain severity with a higher efficacy compared with phenytoin cream.


Effect of muscle relaxation on the oxygenation of human skeletal muscle: A prospective in-vivo experiment using an isolated forearm technique.
Rhee KY, Kim TY, et al.

Needle tract seeding following percutaneous biopsy of renal cell carcinoma.
Chang DT, Sur H, et al.
Chang,Dwayne T S. Department of Urology, Rockingham General Hospital, Perth, Australia. Sur,Hariom. Department of Urology, Rockingham General Hospital, Perth, Australia. Lozinsky,Mikhail. Department of Urology, Rockingham General Hospital, Perth, Australia. Wallace,David M A. Department of Urology, Rockingham General Hospital, Perth, Australia. A 66-year-old man underwent computed tomography-guided needle biopsy of a suspicious renal mass. Two months later he underwent partial nephrectomy. Histology revealed a 30-mm clear cell renal cell carcinoma, up to Fuhrman grade 3. An area of the capsule was interrupted, which corresponded to a hemorrhagic area on the cortical surface. Under microscopy, this area showed a tongue of tumor tissue protruding through the renal capsule. A tumor deposit was found in the perinephric fat. These features suggest that tumor seeding may have occurred during the needle biopsy.


Familial hypercholesterolaemia: PCSK9 inhibitors are coming.
Santos RD, Watts GF.
(Santos) Lipid Clinic, Hospital Israe11a Albert Einstein, University of Sao Paulo, Sao Paulo, SP 05403, Brazil (Watts) Lipid Disorders Clinic, Royal Perth Hospital, University of Western Australia, Perth, WA, Australia
**Central arteriovenous anastomosis in resistant hypertension?**

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**Publication Types:** Comment

**Publication:** Lancet. 2015; 385(9976): 1596-7.

**Central arteriovenous anastomosis in resistant hypertension?**

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**Publication Types:** Comment

**Publication:** Lancet. 2015; 385(9976): 1406-17.

**Crohn's disease management after intestinal resection: a randomised trial.**

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**BACKGROUND:** Most patients with Crohn's disease need an intestinal resection, but a majority will subsequently experience disease recurrence and require further surgery. This study aimed to identify the optimal strategy to prevent postoperative disease recurrence.

**METHODS:** In this randomised trial, consecutive patients from 17 centres in Australia and New Zealand undergoing intestinal resection of all macroscopic Crohn's disease, with an endoscopically accessible anastomosis, received 3 months of metronidazole therapy. Patients at high risk of recurrence also received a thiopurine, or adalimumab if they were intolerant to thiopurines. Patients were randomly assigned to parallel groups: colonoscopy at 6 months (active care) or no colonoscopy (standard care). We used computer-generated block randomisation to allocate patients in each centre to active or standard care in a 2:1 ratio. For endoscopic recurrence (Rutgeerts score >12) at 6 months, patients stepped-up to thiopurine, fortnightly adalimumab with thiopurine, or weekly adalimumab. The primary endpoint was endoscopic recurrence at 18 months. Patients and treating physicians were aware of the patient's study group and treatment, but central reading of the endoscopic findings was undertaken blind to the study group and treatment. Analysis included all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT00989560.

**FINDINGS:** Between Oct 13, 2009, and Sept 28, 2011, 174 (83% high risk across both active and standard care groups) patients were enrolled and received at least one dose of study drug. Of 122 patients in the active care group, 47 (39%) stepped-up treatment. At 18 months, endoscopic recurrence occurred in 60 (49%) patients in the active care group and 35 (67%) patients in...
the standard care group (p=0.03). Complete mucosal normality was maintained in 27 (22%) of 122 patients in the active care group versus four (8%) in the standard care group (p=0.03). In the active care arm, of those with 6 months recurrence who stepped up treatment, 18 (38%) of 47 patients were in remission 12 months later; conversely, of those in remission at 6 months who did not change therapy recurrence occurred in 31 (41%) of 75 patients 12 months later. Smoking (odds ratio [OR] 2.4, 95% CI 1.2-4.8, p=0.02) and the presence of two or more clinical risk factors including smoking (OR 2.8, 95% CI 1.01-7.7, p=0.05) increased the risk of endoscopic recurrence. The incidence and type of adverse and severe adverse events did not differ significantly between patients in the active care and standard care groups (100 [82%] of 122 vs 45 [87%] of 52; p=0.51) and (33 [27%] of 122 vs 18 [35%] of 52; p=0.36), respectively.

INTERPRETATION: Treatment according to clinical risk of recurrence, with early colonoscopy and treatment step-up for recurrence, is better than conventional drug therapy alone for prevention of postoperative Crohn's disease recurrence. Selective immune suppression, adjusted for early recurrence, rather than routine use, leads to disease control in most patients. Clinical risk factors predict recurrence, but patients at low risk also need monitoring. Early remission does not preclude the need for ongoing monitoring.

FUNDING: AbbVie, Gutsy Group, Gandel Philanthropy, Angior Foundation, Crohn's Colitis Australia, and the National Health and Medical Research Council. Copyright © 2015 Elsevier Ltd. All rights reserved.

Publication Types: Randomized Controlled Trial
Research Support, Non-U.S. Gov't


**Fall rates in hospital rehabilitation units after individualised patient and staff education programmes: a pragmatic, stepped-wedge, cluster-randomised controlled trial.**

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**BACKGROUND:** Falls are the most frequent adverse events that are reported in hospitals. We examined the effectiveness of individualised falls-prevention education for patients, supported by training and feedback for staff, delivered as a ward-level programme.

**METHODS:** Eight rehabilitation units in general hospitals in Australia participated in this stepped-wedge, cluster-randomised study, undertaken during a 50 week period. Units were randomly assigned to intervention or control groups by use of computer-generated, random allocation sequences. We included patients admitted to the unit during the study with a Mini-Mental State Examination (MMSE) score of more than 23/30 to receive individualised education that was based on principles of changes in health behaviour from a trained health professional, in addition to usual care. We provided information about patients' goals, feedback about the ward environment, and perceived barriers to engagement in falls-prevention strategies to staff who were trained to support the uptake of strategies by patients. The coprimary outcome measures were patient rate of falls per 1000 patient-days and the proportion of patients who were fallers. All analyses were by intention to treat. This trial is registered with the Australian New Zealand Clinical Trials registry, number ACTRN12612000877886.

**FINDINGS:** Between Jan 13, and Dec 27, 2013, 3606 patients were admitted to the eight units (n=1983 control period; n=1623 intervention period). There were fewer falls (n=196, 780/1000 patient-days vs n=380, 1378/1000 patient-days, adjusted rate ratio 0.60 [robust 95% CI 0.42-0.94], p=0.003), injurious falls (n=66, 263/1000 patient-days vs 131, 475/1000 patient-days, 0.65 [robust 95% CI 0.42-0.88], p=0.006), and fallers (n=136 [838%] vs n=248 [1251%] adjusted odds ratio 0.55 [robust 95% CI 0.38 to 0.81], p=0.003) in the intervention compared with the control group. There was no significant difference in length of stay (intervention median 11 days [IQR 7-19], control 10 days [6-18]).

**INTERPRETATION:** Individualised patient education programmes combined with training and feedback to staff added to usual care reduces the rates of falls and injurious falls in older patients in rehabilitation hospital-units.

**FUNDING:** State Health Research Advisory Council, Department of Health, Government of Western Australia. Copyright © 2015 Elsevier Ltd. All rights reserved.

Publication Types: Research Support, Non-U.S. Gov't


**Type 2 diabetes and cognitive function: Many questions, few answers.**

Bruce DG.
Baseline concentrations of two neoepitopes were associated with increased mortality (C1M: HR 1.62 [95% CI 1.14-2.31], p=0.0069; C6M: 1.042 [1.007-1.078], p=0.017; and CRPM: 1.38 [1.16-1.63], p=0.0002) was strongly predictive of overall survival, and the increased risk was proportional to the magnitude of change in neoepitope concentrations. The strongest association with 3-month biomarker change was recorded for CRPM; greater than 0 ng/mL per month conferred a HR of 2.16 (95% CI 1.15-4.07), whereas a rate greater than 1 ng/mL per month resulted in an HR 4.08 (2.14-7.8), and a rate greater than 1.7 ng/mL per month was associated with an HR 6.61 (2.74-15.94). INTERPRETATION: Concentrations of protein fragments generated by MMP.
activity are increased in the serum of individuals with idiopathic pulmonary fibrosis compared with healthy controls. Increased neoepitope concentrations were associated with disease progression, and the rate of this increase predicted survival. Serial measurements of neoepitopes have potential to be used as theragnostic biomarkers in clinical trials and to guide management of idiopathic pulmonary fibrosis. FUNDING: GlaxoSmithKline R&D and the Medical Research Council.


**Tea consumption reduces the risk of de novo myelodysplastic syndromes.**


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Epidemiologic data suggest that green tea consumption may protect against certain cancers, but no previous study has examined myelodysplastic syndromes (MDS). A hospital-based case-control study was conducted in China in 2012-2013 to investigate the association between tea intake and the risk of de novo MDS in adults. The study included 208 cases aged 19-85 years with MDS and 208 controls individually matched to the cases by gender, 5-year age group and residential locality. Odds ratios (ORs) were estimated using conditional logistic regression. Compared with non-tea drinkers, the adjusted ORs (95% confidence intervals) for all MDS combined were 0.39 (0.20-0.74), 0.45 (0.25-0.79), and 0.40 (0.21-0.77) for those who consumed tea >20 years, >/=2 cups daily, and >750g per annum, respectively. Significant dose-response trends were observed across all the measures. The inverse association existed in both genders, in the refractory anemia with excessive blasts subtype, in cytogenetic 'good' and 'intermediated/poor' prognosis groups, and in the International Prognostic Scoring System lower and higher risk groups, but not in the refractory cytopenia with multilineage dysplasia subtype. The study suggests that regular tea consumption reduces the risk of de novo MDS in the Chinese population.


Leukemia. 2015; 29(2): 369-76.

**A certified plasmid reference material for the standardisation of BCR-ABL1 mRNA quantification by real-time quantitative PCR.**

White H, Deprez L, et al.


Leukemia. 2015; 29(2): 369-76.

**A certified plasmid reference material for the standardisation of BCR-ABL1 mRNA quantification by real-time quantitative PCR.**

White H, Deprez L, et al.

Leukemia and Lymphoma. 2015; 56(5): 1271-1277.

Phase II study of first-line <sup>131</sup>I-l-rituximab radioimmunotherapy in follicular non-Hodgkin lymphoma and prognostic <sup>18</sup>F-fluorodeoxyglucose positron emission tomography.

McQuillan AD, Macdonald WBG, et al. (McQuillan) Department of Hematology, Fremantle Hospital, University of Western Australia, Fremantle, Australia (Macdonald, Turner) Department of Nuclear Medicine, Fremantle Hospital, University of Western Australia, Fremantle, WA 6160, Australia J.H. Turner, Department of Nuclear Medicine, Fremantle Hospital, University of Western Australia, Fremantle, WA 6160, Australia First-line <sup>131</sup>I-I-anti-CD20 radioimmunotherapy of indolent non-Hodgkin lymphoma (NHL) achieves durable remission with low toxicity. The phase II INITIAL study comprised 68 patients with follicular NHL followed up to 7 years (median 4 years) after outpatient <sup>131</sup>I-l-rituximab radioimmunotherapy (RIT) in conjunction with rituximab, followed by maintenance therapy for 1 year. Baseline and 3-month <sup>18</sup>F-fluorodeoxyglucose positron emission tomography (<sup>18</sup>F-FDG PET) imaging, analyzed according to Deauville criteria, was used to evaluate response and predict prognosis. The overall response rate at 3 months was 99%, with 88% achieving Deauville category 1-3. These satisfactory responders did not reach median time-to-next-treatment, versus a median of 29 months for a category 4-5 response (p < 0.0001). Grade IV hematological toxicity (9%) was self-limited without clinical sequelae. <sup>131</sup>I-I-rituximab radioimmunotherapy in newly diagnosed, advanced stage, asymptomatic follicular NHL is an effective, practical and affordable alternative to existing conventional chemotherapies, with lower toxicity and durable remissions. Response assessment at 3 months by <sup>18</sup>F-FDG PET Deauville five-point scale permits prognostic stratification.


MDS patient characteristics associated with use of disease-modifying therapy: Results of a patient survey.

**Artemether-lumefantrine versus artemisinin-naphthoquine in Papua New Guinean children with uncomplicated malaria: A six months post-treatment follow-up study.**

Laman M, Benjamin JM, et al.

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Background: In a recent trial of artemisinin-naphthoquine (artemisinin-NQ) and artemether-lumefantrine (AM-LM) therapy in young children from Papua New Guinea (PNG), there were no treatment failures in artemisinin-NQ-treated children with *Plasmodium falciparum* or *Plasmodium vivax* compared with 2.2% and 30.0%, respectively, in AM-LM-treated children during 42 days of follow-up. To determine whether, consistent with the long elimination half-life of NQ, this difference in efficacy would be more durable, clinical episodes of malaria were assessed in a subset of trial patients followed for six months post-treatment. Methods: For children completing trial procedures and who were assessable at six months, all within-trial and subsequent clinical malaria episodes were ascertained, the latter by clinic attendances and/or review of hand-held health records. Presentations with non-malarial illness were also recorded. Differences between allocated treatments for pre-specified endpoints were determined using Kaplan-Meier survival analysis. Results: Of 247 children who were followed to Day 42, 176 (71.3%) were included in the present sub-study, 87 allocated to AM-LM and 89 to artemisinin-NQ. Twenty children in the AM-LM group (32.8%) had been diagnosed for <3 years; 72% were lower-risk (IPSS ‘low’/ ‘intermediate 1’); 28% were higher-risk (‘intermediate 2’/’high’); and 58% were on Medicare. Almost all (96%) reported having BMB performed at diagnosis; fewer (58%) since diagnosis. Mean FACT-G was 73.1 (scale: 0 - 108). Approximately half (53%) of respondents had ever received DMT (Table). Of those: the majority had received HMA(s); more received azaclotide than decitabine; few received clinical trial medication; a minority received >2 DMTs; and a majority were still receiving DMT. More lower- than higher-risk patients reported DMT use, although more higher-risk patients received HMA(s). DMT use was not significantly associated with QoL (p=0.67). Conclusions: Our findings indicate that many MDS patients still do not receive DMT and that DMT is not associated with disease risk or worsening QoL. Further, only a small minority of patients enrolls in clinical trials. More research is needed to determine the barriers to DMT use and trial participation, and to demonstrate the value of adding more options to the existing therapeutic paradigm. (Table Presented).

Publication Types: Conference Abstract


**Temporal changes in Plasmodium falciparum anti-malarial drug sensitivity in vitro and resistance-associated genetic mutations in isolates from Papua New Guinea.**

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METHODS: A validated fluorescence-based assay was used to assess growth inhibition of 52 P. falciparum isolates from children in a clinical trial in Madang Province. Responses to CQ, lumefantrine, piperinequine, naphthoquine, pyranartemine, dihydroartesinmin, artesunate were assessed. Molecular resistance markers were detected using a multiplex PCR ligase detection reaction fluorescent microsphere assay.

RESULTS: CQ resistance (in vitro concentration required for 50% parasite growth inhibition (IC50) >100 nM) was present in 19% of isolates. All piperinequine and naphthoquine IC50s were <100 nM and those for lumefantrine, pyranartemine, dihydroartesinmin, artesunate were in low nM ranges. Factor analysis of IC50s showed three groupings (lumefantrine; CQ, piperinequine, naphthoquine; pyranartemine, dihydroartesinmin, artesunate). Most IC50s (96%) were monophasic pfcr K767 (5VMNT) mutants and most (98%) contained pfmdr1 N86Y (YYSND). No wild-type pfmdr1 was found but most isolates contained wild-type (SAKAA) pfmdr1.

CONCLUSIONS: Reflecting less drug pressure, in vitro CQ sensitivity appears to be improving in Madang Province despite continued use of sulphadoxine-pyrimethamine and pyrimethamine in the study area including through paediatric intermittent preventive treatment. The susceptibility of local isolates to lumefantrine may be unrelated to those of other ACT partners.


Ultrasonographic assessment of splenic volume at presentation and after anti-malarial therapy in children with malarial anaemia.

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BACKGROUND: Splenic enlargement is a component of the host response to malaria and may also influence the genesis and progression of malarial anaemia. Few cross-sectional and no longitudinal studies have assessed the relationship between splenic volume measured ultrasonographically and haemoglobin concentrations in children with malaria.

METHODS: Fifteen Papua New Guinea children with severe malarial anaemia (SMA; haemoglobin<50 g/L) and ten with moderate...
malarial anaemia (MMA; 51-99 g/L) were recruited. The SMA patients were given intramuscular artemether followed by oral artesinin combination therapy (ACT), and were transfused one unit of packed cells 0.3-4.0 days post-admission. The MMA patients were treated with ACT. Splenic enlargement (Hackett's grade, subcostal distance and ultrasonographically determined volume) and haemoglobin concentrations were measured on days 0, 1, 2, 3, 7, 14, 28, and 42.

RESULTS: Associations between Hackett's grade, subcostal distance and splenic volume were modest (rs<0.62, P<0.001). Baseline splenic volume was not associated with age or haemoglobin (P>0.90). Mean splenic volume had fallen by approximately 50% at day 14 in children with MMA (P<0.011 vs days 0, 1 and 2), but there was no change in the SMA group (P>0.30). There was no change in haemoglobin in the MMA group during follow-up but a rise in the SMA group to day 7 (P<0.05 vs days 0, 1, 2, and 3) which paralleled the packed cell volume transfused.

CONCLUSIONS: Clinical assessment of splenomegaly is imprecise compared with ultrasonography. Serial splenic volumes and haemoglobin concentrations suggest that the spleen does not influence post-treatment haemoglobin, including after transfusion.

Publication Types: Research Support, Non-U.S. Gov't


Vitamin D concentration and its association with past, current and future depression in older men: The Health In Men Study.
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BACKGROUND: Vitamin D deficiency has been associated with depression in later life, but it remains unclear whether this association is truly causal.

METHODS: Observational study examining the retrospective, cross-sectional and prospective associations between vitamin D concentration and depressed mood in a community-derived sample of 3105 older men living in metropolitan Perth, Western Australia. We measured the plasma concentration of 25-hydroxyvitamin D using standard procedures. Past depression was ascertained by direct questioning and through the use of administrative health data linkage. A geriatric depression scale score equal or greater than 7/15 established the presence of current depression. Incident depression was established by a patient health questionnaire (PHQ-9) score >10 or by administrative health data linkage during the 6-year follow up (range 0.1-10.9 years).

RESULTS: Vitamin D concentration <50nmol/L was associated with greater odds of current (OR=1.65, 95% CI=1.13, 2.42) but not past depression (OR=1.15, 95% CI=0.83, 1.58). Of the 2740 men with no past or current history of depression, 81 developed clinically significant symptoms during follow up. The adjusted hazard ratio of incident depression for men with plasma vitamin D <50nmol/L was 1.03 (95% CI=0.59, 1.79; adjusted for age, living arrangements, season, and prevalent cardiovascular diseases).

CONCLUSIONS: Our results do not support a role for vitamin D in the causation of depression, although a small antidepressant effect of vitamin D cannot be entirely discarded. Large randomised placebo-controlled trials are required to dismiss or establish with certainty the causal link between vitamin D deficiency and depression.


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Thyroid hormone: Influences on mood and cognition in adults.
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The association of thyroid dysfunction with alterations in mood and cognition has been recognised since some of the earliest descriptions of thyroid disease. Over the years, researchers have aimed to further define these effects throughout the spectrum of thyroid disorders, to better understand the underlying condition and refine indications for treatment. More recently, attention has turned towards examining the impact of thyroid hormones within the normal reference range, particularly in older adults, providing new insights into the association of thyroid hormone with cognitive decline. This review summarises the evidence assessing the influence of thyroid hormone on mood and cognition in overt and subclinical hypothyroidism, within the reference range, and in subclinical and overt hyperthyroidism. Treatment of overt thyroid dysfunction largely resolves associated disturbances in mood and cognitive dysfunction, however in the setting of overt hyperthyroidism subtle detrimental effects on cognition may not be fully reversed. Subclinical hyperthyroidism and higher free thyroxine (FT4) within the normal range have been associated with poorer cognitive outcomes. Future research including randomised controlled trials are required to confirm causality and guide the assessment of benefits vs risks of intervention in the increasing population of older adults with subclinical thyroid disease.

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Hypovitaminosis D and frailty: Epiphenomenon or causal?
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Vitamin D is not only a key component in the maintenance of calcium homeostasis and bone health, but has also been implicated in a myriad of other non-skeletal biologic systems. The frailty syndrome, an emerging and increasingly important concept in the field of aging, with the "physical" clinical phenotype being initially presented as the operational definition. The relationship between vitamin D and frailty is postulated to be largely mediated via the development of sarcopenia, a condition characterised by a combination of the reduction of muscle mass, plus either muscle strength or performance. Several molecular pathways may account for the development of muscle wasting in sarcopenia, and there is mounting epidemiological and laboratory evidence that supports a role of vitamin D on muscle cell proliferation and function. Although observational studies on vitamin D and frailty have not definitively established an independent relationship, interventional studies of the effect of supplemental vitamin D have yielded a positive influence on the frailty status, mainly via improvements in the physical performance. Further studies that are adequately powered and well-designed are warranted in an attempt to establish a causal relationship between vitamin D and frailty. In the absence of a consensus on the definition of the frailty syndrome, an appropriate and well-validated measure instrument for this health outcome would be recommended in the realm of frailty research.


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Convergent adaptation in the dominant global hospital clone ST239 of methicillin-resistant Staphylococcus aureus.
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Infections caused by highly successful clones of hospital-associated methicillin-resistant Staphylococcus aureus (HAMRSA) are a major public health burden. The globally dominant sequence type 239 (ST239) HA-MRSA clone has persisted in the health care setting for decades, but the basis of its success has not been identified. Taking a collection of 123 ST239 isolates spanning 32 years, we have used population-based functional genomics to investigate the evolution of this highly persistent and successful clone. Phylogenetic reconstruction and population modeling uncovered a previously unrecognized distinct clade of ST239 that was introduced into Australia from Asia and has perpetuated the epidemic in this region. Functional analysis demonstrated attenuated virulence and enhanced resistance to last-line antimicrobials, the result of two different phenomena, adaptive evolution within the original Australian ST239 clade and the introduction of a new clade displaying shifts in both phenotypes. The genetic diversity between the clades allowed us to employ genome-wide association testing and identify mutations in other essential regulatory systems, including walKR, that significantly associate with and may explain these key phenotypes. The phenotypic convergence of two independently evolving ST239 clades highlights the very strong selective pressures acting on HA-MRSA, showing that hospital environments have favored the accumulation of mutations in essential MRSA genes that increase resistance to antimicrobials, attenuate virulence, and promote persistence in the health care environment. Combinations of comparative genomics and careful phenotypic measurements of longitudinal collections of clinical isolates are giving us the knowledge to intelligently address the impact of current and future antibiotic usage policies and practices on hospital pathogens globally.

IMPORTANCE Methicillin-resistant Staphylococcus aureus (MRSA) is responsible for innumerable drug-resistant healthcare-associated infections globally. This study, the first to investigate the evolutionary response of hospital-associated MRSA (HAMRSA) over many decades, demonstrates how MRSA can persist in a region through the reintroduction of a previously unrecognized distinct clade. This study also demonstrates the crucial adaptive responses of HA-MRSA to the highly selective environment of the health care system, the evolution of MRSA isolates to even higher levels of antibiotic resistance at the cost of attenuated virulence. However, in vivo persistence is maintained, resulting in a clone of HA-MRSA able to resist almost all antimicrobial agents and still cause invasive disease in the heavily compromised hosts found in modern health care settings.


**Success in Closing the Gap: favourable neonatal outcomes in a metropolitan Aboriginal Maternity Group Practice Program.**

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**OBJECTIVES:** To report differences in neonatal health outcomes for a community-based antenatal program, the Aboriginal Maternity Group Practice Program (AMGPP; the intervention group), compared with two matched control groups eligible for standard antenatal care. **DESIGN:** Non-randomised intervention study using data from the Western Australian Midwives Notification System. Regression models were used to report adjusted odds ratios (aORs) for defined neonatal health outcomes. **SETTING:** The AMGPP employed Aboriginal grandmothers, Aboriginal Health Officers, and midwives working in partnership with existing antenatal services to provide care for pregnant Aboriginal women residing in south metropolitan Perth. **PARTICIPANTS:** 343 women (with 350 pregnancies) who participated in the AMGPP and gave birth between 1 July 2011 and 31 December 2012; historical and contemporary control groups of pregnant Aboriginal women (each including 350 pregnancies), frequency matched for maternal age and gravidity. **MAIN OUTCOME MEASURES:** Preterm births, birthweight, neonatal resuscitation, neonatal hospital length of stay longer than 5 days. **RESULTS:** Babies born to AMGPP participants were significantly less likely to be born preterm (AMGPP, 9.1% v historical controls, 15.9% [aOR, 0.56; 95% CI, 0.35-0.92]; v contemporary controls, 15.3% [aOR, 0.71; 95% CI, 0.58-0.95]); to require resuscitation at birth (AMGPP, 17.8% v historical controls, 24.4% [aOR, 0.68; 95% CI, 0.47-0.98]; v contemporary controls, 31.2% [aOR, 0.71; 95% CI, 0.60-0.85]), or to have a hospital length of stay of more than 5 days (AMGPP, 4.0% v historical controls, 11.3% [aOR, 0.34; 95% CI, 0.18-0.64]; v contemporary controls, 11.6% [aOR, 0.56; 95% CI, 0.41-0.77]). **CONCLUSION:** Participation in the AMGPP in south metropolitan Perth was associated with significantly improved neonatal health outcomes.


**Anticholinergic burden in older women: Not seeing the wood for the trees?**

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**Objectives:** To identify medicines contributing to and describe predictors of anticholinergic burden among community-dwelling older Australian women. Design, setting and participants: Retrospective longitudinal analysis of data from the Australian Longitudinal Study on Women's Health linked to Pharmaceutical Benefits Scheme medicines data from 1 January 2008 to 30 December 2010; for 3694 women born in 1921-1926. Main outcome measures: Anticholinergic burden calculated from Anticholinergic Drug Scale (ADS) scores derived from ADS levels (0 to 3) for all medicines used by each woman, summed over each 6-month period (semester), medicines commonly used by women with high semester ADS scores (defined as 75th percentile of scores). Results: 1126 women (59.9%) used at least one medicine with anticholinergic properties. The median ADS score was 4 or 5 across all semesters. Most anticholinergic medicines used by women who had a high anticholinergic burden (ADS score, >9) had a low anticholinergic potency (ADS level 1). Increasing age, cardiovascular disease, and number of other medicines used were predictive of a higher anticholinergic burden. Conclusions: A high anticholinergic medicines burden in this group was driven by the use of multiple medicines with lower anticholinergic potency rather than the use of medicines with higher potency. This is a novel and important finding for clinical practice as doctors would readily identify the risk of a high anticholinergic burden for patients using high potency medicines, but may be less likely to identify this risk for users of multiple medicines with low anticholinergic potency.


**Controversies and consensus regarding vitamin D deficiency in 2015: whom to test and whom to treat?**

Glendenning P, Chew GT.


**Heatwave and risk of heat-related burn injury in children in Western Australia.**

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Successful treatment of ACE inhibitor-induced angioedema with icatibant, a bradykinin B2 receptor antagonist.
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A 65-year-old woman of European ancestry presented to the emergency department (ED) of our tertiary hospital at 09:30 with isolated tongue swelling without rash, gastrointestinal symptoms or wheeze, which had progressed over the previous 4 hours and was non-responsive to adrenaline administered by her general practitioner at 08:15. She recalled a single episode of mild self-limiting tongue swelling several months earlier and had no family history of angioedema. The patient had well controlled hypertension managed with perindopril (5 mg daily) for the past 10 years. Other comorbidities included gastroesophageal reflux disease, hypercholesterolaemia and osteopaenia. She was an active smoker. Other medications included atorvastatin, calcium carbonate, dothiepin, esomeprazole and oestradiol valerate, and she denied over-the-counter medication use. Despite treatment with intravenous dexamethasone (6 mg), intravenous glycopyrrolate (0.2 mg) and intramuscular promethazine (25 mg), the patient's condition continued to deteriorate. Fibreoptic nasoendoscopy (FNE) revealed epiglottic and left arytenoid oedema. Her treating team planned awake fibreoptic intubation as a priority one case, with a surgical team on standby for emergency tracheostomy. Icatibant, a competitive bradykinin B2 receptor (B2R) antagonist, was administered subcutaneously at a dose of 30 mg at 10:30, without development of a local injection site reaction. On repeat FNE 10 minutes later, there was a significant improvement in her condition. Intubation was ultimately avoided and she was observed in the intensive care unit (ICU) for 2 hours before being transferred to a highdependency ward area overnight. Complete resolution of symptoms was seen within 5 hours, and she was discharged the next morning after a normal FNE. Perindopril was implicated in the patient's angioedema. It was discontinued and replaced with amiodipine (5 mg daily) and hydrochlorothiazide (12.5 mg daily). At follow-up 9 months later, she reported no further episodes of angioedema. Despite thorough investigation, no other cause aside from angiotensin-converting enzyme (ACE) inhibitor-induced angioedema was identified. An infective focus was excluded, with urinalysis, chest x-ray and white cell count yielding normal results. Hereditary angioedema and acquired C1 esterase inhibitor deficiency were excluded by a normal C4 concentration of 0.4 g/L (reference interval, 0.16-0.52 g/L) at presentation. Quantitative and functional C1 inhibitor studies at a subsequent follow-up visit did not find reduced values.

Consensus guidelines for the investigation and management of encephalitis.
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A bolt out of the blue: The night of the blue pills.
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Snapshot eagle syndrome as a potential cause of tapia syndrome.
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Malondialdehyde-Modified LDL IgG Antibody Levels and Indices of Cardiac Function in Valvular Heart and Coronary Artery Disease Patients.

Rahsepar AA, Mirzaee A, et al.

Objective: To compare the changes in anti-malondialdehyde-modified low-density lipoprotein (MDA-LDL) IgG levels among patients undergoing off-pump and on-pump coronary artery bypass grafting (CABG) or valvuloplasty. Subjects and Methods: A total of 38, 39 and 34 patients who underwent off-pump CABG, on-pump CABG and valvuloplasty, respectively, were enrolled in this study. Serum anti-MDA-LDL IgG values were measured 24 h before and after the operative procedures and at discharge. Echocardiography was also done before surgery and before discharge. The results were compared with values from 50 healthy controls. Results: In all patients, a reduction in antibody titers was observed post-operatively. However, the decrease was significant only in the off-pump CABG - before surgery: 42.33 (25.83-58.51), after surgery: 30.86 (16.36-51.33) and at discharge: 10.96 (6.82-23.57; p = 0.027). There was a significant positive association between anti-MDA-LDL IgG levels and ejection fraction (r = 0.248, p = 0.036) and the SOL and medial gastrocnemius physiological cross-sectional area were statistically different between groups after normalizing to lean body mass and body surface area, respectively. Total lower limb lean mass did not differ between CHF and controls. Results: In all patients, a reduction in antibody titers was observed post-operatively. However, the decrease was significant only in the off-pump CABG - before surgery: 42.33 (25.83-58.51), after surgery: 30.86 (16.36-51.33) and at discharge: 10.96 (6.82-23.57; p = 0.027). There was a significant positive association between anti-MDA-LDL IgG levels and ejection fraction (r = 0.248, p = 0.036) and the SOL and medial gastrocnemius physiological cross-sectional area were statistically different between groups after normalizing to lean body mass and body surface area, respectively. Total lower limb lean mass did not differ between CHF and controls.

Methods: Eleven patients with CHF and 15 age-matched controls were recruited. Lower limb lean mass was assessed by dual energy x-ray absorptiometry and the architecture of skeletal muscle and tendon properties by ultrasound. Plantarflexor strength was assessed by dynamometry.

Results: Patients with CHF exhibited approximately 25% lower combined triceps surae volume and physiological cross-sectional area (PCSA) compared with those of control subjects (P < 0.05), driven in large part by reductions in the SOL. The SOL volume and the SOL and medial gastrocnemius physiological cross-sectional area were statistically different between groups after normalizing to lean body mass and body surface area, respectively. Total lower limb lean mass did not differ between CHF and control subjects, further highlighting the SOL specificity of muscle wasting in CHF. Moreover, the volume of the SOL and plantarflexor strength correlated strongly with peak oxygen uptake (VO2peak) in patients with CHF.

Conclusions: These findings suggest that the SOL may be a sentinel skeletal muscle in CHF and provide a rationale for including plantarflexor muscle training in CHF care.

Publication Types: Research Support, Non-U.S. Gov't


Familial hypercholesterolaemia: Challenges in primary care.

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defect. Using the MARF technique, the maxillectomy defect was obliterated with vascularized adipose tissue overlying the rectus muscle and was trimmed to fit the maxillectomy defect. The adipose tissue was allowed to granulate and mucosalize. RESULTS: The length of stay at the hospital ranges from 9 to 22 days. On follow-up ranging 7.5-32.8 months, two patients died from their malignancies. The other three patients were able to tolerate oral soft diet. CONCLUSION: The MARF may be considered as an alternative to myocutaneous rectus free flap particularly for the reconstruction of maxillary defects in patients with central obesity. (c) 2015 Wiley Periodicals, Inc. Microsurgery, University of Western Australia, Perth, Australia


Metabolism: Clinical & Experimental. 2015; 64(11): 1466-76

**Does statin therapy reduce plasma VEGF levels in humans? A systematic review and meta-analysis of randomized controlled trials.**


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**BACKGROUND:** The effect of statins on plasma concentrations of vascular endothelial growth factor (VEGF), the main angiogenic growth factor with pro-inflammatory and atherogenic properties, is controversial. A systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted to obtain a conclusive result in humans.

**METHODS:** PubMed-Medline, SCOPUS, Web of Science and Google Scholar databases were searched to identify RCTs investigating the impact of statins on plasma VEGF concentrations. A random-effects model and the generic inverse variance method were used for quantitative data synthesis. Meta-regression, sensitivity analysis and publication bias assessments were performed using standard methods.

**RESULTS:** Eight RCTs examining the effects of statins on plasma VEGF concentrations were included. Meta-analysis suggested a significant reduction of plasma VEGF levels following statin therapy (weighted mean difference: -19.88 pg/mL, 95% CI: -35.87, -3.89, p=0.015). VEGF reductions were observed in the subsets of trials with treatment durations >4 weeks (-19.54, -37.78, -1.30, p=0.036), LDL-C reductions >50mg/dL (-28.59, -43.68, -13.50, p<0.001), lipophilic statins (-22.31, -40.65, -3.98, p=0.017), and diseased populations (-21.08, -39.97, -2.18, p=0.029), but not in the opposite subsets. Meta-regression also suggested a significant association between changes in plasma VEGF levels and LDL-C changes, treatment duration, but not molar dose of statins.

**CONCLUSIONS:** These results suggest a significant reduction in plasma VEGF concentrations following statin therapy. This effect depends on duration of treatment, LDL-lowering activity, lipophilicity of statins, and health status of studied individuals. Further RCTs are needed to explore if the VEGF reduction is implicated in the statin benefits on cardiovascular outcomes. Copyright © 2015 Elsevier Inc. All rights reserved.


**Reconstruction of maxillary defect with musculo-adipose rectus free flap.**

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**BACKGROUND:** The rectus myocutaneous free flap (RMFF) is used for medium to large maxillectomy defects. However, in patients with central obesity the inset could be difficult due to the bulk from excessive layer of adipose tissue. We describe a modification of the RMFF for patients with excessive central obesity with a flap consisting of adipose tissue with minimal rectus muscle; the musculo-adipose rectus free flap (MARF). **METHODS:** Five cases of MARF reconstruction were performed between 2003 and 2013, with patients' body mass indexes ranging from 29.0 to 41.2 kg/m². All patients had sinonasal tumor, of which three were adenoid cystic carcinoma, one squamous cell carcinoma, and one melanoma. Four patients had Codeir I/Ib defects and one had Codeir II defect. Using the MARF technique, the maxillectomy defect was obliterated with vascularized adipose tissue overlying the rectus muscle and was trimmed to fit the maxillectomy defect. The adipose tissue was allowed to granulate and mucosalize. **RESULTS:** The volume of adipose tissue harvested was between 120 and 160 mL. All flaps survived with no requirement for re-exploration. Complete oro-nasal separation was achieved in all patients. The time to commencement of oral intake ranges from 5 to 15 days. One patient developed seroma and one developed wound breakdown on the donor site. The length of stay at the hospital ranges from 9 to 22 days. On follow-up ranging 7.5-32.8 months, two patients died from their malignancies. The other three patients were able to tolerate oral soft diet. **CONCLUSION:** The MARF may be considered as an alternative to myocutaneous rectus free flap particularly for the reconstruction of maxillary defects in patients with central obesity. (c) 2015 Wiley Periodicals, Inc. Microsurgery, 2015.

Molecular Imaging and Biology. 2015; 1).

**Gallium 68 octreotate PET in head and neck squamous cell carcinoma.**

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Squamous cell carcinoma (SCC) is a common malignancy of the head and neck (H&N). Fluorine-18 FDG (18F-FDG) PET/CT is a standard modality in the initial staging and re-staging of this common malignancy, however, it has limitations in the head and neck region due to physiological oropharyngeal activity and uptake in non malignant inflammatory conditions. Somatostatin receptors are known to be expressed and upregulated in SCC and radiotracers such as gallium-68 octreotate (68Ga-OCT) may be contemplated as a complimentary imaging modality for H&N SCC. In this study we have imaged patients with both 18F-FDG and 68Ga-OCT PET/CT to localise and stage H&N SCC and also evaluate the potential for neoadjuvant or salvage radioligand therapy. Methods and Results: Nineteen patients with histologically confirmed SCC of H&N underwent semi quantitative whole body PET/CT imaging with both 18F-FDG and 68Ga-OCT within 2 weeks on a General Electric 710 PET-CT scanner. All 19 patients showed 18F-FDG positivity, 18 of whom were also positive on 68Ga-OCT. The singular exception being in a patient with verrucous variant SCC. The SUV values were consistently higher in 18F-FDG studies, both in primary and metastatic tumours, however, the 68Ga-OCT scans showed no significant inflammatory or physiological activity in the oropharynx. One patient with extensive FDG and 68Ga-OCT positive SCC was treated with adjuvant Lutetium-177 octreotate (177Lu-OCT) radioligand therapy. Interpretation: Both primary and metastatic H&N SCC may be imaged with 68Ga-OCT PET/CT targeting tumour somatostatin receptors. Although tumour activity is less prominent than that of 18F-FDG there is no confounding uptake in normal oropharynx or inflamed tissues. Complementary imaging with 68Ga-OCT may thus offer an advantage in assessment of SCC of unknown primary location in H&N and in post-operative evaluation. Proof of concept of the use of 177Lu-OCT for adjuvant targeted radioligand therapy of H&N SCC has been shown.

Publication Types: Conference Abstract


**Is the Parkinson anxiety scale comparable across raters?**

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The Parkinson Anxiety Scale is a new scale developed to measure anxiety severity in Parkinson's disease specifically. It consists of three dimensions: persistent anxiety, episodic anxiety, and avoidance behavior. This study aimed to assess the measurement properties of the scale while controlling for the rater (self- vs. clinician-rated) effect. The Parkinson Anxiety Scale was administered to a cross-sectional multicenter international sample of 362 Parkinson’s disease patients. Both patients and clinicians rated the patient's anxiety independently. A many-facet Rasch model design was applied to estimate and remove the rater effect. The following measurement properties were assessed: fit to the Rasch model, unidimensionality, reliability, differential item functioning, item local independency, interrater reliability (self or clinician), and scale targeting. In addition, test-retest stability, construct validity, precision, and diagnostic properties of the Parkinson Anxiety Scale were also analyzed. A good fit to the Rasch model was obtained for Parkinson Anxiety Scale dimensions A and B, after the removal of one item and rescaling of the response scale for certain items, whereas dimension C showed marginal fit. Self versus clinician rating differences were of small magnitude, with patients reporting higher anxiety levels than clinicians. The linear measure for Parkinson Anxiety Scale dimensions A and B showed good convergent construct with other anxiety measures and good diagnostic properties. Parkinson Anxiety Scale modified dimensions A and B provide valid and reliable measures of anxiety in Parkinson's disease that are comparable across raters. Further studies are needed with dimension C.


Muscle Nerve. 2015.

**Muscle Histopathology in Children with Spastic Cerebral Palsy Receiving Botulinum toxin Type A.**

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INTRODUCTION: Botulinum toxin A (BoNTA) is routine treatment for hypertonicity in children with cerebral palsy (CP). METHOD: Single blind prospective cross sectional study of 10 participants (mean age 11 years, 7 months) was done to determine the relationship between muscle histopathology and BoNTA in treated medial gastrocnemius muscle of children with CP. Open muscle
biopsies were taken from medial gastrocnemius muscle and vastus lateralis (control) during orthopedic surgery. RESULTS: Neurogenic atrophy in the medial gastrocnemius was seen in 6 participants between 4 months to 3 years post BoNTA. Type 1 fiber loss with type 2 fiber predominance was significantly related to the number of BoNTA injections (r = 0.89, P < 0.001).

DISCUSSION: The impact of these changes in muscle morphology on muscle function in CP is not clear. It is important to consider rotating muscle selection or injection sites within the muscle or allowing longer time between injections. This article is protected by copyright. All rights reserved.


Genomic signatures of human and animal disease in the zoonotic pathogen Streptococcus suis.

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Streptococcus suis causes disease in pigs worldwide and is increasingly implicated in zoonotic disease in East and South-East Asia. To understand the genetic basis of disease in S. suis, we study the genomes of 375 isolates with detailed clinical phenotypes from pigs and humans from the United Kingdom and Vietnam. Here, we show that isolates associated with disease contain substantially fewer genes than non-clinical isolates, but are more likely to encode virulence factors. Human disease isolates are limited to a single-virulent population, originating in the 1920s when pig production was intensified, but no consistent genomic differences between pig and human isolates are observed. There is little geographical clustering of different S. suis subpopulations, and the bacterium undergoes high rates of recombination, implying that an increase in virulence anywhere in the world could have a global impact over a short timescale.


Whole-genome sequencing provides new insights into the clonal architecture of Barrett’s esophagus and esophageal adenocarcinoma.

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The molecular genetic relationship between esophageal adenocarcinoma (EAC) and its precursor lesion, Barrett's esophagus, is poorly understood. Using whole-genome sequencing on 23 paired Barrett's esophagus and EAC samples, together with one in-depth Barrett's esophagus case study sampled over time and space, we have provided the following new insights: (i) Barrett's esophagus is polyclonal and highly mutated even in the absence of dysplasia; (ii) when cancer develops, copy number increases and heterogeneity persists such that the spectrum of mutations often shows surprisingly little overlap between EAC and adjacent Barrett's esophagus; and (iii) despite differences in specific coding mutations, the mutational context suggests a common causative insult underlying these two conditions. From a clinical perspective, the histopathological assessment of dysplasia appears to be a poor reflection of the molecular disarray within the Barrett's epithelium, and a molecular Cytosponge technique overcomes sampling bias and has the capacity to reflect the entire clonal architecture.


Factors influencing success of clinical genome sequencing across a broad spectrum of disorders.

Taylor JC, Martin HC, et al.
To assess factors influencing the success of whole-genome sequencing for mainstream clinical diagnosis, we sequenced 217 individuals from 156 independent cases or families across a broad spectrum of disorders in whom previous screening had identified no pathogenic variants. We quantified the number of candidate variants identified using different strategies for variant calling, filtering, annotation and prioritization. We found that jointly calling variants across samples, filtering against both local and external databases, deploying multiple annotation tools and using familial transmission above biological plausibility contributed to accuracy. Overall, we identified disease-causing variants in 21% of cases, with the proportion increasing to 34% (23/68) for mendelian disorders and 57% (8/14) in family trios. We also discovered 32 potentially clinically actionable variants in 18 genes unrelated to the referral disorder, although only 4 were ultimately considered reportable. Our results demonstrate the value of genome sequencing for routine clinical diagnosis but also highlight many outstanding challenges.

Whole genomes redefine the mutational landscape of pancreatic cancer.

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Dual effect of curcumin in preventing atherosclerosis: The potential role of pro-oxidant-antioxidant mechanisms.

A. Sahebkar


Whole genomes redefine the mutational landscape of pancreatic cancer.

Sahebkar A.

Dual effect of curcumin in preventing atherosclerosis: The potential role of pro-oxidant-antioxidant mechanisms.

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Whole genomes redefine the mutational landscape of pancreatic cancer.

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Dual effect of curcumin in preventing atherosclerosis: The potential role of pro-oxidant-antioxidant mechanisms.

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Whole genomes redefine the mutational landscape of pancreatic cancer.

Sahebkar A.
Whole genomes redefine the mutational landscape of pancreatic cancer.


Whole genomes redefine the mutational landscape of pancreatic cancer.

Pancreatic cancer remains one of the most lethal of malignancies and a major health burden. We performed whole-genome sequencing and copy number variation (CNV) analysis of 100 pancreatic ductal adenocarcinomas (PDACs). Chromosomal rearrangements leading to gene disruption were prevalent, affecting genes known to be important in pancreatic cancer (TP53, SMAD4, CDKN2A, ARID1A and ROBO2) and new candidate drivers of pancreatic carcinogenesis (KDM6A and PREX2). Patterns of rearrangements leading to gene disruption were prevalent, affecting genes known to be important in pancreatic cancer (TP53, SMAD4, CDKN2A, ARID1A and ROBO2) and new candidate drivers of pancreatic carcinogenesis (KDM6A and PREX2). Patterns of structural variation (variation in chromosomal structure) classified PDACs into 4 subtypes with potential clinical utility: the subtypes were termed stable, locally rearranged, scattered and unstable. A significant proportion harboured focal amplifications, many of which contained druggable oncogenes (ERBB2, MET, FGFR1, CDK6, PIK3R3 and PIK3CA), but at low individual patient prevalence. Strikingly, structural variation also led to the inactivation of DNA maintenance genes (BRCA1, BRCA2 or PALB2) and a mutational signature of DNA damage repair deficiency. Of 8 patients who received platinum therapy, 4 of 5 individuals with these measures of response to platinum were found to have a structural DNA variant.
those with rs12979860CC also have greater stage-constant and stage-specific fibrosis progression rates (P<0.0001 for all). The impact of rs12979860 genotypes on fibrosis is maximal in young females, especially those with HCV genotype 3. These findings establish rs12979860 genotype as a strong aetiology-independent predictor of tissue inflammation and fibrosis.


High-density mapping of the MHC identifies a shared role for HLA-DRB1*01:03 in inflammatory bowel diseases and heterozygous advantage in ulcerative colitis.


HLA variants and heterozygous advantage observed in ulcerative colitis, suggesting an important role of the adaptive immune power to define the architecture of association and causal alleles. To address this, we performed high-density SNP typing of the MHC in >32,000 individuals with IBD, implicating multiple HLA alleles, with a primary role for HLA-DRB1*01:03 in both Crohn's disease and ulcerative colitis. Noteworthy differences were observed between these diseases, including a predominant role for class II HLA variants and heterozygous advantage observed in ulcerative colitis, suggesting an important role of the adaptive immune response in the colonic environment in the pathogenesis of IBD.


Nephrol Dial Transplant. 2015. Insulin resistance and vascular dysfunction in chronic kidney disease: mechanisms and therapeutic interventions. Chan DT, Watts GF, et al. Department of Renal Medicine, Sir Charles Gairdner Hospital, Nedlands, WA, Australia. Lipid Disorders Clinic, Cardiovascular Medicine, Royal Perth Hospital, Perth, WA, Australia School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia. Department of Nephrology, Fiona Stanley Hospital, Murdoch, WA, Australia.

Insulin resistance (IR) is a novel cardiovascular risk factor that has been implicated in the pathogenesis of cardiovascular disease (CVD) in patients with chronic kidney disease (CKD). Beyond its metabolic effects, insulin can potentially mediate the increased risk for CVD through its vasoactive properties. This review examines key clinical data and potential mechanisms linking IR and vascular risk in CKD. While lifestyle interventions and pharmacotherapies with known insulin-sensitizing properties are promising therapeutic efforts to reduce the CVD burden in this population, clinical trial data on the effect of insulin sensitization on vascular function in CKD are either lacking or conflicting and are limited by small sample size and short duration of intervention. Affirming the role of IR in lowering CVD risk in CKD will require prospective randomized controlled studies with sufficient sample size and hard clinical outcomes. Future research efforts should be directed at assessing the efficacy, safety and mechanisms by which novel insulin sensitizers such as bile acid sequestrant, selective and dual peroxisome proliferator-activated receptor modulators and modulators of gut microbiota and uraemic toxins alter vascular function in patients with CKD.


Nephrology. 2015; 20(8): 583-4. Hypocalcaemic tetany occurring post a single denosumab dose in a patient with stage 4 chronic kidney disease, followed by calcium- and calcitriol-induced hypercalcaemia. Lambe G, Malvathu R, et al. Lambe, Gerard. General Medicine Department, Rockingham General Hospital, Rockingham, Western Australia, Australia. Malvathu, Rajasekar. General Medicine Department, Rockingham General Hospital, Rockingham, Western Australia, Australia. Thomas, Helen M. General Medicine Department, Rockingham General Hospital, Rockingham, Western Australia, Australia. Graves, Angela. General Medicine Department, Rockingham General Hospital, Rockingham, Western Australia, Australia. Publication Types: Letter


Nephrology. 2015; 20: 83-84. An observational, non-interventional, multicentre, multinational registry of patients with atypical haemolytic uraemic syndrome (AHUS): Initial characteristics of the australian cohort. Isbel N, Hughes P, et al. (Isbel) Department of Nephrology, Princess Alexandra Hospital, Brisbane, QLD, Australia (Isbel) University of Queensland, Melbourne, VIC, Australia (Hughes) Department of Nephrology, Royal Melbourne Hospital, Melbourne, VIC, Australia (Ferrari) Department of Nephrology, Fremantle Hospital, Fremantle, WA, Australia (Kausman) Department of Nephrology, Royal Childrens Hospital, Melbourne, VIC, Australia (Lim) Department of Nephrology, Sir Charles Gairdner Hospital, Perth, WA, Australia (Chadban) Renal Transplant Unit, Westmead Hospital, Sydney, NSW, Australia (Chadban) Department of Renal Medicine, Royal Prince Alfred Hospital, Sydney, NSW, Australia (Mantha) Renal Services, Cairns Base Hospital, Cairns, QLD, Australia (Brown) Department of Nephrology, Monash Medical Centre, Melbourne, VIC, Australia (Hsu) Haematology Department, Liverpool Hospital, Sydney, NSW, Australia (Licht) Hospital for Sick Children, Toronto, ON, Canada (Fremeaux-Bacchi) Assistance Publique-Hopitaux de Paris, Paris,
Aim: To report baseline demographics of the Australian Cohort of patients with aHUS enrolled into the global aHUS Registry. Background: aHUS is an ultra-rare, genetic, life-threatening disease of chronic complement activation leading to systemic thrombotic microangiopathy, with renal and other end-organ damage. There is a paucity of information on incidence, diagnosis, treatment and patient outcomes. The global aHUS Registry is a multi-centre, multi-national non-interventional registry, initiated in April 2012, that prospectively collects information on patients with aHUS. Methods: Patients with aHUS are enrolled by the treating physician and demographic, disease history, laboratory data, treatments, efficacy and safety outcome data are collected at baseline and every 6 months thereafter. Results: By March 30, 2015, 39 Australian pts from 11 centres were enrolled in the aHUS registry. 36 (92%) patients were >18 years and 29 (74.4%) patients were female. 7 pts (17.9%) had a family member diagnosed with aHUS. 35.3% of these patients had received a kidney transplant, 76.5% received dialysis and 85.3% had received plasma exchange or infusion. 15 (41.7%) were treated with eculizumab [ECU] therapy with a median duration of treatment of 2 years (0.0-4.8 years). Mean age at ECU treatment initiation was 28.76 years (1.7-43.2 years). Conclusions: Analyses of data obtained through the aHUS Registry will increase our understanding of the history and disease progression in patients with aHUS, and may help optimize management of patients with this rare and lifethreatening disease. New clinical sites are encouraged to participate.

Publication Types: Conference Abstract

Fabry's disease-a multi-disciplinary approach.
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Aim: To evaluate patient satisfaction with a multi-disciplinary Fabry's Disease clinic. Background: Multi-system Fabry's Disease requires many different specialities, usually with separate clinic appointments. To reduce patient appointment burden, we established a multi-disciplinary public outpatient clinic, with staff specialists and advanced trainees from nephrology, cardiology, neurology, pain management, psychiatry and genetic counselling, plus senior nurse coordinator. Methods: The clinic commenced in December 2012, increasing from 6th to 3rd monthly to meet demand. At each visit, patients nominate a prime problem area, directed to the relevant clinician, with supplementary briefier reviews as required. All prior letters, pathology and imaging results are available via a shared electronic database. Patient reports from each clinician are unifed into a single letter (including trendslines), and copied to each patient. Pharmaceutical company preceptorships (after formal confidentiality/consent) have provided useful advice for clinic patient flow, patient home support programs, and clinician education. Patient satisfaction is surveyed at each clinic, inviting improvement suggestions. Results: The clinic currently cares for 26 patients with Fabry's Disease in Western Australia, 10 on enzyme replacement or chaperone therapy. Patient satisfaction surveys favour multi-disciplinary clinic over previous single specialty clinic (43% vs 18%, neutral 39%). 86% were "happy" or "very happy" with their clinic times. Overall satisfaction scores were "good" 19%, "very good" 19% or "excellent" 62%. Conclusions: A multi-disciplinary approach in assessing and managing patients with Fabry's Disease is favoured over a single specialty set up, and is facilitated by public outpatient collaborative approach.

Publication Types: Conference Abstract

I neffectiveness of abatacept in steroid and rituximab resistant FSGS.
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Background: Treatment options in steroid-resistant focal segmental glomerulosclerosis (FSGS) have limited efficacy and considerable cumulative toxicity. Novel therapies are emerging with some (eg. Rituximab, abatacept, adalimumab and stem cells) showing optimistic outcomes in steroid resistant FSGS. We report a case of steroid-resistant FSGS who failed on novel T-cell co-stimulatory inhibitor Abatacept. Case report: A 62-year-old Caucasian male presented with overt nephrotic syndrome. Secondary causes were excluded and a renal biopsy confirmed diagnosis of primary FSGS. He achieved remission with 3 month tapering course of oral prednisolone. He re-presented 2 years later with worsening proteinuria and received a second course of prednisolone therapy. As a result of minimal response to this therapy he was changed to a calcineurin inhibitor (CNI) (Cyclosporin). However due to intolerance and raising creatinine CNI therapy was ceased. A renal biopsy at this stage revealed CNI toxicity changes. He was switched to a six month regimen of high dose alternate day prednisolone and cyclophosphamide therapy. Five months post therapy, his proteinuria continued to worsen resulting in change of therapy to a B lymphocyte depleting agent (Rituximab). Due to poor response to Rituximab, an informed decision was made to trial patient on abatacept. He received 4 doses of abatacept (750 mg IV) over a 4 month period. Although he tolerated this regimen, he did not have noticeable improvement in either proteinuria or creatinine. Conclusion: Abatacept may not be the answer for every patient with glucocorticoid and/or rituximab resistant FSGS, nevertheless subset of these patients may respond as shown in the recently published case series. Reporting bias tends to favour case reports with positive outcomes. Controlled trials are necessary to find the cohort of patients who may respond to Abatacept therapy.

Publication Types: Conference Abstract
Cholecalciferol (VIT D) therapy for low serum VIT D levels (LSVDL) in haemodialysis (HD) over 52 months—a prospective observational study.
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Aim: To study the effect of long term oral Vit D therapy in HD population with LSVDL on the haematological and biochemical parameters of bone chemistry. Background: Effects of long term Vit D therapy in HD patients with LSVDL are unknown. Short term trials have shown limited benefits with Vit D treatment. Methods: A prospective observational study at outer metropolitan HD unit from August 2009-January 2014 in 72 (M = 49, F = 23) eligible adult patients (≥3 month follow-up; PTH ≥ 10 pmol/L, and Vit D < 75 nmol/L) was analysed. Vit D is nurse administered at 6000 Units/week (Serum Vit D 50-75 nmol/L) or 18000 Units/week (<50 nmol/L) with 3 monthly monitoring of parathyroid hormone (PTH), Serum Vit D levels. Effect of treatment on PTH, haemoglobin, Erythropoietin (ESA) use, calcimimetic use, and parathyroidectomy is studied. Study was terminated in January 2014 due to PTH assay change. Comparison was made with other satellite unit without use of Vit D therapy. Results: Median (IQR) age (years), dialysis duration (years), follow-up period (weeks) was 61.3 (51.8-71.6); 0.93 (0.25-2.65) and 21 (12-156) respectively. 25 patients died, 5 received renal transplant and 9 transferred to other units. Although mean Vit D levels were normalised, PTH reduction was not significant beyond first 6 months. At baseline (n = 72), 72 (n 51), 24 (n 28), 36 (n 19) and 48 (n 11) months, mean (SD) for PTH were 47 (16), 51 (34), 60 (32), 62 (36), 74 (45) and Vit D levels were 44 (16), 73 (19), 83 (28), 95 (31) and 76 (23) respectively. PTH trend did not differ from the comparative dialysis unit. Conclusions: Vit D therapy in LSVDL seems to have limited impact on biochemical bone mineral parameters in HD population in prospective observational study. Larger randomised study is needed.

Disparities in survival of dialysis patients in Australia based upon ethnicity and country of birth.
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Aim: To compare survival of Australian-born Caucasian dialysis patients with that of first generation migrants and their naturalized immigrant counterparts. Background: Disparities in clinical outcomes have been demonstrated within dialysis populations, including differences with Indigenous Australians and residents in rural/remote locations. Ethnicity appears to confer an effect on dialysis patient survival. Methods: We identified, using the ANZDATA registry, patients who initiated dialysis between 1st January 1993 and 31st December 2013. The patient cohort was divided into 4 groups: Australian-born Caucasians, Caucasians born overseas, non-Caucasians born in Australia, and non-Caucasians born overseas. Adjusted Cox proportional hazards models were used to estimate the hazard ratios (HR) for mortality for the latter 3 groups compared with Australian-born Caucasians. A secondary analysis censored for transplantation. Results: 39,618 patients were included in this study (Australian-born Caucasian = 22771; Caucasian-born overseas = 8387; Non-Caucasian-Australian born = 3964; and Non-Caucasian-born overseas = 4496). The median age was 63, 67, 50 and 58.5 years respectively (p < 0.001). Males made up 59.7%, 67.5%, 44.8% and 57.1% respectively (p < 0.001). Compared with Australian-born Caucasians, Caucasians born overseas had a reduced mortality, HR = 0.86 (95% confidence interval (95 CI): 0.83, 0.89) and Non-Caucasians born overseas had lower mortality risk than Australia-born Caucasians, HR = 0.73 (95 CI: 0.69, 0.77), whereas non-Caucasians born in Australia had increased mortality, HR = 1.32 (95 CI: 1.25, 1.38) although this was markedly attenuated when data was censored for transplantation, HR 1.04, (95% CI 1.03-1.04, p = 0.04). Conclusions: Both ethnicity and the place of birth appear to significantly impact on survival of dialysis patients. Being born in Australia appears to confer an increased mortality risk, more pronounced for Non-Caucasian dialysis patients. This may be related to differences in access to transplantation.

Lunar: Lupus nephritis Australian registry baseline demographics.
Phoon R, Isbel N, et al. (Phoon) Westmead Hospital, NSW, Australia (Isbel) Princess Alexandria Hospital, QLD, Australia (Brown) Monash Medical Centre, VIC, Australia (Coates) Royal Adelaide Hospital, SA, Australia (Wyburn) Royal Prince Alfred Hospital, NSW, Australia (Langham) St Vincent's Hospital, VIC, Australia (Kurts, Lobb) Westmead Hospital, NSW, Australia (Irish) Fiona Stanley Hospital, WA, Australia
R. Phoon, Westmead Hospital, NSW, Australia
Aim: To collect and analyse long-term safety and efficacy data in patients with Lupus Nephritis (LN) and to characterise and describe the population of patients receiving Myfortic and other immunosuppressant therapies. Background: Long term monitoring of outcomes and safety provides an invaluable opportunity to generate significant insights about the nature of the disease, temporal and treatment induced changes within the natural history of the disease, as well as to pick up early signs of any safety signals that
Nephrology. 2015; 20: 34.

**Analysis of clinical presentation, pathological spectra, treatment and outcomes of biopsy-proven acute post infectious glomerulonephritis (APIGN) in the Northern Territory.**

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**Aim:** To describe the presentation and outcomes of biopsy proven APIGN in the Northern Territory of Australia. **Background:** APIGN is common in Indigenous communities in the Northern Territory. It is a major risk factor for the very high prevalence of chronic kidney disease. **Methods:** We performed a retrospective cohort analysis of adult patients (>18 years) who had renal biopsies from 01/01/2004 to 31/05/2014. Demographic, microbiological, pathology and renal biopsy data were obtained through clinical coding department, electronic medical, pathology and hard copy medical records. All native renal biopsy results with the diagnosis of APIGN were reviewed and analysed. The outcome measure was ESRD or dialysis requirement. Results: 43 (12.7%) (Median age 44 years) of 340 patients with 377 biopsies had APIGN (11.4%). 38 (88.4%) were Aboriginal. Comorbidities included diabetes mellitus 26 (60.5%), hypertension 26 (60.5%) and smoking 22 (56.4%). 49% had multiple pathologies on biopsy. Predominant histological pattern was diffuse proliferative glomerulonephritis (72%). Main sites of infections were skin (47.6%) and throat (26.2%) with streptococcus/staphylococcus as predominant organism. 50% required long-term dialysis. Unadjusted analysis revealed older patients (p = 0.030), lower baseline eGFR (p < 0.001), higher serum creatinine (p < 0.001), ACR (p = 0.02) and serum urea (p = < 0.01) and lower serum sodium (p = 0.01) at presentation, higher interstitial fibrosis (p = 0.01), number of obsolete glomeruli (p < 0.001), different pathologies (p < 0.001) and had diabetes (p = 0.01) or hypertension (p = 0.01). Infecting organism (p < 0.001) was also significant. On adjusting for all covariates in a logistic regression, only higher ACR (p = 0.023) and serum creatinine (0.02) at presentation were significant. Conclusions: APIGN was associated with poor renal outcomes with 50% requiring long-term dialysis. Most patients had pre-existing pathology with superimposed APIGN that led to significant and permanent deterioration in kidney function. **Publication Types:** Conference Abstract  


**Booster hepatitis b vaccination in haemodialysis patients-a 5-year prospective study.**

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**Aim:** To study the efficacy of 3 yearly Hepatitis B booster vaccines in haemodialysis population. **Background:** The duration of booster re-vaccination of Hepatitis B in nonresponsive haemodialysis population is unclear. Impact of the new protocol of 3 annual boosters after initial vaccination over 5 years was reviewed. **Methods:** Protocol with up to 3 yearly Hepatitis B booster vaccinations after a standard course was established in 2008, with ongoing monitoring in 4th and 5th year. Patients were classed according to the response to “initial” and “boosters” as initial and subsequent responders (Anti HBsAb > 10 mIU/mL). Blood transfections and Hepatitis B infection related data was reviewed in this population. Results: 46 HD patients (M = 26; F = 20) completed 5 years of vaccination regime, were evaluated for protocol efficacy. None of the 20 “initial” responders needed booster vaccination over 5 years (8 deaths, 1 transplant and 1 transfer). Of the 26 non-responders to primary vaccination, 26, 21 and 15 patients received vaccination in Year 1, 2 and 3 respectively. 3 patients responded to the 2 boosters, with short term (<12 months) response in 2 (Anti HbsAb < 21 mIU/mL) and long term response (>36 months) in one (Anti HBsAb > 100 mIU/mL). 141 patients were dialysed in the unit from 2008-2014, 68 patients receiving 488 transfusions. 2 patients were Hepatitis B positive prior to arrival to the unit, there was no reported acquired transmission over the study period. Conclusions: Our findings suggest limited or no benefit of surveillance or vaccinations in unresponsive haemodialysis patients beyond 3 years. Use of standard precautions and targeted surveillance should suffice in this population. Larger studies confirming the benefit are useful. **Publication Types:** Conference Abstract  
sympathetic hyperactivity is a characteristic feature of obesity, the metabolic syndrome and type 2 diabetes. Sympathetic inhibition expression are not fully understood. The sympathetic nervous system is an important modulator of glucose homeostasis and of this glucose transporter for the treatment of type 2 diabetes, the mechanisms that regulate sodium glucose co-transporter 2 are therefore of high clinical relevance. However, despite recent advances in the field and the availability of pharmacological inhibitors there are no products currently available for the treatment of type 2 diabetes.

Is it time to think about the sodium glucose co-transporter 2 sympathetically?
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Disturbances in glucose homeostasis are a key feature of the metabolic syndrome and type 2 diabetes. Renal glucose reabsorption is an important factor in glycaemic control. Glucose reabsorption in the proximal tubules is mediated by the sodium glucose co-transporter 2. The capacity for glucose reabsorption is increased in type 2 diabetes and contributes significantly to hyperglycaemia and impaired glucose control. Understanding the mechanisms underpinning the regulation of the sodium glucose co-transporter 2 is therefore of high clinical relevance. However, despite recent advances in the field and the availability of pharmacological inhibitors of this glucose transporter for the treatment of type 2 diabetes, the mechanisms that regulate sodium glucose co-transporter 2 expression are not fully understood. The sympathetic nervous system is an important modulator of glucose homeostasis and sympathetic hyperactivity is a characteristic feature of obesity, the metabolic syndrome and type 2 diabetes. Sympathetic inhibition either achieved pharmacologically or by renal sympathetic denervation has been associated with improved glucose control. Importantly, sympathetic nerves innervate the proximal tubules of the kidney where they have been shown to regulate the expression of other transporters such as the sodium hydrogen exchanger 3. This review aims to explore the evidence for the regulation of sodium glucose co-transporter 2-mediated glucose reabsorption by the sympathetic nervous system.

Kidney paired donation: principles, protocols and programs.
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Due to the ongoing shortage of deceased-donor organs, novel strategies to augment kidney transplantation rates through expanded living donation strategies have become essential. These include desensitization in antibody-incompatible transplants and kidney paired donation (KPD) programs. KPD enables kidney transplant candidates with willing but incompatible living donors to join a registry of other incompatible pairs in order to find a suitable match to each other. Multicenter KPD programs use sophisticated algorithms to identify optimal match potential, with simultaneous two-, three- or more complex multiway exchanges. The article focuses on the recent progresses in KPD and it also reviews some of the differences and commonalities across four different national KPD programs. Copyright © The Author 2014. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved.


**Hyperfiltration in Indigenous Australians with and without diabetes.**
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**BACKGROUND:** Hyperfiltration (HF) has been linked to the development of diabetic kidney disease (DKD), but the causative or predictive role of HF in the pathogenesis of DKD still remains unclear. To date, there have been no studies of HF in Indigenous Australians, a population with high rates of both diabetes and end-stage kidney disease. We aimed to compare the characteristics and frequency of HF in Indigenous Australians with and without type 2 diabetes.

**METHODS:** Indigenous Australian participants, recruited across five pre-defined strata of health, diabetes status and kidney function, had a reference glomerular filtration rate (GFR) measured using plasma disappearance of iohexol [measured GFR(mGFR)] over 4 h. HF was defined in various ways: (i) mgFR > 144 mL/min/1.73 m(2), which is mgFR > 1.96 x SD above the mean of the mgFR in non-diabetic participants with normal albuminuria and normal renal function (mgFR > 90 mL/min/1.73 m(2)); (ii) age-corrected mgFR (>144 mL/min/1.73 m(2)) to account for the effect of ageing on GFR in subjects over 40 years of age with cut-off 1 mL/min/1.73 m(2) lower for every year; (iii) mgFR > 144 mL/min, without correction for body surface area or age, as well as (iv) mgFR > 125 mL/min/1.73 m(2), without adjustment for age.

**RESULTS:** A total of 383 Indigenous participants, 125 with and 258 without diabetes, with mgFR > 90 mL/min/1.73 m(2) were studied. The proportion of participants with HF was 7% using mgFR > 144 mL/min/1.73 m(2), 11% using the age-adjusted definition, 19% using mgFR > 144 mL/min and 27% using mgFR > 125 mL/min/1.73 m(2). Diabetes was more common in participants with HF (40-74%) compared with normofiltering participants (28-31%), regardless of the definition of HF. A greater proportion of participants had diabetes in HF group compared with normofiltration group. Long-term follow-up of this cohort is necessary to determine if HF plays a role in the development of DKD and non-DKD. Copyright © The Author 2015. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved.

**Neuroendocrinology, 2015.**

**Pancreatic Neuroendocrine Tumor Control: Durable Objective Response to Combination Lu-Octreotate-Capecitabine-Temozolomide Radiopeptide Chemotherapy.**
Claringbold PG, Turner JH.
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**BACKGROUND:** Thirty patients with advanced progressive Grade 1 or 2 pancreatic neuroendocrine tumors (pNETS), treated on a prospective Phase II single-center study, were followed for up to 4 years after 4 cycles of 7.9 Gbq 177Lu-octreotate combined with capecitabine and chemotherapy. Each 8 week cycle of treatment combined radipeptide with14 days of capecitabine 1,500 mg/m2 and 5 days of temozolomide 200 mg/m2. RESULTS: Overall response rate (ORR) was 80% (95% CI , 66-93%), complete remission (CR) 13% (95% CI 4-30%) and partial response (PR) 70% ((95% CI 52-83%). No patient manifested progressive disease (PD) on treatment. Median progression-free survival (PFS) was 48 months. Median overall survival (OS) had not been reached at a median follow-up of 33 months. No patient was lost to follow-up, all but one received 4 cycles of outpatient therapy and all were evaluated for response and toxicity. One patient required hospital admission. Treatment was well tolerated and no serious dose-limiting toxicities were seen. The commonest toxicities were transient nausea grade 2 (33%), grade 3 (7%). Hematological toxicity was limited to grade 3 thrombopenia (10%) and anemia (10%). There were no grade 4 adverse events and no renal function impairment was evident. CONCLUSION: Combined 177Lu-octreotate radiopeptide-capecitabine-temozolomide chemotherapy is a well-tolerated, highly...
Nuclear actin aggregation is a hallmark of anti-synthetase syndrome-induced dysimmune myopathy.

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Stenzel W, Preuse C, et al.
OBJECTIVE: To analyze antisynthetase syndrome-associated myositis by modern myopathologic methods and to define its place in the spectrum of idiopathic inflammatory myopathies (IIMs).

METHODS: Skeletal muscle biopsies from antisynthetase syndrome-associated myositis and other IIMs from different institutions worldwide were analyzed by histopathology, quantitative PCR, and electron microscopy.

RESULTS: Myonuclear actin filament inclusions were identified as a unique morphologic hallmark of antisynthetase syndrome-associated myositis. Nuclear actin inclusions were never found in dermatomyositis, polymyositis, sporadic inclusion body myositis, autoimmune necrotizing myopathy associated with signal recognition particle or 3-hydroxy-3-methylglutaryl-coenzyme A reductase autoantibodies, or nonspecific myositis associated with other systemic diseases, harboring myositis-associated autoantibodies, and myofiber necrosis. We show that molecules involved in actin filament formation and actin shuffling mechanisms are altered in antisynthetase syndrome, and may thus be involved in pathologic myonuclear actin aggregation. In addition, we have identified a typical topographic distribution of necrotic myofibers predominantly located at the periphery of muscle fascicles accompanied by inflammation and destruction of the perimysial connective tissue.

CONCLUSION: Antisynthetase syndrome-associated myositis is characterized by distinctive myonuclear actin filament inclusions, including rod formation and a typical necrotizing perimysial myositis. This supports the hypothesis that antisynthetase syndrome-associated myositis is unique and should not be grouped among dermatomyositis, polymyositis, sporadic inclusion body myositis, necrotizing autoimmune myositis, or nonspecific myositis.

CLASSIFICATION OF EVIDENCE: This study provides Class II evidence that for patients with IIMs, the presence of myonuclear actin filament inclusions accurately identifies patients with antisynthetase syndrome-associated myositis (sensitivity 81%, specificity 100%).

Type 2 diabetes mellitus and biomarkers of neurodegeneration.


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CONCLUSIONS: T2DM may promote neurodegeneration independent of AD dementia diagnosis, and its effect may be driven by tau phosphorylation. The mechanisms through which T2DM may promote tau phosphorylation deserve further study. Copyright © 2015 American Academy of Neurology.


**Origin-of-transfer sequences facilitate mobilisation of non-conjugative antimicrobial-resistance plasmids in *Staphylococcus aureus***.

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*Staphylococcus aureus* is a common cause of hospital, community and livestock-associated infections and is increasingly resistant to multiple antimicrobials. A significant proportion of antimicrobial-resistance genes are plasmid-borne, but only a minority of *S. aureus* plasmids encode proteins required for conjugative transfer or Mob relaxase proteins required for mobilisation. The pWBG749 family of *S. aureus* conjugative plasmids can facilitate the horizontal transfer of diverse antimicrobial-resistance plasmids that lack Mob genes. Here we reveal that these mobilisable plasmids carry copies of the pWBG749 origin-of-transfer (oriT) sequence and that these oriT sequences facilitate mobilisation by pWBG749. Sequences resembling the pWBG749 oriT were identified on half of all sequenced *S. aureus* plasmids, including the most prevalent large antimicrobial-resistance/virulence-gene plasmids, pB485, pMW2 and pUSA300HOUMR. oriT sequences formed five subfamilies with distinct inverted-repeat-2 (IR2) sequences. pWBG749-family plasmids encoding each IR2 were identified and pWBG749 mobilisation was found to be specific for plasmids carrying matching IR2 sequences. Specificity of mobilisation was conferred by a putative ribbon-helix-helix-protein gene smpO. Several plasmids carried 2-3 oriT variants and pWBG749-mediated recombination occurred between distinct oriT sites during mobilisation. These observations suggest this relaxase-in trans mechanism of mobilisation by pWBG749-family plasmids is a common mechanism of plasmid dissemination in *S. aureus*.


Nutrients. 2015; 7(6): 4416-4425.

**Effect of dietary fatty acids on human lipoprotein metabolism: A comprehensive update.**

Ooi EMM, Watts GF, et al.
(Ooi, Watts, Ng, Barrett) Metabolic Research Centre, School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6000, Australia (Watts) Lipid Disorders Clinic, Cardiometabolic Service, Department of Internal Medicine, Royal Perth Hospital, WA 6000, Australia (Barrett) Computing and Mathematics, University of Western Australia, Perth, WA 6000, Australia
P.H.R. Barrett, Metabolic Research Centre, School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6000, Australia

Dyslipidemia is a major risk factor for cardiovascular disease (CVD). Dietary fatty-acid composition regulates lipids and lipoprotein metabolism and may confer CVD benefit. This review updates understanding of the effect of dietary fatty-acids on human lipoprotein metabolism. In elderly participants with hyperlipidemia, high n-3 polyunsaturated fatty-acids (PUFA) consumption diminished hepatic triglyceride-rich lipoprotein (TRL) secretion and enhanced TRL to low-density lipoprotein (LDL) conversion. n-3 PUFA also decreased TRL-apoB-48 secretion by decreasing TRL-apoB-48 secretion. High n-6 PUFA intake decreased very low-density lipoprotein (VLDL) cholesterol and triglyceride concentrations by up-regulating VLDL lipolysis and uptake. In a study of healthy subjects, the intake of saturated fatty-acids with increased palmitic acid at the sn-2 position was associated with decreased postprandial lipemia. Low medium-chain triglyceride may not appreciably alter TRL metabolism. Replacing carbohydrate with monounsaturated fatty-acids increased TRL catabolism. Trans-fatty-acid decreased LDL and enhanced high-density lipoprotein catabolism. Interactions between APOE genotype and n-3 PUFA in regulating lipid responses were also described. The major advances in understanding the effect of dietary fatty-acids on lipoprotein metabolism has centered on n-3 PUFA. This knowledge emphasizes the importance of regulating lipoprotein metabolism as a mode to improve OPEN plasma lipids and potentially CVD risk. Additional studies are required to better characterize the cardiometabolic effects of other dietary fatty-acids.

Publication Types: Review


**Oral Nucleotides Only Minimally Improve 5-Fluorouracil-Induced Mucositis in Rats.**

Nutrients. 2015; 7(6): 4416-4425.

**Effect of dietary fatty acids on human lipoprotein metabolism: A comprehensive update.**

Ooi EMM, Watts GF, et al.
(Ooi, Watts, Ng, Barrett) Metabolic Research Centre, School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6000, Australia (Watts) Lipid Disorders Clinic, Cardiometabolic Service, Department of Internal Medicine, Royal Perth Hospital, WA 6000, Australia (Barrett) Computing and Mathematics, University of Western Australia, Perth, WA 6000, Australia
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Dyslipidemia is a major risk factor for cardiovascular disease (CVD). Dietary fatty-acid composition regulates lipids and lipoprotein metabolism and may confer CVD benefit. This review updates understanding of the effect of dietary fatty-acids on human lipoprotein metabolism. In elderly participants with hyperlipidemia, high n-3 polyunsaturated fatty-acids (PUFA) consumption diminished hepatic triglyceride-rich lipoprotein (TRL) secretion and enhanced TRL to low-density lipoprotein (LDL) conversion. n-3 PUFA also decreased TRL-apoB-48 secretion by decreasing TRL-apoB-48 secretion. High n-6 PUFA intake decreased very low-density lipoprotein (VLDL) cholesterol and triglyceride concentrations by up-regulating VLDL lipolysis and uptake. In a study of healthy subjects, the intake of saturated fatty-acids with increased palmitic acid at the sn-2 position was associated with decreased postprandial lipemia. Low medium-chain triglyceride may not appreciably alter TRL metabolism. Replacing carbohydrate with monounsaturated fatty-acids increased TRL catabolism. Trans-fatty-acid decreased LDL and enhanced high-density lipoprotein catabolism. Interactions between APOE genotype and n-3 PUFA in regulating lipid responses were also described. The major advances in understanding the effect of dietary fatty-acids on lipoprotein metabolism has centered on n-3 PUFA. This knowledge emphasizes the importance of regulating lipoprotein metabolism as a mode to improve OPEN plasma lipids and potentially CVD risk. Additional studies are required to better characterize the cardiometabolic effects of other dietary fatty-acids.

Publication Types: Review


**Oral Nucleotides Only Minimally Improve 5-Fluorouracil-Induced Mucositis in Rats.**
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Chemotherapy-induced mucositis is characterized by inflammation and ulceration of the intestinal mucosa, compromising intestinal function. Exogenous nucleotides have been reported to repair the mucosa. The nucleotide preparation, Nucleoforce F0328 (Nucleoforce), was investigated for its potential to ameliorate intestinal mucositis in rats. Female Dark Agouti rats (n = 8/group) were gavaged once daily with Nucleoforce (175 mg/kg) or water from Days 0 to 8 and injected (i.p.) with 5-fluorouracil (5-FU; 150 mg/kg) or saline on Day 5. Histological parameters (disease severity, crypt depth, and villus height measurements) and myeloperoxidase activity were quantified. P < 0.05 was considered significant. Jejunal and ileal histological disease severity scores were significantly increased by 5-FU, compared to normal controls (P < 0.05). Nucleoforce treatment in 5-FU-injected rats significantly reduced jejunal and ileal disease severity compared to 5-FU controls (P < 0.05). In 5-FU-injected rats, jejunal and ileal villus heights and crypt depths were significantly decreased compared to 5-FU controls, with no additional Nucleoforce effect (P > 0.05). Intestinal myeloperoxidase activity was significantly elevated by 5-FU (8.8-fold), compared to normal controls (P < 0.05), which was not normalized by Nucleoforce treatment (P > 0.05). Nucleoforce only partially improved parameters associated with experimentally-induced mucositis. Future studies could investigate increased concentrations, more frequent administration, or protective microencapsulation delivery methods, to increase bioavailability.


Paternal dietary folate, B6 and B12 intake, and the risk of childhood brain tumors.

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It is biologically plausible that a paternal preconception diet low in nutrients related to DNA integrity could affect sperm DNA and subsequently risk of cancer in the offspring. The aim of this analysis was to investigate whether paternal preconception dietary folate, B6, or B12 intake was associated with the risk of childhood brain tumors (CBT) in an Australian case-control study. Cases <15 years of age were recruited from 10 Australian pediatric oncology centers between 2005 and 2010, and controls from random-digit dialing, frequency-matched to cases on age, sex, and state of residence. Paternal dietary information was obtained by food-frequency questionnaires. Nutrient values were energy adjusted and divided into tertiles for analysis by unconditional logistic regression. In fathers with relevant data (237 cases and 629 controls), no association with dietary folate and B6 and risk of CBT was seen; high B12 intake was associated with an increased risk of CBT (odds ratio highest vs. lowest tertile: 1.74, 95% confidence interval: 1.14, 2.66) without an increasing trend. These results do not support the hypothesis that paternal dietary folate intake influences the risk of CBT. The increased OR observed between dietary B12 intake and risk of CBT is without any certain explanation.


The effect of yoghurt and its probiotics on blood pressure and serum lipid profile; a randomised controlled trial.

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Background and aims: Despite strong mechanistic data, and promising results from invitro and animal studies, the ability of probiotic bacteria to improve blood pressure and serum lipid concentrations in humans remains uncertain. The aim of this study was to determine the effect of Lactobacillus acidophilus La5 and Bifidobacterium animalis subsp lactis Bb12 dose of 3.0x10<sup>9</sup>CFU/d. Home blood pressure monitoring, consisting of 7-day bi-daily repeat measurements, were collected at baseline and week 6. Fasting total cholesterol, low density lipoprotein cholesterol (LDLC), and serum triglyceride were performed at baseline and week 6. When compared to
control milk, probiotic yoghurt did not significantly alter blood pressure, heart rate or serum lipid concentrations (P>0.05). Similarly, when compared to placebo capsules, supplementation with probiotic capsules did not alter blood pressure or concentrations of total cholesterol LDL-C, HDL-C, or triglycerides (P>0.05). Conclusions: The probiotic strains L. acidophilus La5 and B. animalis subsp. lactis Bb12 did not improve cardiovascular risk factors.


Oncogene. 2015. Regulation of sarcoma cell migration, invasion and invadopodia formation by AFAP1L1 through a phosphotyrosine-dependent pathway.
Tie SR, McCarthy DJ, et al.
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Invasion and metastasis are controlled by the invadopodia, which delivers matrix-degrading enzymes to the invasion interface permitting cancer cell penetration and spread into healthy tissue. We have identified a novel pathway that directs Lyn/Src family tyrosine kinase signals to the invadopodia to regulate sarcoma cell invasion via the molecule AFAP-1-like-1 (AFAP1L1), a new member of the AFAP (actin filament-associated protein) family. We show that AFAP1L1 can transform cells, promote migration and co-expression with active Lyn profoundly influences cell morphology and movement. AFAP1L1 intersects several invadopodia pathway components through its multiple domains and motifs, including the following (i) pleckstrin homology domains that bind phospholipids generated at the plasma membrane by phosphoinositide 3-kinase, (ii) a direct filamentous-actin binding domain and (iii) phospho-tyrosine motifs (pY136 and pY566) that specifically bind Vav2 and Nck2 SH2 domains, respectively. These phosphotyrosine motifs are essential for AFAP1L1-mediated cytoskeleton regulation. Through its interaction with Vav2, AFAP1L1 regulates Rac activity and downstream control of PAK1/2/3 (p21-activated kinases) phosphorylation of myosin light chain (MLC) kinase and MLC2. AFAP1L1 interaction with Nck2 recruits actin-nucleating complexes. Significantly, in osteosarcoma cell lines, knockdown of AFAP1L1 inhibits phosphorylated MLC2 recruitment to filamentous-actin structures, disrupts invadopodia formation, cell attachment, migration and invasion. These data define a novel pathway that directs Lyn/Src family tyrosine kinase signals to sarcoma cell invadopodia through specific recruitment of Vav2 and Nck2 to phosphorylated AFAP1L1, to control cell migration and invasion. Oncogene advance online publication, 27 July 2015; doi:10.1038/onc.2015.272.


Assessing expression of muc1 and zag protein biomarkers in prostate biopsies improves prediction of adverse pathology following radical prostatectomy.

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Objectives: To determine whether assessing expression of MUC1 and ZAG proteins in prostate biopsies, by immunohistochemistry, improves prediction of radical prostatectomy histopathology, which in turn predicts longer-term outcomes. Methods: We studied 231 consecutive patients managed by two experienced urologic surgeons (MF, LH). Each patient had prostate biopsies revealing cancer followed by a radical prostatectomy. Expression of MUC1 and ZAG in biopsy tissue was assessed by immunohistochemistry, masked to the radical prostatectomy histopathology. Data were analysed by Chi-square, Fischer exact test & Mann Whitney U test followed by multivariate analysis using binary logistic regression. Results: By univariate analysis, MUC1 expression in prostate biopsies was associated with worse histopathology in the radical prostatectomy specimen (p<0.023), while ZAG expression was associated with better pathology (p=0.03). By multivariate analysis decreased expression of ZAG in biopsies (p=0.02), but not MUC1 expression, improved prediction of high-risk radical prostatectomy pathology beyond conventional biopsy variables; neither MUC1 nor ZAG staining improved prediction of minimal-risk cancers. Conclusions: Assessment of ZAG expression in prostate biopsies, and possibly MUC1 expression, may improve knowledge of prostate cancers in vivo or after radical prostatectomy.


Open Urology and Nephrology Journal. 2015; 8: 45-52.
Cardio renal syndromes 2015: Is there a silver lining to the dark clouds?
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Kidneys have a pivotal role in maintaining our homeostasis. Kidneys and heart work in tandem to maintain volume homeostasis. Heart failure impacts renal function in many ways including renal hypoperfusion but also due to increased venous pressure along with stimulation of various neuro-humoral responses. Renal failure induces cardiac damage and dysfunction by causing volume overload, inflammation, and cardiomyocyte fibrosis. Concomitant comorbidities like Hypertension and Diabetes also play important role resulting in Cardiorenal Syndrome (CRS). Acute Dialysis Quality Initiative, 2007 recognized the bidirectional nature and different manifestations of CRS in acute and chronic settings. Diuretics are the most common drugs to treat the most common symptoms of CRS i.e., peripheral edema and pulmonary congestion. Diuretics could nevertheless contribute to worsening renal function (WRF). Initially it was accepted that WRF during the course of treatment of acute decompensated heart failure (ADHF) uniformly resulted in worse prognosis. However, in view of a few recent studies, the significance of WRF early in response to treatment of ADHF is being debated. The optimal dose and method of delivery of diuretics is still undecided. Isolated ultrafiltration does not improve renal function in patients with CRS despite the early promise. A large, multicentre trial ruled out any survival benefits with Recombinant Brain Natriuretic Peptide (Nesiritide). Despite good physiological basis and early promise with smaller studies, many drugs like Dobutamine, Rolofylline and Tolvaptan failed to show survival benefit in larger studies. However, two recent studies involving Relaxin and Nephrilysin have shown good survival advantage. There had been little progress in treatment of CRS until studies involving Relaxin and Nephrilysin inhibitor combination with ARB were published. There may after all, be a glimmer of hope in the field of CRS boggied by multiple negative studies.


Ophthalmoology. 2015; 122(9): 1951-3.

**Charles Bonnet Syndrome in Advanced Retinitis Pigmentosa.**

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**Analgesic efficacy and safety of curcuminoids in clinical practice: A systematic review and meta-analysis of randomized controlled trials.**

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Purpose: Curcuminoids are natural products with potent anti-inflammatory and antioxidant properties. There have been a number of reports on the analgesic effects of curcuminoids in clinical trials, yet data have not been fully conclusive. The objective of this study was to provide the highest level of evidence on the efficacy of curcuminoids in patients with painful conditions through meta-analysis of data from randomized controlled trials (RCTs). Methods: A systematic review and meta-analysis was conducted using data reported by RCTs. The primary efficacy measure was pain intensity or algofunctional status. Treatment effect was summarized with standardized mean difference (SMD) calculated from differences in means of pain measures between treatment and control groups using a random-effects model. Results: A total of 8 RCTs met our inclusion criteria, that included 606 randomized patients with different painful conditions (osteoarthritis, rheumatoid arthritis, fibromyalgia). Curcuminoids were found to significantly reduce pain (SMD: -0.57, 95% CI: -1.11 to -0.03, p = 0.04). This pain-relieving effect was found to be independent of administered dose and duration of treatment with curcuminoids, and was free from publication bias. Curcuminoids were safe and well tolerated in all evaluated RCTs. Conclusions: This meta-analysis of RCTs showed that supplementation with curcuminoids is a safe and effective strategy to reduce pain severity.

Publication Types: Conference Abstract


**Cochlear implantation in children with congenital and noncongenital unilateral deafness: a case series.**

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OBJECTIVES: Cochlear implantation is rapidly gaining acceptance as the most effective treatment for adult patients with unilateral deafness. The benefits for the pediatric population remain to be investigated. This study aimed to investigate the implications of cochlear implantation in children with congenital and noncongenital unilateral deafness.

DESIGN: Four children, three with congenital and one with a sudden unilateral deafness, were studied after implantation. The children were aged 17 months, 4.5 years, 6.8 years, and 9 years at the time of implantation. Speech perception in noise and sound localization ability were evaluated using age-appropriate materials.

RESULTS: The child with postlingual unilateral deafness rapidly integrated the normal acoustic hearing with the electrical signal from the cochlear implant and showed binaural benefits, as indicated by the localization ability and the improvement of speech perception in noise scores. The younger child with congenital unilateral deafness showed some clinical evidence of binaural
integration and the two older children with congenital deafness have not yet indicated signs of binaural benefits.

CONCLUSION: It seems that cochlear implantation in children with congenital unilateral deafness may provide some of the benefits of binaural hearing if implantation occurs within the critical period for bilateral auditory development.


The impact of cochlear implantation on speech understanding, subjective hearing performance, and tinnitus perception in patients with unilateral severe to profound hearing loss.

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OBJECTIVES: This study aimed to determine the impact of cochlear implantation on speech understanding in noise, subjective perception of hearing, and tinnitus perception of adult patients with unilateral severe to profound hearing loss and to investigate whether duration of deafness and age at implantation would influence the outcomes. In addition, this article describes the auditory training protocol used for unilaterally deaf patients.

DESIGN: This is a prospective study of subjects undergoing cochlear implantation for unilateral deafness with or without associated tinnitus.

METHODS: Speech perception in noise was tested using the Bamford-Kowal-Bench speech-in-noise test presented at 65 dB SPL. The Speech, Spatial, and Qualities of Hearing Scale and the Abbreviated Profile of Hearing Aid Benefit were used to evaluate the subjective perception of hearing with a cochlear implant and quality of life. Tinnitus disturbance was measured using the Tinnitus Reaction Questionnaire. Data were collected before cochlear implantation and 3, 6, 12, and 24 months after implantation.

RESULTS: Twenty-eight postlingual unilaterally deaf adults with or without tinnitus were implanted. There was a significant improvement in speech perception in noise across time in all spatial configurations. There was an overall significant improvement on the subjective perception of hearing and quality of life. Tinnitus disturbance reduced significantly across time. Age at implantation and duration of deafness did not influence the outcomes significantly.

CONCLUSION: Cochlear implantation provided significant improvement in speech understanding in challenging situations, subjective perception of hearing performance, and quality of life. Cochlear implantation also resulted in reduced tinnitus disturbance. Age at implantation and duration of deafness did not seem to influence the outcomes.


Piezosurgery for the repair of middle cranial fossa meningoencephaloceles.

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OBJECTIVES: To describe the use of a piezosurgery medical device to perform a craniotomy and produce a split calvarial graft for the repair of middle cranial fossa meningoencephaloceles.

STUDY DESIGN: Retrospective case review.

SETTING: Tertiary referral hospital.

PATIENTS: Ten consecutive patients undergoing middle cranial fossa approach for the repair of meningoencephaloceles.

INTERVENTION: Therapeutic.

MAIN OUTCOME MEASURES: Intraoperative and postoperative complications, success rate as defined by the ability to fashion a split calvarial graft that achieves complete closure of the tegmen defect. As a secondary outcome measure, evidence of integration of the split calvarial bone graft with the adjacent skull base was assessed.

RESULTS: There were no intraoperative or postoperative complications. An appropriately sized calvarial bone graft was produced, and complete closure of the tegmen defect was achieved in all 10 cases. Computed tomography demonstrated evidence of integration of the bone graft in eight cases between 4 and 9 months after surgery.

CONCLUSION: The piezosurgery medical device provides a safe and effective means by which the middle fossa craniotomy and split calvarial bone graft can be produced to repair defects of the middle fossa tegmen, with integration of the bone graft in the majority of cases.


Does Coupling and Positioning in Vibroplasty Matter? A Prospective Cohort Study.

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OBJECTIVE: Vibroplasty has offered a new modality of hearing rehabilitation in patients with mixed, conductive, and sensorineural hearing loss who cannot wear hearing aids. Potentially, the positioning of the floating mass transducer (FMT) in vibroplasty surgery has a critical effect on hearing outputs. In this study, the impact on hearing outputs and coupling efficiency are evaluated by comparing various vibroplasty applications in the middle ear. No other study to date has examined the coupling efficiency of round window (RW) versus an ossicular vibroplasty application.


STUDY DESIGN: Prospective cohort study of patients with underlying ear pathologies who were not able to wear hearing aids. METHODS: This is an ongoing prospective study of 16 patients. All patients had a standard audiological test battery. Direct drive transfer function analysis results were correlated with bone conduction thresholds to assess the efficiency of the FMT coupling. Speech perception in quiet and quality of life measure questionnaires were used to assess outcomes. Nine patients had round window vibroplasty, six patients had stapes vibroplasty, and one patient had traditional incus vibroplasty. RESULTS: Patients with a soft tissue coupler between the FMT and the RW had significantly reduced coupling efficiency. Patients who had direct RW contact had significantly improved coupling efficiency. Patients who underwent stapes or incus vibroplasty had the greatest coupling efficiency.

CONCLUSION: This study demonstrates that attachment to the stapes or incus provides the best coupling when compared to round window vibroplasty. When applicable, stapes or incus coupling should be the first choice when implementing vibroplasty.


Cochlear Implantation in Children with Congenital and Noncongenital Unilateral Deafness.
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Publication Types: Comment Letter


Changes in Caesarean Delivery Rates in Western Australia from 1995 to 2010 by Gestational Age at Birth.
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BACKGROUND: The caesarean delivery rate in the developed world has been increasing. It is not well understood how caesarean delivery rates have changed by gestational age at birth in Western Australia, particularly in relation to the introduction of the early-term delivery guidelines in Australia in 2006. METHODS: Data from the Western Australian Midwives Notification System were used to identify 193,136 singletons born to primiparous women at 34-42 weeks’ gestation during 1995-2010. Caesarean delivery rates were calculated by gestational age group (34-36 weeks, 37-38 weeks, and 39-42 weeks) and stratified into pre-labour and in-labour caesarean delivery. The average annual percent change (AAPC) for the caesarean delivery rates was calculated using joinpoint regression. Log-binomial regression was used to estimate the risk of having a caesarean delivery while adjusting for maternal and antenatal factors. RESULTS: Caesarean delivery rates rose steadily from 1995 to 2005 (AAPC = 5.9%, [95% confidence interval (CI) 4.9, 6.9]), but stabilised since then (AAPC = 0.9%, [95% CI -1.9, 3.8])). The rate of in-labour caesarean deliveries rose consistently from 1995 to 2010 across all gestational age groups. The pre-labour caesarean delivery rate rise was most dominant at 37-38 weeks’ gestation from 1995 to 2005 (AAPC = 6.8%, [95% CI 5.4, 8.2]), but declined during 2006-10 (AAPC = -4.5, [95% CI -6.7, -2.3]) while the same time the rise in pre-labour caesarean deliveries during 1995-2005 occurred predominantly at 37-38 weeks’ gestation, but declined again from 2006 to 2010. This suggests that the recently developed Australian early-term delivery guidelines may have had some success in reducing early-term deliveries in Western Australia.


Paediatric Anaesthesia. 2015; 25(4): 400-404.
The 'Can't Intubate Can't Oxygenate' scenario in pediatric anaesthesia: A comparison of the Melker cricothyroidotomy kit with a scalpel bougie technique.
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Summary Background While the majority of pediatric intubations are uncomplicated, the 'Can't intubate, Can't Oxygenate' scenario (CICO) does occur. With limited management guidelines available, CICO is still a challenge even to experienced pediatric anesthetists. Objectives To compare the COOK Melker cricothyroidotomy kit (CM) with a scalpel bougie (SB) technique for success

**A classification of chronic pain for ICD-11.**
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**Community-based palliative care is associated with reduced emergency department use by people with dementia in their last year of life: A retrospective cohort study.**
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Objective: To describe patterns in the use of hospital emergency departments in the last year of life by people who died with dementia and whether this was modified by use of community-based palliative care. Design: Retrospective population-based cohort study of people in their last year of life. Time-to-event analyses were performed using cumulative hazard functions and flexible parametric proportional hazards regression models. Setting/participants: All people living in Western Australia who died with dementia in the 2-year period 1 January 2009 to 31 December 2010 (dementia cohort; N=5261). A comparative cohort of decedents without dementia who died from other conditions amenable to palliative care (N=2685). Results: More than 70% of both the dementia and comparative cohorts attended hospital emergency departments in the last year of life. Only 6% of the dementia cohort used community-based palliative care compared to 26% of the comparative cohort. Decedents with dementia who were not receiving community-based palliative care attended hospital emergency departments more frequently than people receiving community-based palliative care. The magnitude of the increased rate of emergency department visits varied over the last year of life from 1.4 (95% confidence interval: 1.1-1.9) times more often in the first 3 months of follow-up to 6.7 (95% confidence interval: 4.7-9.6) times more frequently in the weeks immediately preceding death. Conclusions: Community-based palliative care of people who die with or of dementia is relatively infrequent but associated with significant reductions in hospital emergency department use in the last year of life.


Parkinsonism & Related Disorders. 2015; 21(2): 142-6.

**Factor analysis of the Hamilton Depression Rating Scale in Parkinson’s disease.**

RESULTS: KMO verified the sample's adequacy for factor analysis and Cronbach's alpha indicated a good internal consistency of the computed to assess factor validity. Cronbach's alpha, Bartlett's test, communality, percentage of non-redundant residuals and the component correlation matrix were combination with oblique rotations were used to identify which variables made up the factors. Kaiser-Meyer-Olkin measure (KMO),

INTRODUCTION: Several studies have validated the Hamilton Depression Rating Scale (HAMD) in patients with Parkinson's disease (PD), and reported adequate reliability and construct validity. However, the factorial validity of the HAMD has not yet been investigated. The aim of our analysis was to explore the factor structure of the HAMD in a large sample of PD patients.

METHODS: A principal component analysis of the 17-item HAMD was performed on data of 341 PD patients, available from a previous cross sectional study on anxiety. An eigenvalue >1 was used to determine the number of factors. Factor loadings >0.4 in combination with oblique rotations were used to identify which variables made up the factors. Kaiser-Meyer-Olkin measure (KMO), Cronbach's alpha, Bartlett's test, communality, percentage of non-redundant residuals and the component correlation matrix were computed to assess factor validity.

RESULTS: KMO verified the sample's adequacy for factor analysis and Cronbach's alpha indicated a good internal consistency of the total scale. Six factors had eigenvalues >1 and together explained 59.19% of the variance. The number of items per factor varied from 1 to 6. Inter-item correlations within each component were low. There was a high percentage of non-redundant residuals and low communality.

CONCLUSION: This analysis demonstrates that the factorial validity of the HAMD in PD is unsatisfactory. This implies that the scale is not appropriate for studying specific symptom domains of depression based on factorial structure in a PD population.


Handling of radioactive seed localisation breast specimens in the histopathology laboratory: the Western Australian experience.

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Radio-guided occult lesion localisation using iodine-125 seeds (ROLLIS) is a novel method of localisation for impalpable in situ and invasive carcinomas that has been the subject of a recent pilot study and pilot study extension in Western Australia. Robust protocols for radiation safety, specimen labelling, specimen tracking, seed retrieval and seed disposal were developed at two Western Australian laboratories to minimise the risk of seed loss. The processes are safe and effective with no significant radiation exposure to pathologists and with acquisitions of all seeds intact and undamaged. The success can be attributed to developing specific seed retrieval techniques, suited to local preferences at each institution, with input from surgeons, radiologists and medical physics personnel. These techniques are now routine and will continue in the randomised control phase of the ROLLIS study.


Evaluation of the BD Max Cdiff assay for the detection of toxigenic Clostridium difficile in human stool specimens.

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The Becton Dickinson (BD) PCR-based GeneOhm Cdiff assay has demonstrated a high sensitivity and specificity for detecting Clostridium difficile. Recently, the BD Max platform, using the same principles as BD GeneOhm, has become available in Australia. This study aimed to investigate the sensitivity and specificity of BD Max Cdiff assay for the detection of toxigenic C. difficile in an Australian setting. Between December 2013 and January 2014, 406 stool specimens from 349 patients were analysed with the BD Max Cdiff assay. Direct and enrichment toxigenic culture were performed on bioMerieux ChromID C. difficile agar as a reference method. isolates from specimens with discrepant results were further analysed with an in-house PCR to detect the presence of toxin genes. The overall prevalence of toxigenic C. difficile was 7.2%. Concordance between the BD Max assay and enrichment culture was 98.5%. The sensitivity, specificity, positive predictive value and negative predictive value for the BD Max Cdiff assay were 95.5%, 99.0%, 87.5% and 99.7%, respectively, when compared to direct culture, and 91.7%, 99.0%, 88.0% and 99.4%, respectively, when compared to enrichment culture. The new BD Max Cdiff assay appeared to be an excellent platform for rapid and
Plasma cholesterol in adults with phenylketonuria.


Phenylketonuria (PKU) is an autosomal recessive disorder of phenylalanine (Phe) catabolism resulting from a deficiency of L-phenylalanine hydroxylase (PAH). An association between hyperphenylalaninaemia (HPA) and hypocholesterolaemia has been reported in children. However, controversy exists as to whether this is due to the low protein diet or to a disruption to cholesterol biosynthesis inherent to those with PKU. We investigated the relationship between blood Phe and plasma cholesterol in 41 apparently healthy adults with PKU (26 female, 15 male, age 18-57 years, median age 26 years) attending a PKU outpatient clinic at an adult tertiary care hospital. Of these patients, 33 (80%) were compliant with a Phe-restricted diet with amino acid supplementation, whereas eight (20%) were not. The PKU subjects had a mean body mass index (BMI) of 30.3 +/- 1.8 kg/m; 72% were obese, 14% overweight, with only 14% having normal BMI. The mean blood Phe was 1194 +/- 522 mmol/L with plasma total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol and apolipoprotein (apo) B concentrations of 4.3 +/- 0.8 mmol/L, 1.6 +/- 0.8 mmol/L, 1.2 +/- 0.3 mmol/L, 2.3 +/- 0.8 mmol/L, and 0.83 +/- 0.21 g/L, respectively. The mean LDL-cholesterol was 19% lower in PKU females than that of 8944 age-matched females from a community population (2.5 +/- 0.8 mmol/L vs. 3.1 +/- 0.9 mmol/L, p < 0.001). Similarly, the mean LDL-cholesterol was 32% lower in PKU males than 3786 age-matched males (2.1 +/- 0.7 mmol/L vs. 3.1 +/- 1.0 mmol/L, p < 0.0001). No correlations were observed between Phe and total cholesterol, LDL-cholesterol or apoB in the PKU cohort. Adults with PKU had low-normal cholesterol concentrations, with no correlation observed between Phe and cholesterol levels. Our findings support the concept that the HPA found in PKU, rather than an effect of a low-protein diet, leads to hypocholesterolaemia. Studies are required to determine whether this cholesterol-lowering effect confers cardioprotection.

Publication Types: Research Support, Non-U.S. Gov't

Eighteen Years of Respiratory Syncytial Virus Surveillance: Changes in Seasonality and Hospitalization Rates in Southwestern Alaska Native Children.

Bruden DJ, Singleton R, et al.

BACKGROUND: Alaska Native infants from the Yukon-Kuskokwim Delta (YKD) experienced respiratory syncytial virus (RSV) hospitalization rates 5 times higher and an RSV season twice as long as the general US infant population. We describe trends in hospitalization rates and seasonality during 18 years of continuous RSV surveillance in this population and explore contributions of climate and sociodemographic factors.

METHODS: We abstracted clinical and RSV test information from computerized medical records at YKD Regional Hospital and Alaska Native Medical Center from 1994 to 2012 to determine hospitalization rates and RSV season timing. Descriptive village and weather data were acquired through the US Census and Alaska Climate Research Center, University of Alaska, Fairbanks, respectively.

RESULTS: During 1994-2012, YKD infant RSV hospitalization rates declined nearly 3-fold, from 177 to 65 per 1000 infants/yr. RSV season onset shifted later, from mid October to late December, contributing to a significantly decreased season duration, from 30 to 11 weeks. In a multivariate analysis, children from villages with more crowded households and lacking plumbed water had higher rates of RSV hospitalizations (relative rate, 1.45; P = 0.0003). No association of temperature or dew point was found with the timing or severity of RSV season.

CONCLUSIONS: Although the RSV hospitalization rate decreased 3-fold, YKD infants still experience a hospitalization rate 3-fold higher than the general US infant population. Overcrowding and lack of plumbed water were associated with RSV hospitalization. Dramatic changes occurred in RSV seasonality, not explained by changes in climate.
BACKGROUND AND OBJECTIVES: Extremely preterm infants and infants born to adolescent mothers are at risk for adverse outcomes. The objectives were to evaluate development and behavior outcomes of extremely low birth weight (ELBW) infants born to adolescent mothers <20 years compared with adult mothers >/>=20 years and to identify socioeconomic risk factors that affect outcomes. METHODS: Retrospective cohort analysis of 211 infants >/>=27 weeks of adolescent mothers and 1723 infants of adult mothers at Neonatal Research Network centers from 2008 to 2011. Groups were compared and regression models were run to predict 18- to 22-month adverse outcomes. Primary outcomes were Bayley-III scores, neurodevelopmental impairment, and Brief Infant Toddler Social Emotional Assessment problem scores (BITSEA/P >/>=75th percentile. RESULTS: Adolescent mothers were more often single, Hispanic, less educated, and had public insurance. By 18 to 22 months, their children had significantly increased rates of having lived >/>=3 places (21% vs 9%), state supervision (7% vs 3%), and significant cerebellar lesions, and serial CUS adverse findings as predictors of outcomes at 18 to 22 months’ corrected age. METHODS: Early and late CUS, and brain MRI were read by masked central readers, in a large cohort (n = 480) of extremely preterm infants born to adolescent mothers <28 weeks’ gestation surviving to near term in the Neonatal Research Network. Outcomes included NDI or death after neuroimaging, and significant gross motor impairment or death, with NDI defined as cognitive composite score <70, significant gross motor impairment, and severe hearing or visual impairment. Multivariable models evaluated the relative predictive value of neuroimaging while controlling for other factors. RESULTS: Of 480 infants, 15 died and 20 were lost. Increasing severity of WMA and significant cerebellar lesions on MRI were associated with adverse outcomes. Cerebellar lesions were rarely identified by CUS. In full multivariable models, both late CUS and MRI, but not early CUS, remained independently associated with NDI or death (MRI cerebellar lesions: odds ratio, 3.0 [95% confidence interval: 1.3-6.8]; late CUS: odds ratio, 9.8 [95% confidence interval: 2.8-35]), and significant gross motor impairment or death. In models that did not include late CUS, MRI moderate-severe WMA was independently associated with adverse outcomes. CONCLUSIONS: Both late CUS and near-term MRI abnormalities were associated with outcomes, independent of early CUS and other factors, underscoring the relative prognostic value of near-term neuroimaging.

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Background: The ability of urinary biomarkers to predict residual renal function (RRF) decline in peritoneal dialysis (PD) patients has not been defined. The present study aimed to explore the utility of established biomarkers from kidney injury models for predicting loss of RRF in incident PD patients, and to evaluate the impact on RRF of using neutral-pH PD solution low in glucose degradation products. Methods: The study included 50 randomly selected participants from the balANZ trial who had completed 24 months of follow-up. A change in glomerular filtration rate (GFR) was used as the primary clinical outcome measure. In a mixed-effects general linear model, baseline measurements of 18 novel urinary biomarkers and albumin were used to predict GFR change. The model was further used to evaluate the impact of biocompatible PD solution on RRF, adjusted for each biomarker. Results: Baseline albuminuria was not a useful predictor of change in RRF in PD patients (p = 0.84). Only clusterin was a significant predictor of GFR decline in the whole population (p = 0.04, adjusted for baseline GFR and albuminuria). However, the relationship was no longer apparent when albuminuria was removed from the model (p = 0.31). When the effect of the administered PD solutions was examined using a model adjusted for PD solution type, baseline albuminuria, and GFR, higher baseline urinary concentrations of trefoil factor 3 (TF3, p = 0.02), kidney injury molecule 1 (KIM-1, p = 0.04), and interferon gamma-induced protein 10 (IP-10, p = 0.03) were associated with more rapid decline of RRF in patients receiving conventional PD solution compared with biocompatible PD solution. Conclusions: Higher urinary levels of kidney injury biomarkers (TF3, KIM-1, IP-10) at baseline predicted significantly slower RRF decline in patients receiving biocompatible PD solutions. Findings from the present investigation should help to guide future studies to validate the utility of urinary biomarkers as tools to predict RFR decline in PD patients.


Lipids, blood pressure and kidney update 2014.

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This paper is an effort to review all the most important studies and guidelines in the topics of lipid, blood pressure and kidney published in 2014. Irrespective of advances, the options for improving simultaneous hypercholesterolemia and hypertension management (as well as its complication - chronic kidney disease) remain a problem. Recommending hypolipidemic, hypotensive and kidney disease drugs to obtain therapy targets in cardiovascular, diabetic, elderly and kidney disease (=high risk) patients might strengthen risk factor control, improve compliance and the therapy efficacy, and in the consequence reduce the risk of cardiovascular events and mortality rate. That is why the authors have decided to summary and discuss the recent scientific achievements in the field of lipid, blood pressure and kidney.


Statin therapy and plasma coenzyme Q10 concentrations - A systematic review and meta-analysis of placebo-controlled trials.

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OBJECTIVE: This study was conducted to assess whether serum homocysteine concentration was associated with the severity of primary chronic venous disease. DESIGN: Cross-sectional study. METHODS: A total of 282 primary chronic venous disease patients were enrolled from outpatient vascular services. The severity of venous disease was graded using the Clinical Etiology Anatomy Pathophysiology classification system. The association of serum homocysteine concentration with advanced primary chronic venous disease (C4-C6) was assessed using the Mann Whitney U test and logistic regression analysis. RESULTS: Median (interquartile range) serum homocysteine concentrations were 9.10 microM (7.55-10.75) and 10.40 microM (8.85-13.10) in patients with primary chronic venous disease.
Conclusions: Most participants ambulated at a low percentage of their measured exercise capacity. The 6MWT appears to be a useful test for inpatients recently discharged from the ICU.

Limitations: The maximum distance ambulated on the ward was estimated with premeasured distances.

1.06-12.09%, p < 0.001). If wounds are present on the hands and/or wrist, then the alternate electrode position described in this study is valid, for whole body and upper limb segmental BIS.

Objective: The study objectives were to investigate how much ground-based walking is undertaken by inpatients recovering from critical illness within 1 week of discharge from an ICU and to evaluate the feasibility and safety of the Six-Minute Walk Test (6MWT) for this population.

Design: This was an observational study.

Methods: Within 1 week of discharge from the ICU, functional exercise capacity was measured with the 6MWT. The maximum distance ambulated on the ward in a single session as part of usual clinical management was extracted from the medical notes. The distance achieved during the 6MWT and the maximum distance ambulated on the ward were compared.

Results: The participants (N=23) were survivors of a critical illness; their mean age was 57 years (SD=11). The median length of ICU stay was 11 days (interquartile range [IQR]=7). The mean 6-minute walk distance (6MWD) was 179 m (SD=101), and the maximum distance ambulated on the ward was 30 m (IQR=65). There was a moderate association between the distance participants ambulated on the ward and the 6MWD (r=.54). The maximum distance ambulated on the ward, expressed as a percentage of the 6MWD, was 29% (IQR=34%). Five participants (22%) experienced oxygen desaturation (oxygen saturation of <85%) and recovered within 1 minute of resting.

Limitations: The maximum distance ambulated on the ward was estimated with premeasured distances.

Conclusions: Most participants ambulated at a low percentage of their measured exercise capacity. The 6MWT appears to be a safe and useful test for inpatients recently discharged from the ICU. Copyright © 2015 American Physical Therapy Association.


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Discordance Between Distance Ambulated as Part of Usual Care and Functional Exercise Capacity in Survivors of Critical Illness Upon Intensive Care Discharge: Observational Study.

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Background: People who have had a prolonged admission to an intensive care unit (ICU) commonly have profound debilitation and weakness. For the delivery of effective exercise training, an accurate assessment of exercise capacity is essential.

Objective: The study objectives were to investigate how much ground-based walking is undertaken by inpatients recovering from critical illness within 1 week of discharge from an ICU and to evaluate the feasibility and safety of the Six-Minute Walk Test (6MWT) for this population.

Design: This was an observational study.

Methods: Within 1 week of discharge from the ICU, functional exercise capacity was measured with the 6MWT. The maximum distance ambulated on the ward in a single session as part of usual clinical management was extracted from the medical notes. The distance achieved during the 6MWT and the maximum distance ambulated on the ward were compared.

Results: The participants (N=23) were survivors of a critical illness; their mean age was 57 years (SD=11). The median length of ICU stay was 11 days (interquartile range [IQR]=7). The mean 6-minute walk distance (6MWD) was 179 m (SD=101), and the maximum distance ambulated on the ward was 30 m (IQR=65). There was a moderate association between the distance participants ambulated on the ward and the 6MWD (r=.54). The maximum distance ambulated on the ward, expressed as a percentage of the 6MWD, was 29% (IQR=34%). Five participants (22%) experienced oxygen desaturation (oxygen saturation of <85%) and recovered within 1 minute of resting.

Limitations: The maximum distance ambulated on the ward was estimated with premeasured distances.

Conclusions: Most participants ambulated at a low percentage of their measured exercise capacity. The 6MWT appears to be a safe and useful test for inpatients recently discharged from the ICU. Copyright © 2015 American Physical Therapy Association.


Alternate electrode placement for whole body and segmental bioimpedance spectroscopy.

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Bioimpedance spectroscopy (BIS) is frequently used to monitor body fluid and body composition in healthy and clinical populations. BIS guidelines state that there should be no skin lesions at the site of electrodes, and if lesions are present, electrode positions should be changed. However, alternate electrode positions are yet to be reported. This study aimed to determine if ventral electrode placements were suitable alternatives for whole body and segmental BIS measurements. Three alternate electrode placements were assessed for whole body BIS using a combination of ventral hand and foot electrode placements. An alternate position was assessed for upper and lower body segmental BIS. The results demonstrated that for whole body BIS, if drive and sense electrodes on the hand are moved to ventral positions, but foot electrodes remain in standard positions, then whole body BIS variables were comparable to standard electrode positioning (percentage difference range = 0.01 to 1.65%, p = 0.211-0.937). The alternate electrode placement for upper limb segmental BIS, results in BIS variables that are comparable to that of the standard positioning (percentage difference range = 0.24-3.51%, p = 0.393-0.604). The alternate lower limb electrode position significantly altered all resistance and predicted BIS variables for whole body and lower limb segmental BIS (percentage difference range = 1.06-12.09%, p < 0.001). If wounds are present on the hands and/or wrist, then the alternate electrode position described in this study is valid, for whole body and upper limb segmental BIS.


Physiol Rep. 2015; 3(8).

Lack of independent effect of type 2 diabetes beyond characteristic comorbidities and medications on small muscle

venous disease classified by C1-3 (n = 209) and C4-6 (n = 73) grades, respectively, p < 0.001. Serum homocysteine concentration was positively associated with clinical grade 4-6 after adjusting for other risk factors including age, diabetes, male sex, hypertension, recurrent varicose veins and stroke. Patients with serum homocysteine in the third (odds ratio 2.76, 95% confidence interval 1.01-7.54) and fourth (odds ratio 3.29, 95% confidence interval 1.15-9.43) quartiles were more likely to have grade C4-6 chronic venous disease than subjects with serum homocysteine in the first quartile. CONCLUSIONS: Serum homocysteine is positively associated with the severity of primary chronic venous disease and therefore could play a role in promoting chronic venous disease complications.

mass exercising muscle blood flow and exercise tolerance.
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Persons with type 2 diabetes (T2D) are believed to have reduced exercise tolerance; this may be partly due to impaired muscle blood flow (MBF). Whether there is an impact of T2D on exercising MBF within the typical constellation of comorbidities (hypertension, dyslipidemia, obesity) and their associated medications has not been investigated. We tested the hypothesis that small muscle mass exercise tolerance is reduced in persons with T2D versus Controls (matched for age, body mass index, fitness, comorbidities, non-T2D medications) and that this is related to blunted MBF. Eight persons with T2D and eight controls completed a forearm critical force (fCFimpulse) test as a measure of exercise tolerance (10-min intermittent maximal effort forearm contractions; the average contraction impulse in the last 30 sec quantified fCFimpulse). Forearm blood flow (FFB; ultrasound) and mean arterial pressure (MAP; finger photoplethysmography) were measured; forearm vascular conductance (FVK) was calculated. Data are means +/- SD, T2D versus Control. fCFimpulse was not different between groups (136.9 +/- 47.3 N.sec vs. 163.1 +/- 49.7 N.sec, P = 0.371) nor was the FBF from rest to during exercise at fCFimpulse (502.9 +/- 144.6 vs. 709.1 +/- 289.2 mL/min, P = 0.092), or its determinants FVK and MAP (both P > 0.05), although there was considerable interindividual variability. FBF was strongly related to fCFimpulse (r = 0.727, P = 0.002), providing support for the relationship between oxygen delivery and exercise tolerance. We conclude that small muscle mass exercising MBF and exercise tolerance are not impaired in representative persons with T2D versus appropriately matched controls. This suggests that peripheral vascular control impairment does not contribute to reduced exercise tolerance in this population.

Phytotherapy Research. 2015; 29(1): 141-143.
Effects of supplementation with Heracleum persicum fruit extract on serum lipids in patients undergoing coronary angiography: A pilot trial.
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Heracleum persicum Desf. ex Fischer (Apiaceae) is a native medicinal plant in the Iranian traditional medicine and also a safe and common dietary spice. The present pilot study aimed to investigate the impact of supplementation with H. persicum fruits on serum lipid concentrations in a group of patients with minimal coronary artery disease. Subjects who were diagnosed with <50% luminal narrowing in any of the major coronary arteries in coronary angiography were recruited for this trial and were randomized to receive either H. persicum hydroalcoholic fruit extract (n = 15; 300 mg/day) or placebo (n = 12) for a period of 6 months. Serum concentrations of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides were measured at baseline and at the end of study. No significant difference in concentrations of total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol was observed between H. persicum extract and placebo groups (p > 0.05). However, serum triglycerides levels were reduced after H. persicum extract supplementation in a borderline significant manner (p = 0.063). Short-term supplementation with H. persicum fruit extract might be used as an adjunctive treatment for patients with hypertriglyceridemia.

Investigation of the efficacy of adjunctive therapy with bioavailability-boosted curcuminoids in major depressive disorder.
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Current medications have limited efficacy in controlling the symptoms of major depressive disorder (MDD), and are associated with several adverse events on long-term use. Curcuminoids are extremely safe and multifunctional phytopharmaceuticals that have been shown to alleviate depressive symptoms in a variety of experimental models. The present study aimed to investigate the efficacy of curcuminoids as an add-on to standard antidepressants in patients with MDD. One hundred and eleven subjects were assigned to standard antidepressive therapy plus curcuminoids-piperine combination (1000-10 mg/day; n = 61) or standard antidepressive therapy alone (n = 50) for a period of 6 weeks. Efficacy measures were changes in the psychological status on the basis of the Hospital Anxiety and Depression Scale (HADS) and Beck Depression Inventory II (BDI-II). The BDI-II and HADS total
and subscale scores were reduced by the end of trial in both study groups. There were significantly greater reductions in total HADS score and subscales of anxiety and depression in the curcuminoids versus control group (p < 0.001). Likewise, reductions in BDI-II total score and scores of somatic and cognitive subscales were found to be greater in the curcuminoids compared with control group (p < 0.001). Co-administration of curcuminoids with piperine may be used as a safe and effective add-on to standard antidepressants in patients with MDD.


Effects of omega-3 and omega-6 fatty acids on human placental cytokine production.


Clinician-Graded Electronic Facial Paralysis Assessment: The eFACE.

Banks CA, Bhma PK, et al.


Selective and genetic constraints on pneumococcal serotype switching.

Croucher NJ, Kagedan L, et al.


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METHODS: To determine whether a pre-existing abacavir reactive memory T-cell population contributes to early abacavir HSR at least in some cases, abacavir HSR is due to re-stimulation of a pre-existing memory T-cell population rather than priming of a high responder. Fifty-five percent of individuals with HLA-B*57:01 exposed to the antiretroviral drug abacavir develop a hypersensitivity reaction (HSR) that has been attributed to naive T-cell responses to neo-antigen generated by the drug. Immunologically confirmed abacavir HSR can manifest clinically in less than 48 hours following first exposure suggesting that, at least in some cases, abacavir HSR is due to re-stimulation of a pre-existing memory T-cell population. Abacavir reactive memory T cells are present in drug naive individuals.

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BACKGROUND: Fifty-five percent of individuals with HLA-B*57:01 exposed to the antiretroviral drug abacavir develop a hypersensitivity reaction (HSR) that has been attributed to naive T-cell responses to neo-antigen generated by the drug. Immunologically confirmed abacavir HSR can manifest clinically in less than 48 hours following first exposure suggesting that, at least in some cases, abacavir HSR is due to re-stimulation of a pre-existing memory T-cell population rather than priming of a high frequency naive T-cell population.

METHODS: To determine whether a pre-existing abacavir reactive memory T-cell population contributes to early abacavir HSR symptoms, we studied the abacavir specific naive or memory T-cell response using HLA-B*57:01 positive HSR patients or healthy controls using ELISPOT assay, intra-cellular cytokine staining and tetramer labelling.

RESULTS: Abacavir reactive CD8+ T-cell responses were detected in vitro in one hundred percent of abacavir unexposed HLA-B*57:01 positive healthy donors. Abacavir-specific CD8+ T cells from such donors can be expanded from sorted memory, and sorted naive, CD8+ T cells without need for autologous CD4+ T cells.

CONCLUSIONS: We propose that these pre-existing abacavir-reactive memory CD8+ T-cell responses must have been primed by earlier exposure to another foreign antigen and that these T cells cross-react with an abacavir-HLA-B*57:01-endogenous peptide ligand complex, in keeping with the model of heterologous immunity proposed in transplant rejection.


**Abacavir-reactive memory T cells are present in drug naive individuals.**

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Lessons learned from whole exome sequencing in multiplex families affected by a complex genetic disorder, intracranial aneurysm.

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Genetic risk factors for intracranial aneurysm (IA) are not yet fully understood. Genomewide association studies have been successful at identifying common variants; however, the role of rare variation in IA susceptibility has not been fully explored. In this study, we report the use of whole exome sequencing (WES) in seven densely-affected families (45 individuals) recruited as part of the Familial Intracranial Aneurysm study. WES variants were prioritized by functional prediction, frequency, predicted pathogenicity, and segregation within families. Using these criteria, 68 variants in 68 genes were prioritized across the seven families. Of the genes that were expressed in IA tissue, one gene (TMEM132B) was differentially expressed in aneurysmal samples (n=44) as compared to control samples (n=16) (false discovery rate adjusted p-value=0.023). We demonstrate that sequencing of densely affected families permits exploration of the role of rare variants in a relatively common disease such as IA, although there are important study design considerations for applying sequencing to complex disorders. In this study, we explore methods of WES variant prioritization, including the incorporation of unaffected individuals, multipoint linkage analysis, biological pathway information, and transcriptome profiling. Further studies are needed to validate and characterize the set of variants and genes that we identify in this study.


An Improved Fst Estimator.
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Brighton and Sussex Medical School, Falmer, Brighton, United Kingdom.
The fixation index Fst plays a central role in ecological and evolutionary genetic studies. The estimators of Wright ([Formula: see text]), Weir and Cockerham ([Formula: see text]), and Hudson et al. ([Formula: see text]) are widely used to measure genetic differences among different populations, but all have limitations. We propose a minimum variance estimator [Formula: see text] using [Formula: see text] and [Formula: see text]. We tested [Formula: see text] in simulations and applied it to 120 unrelated East African individuals from Ethiopia and 11 subpopulations in HapMap 3 with 464,642 SNPs. Our simulation study showed that [Formula: see text] has smaller bias than [Formula: see text] for small sample sizes and smaller bias than [Formula: see text] for large sample sizes. Also, [Formula: see text] has smaller variance than [Formula: see text] for small Fst values and smaller variance than [Formula: see text] for large Fst values. We demonstrated that approximately 30 subpopulations and 30 individuals per subpopulation are required in order to accurately estimate Fst.

Anti-hepatitis C virus T-cell immunity in the context of multiple exposures to the virus.

Pfafferott K, Deshpande P, et al.

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Characterisation of Hepatitis C virus (HCV)-specific CD8+ T-cell responses in the context of multiple HCV exposures is critical to identify broadly protective immune responses necessary for an effective HCV vaccine against the different HCV genotypes. However, host and viral genetic diversity complicates vaccine development. To compensate for the observed variation in circulating autologous viruses and host molecules that restrict antigen presentation (human leucocyte antigens; HLA), this study used a reverse genomics approach that identified sites of viral adaptation to HLA-restricted T-cell immune pressure to predict genotype-specific HCV CD8+ T-cell targets. Peptides representing these putative HCV CD8+ T-cell targets, and their adapted form, were used in individualised IFN-gamma ELISpot assays to screen for HCV-specific T-cell responses in 133 HCV-seropositive subjects with high-risk of multiple HCV exposures. The data obtained from this study i) confirmed that genetic studies of viral evolution is an effective approach to detect novel in vivo HCV T-cell targets, ii) showed that HCV-specific T-cell epitopes can be recognised in their adapted form and would not have been detected using wild-type peptides and iii) showed that HCV-specific T-cell (but not antibody) responses against alternate genotypes in chronic HCV-infected subjects are readily found, implying clearance of previous alternate genotype infection. In summary, HCV adaptation to HLA Class I-restricted T-cell responses plays a central role in anti-HCV immunity and multiple HCV genotype exposure is highly prevalent in at-risk exposure populations, which are important considerations for future vaccine design.


Hospital mental health admissions in women after unsuccessful infertility treatment and in vitro fertilization: an Australian population-based cohort study.


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School of Women’s and Infants’ Health, The University of Western Australia, King Edward Memorial Hospital, Subiaco, Western Australia, Australia, and Fertility Specialists of Western Australia, Bethesda Hospital, Claremont, Western Australia, Australia.

OBJECTIVE: To examine the association between in vitro fertilization (IVF) and later admission to hospital with a mental health diagnosis in women who remained childless after infertility treatment. METHODS: This was a population-based cohort study using linked administrative hospital and registry data. The study population included all women commencing hospital treatment for infertility in Western Australia between the years 1982 and 2002 aged 20-44 years at treatment commencement who did not have a recorded birth by the end of follow-up (15 August 2010) and did not have a hospital mental health admission prior to the first infertility admission (n=6,567). Of these, 2,623 women had IVF and 3,944 did not. We used multivariate Cox regression modeling of mental health admissions and compared women undergoing IVF treatment with women having infertility treatment but not IVF.

RESULTS: Over an average of 17 years of follow-up, 411 women in the cohort were admitted to hospital with a mental health diagnosis; 93 who had IVF and 318 who did not. The unadjusted hazard ratio (HR) for a hospital mental health admission comparing women who had IVF with those receiving other infertility treatment was 0.50 (95% confidence interval [CI] 0.40-0.63). After adjustment for age, calendar year and socio-economic status the HR was 0.56 (95% CI 0.44-0.71). CONCLUSIONS: IVF treatment is associated with a reduced risk of hospital mental health admissions in women after unsuccessful infertility treatment. This may be explained by the healthy cohort effect.


Clinical setting influences off-label and unlicensed prescribing in a paediatric teaching hospital.

Czarniak P, Bint L, et al.

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PURPOSE: To estimate the prevalence of off-label and unlicensed prescribing during 2008 at a major paediatric teaching hospital in Western Australia. METHODS: A 12-month retrospective study was conducted at Princess Margaret Hospital using medication chart records randomly selected from 145,550 patient encounters from the Emergency Department, Inpatient Wards and Outpatient Clinics. Patient and prescribing data were collected. Drugs were classified as off-label or unlicensed based on Australian registration data. A hierarchical system of age, indication, route of administration and dosage was used. Drugs were classified according to the

Anatomical Therapeutic Chemical Code. RESULTS: A total of 1,037 paediatric patients were selected where 2,654 prescriptions for 330 different drugs were prescribed to 699 patients (67.4%). Most off-label drugs (n = 295; 43.3%) were from the nervous system; a majority of unlicensed drugs were systemic hormonal preparations excluding sex hormones (n = 22; 32.4%). Inpatients were prescribed more off-label drugs than outpatients or Emergency Department patients (p < 0.0001). Most off-label prescribing occurred in infants and children (31.7% and 35.9% respectively) and the highest percentage of unlicensed prescribing (7.2%) occurred in infants (p < 0.0001). There were 25.7% of off-label and 2.6% of unlicensed medications prescribed across all three settings. Common reasons for off-label prescribing were dosage (47.4%) and age (43.2%). CONCLUSION: This study confirmed off-label and unlicensed use of drugs remains common. Further, that prevalence of both is influenced by the clinical setting, which has implications in regards to medication misadventure, and the need to have systems in place to minimise medication errors. Further, there remains a need for changes in the regulatory system in Australia to ensure that manufacturers incorporate, as it becomes available, evidence regarding efficacy and safety of their drugs in children in the official product information.


The journey from traffic offender to severe road trauma victim: destiny or preventive opportunity?
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BACKGROUND: Road trauma is a leading cause of death and injury in young people. Traffic offences are common, but their importance as a risk indicator for subsequent road trauma is unknown. This cohort study assessed whether severe road trauma could be predicted by a history of prior traffic offences.

METHODOLOGY AND PRINCIPAL FINDINGS: Clinical data of all adult road trauma patients admitted to the Western Australia (WA) State Trauma Centre between 1998 and 2013 were linked to traffic offences records at the WA Department of Transport. The primary outcomes were alcohol exposure prior to road trauma, severe trauma (defined by Injury Severity Score >15), and intensive care admission (ICU) or death, analyzed by logistic regression. Traffic offences directly leading to the road trauma admissions were excluded. Of the 10,330 patients included (median age 34 years-old, 78% male), 1955 (18.9%) had alcohol-exposure before road trauma, 2415 (23.4%) had severe trauma, 1360 (13.2%) required ICU admission, and 267 (2.6%) died. Prior traffic offences were recorded in 6269 (60.7%) patients. The number of prior traffic offences was significantly associated with alcohol-related road trauma (odds ratio [OR] per offence 1.03, 95% confidence interval [CI] 1.02-1.05), severe trauma (OR 1.13, 95%CI 1.14-1.15), and ICU admission or death (OR 1.10, 95% CI 1.08-1.11). Drink-driving, seat-belt, and use of handheld electronic device offences were specific offences strongly associated with road trauma leading to ICU admission or death—all in a 'dose-related' fashion. For those who recovered from road trauma after an ICU admission, there was a significant reduction in subsequent traffic offences (mean difference 1.8, 95% CI 1.5 to 2.0) and demerit points (mean difference 7.0, 95% CI 6.5 to 7.6) compared to before the trauma event.

SIGNIFICANCE: Previous traffic offences were a significant risk factor for alcohol-related road trauma and severe road trauma leading to ICU admission or death.


Breast Tissue Composition and Immunophenotype and Its Relationship with Mammographic Density in Women at High Risk of Breast Cancer.
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AIM: To investigate the cellular and immunophenotypic basis of mammographic density in women at high risk of breast cancer.

METHODS: Mammograms and targeted breast biopsies were accrued from 24 women at high risk of breast cancer. Mammographic density was classified into Wolfe categories and ranked by increasing density. The histological composition and immunophenotypic profile were quantified from digitized haematoxylin and eosin-stained and immunohistochemically-stained (ERalpha, ERbeta, PgR, HER2, Ki-67, and CD31) slides and correlated to mammographic density.

RESULTS: Increasing mammographic density was significantly correlated with increased fibrous stroma proportion (rs (22) = 0.5226, p = 0.0088) and significantly inversely associated with adipose tissue proportion (rs (22) = -0.5409, p = 0.0064). Contrary
to previous reports, stromal expression of ERalpha was common (19/20 cases, 95%). There was significantly higher stromal PgR expression in mammographically-dense breasts (p=0.026).

CONCLUSIONS: The proportion of stroma and fat underlies mammographic density in women at high risk of breast cancer. Increased expression of PgR in the stroma of mammographically dense breasts and frequent and unexpected presence of stromal ERalpha expression raises the possibility that hormone receptor expression in breast stroma may have a role in mediating the effects of exogenous hormonal therapy on mammographic density.


Association between the Advanced Glycosylation End Product-Specific Receptor Gene and Cardiovascular Death in Older Men.

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Advanced glycosylation end product-specific receptor (AGER) signaling has been implicated in atherosclerosis. The aim of this study was to evaluate whether a common genetic variation in the AGER gene is associated with cardiovascular (CV) death. We included 1304 older men who were genotyped for rs1035798:C>T, which is a single nucleotide polymorphism (SNP) mapped to the third intron of AGER. Cox proportional hazard analysis was used to estimate the association of rs1035798:C>T with CV death. In addition we analyzed total RNA extracted from carotid atherosclerosis biopsies of 18 patients that did or did not have recent symptoms of cerebrovascular embolization by quantitative real-time reverse transcription PCR (qRT-PCR). The minor T-allele of rs1035798:C>T was found to be associated with CV death under dominant (HR = 1.43, 95% CI: 1.01-2.02, P = 0.04) and recessive (HR = 2.05, 95% CI: 1.11-3.81, P = 0.02) models of inheritance even after adjustment for traditional cardiovascular risk factors. No association was found between rs1035798:C>T and non-CV death. qRT-PCR results suggested that median relative expression of AGER isoform 1 and isoform 6 transcripts were approximately 6- (P = 0.01) and 2-fold (P = 0.02) greater, respectively, within carotid biopsies of symptomatic compared to asymptomatic patients. These data suggest that the minor (T) allele of rs1035798:C>T represents an independent susceptibility factor for CV death. The expression of AGER isoforms is different in atheroma from patients with recent symptoms. Further studies are needed to investigate if rs1035798:C>T influences the alternative splicing of AGER.


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A comparison of two methods of foot health education: The Fremantle Diabetes Study Phase II.

Baba M, Duff J, et al.

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Aims To compare the effectiveness of two different methods of education on foot health, behaviours and attitudes in patients with type 2 diabetes. Methods Community-based patients were consecutively allocated to written education (Group A) or an interactive educator-led session (Group B). A quantitative Foot Score (maximum 90 points score based on severity of treatable pathology), the Nottingham Assessment of Functional Foot Care (NAFFC) survey score (maximum 30 points reflecting frequency of foot care behaviours) and a 6-question survey of attitudes to foot complications were administered at baseline and 3 months. Results 154 patients (mean +/- SD age 68 +/- 10 years, 59.7% males, median [interquartile range] diabetes duration 11.5 [5.6-18.9] years) were recruited. There was a greater change (Δdelta) in Foot Score from baseline to 3 months in Group A (8.3 +/- 3.5, Δdelta; -1.8 (95% CI: -2.4 to -1.2) vs Group B (6.8 +/- 2.6, Δdelta; -0.1 (-0.7 to 0.4); P < 0.001), but no change in NAFFC survey score in either group (P = 0.13). In the attitudes survey, Group B felt they better understood how to prevent foot complications than Group A after education (P = 0.031). Conclusions Written information was more effective at improving foot health while interactive education improved confidence in undertaking preventive measures, suggesting that the most effective foot care education should include both components.

Publication Types: Review

**Long term locomotor function in individuals with lower limb amputation following discharge from rehabilitation.**

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Background: In Australia there is limited information on long term locomotor outcomes of people with lower limb amputation after rehabilitation discharge1,2. Roffman et al demonstrated that indigenous status was not predictive of prosthetic non-use however locomotor function of Aboriginal people has not been reported despite high rates of diabetes related amputation and poor health outcomes. The Locomotor Capabilities Index 5 (LCI5) is a reliable and valid measure of self reported locomotor function for people with lower limb amputation3, Aim: The study aims were to: 1. Quantify prosthetic use for locomotor activities in people with lower limb amputation who have been discharged from rehabilitation in Western Australia. 2. Determine if self reported locomotor function after rehabilitation discharge was different between prosthetic users and non-users, and diagnostic user groups including those with Aboriginal ethnicity, age >58 years, amputation above transtibial level, bilateral amputation, diabetes, high comorbidities, atraumatic amputation, males and the remaining prosthetic user cohort. Method: 201 consecutive participants with lower limb amputation from Royal Perth Hospital, the state amputee rehabilitation centre were recruited. Medical records were audited for descriptive characteristics. Participants were prospectively interviewed at median, 1.5 (IQR, 1.2 to 2.2) years after discharge using the LCI5 and a previously piloted questionnaire regarding their prosthetic use, falls history, functional ability, amputation, general health and demographic details. Time prosthetic use ceased relative to physiotherapy discharge and reasons for prosthetic non-use were recorded for non-users. Descriptive statistics and Mann Whitney U Tests were used to determine if locomotor capabilities were significantly different between prosthetic users and non-users and the diagnostic user groups. Results: A total of 26% (52) of participants were prosthetic non-users and 74% (149) users. Prosthetic non-users (median, 4 IQR, 1 to 11) reported significantly lower Basic, Advanced and Total locomotor capabilities (z = 8.13, p < .001) than users (median, 24 IQR, 18 to 28). LCI5 scores were significantly different (z > 2.10, p < .036) for all diagnostic groups except the Aboriginal (z = 1.17, p = .25) and amputation above transtibial level (z = 1.56, p = .12) sub-groups. Ceiling effect was 25% for Total LCI5 score and greatest in the <58 years and traumatic amputation sub-groups. Discussion & Conclusion: This was the first study in an Australian cohort with lower limb amputation to report long term locomotor function after rehabilitation discharge and demonstrate that locomotor function was not significantly different for Aboriginal people. Ceiling effect in younger participants with traumatic amputation and significantly poorer LCI5 scores for prosthetic non-users and the diagnostic user groups were consistent with past findings. Self reported locomotor performance after rehabilitation discharge using the LCI5 may inform clinical decision making and service model planning.

Publication Types: Conference Abstract


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**Locomotor performance characteristics following lower limb amputation.**

Roffman CE, Buchanan J, et al.

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Background: Locomotor skills have been demonstrated as predictors of prosthetic non-use1. However, there is a lack of consensus on which performance measures should be used to evaluate people with lower limb amputation during rehabilitation2 and limited knowledge on how performance in the functional domains of velocity, distanced walked and balance during rehabilitation relates to future ability to use a prosthesis. Aims: The study objectives were to determine: 1. If performance measures assessed during rehabilitation could identify individuals at high risk of prosthetic non-use 12 months post-discharge. 2. If diagnostic groups at risk of prosthetic non-use including people with Aboriginal ethnicity, older age, amputation above transtibial level, bilateral lower limb amputation, atrumatic amputation, diabetes and high comorbidities had poorer performance measure results. Method: Medical records of 201 consecutive participants with lower limb amputation from Royal Perth Hospital, the state amputee rehabilitation centre were retrospectively audited for 10m walk (10MWT), timed up and go (TUGT), 6 minute walk (6MWT) and four square step (FSST) tests and descriptive variables. Participants were interviewed at median 1.5 (interquartile range, 1.2 to 2.2) years post-discharge to identify prosthetic users, non-users and time prosthetic use ceased. Receiver operator characteristic curves were generated to determine performance measure thresholds and relative risk (RR) for prosthetic non-use. Mann Whitney U Tests were used to determine if locomotor performance of diagnostic groups at risk of non-use were significantly different from the remaining cohort. Results: At 12 months post-discharge 18% (36) of participants were prosthetic non-users. Performance measure thresholds and RR of prosthetic non-use (95% CI) were: 10MWT: If velocity was < 0.44 ms-1 (Area Under the Curve (AUC) = 0.743), RR of non-use = 2.76 (Confidence Interval (CI), 1.83 to 3.79, p < .0001). 6MWT: If distance walked was < 191 m (AUC = 0.788), RR of non-use = 2.84 (CI, 2.05 to 3.48, p < .0001). TUGT: If time was > 21.4s (AUC = 0.796), RR of non-use = 3.17 (CI, 2.17 to 4.14, p < .0001). FSST: If time was > 36.6s (AUC = 0.762), RR of non-use = 2.76 (CI, 1.99 to 3.39, p < .0001). Only 25% of the total cohort were able to perform the FSST. 10MWT was systematically different (p < .025) for diagnostic groups including age >58 years, high comorbidities, bilateral and above transtibial amputation but was better at predicting prosthetic non-use than locomotor performance of diagnostic groups. Discussion & Conclusion: Locomotor performance during rehabilitation may identify future risk of prosthetic non-use. Similar to past studies locomotor performance was poorer in those with amputation above transtibial level, high comorbidities, bilateral lower limb amputation and older age. Clinical utility was greatest for the 10MWT. Validation is warranted.

Publication Types: Conference Abstract

Lipids were extracted for fatty acid analysis and SPMs were quantitated by mass spectrometry. Gene expression was determined from women (n = 51) enrolled in a randomised, placebo controlled trial of n-3 PUFA supplementation from 20-week gestation. In all placentas, but concentrations were not significantly increased by n-3 PUFA supplementation. Placental DHA levels were negatively associated with maternal and cord blood erythrocytes. Supplementation with n-3 PUFAs increased placental docosahexaenoic acid (DHA) levels, but not eicosapentaenoic acid (EPA) levels (P<0.05), and increased the levels of the SPM precursors 18-hydroxyeicosapentaenoic acid and 17-hydroxydocosahexaenoic acid (17-HDHA) by two- to threefold (P<0.0005). RvD1, 17R-RvD1, RvD2 and PD1 were detectable in all placentas, but concentrations were not significantly increased by n-3 PUFA supplementation. Placental DHA levels were positively associated with maternal and cord DHA levels (P<0.005), and with placental 17-HDHA concentrations (P<0.0001). Placental mRNA expression of PTG52, IL1beta, IL6 and IL10 was unaffected by n-3 PUFA supplementation, but TNFalpha expression was increased by 14-fold (P<0.05). We conclude that n-3 PUFA supplementation in pregnancy i) enhances placental accumulation of DHA and SPM precursors, ii) does not alter placental EPA levels, and iii) has no stimulatory effects on inflammatory gene expression. Further studies are required to ascertain the biological significance of SPMs in the placenta and the potential immunomodulatory effects of elevating placental SPM levels.


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Letter to the Editor: "Risk factors for postoperative pneumonia after lung cancer surgery and impact of pneumonia on survival".
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Impairments after curative intent treatment for non-small cell lung cancer: A comparison with age and gender-matched healthy controls.
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BACKGROUND: The aim of this study was to compare measures of exercise capacity, health-related quality of life (HRQoL), muscle force, lung function and feelings of anxiety and depression in people after curative intent treatment for NSCLC with age and gender-
matched healthy controls.

METHODS: This cross-sectional study included 23 participants (68 +/- 10yr; 16 females), 6-10 weeks after lobectomy for NSCLC or, for those who received adjuvant chemotherapy, 4-8 weeks after their last cycle. The study also included 20 age and gender-matched healthy controls (69 +/- 5yr; 13 females). All participants underwent measurements of exercise capacity (cycle-ergometry test [CPET] and 6-min walk test [6MWT]), HRQoL (Short-Form 36 general health survey [SF-36]), handgrip force, quadriceps torque, lung function and feelings of anxiety and depression.

RESULTS: When compared with data collected in healthy controls, those in the NSCLC group demonstrated impairments in the peak rate of oxygen consumption (15 +/- 3 versus 24 +/- 7 ml kg(-1)min(-1); p < 0.001) and maximum work rate (75 +/- 25 versus 127 +/- 51Watts; p < 0.001) measured during the CPET, and 6-min walk distance (494 +/- 77 versus 649 +/- 61 m; p < 0.001). Similarly, impairments were demonstrated in all domains of the SF-36 (p < 0.01 for all), isometric handgrip force (28 +/- 7 versus 34 +/- 10 kg; p = 0.02), and all measures of lung function (p < 0.001 for all). A higher score for depression was also seen (3.0 +/- 2.5 versus 1.5 +/- 1.6; p = 0.03). There was no difference between the groups in isometric quadriceps torque or feelings of anxiety.

CONCLUSIONS: After curative intent treatment for NSCLC, compared to healthy controls, impairments were demonstrated in laboratory and field-based measures of exercise capacity, HRQoL, isometric handgrip force and lung function. Although people after curative intent treatment for NSCLC reported greater feelings of depression, these levels were below those considered clinically relevant. These findings suggest that people after curative intent treatment for NSCLC may benefit from rehabilitative strategies to optimise exercise capacity and HRQoL. Copyright © 2015 Elsevier Ltd. All rights reserved.


Pleural empyema caused by Klebsiella oxytoca: A case series.

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We report on 19 patients from Western Australia of pleural empyema with Klebsiella oxytoca, an organism never before reported in association with this condition. Median age was 65 years, 14/17 (83%) had been in hospital within 30 days prior to diagnosis, 12/18 (67%) had active cancer, 9/17 (53%) had been in intensive care and 7/17 (41%) had prior surgery. Nine patients died at the time of censure, five within 90 days of infection.


Do all patients with idiopathic pulmonary fibrosis warrant a trial of therapeutic intervention? A pro-con perspective.

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Idiopathic pulmonary fibrosis (IPF) is an incurable condition that is characterized by progressive pulmonary fibrosis, architectural distortion of the lung and loss of gas exchange units. Until recently, there was no effective treatment for this condition. However, there were two landmark trials published earlier this year, which have changed the management of this condition. Pirfenidone (Assessment of Pirfenidone to Confirm Efficacy and Safety in Idiopathic Pulmonary Fibrosis trial) and nintedanib (Efficacy and Safety of Nintedanib in Idiopathic Pulmonary Fibrosis-1 and -2 trials) have both demonstrated positive outcomes in patients with IPF. In this perspective, we critically discuss the role of these agents in IPF and in the broader pulmonary fibrosis population.

Publication Types: Review


Respirology. 2015; 20: 142.

Effects of human rhinovirus infection in large and small airway of lung transplant recipients.

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Respirology. 2015; 20: 126.

**Human pleural fluid is a potent growth medium for bacteria especially Streptococcus pneumoniae.**

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Aim: Empyema can complicate pneumonia, and is defined by the presence of bacteria and/or pus in pleural effusions. Streptococcus pneumoniae is one of the commonest bacteria isolated from empyema fluid. It is believed that bacteria are shed from infected lung/pleural tissue into the fluid. However, the subsequent biological interactions between bacteria and pleural fluid (and its cellular content) have not been studied adequately. We hypothesize that pleural fluid presents a rich culture medium that facilitates bacterial growth. This study aims to determine whether pleural fluid, with/without its cellular content, enhances proliferation of *S. pneumoniae* and other common pneumonia/empyema pathogens. Methods: LAEC and SAEC primary cell cultures were established from bronchial brushings obtained at surveillance bronchosopies and infected with human rhinovirus 1B (HRV1B) at various multiplicities of infection (MOI). In addition specific cultures were also treated with azithromycin (1 mug/ml) prior to HRV1B infection. Cell viability and apoptosis were measured post infection. RNA and supernatants were collected and viral receptor, inflammatory cytokine production measured. Results: Cell viability was significantly decreased in both LAEC and SAEC after infection with HRV1B and appeared enhanced in LAEC. HRV1B receptor, namely low-density lipoprotein (LDL) receptor, gene expression was up-regulated more so in LAEC (-2 fold) than SAEC (-1.1 fold). Viral replication was also found to be similar between LAEC (-4671 HRV copy/#ng RNA) and SAEC (-3577 HRV copy/#ng RNA) and did not differ to LAEC of healthy controls. Apoptosis was significantly elevated in both LAEC and SAEC (-400 fold in both) after HRV1B infection in a MOI-dependant manner (p < 0.001). Treatment of cells with azithromycin did not reduce viral replication or apoptotic activity in both LAEC and SAEC. However, azithromycin did significantly reduce IL-6 (>2 fold), IL-8 (>2 fold) and RANTES (>4 fold) production in both LAEC and SAEC (p < 0.05). Conclusion: HRV1B actively infects LAEC and more significantly SAEC of lung transplant recipients which may have severe long term consequences. Although azithromycin was ineffectively at reducing viral replication, its anti-inflammatory effects warrant further investigation.

Publication Types: Conference Abstract


Respirology. 2015; 20: 118.

**A case of fatal hyperammonemia in a lung transplant recipient in Australia.**

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Background: We describe a case of fatal encephalopathy and seizures 11 days post-bilateral sequential lung transplantation associated with significantly elevated plasma ammonia levels. Idiopathic hyperammonemia is recognised as a rare, life-threatening complication of lung transplantation. Findings: A 59 year old Chinese Australian gentleman underwent bilateral sequential lung transplantation for idiopathic pulmonary fibrosis. Both recipient and donor were cytomegalovirus (CMV) IgG positive. Surgery was uncomplicated. Standard induction immunosuppression with basiliximab and methylprednisolone was given, with subsequent addition of cyclosporin, mycophenolate mofetil and empiric peri-operative antibiotics. Early post-operative complications included pulmonary hypertension, atrial fibrillation, fevers and agitation when weaning sedation. By day 8, the patient was fully orientated and conversing with family members. He subsequently deteriorated with confusion and decreased conscious level requiring reintubation on day 10. Computed tomography of the brain showed no acute intracranial pathology. Plasma ammonia level was

significantly elevated at 359 umol/L (normal < 50 umol/L). Hepatic dysfunction was excluded. Urgent therapy including high-dose haemodialfiltration, cessation of cyclosporin, low protein feeds and gut decontamination was commenced. Unfortunately, within 12 hours of the ammonia result, the patient developed generalised tonic-clonic seizures, profound hypotension and cardiopulmonary arrest (pulseless electrical activity) with no return of spontaneous circulation despite prolonged cardiopulmonary resuscitation. We postulate that the unexpected deterioration was secondary to idiopathic hyperammonemia associated with lung transplantation, leading to fatal cerebral oedema. Coroner’s post-mortem revealed no other cause of death and no underlying urea-cycle abnormality. Conclusion: This is the first case of fatal post-transplantation hyperammonemia described in Western Australia. Idiopathic hyperammonemia is a serious complication of lung transplantation. Its aetiology is unknown and precipitants unclear. Successful management has previously been described in case reports. Prompt diagnosis is essential and urgent treatment advised. Further research is warranted for this rare but fatal condition.

Respirology. 2015; 20: 108.

**Bronchoscopic endobronchial valve insertion for bronchopleural fistula in a patient with ARDS and severe hypoxaemia on mechanical ventilation.**

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Background: We describe a patient with severe pneumonia complicated by acute respiratory distress syndrome (ARDS), lung abscess and bilateral pneumothoraces with pneumomediastinum secondary to a bronchopleural fistula. The bronchopleural fistula was managed by bronchoscopic insertion of endobronchial valves to collapse the left lower lobe. Findings: A 35 year old alcoholic man was admitted to intensive care with severe sepsis, bilateral pneumonia and alcoholic ketoacidosis. He developed ARDS requiring mechanical ventilation and subsequently extracorporeal membrane oxygenation (ECMO) for 10 days and tracheostomy formation. Following ECMO wean, the patient developed a left intra-parenchymal lung abscess and possible empyma for which an intercostal chest catheter was inserted. He then developed pneumomediastinum, pneumomediastinum and pneumothorax secondary to a bronchopleural fistula. This compromised effective mechanical ventilation with the patient requiring airway pressure release ventilation (APRV) on FiO<sub>2</sub> 0.8 and peak pressures 27-33 cm H2O, with a PaO<sub>2</sub> 60 mm Hg and PaCO<sub>2</sub> of 64 mm Hg. A temporary bronchial blocker was inserted to collapse the left lower lobe. Definitive therapy with bronchoscopic insertion of 7 endobronchial valves (PulmonX Inc Zephyr valves) was achieved. The patient required 3 months in intensive care and 4 months in hospital. He was transferred to a rehabilitation unit before return to independent living. The endobronchial valves were removed 6 months after insertion with good clinical and radiological outcomes. Conclusion: We describe the successful use of endobronchial valve insertion in a septic patient with ARDS and profound hypoxaemia on mechanical ventilation with a bronchopleural fistula. Radiological differentiation between intra-parenchymal abscess and empyma can be difficult but is important to guide appropriate therapy. Bronchoscopic insertion of endobronchial valves to treat bronchopleural fistulae has been described in a variety of settings. This case illustrates its potential usage in a critically unwell and hypoxaemic patient who would not have tolerated surgical intervention.

Respirology. 2015; 20: 108.

**Low rates of beta-blocker use for incident events of ischaemic heart disease in hospitalised patients with acute exacerbations of COPD.**

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Aim: The prevalence of ischaemic heart disease (IHD) in chronic obstructive pulmonary disease (COPD) is high and associated with increased mortality.1 Beta-blockers reduce mortality after myocardial infarction by 40% with similar risk-reduction profile in COPD patients on subgroup analysis.2 Beta-blockers have been shown to be safe to use in COPD.3 We aim to determine the prevalent use and incident in-hospital initiation of beta-blockers in patients admitted with acute exacerbations of COPD (AECOPD) complicated by inpatient IHD events. We compare these with use of other drug classes used in primary and secondary IHD prevention. Methods: We conducted a retrospective cohort study on patients aged >40 years admitted to a tertiary referral centre between 1st January 2012 and 31st December 2012 with a diagnosis of AECOPD. Only the first admission of the year for each patient was included in the analysis. Data was collected from hospital electronic databases and discharge summaries. IHD events included acute coronary syndromes and stable angina. We measured the prevalent use and incident initiation of beta-blockers, antiplatelet agents, statins and angiotensin-converting enzyme inhibitors (ACEI)/ angiotensin II receptor blockers (ARB). Results: 366 cases were identified as the first admission in 2012 for AECOPD. 6.8% (25/366) of patients had an IHD event during their admission. 64% (16/25) of these patients had a prior history of IHD. Inpatient mortality rate was 16% (4/25). The prevalent use and incident initiation of cardiovascular medications are displayed in Table 1. Conclusion: The prevalent use of beta-blockers in patients with incident IHD events was low compared to other risk-modifying agents. Furthermore, there is a lower incident initiation of beta-blockers compared to anti-platelet agents despite established evidence for utility of both for secondary prevention in IHD. (Table Presented).

Publication Types: Conference Abstract

Respirology. 2015; 20: 108.

**Low rates of beta-blocker use for incident events of ischaemic heart disease in hospitalised patients with acute exacerbations of COPD.**

Respirology. 2015; 20: 108.

**Low rates of beta-blocker use for incident events of ischaemic heart disease in hospitalised patients with acute exacerbations of COPD.**

Publication Types: Conference Abstract

Respirology. 2015; 20: 104.

**Low rates of beta-blocker use for incident events of ischaemic heart disease in hospitalised patients with acute exacerbations of COPD.**

Publication Types: Conference Abstract
Is idiopathic pulmonary fibrosis more indolent in the elderly population?

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Background: Idiopathic pulmonary fibrosis (IPF) results in severe progressive fibrosis of the lung parenchyma, and occurs more frequently in the elderly population. Survival from diagnosis has a mean of 2.5 yrs, with considerable variation in the natural history of this condition. It has been hypothesized elderly IPF patients may have less rapidly progressive disease than younger IPF patients.

Aim: To determine whether elderly IPF patients have a different disease course than younger IPF patients. Methods: The Australian IPF Registry recruits IPF patients across Australia, collating patient questionnaires, physiological data and vital status every six months. Disease progression was considered present when either there was a relative fall in FVC > 10% or DLco > 15%. We explored the relationship between age tertiles and change in physiological measures and outcome. Results: In October 2014, 535 IPF patients have consented to the Registry (365 male; mean age 71.1 +/- 8.7 yrs, range 32-91 yrs). Age was divided into equal tertiles including: 32-66 yrs, 67-73 yrs and 74-91 yrs. Baseline pulmonary function included: FVC 2.7 +/- 0.8 L (82.0 +/- 21.0%), DLco 47.9 +/- 21.1%. Six-minute walk test (6MWT) distance: median 440.5 (range 48-706) m, with resting SpO2 < 94% and end-exercise 88.6 +/- 7.5%. Over 32 months follow-up, 223 patients had serial pulmonary function tests. Of these patients, median change in FVC was -26.3% (-100.3% to 89.2%) and DLco was -9.3% (-78.0% to 173.4%), with 169 (75.6%) having significant disease progression and 44 (19.7%) dying during the follow-up period. Participants in the oldest tertile (>74 yrs) did have less severe decline in FVC (19.6 +/- 19.9%) compared to younger patients (<74 yrs, 28.9 +/- 26.8%); p = 0.005 (Wilcoxon's ranksum test). However, there was no difference in disease progression and/or death between the age tertiles (Cox regression analysis). Conclusion: Older IPF patients may have less rapid decline in FVC than younger IPF patients. However, disease progression and death occur uncommonly, and no significant difference in disease progression and/or death was demonstrated between age groups.

Prevalence of occupational and environmental exposures in Australian patients with idiopathic pulmonary fibrosis (1 PF).

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Background: Idiopathic pulmonary fibrosis (IPF) is a fatal lung disease, with no current cure. IPF is currently considered idiopathic by definition, but key environmental exposures may actually be important to its pathogenesis. Aim: To use the Australian IPF Registry to undertake a preliminary analysis of the prevalence of occupational and environmental exposures from the first 30 months of Registry data. To demonstrate how collaborating can create a national research platform. Methods: The Australian IPF Registry is a national cohort of IPF patients established in 2012 by the Lung Foundation Australia. Data collected include a questionnaire with a detailed exposure history to tobacco, environment, and dust exposures. The prevalence of exposures and associations between rate of exposure. Results: 501 patients have consented to the Registry. 389 (77.6%) have completed their exposure questionnaires (mean +/- SD: age 72.3 +/- 8.9 yrs; 337 male; FVC 81.6 +/- 21.8% predicted; DLco 47.0 +/- 19.5% predicted ). Smoking history: 266 ex-smokers, 11 current smokers, 110 non-smokers. Environmental exposures are reported in the table. Occupational exposures include asbestos in 150 (40.2%; 95% CI: 35.4, 45.3), silica in 47 (12.4%; 9.4, 16.2), chemicals/ gases in 181 (47.6%; 42.7, 52.7) and dusty environments in 196 (51.0%; 46.1, 56.0). Conclusion: IPF patients report a high prevalence of potentially adverse exposures. A case control study is needed to determine if these exposures are more relevant to IPF. (Table Presented).

Beta-blockers are underutilised in patients with COPD.

Lim K, Loughrey S, et al.
Multidisciplinary review of idiopathic pulmonary fibrosis (IPF) patients: Review of clinical diagnosis for patients referred to the Australian IPF Registry.

Glaspole I, Goh N, et al.

Aim: Idiopathic pulmonary fibrosis (IPF) is a severe progressive condition with a median survival from diagnosis of 3-5 yrs. Diagnostic accuracy improves following multidisciplinary discussion. In Australia, the collaborative national initiative, the Australian IPF Registry has three review (Radiology, Histopathology and Clinical) panels that consider the IPF diagnosis according to ATS/ERS Guidelines. Methods: The Australian IPF Registry, established by the Lung Foundation Australia, recruits IPF patients across Australia collating data including patient questionnaires and physiological data every six-months. All HRCTs and surgical biopsies are reviewed independently by 3 reviewers, a consensus result is decided by the final reviewer. Three clinical reviewers independently review Registry data to decide a MDT "Registry diagnosis". We report the Registry diagnosis in the first 68 patients undergoing MDT review. Results: 535 IPF patients have consented (365 male; mean age 71.1 +/- 8.7 yrs). To date, the MDT panels have reviewed 68 subjects for a Registry diagnosis. Of these, 34 (50%) had a diagnosis of IPF, 3 (4.4%) probable IPF, 13 possible IPF (19.1%) and 18 (26.5%) were inconsistent with IPF. Baseline pulmonary function for Registry participants included: FVC 2.7 +/- 0.8 L (82.0 +/- 21.0%) (SD), DLco 47.9 +/- 21.1% (SD). Six-minute walk test (6MWT) distance: median 440.5 (range 48 to 706)m, with resting SpO2 95.2 +/- 3.5% (SD) and end-exercise 86.3 +/- 7.5% (SD). Conclusion: Although the majority of IPF patients referred had a diagnosis consistent with IPF, a minority were inconsistent with IPF. Given the profound prognostic implications of this diagnosis, this suggests that all patients undergo multidisciplinary review at diagnosis. 

Publication Types: Conference Abstract

Vitamin d and respiratory health in the busselton healthy ageing study.


Aim: Several studies have reported an association between respiratory disease such as asthma, COPD, respiratory infections and low serum Vitamin D (25(OH)D) levels. Serum 25(OH)D level was assessed as an independent risk factor for respiratory health outcomes in the Busselton Healthy Ageing Study (BHAS) after adjustment for potential confounders. Methods: A cross-sectional questionnaire-
Compared with any change seen in the control group, those in the exercise training group demonstrated greater gains in the peak decrements in physical and mental components of HRQoL, handgrip force, daily physical activity and all measures of lung function associated with VitD level but not after adjustment for chronic illness. The trend across all Models will be further tested in the full BHAS cohort (~4000).

Aim: Anxiety and depression are common in people with chronic obstructive pulmonary disease (COPD). This study investigated the efficacy of two formats of cognitive behavioural therapy (CBT): group therapy versus a self-paced simulation-based learning resource (DVD) to reduce anxiety and depression, and improve quality of life amongst COPD patients compared to usual care (UC). Methods: COPD patients were screened for anxiety or depression via the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI-II). Those with symptomatology were randomised into three interventions: CBT, DVD or UC. All groups were followed-up at post-intervention, three and six months via telephone or home visit. Results of the BAI, BDI-II and St George's Respiratory Questionnaire (SGRQ) were assessed and provided as mean +/- SEM. Results: In total, 242 participants were recruited, of whom 51.2% (n = 124) had anxiety and/or depression. There was a significant treatment by time effect for the SGRQ 'impact' score that examines psycho-social functioning factors; higher scores suggest poorer quality of life (QoL). Compared to baseline, the UC group's average impact score was significantly worse at six months (57.0 +/- 3.55 vs. 57.4 +/- 3.55, p < 0.001). Both UC and CBT groups also had significantly poorer impact scores than the DVD group (57.0 +/- 3.55 vs. 57.4 +/- 4.99 vs. 40.2 +/- 5.40, p < 0.05). There were no differences over time within the DVD group, suggesting it was the only group not to see significant deterioration. There was no effect of treatment over time by BAI, BDI and SGRQ symptoms scores or SGRQ activity score. Conclusion: Overall, the DVD appears to improve QoL of COPD patients but not anxiety or depression symptomatology. In comparison, group CBT did not appear to be efficacious for improving anxiety, depression or quality of life, possibly due to practicalities of attendance leading to high drop-out rates.

Aims: In people following curative intent treatment for non-small cell lung cancer (NSCLC) to; (i) compare measures of exercise capacity, health-related quality of life (HRQoL), muscle force, physical activity and lung function with healthy controls and, (ii) investigate the effects of supervised exercise training on these outcomes. Methods: Part A included people 6 to 10 weeks after lobectomy for NSCLC or, for those who required adjuvant chemotherapy, 4 to 8 weeks after completion of their last cycle. Stratified sampling was used to recruit age and gender-matched healthy controls. Measurements were collected of the aforementioned outcomes. Part B was a single-blinded randomised controlled trial. After completing the pre-intervention assessments, participants were randomised to 8 weeks of exercise training or phone calls (control group). Post-intervention assessments were completed and intention-to-treat analyses were undertaken. Results: Part A included 23 people with NSCLC (68 +/- 10 yr; 16 females) and 20 healthy controls (69 +/- 5 yr; 13 females). Compared with healthy controls, people with NSCLC had reduced exercise capacity and decrements in physical and mental components of HRQoL, handgrip force, daily physical activity and all measures of lung function (p < 0.03 for all). For Part B, 9 and 8 participants were randomised to the exercise training and control groups, respectively. Compared with any change seen in the control group, those in the exercise training group demonstrated greater gains in the peak
Cardiovascular and cerebrovascular events occur frequently in acute exacerbations of COPD and are associated with poor outcomes.

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Aim: 1-year mortality following acute exacerbation of chronic obstructive pulmonary disease (AECOPD) has been described at 20-35%, with cardiovascular events accounting for 19-37% of deaths. We aim to determine the incidence of cardiovascular and cerebrovascular (CV) events during admissions for AECOPD and their impact on patient outcomes. Methods: We conducted a retrospective cohort study on patients aged > 40 years admitted to a tertiary referral centre between 1st January 2012 and 31st December 2012 with a primary or secondary diagnosis of AECOPD. Only the first admission of the year for each patient was included in the analysis. The cardiovascular events analysed were ischaemic heart disease (IHD), congestive cardiac failure (CCF) and tachyarrhythmias. The cerebrovascular events included transient ischaemic attacks (TIA) and strokes (ischaemic/haemorrhagic). Results: 366 unique presentations for AECOPD in 2012 were identified. 16% (57/366) of patients were found to have had one or more incident CV events during their admission. A total of 70 events were identified - 25 IHD, 27 CCF, 16 tachyarrhythmias and 2 cerebrovascular events. Hospital morbidity and mortality are presented in Table 1. Of the 11 patients who died, 4 patients had cardiovascular events and 1 patient had a cerebrovascular event. (P values are compared against AECOPD without CV events.) Conclusion: Cardiovascular and cerebrovascular events are frequent in patients admitted with AECOPD. Patients with CV events have a significantly longer length of stay and increased in-hospital mortality. Further research is warranted to address the potential role of primary prevention of cardiovascular and cerebrovascular complications in COPD patients. (Table Presented).

Children with bronchopulmonary dysplasia have a normal response to a maximal exercise test.

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Aim: Evidence regarding the ventilatory response to exercise in children born preterm is limited. The aim of this study was to determine the ventilatory response to exercise in term born and preterm children at age 9-11. Method: Pre-term children (<32 weeks gestation), with and without a diagnosis of BPD (>28 days supplemental O2, assessed at 36 week post menstrual age), and term born healthy controls were included in the study. Subjects performed spirometry and an incremental treadmill exercise test to volitional exhaustion with breath by breath analysis. Group differences were assessed by one way analysis of variance. The effect of development (gestational age and birth weight z-score), neonatal lung disease (days of supplemental oxygen and ventilatory support), age, weight and lung function (FEV1 and FVC z-scores) were assessed by multivariate linear regression. Results: 88 Children (31 BPD, 28 nonBPD, 29 controls) performed acceptable exercise tests. There were no differences in the following outcome measures for BPD, nonBPD and Controls, respectively: Peak oxygen uptake (peak VO2) (median (SD) (48.5 (6.97) vs. 47.1 (6.29) vs. 47.0 (5.32)ml/min/kg), peak tidal volume (826 (231) vs.1008 (254) vs 861 (252) ml), breathing frequency at peak exercise (66 vs. 54 vs. 59 breaths/min) or breathing reserve (35 (9.6) vs. 35 (9.8) vs 29 (10.8) %). After accounting for age and weight, regression analysis showed peak VO2 was influenced by ventilatory support (r2) (0.255, p < 0.001) and birth weight z-score (0.168, p < 0.05). Tidal volume and breathing frequency were influence by gestational age (0.232 p < 0.05, -0.701 p < 0.05) and birth weight z-score (0.254 p < 0.005, -0.439 p < 0.05). Conclusion: Children with BPD do not have an altered response to exercise compared to healthy children. Peak exercise capacity is reduced in small for gestational age children and those with worse neonatal lung disease. The ventilatory response to exercise is associated with foetal lung development and not the severity of neonatal lung disease. The clinical significance of these findings is unclear.

Use of non-pharmaceutical interventions to reduce the transmission of influenza in adults: A systematic review.

Smith SM, Sonego S, et al.
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transmission by non-pharmaceutical interventions (NPI) has a significant appeal and is often recommended. However, the efficacy of such interventions is unclear. A systematic literature review was undertaken to identify and evaluate the published literature on NPI efficacy to prevent human transmission of influenza virus in adults. Reviewers assessed the quality of eligible studies utilizing the Critical Appraisal Skills Programme for bias and the Scottish Intercollegiate Guidelines Network for methodological quality. Studies were assessed for risk of bias domains of random sequence generation, allocation concealment, attribution bias, selective reporting and blinding. Relevant citations of 2247 were reduced to 100 for full-text evaluation. Only seven met all selection criteria and pooled analysis was not feasible. Of the seven studies, two were randomized controlled trials (RCT) and five were cluster RCT. The main NPI studied were disinfection and hygiene; barriers; and combined NPI. However, these seven RCT had significant design flaws. Only two studies used laboratory confirmed influenza and poor statistical power was a major problem. Positive significant interventions included professional oral hygiene intervention in the elderly and hand washing. Despite the potential for NPI in preventing influenza transmission, there is very limited data available. Hand washing and dental hygiene may be useful, but other interventions have not been fully assessed. Properly designed studies evaluating large populations including 'at risk' patients and in a variety of communities are needed. Copyright © 2015 Asian Pacific Society of Respirology.


Prevalence of oropharyngeal antibiotic-resistant flora among residents of aged care facilities: a pilot study.

Etherton-Beer CD, Inglis T, et al.

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Residents in 11 long-term care facilities, and presenting to a single tertiary hospital site, were sampled to estimate prevalence of oropharyngeal colonization with resistant Gram-negative bacteria. From 124 residents, only one isolate (0.8%; 95% confidence interval 0.0%, 4.4) was multi-resistant (an extended-spectrum beta-lactamase producing Escherichia coli) indicating that different treatment recommendations for respiratory infections in this population may not be justified. Copyright © 2015 Asian Pacific Society of Respirology.

Publication Types: Letter


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PURPOSE: We evaluated the association between chest compression release velocity (CCRV) and outcomes after out-of-hospital cardiac arrest (OHCA). MATERIALS AND METHODS: CPR quality was measured using a defibrillator with accelerometer-based technology (E Series, ZOLL Medical) during OHCA resuscitations by 2 EMS agencies in Arizona between 10/2008 and 06/2013. All non-EMS-witnessed adult (> = 18 years) arrests of presumed cardiac etiology were included. The association between mean CCRV
Rheumatology. 2015; 54(10): 1797-805.

International Consensus for ultrasound lesions in gout: results of Delphi process and web-reliability exercise.

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OBJECTIVE: To produce consensus-based definitions of the US elementary lesions in gout and to test their reliability in a web-based exercise.

METHODS: The process consisted of two steps. In the first step a written Delphi questionnaire was developed from a systematic literature review and expert international consensus. This collated information resulted in four statements defining US elementary lesions: double contour (DC), tophus, aggregates and erosion. The Delphi questionnaire was sent to 35 rheumatology experts in US, asking them to rate their level of agreement or disagreement with each statement. The second step tested the reliability by a web-exercise. US images of both normal and gouty elementary lesions were collected by the participants. A facilitator then constructed an electronic database of 110 images. The database was sent to the participants, who evaluated the presence/absence of US elementary lesions. A group of 20 images was displayed twice to evaluate intra-reader reliability.

RESULTS: A total of 32 participants responded to the questionnaires. Good agreement (>80%) was obtained for US definitions on DC, tophus, aggregates and erosion in the Delphi exercise after three rounds. The reliability on images showed inter-reader kappa values for DC, tophus, aggregates, erosion findings of 0.98, 0.71, 0.54 and 0.85, respectively. The mean intra-reader kappa values were also acceptable: 0.93, 0.78, 0.65 and 0.78, respectively.

CONCLUSION: This, the first consensus-based US definition of elementary lesions in gout, demonstrated good reliability overall. It constitutes an essential step in developing a core outcome measurement that permits a higher degree of homogeneity and comparability between multicentre studies. Copyright © The Author 2015. Published by Oxford University Press on behalf of the British Society for Rheumatology. All rights reserved. For Permissions, please email: journals.permissions@oup.com.


Autosomal recessive transmission of TRAPS in a family with a novel TNFRSF1A mutation.

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Publication Types: Letter


**No additive effect of cannabis on cognition in schizophrenia.**


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BACKGROUND: We aimed to examine the association between lifetime cannabis use and estimates of both premorbid and current cognitive function in psychotic disorders in an Australian cohort.

METHODS: In an Australian multicenter cohort, 1237 participants with an established ICD-10 diagnosis of psychotic disorder were categorised according to history of lifetime cannabis use (non-users, n=354; cannabis users, n=221; cannabis dependency, n=662).

Groups were analyzed according to available indices of cognitive ability: the National Adult Reading Test - Revised (NART-R) for ability prior to illness onset; and the Digit Symbol Coding Test (DSCT) for current ability. Two-way analysis of variance was conducted without any covariate, followed by a two-way analysis of covariance (using age, age at onset of psychiatric illness, premorbid IQ and the Socio-Economic Index for Areas (SEIFA) rankings).

RESULTS: Whilst there appeared to be a significant association between cannabis use and mean DSCT (higher DSCT scores in premorbid IQ and the Socio-Economic Index for Areas (SEIFA) rankings).

No additive effect of cannabis on cognition in schizophrenia. (McKitrick) University of Western Australia, Cardiology Department, Royal Perth Hospital, Perth, WA 6000, Australia (Charles) Anatomical Pathology, Sidra Medical and Research Center, Doha 26999, Qatar

Power, Brian D. School of Medicine, Fremantle, The University of Notre Dame Australia, Fremantle, Australia; South Metropolitan Area Health Service, Perth, Australia; Clinical Research Centre, North Metropolitan Health Service - Mental Health, Perth, Australia.


**Regulator of G protein signaling 5 is a determinant of gestational hypertension and preeclampsia.**

Holobotovsky V, Chong YS, et al.

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Preeclampsia is a systemic vascular disorder of pregnancy and is associated with increased sensitivity to angiotensin II (AngII) and hypertension. The cause of preeclampsia remains unknown. We identified the role of regulator of G protein (heterotrimeric guanine nucleotide-binding protein) signaling 5 (RG5) in blood pressure regulation during pregnancy and preeclampsia. RG5 expression in human myometrial vessels is markedly suppressed in gestational hypertension and/or preeclampsia. In pregnant RG5-deficient mice, reduced vascular RG5 expression causes gestational hypertension by enhancing vascular sensitivity to AngII. Further challenge by increasing AngII results in preeclampsia-like symptoms, namely, more severe hypertension, proteinuria, placental pathology, and reduced birth weight. In pregnant heterozygote null mice, treatment with peroxisome proliferator-activated receptor (PPAR) agonists normalizes vascular function and blood pressure through effects on RG5. These findings highlight a key role of RG5 at the interface between AngII and PPAR signaling. Because preeclampsia is refractory to current standard therapies, our study opens an unrecognized and urgently needed opportunity for treatment of gestational hypertension and preeclampsia.

A systematic review and meta-analysis of the effect of statins on plasma asymmetric dimethylarginine concentrations.


Scientific Reports. 2015; 5: 9902.
tissues. tissue-mimicking phantoms and demonstrate the ability to map elasticity of freshly excised malignant and benign human breast samples. We show that quantification of elasticity can improve the ability of compression OCE to distinguish between tissues, thereby extending the potential for inter-sample comparison and longitudinal studies of tissue elasticity. We validate the technique using a significant reduction in plasma ADMA concentrations following therapy with hydrophilic statins. A weighted meta-regression (WMD) using unrestricted maximum likelihood model was performed to assess the impact of statin dose, duration of statin therapy and baseline ADMA concentrations as potential variables on the WMD between statin and placebo group. In total, 1134 participants in 9 selected RCTs were randomized; 568 were allocated to statin treatment and 566 were controls. There was a significant reduction in plasma ADMA concentrations following statin therapy compared with placebo (WMD: -0.101μM, 95% confidence interval: -0.131 to -0.077, Z = -7.577, p < 0.0001). Subgroups analysis has shown a significant impact of hydrophilic statins (WMD: -0.207μM, 95% CI: -0.427 to +0.013, Z = -7.250, p < 0.0001) and a non-significant effect of hydrophobic statins (WMD: -0.101μM, 95% CI: -0.128 to -0.074, Z = -1.845, p = 0.065). In conclusion, this meta-analysis of available RCTs showed a significant reduction in plasma ADMA concentrations following therapy with hydrophilic statins.

Scientific Reports. 2015; 5: 15538.

Quantitative micro-elastography: imaging of tissue elasticity using compression optical coherence elastography.
Kennedy KM, Chin L, et al.

Kennedy,Kelsey M. Optical+Biomedical Engineering Laboratory, School of Electrical, Electronic & Computer Engineering, The University of Western Australia, 35 Stirling Highway, Crawley WA 6009, Australia. Chin,Lixin. Optical+Biomedical Engineering Laboratory, School of Electrical, Electronic & Computer Engineering, The University of Western Australia, 35 Stirling Highway, Crawley WA 6009, Australia. McLaughlin,Robert A. Optical+Biomedical Engineering Laboratory, School of Electrical, Electronic & Computer Engineering, The University of Western Australia, 35 Stirling Highway, Crawley WA 6009, Australia. Latham,Bruce. PathWest, Fiona Stanley Hospital, Robin Warren Drive, Murdoch, WA 6150, Australia. Saunders,Christobel M. School of Surgery, The University of Western Australia, 35 Stirling Highway, Crawley, WA 6009, Australia. Saunders,Christobel M. Breast Clinic, Royal Perth Hospital, 197 Wellington Street, Perth, WA 6000, Australia. Sampson,David D. Optical+Biomedical Engineering Laboratory, School of Electrical, Electronic & Computer Engineering, The University of Western Australia, 35 Stirling Highway, Crawley WA 6009, Australia. Kennedy,Brendan F. Optical+Biomedical Engineering Laboratory, School of Electrical, Electronic & Computer Engineering, The University of Western Australia, 35 Stirling Highway, Crawley WA 6009, Australia. Probing the mechanical properties of tissue on the microscale could aid in the identification of diseased tissues that are inadequately detected using palpation or current clinical imaging modalities, with potential to guide medical procedures such as the excision of breast tumours. Compression optical coherence elastography (OCE) maps tissue strain with microscale spatial resolution and can delineate microstructural features within breast tissues. However, without a measure of the locally applied stress, strain provides only a qualitative indication of mechanical properties. To overcome this limitation, we present quantitative micro-elastography, which combines compression OCE with a compliant stress sensor to image tissue elasticity. The sensor consists of a layer of translucent silicone with well-characterized stress-strain behaviour. The measured strain in the sensor is used to estimate the two-dimensional stress distribution applied to the sample surface. Elasticity is determined by dividing the stress by the strain in the sample. We show that quantification of elasticity can improve the ability of compression OCE to distinguish between tissues, thereby extending the potential for inter-sample comparison and longitudinal studies of tissue elasticity. We validate the technique using tissue-mimicking phantoms and demonstrate the ability to map elasticity of freshly excised malignant and benign human breast tissues.

Seizure. 2015; 26: 36-42.

Evidence for an excitatory GABAA response in human motor cortex in idiopathic generalised epilepsy.
Silbert BI, Heaton AE, et al.
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Purpose Impaired GABAergic inhibition has been implicated in the pathophysiology of epilepsy. The possibility of a paradoxical excitatory effect of GABA in epilepsy has been suggested, but has not been investigated in vivo. We investigated pre- and post-synaptic GABAergic mechanisms in patients with idiopathic generalised epilepsy (IGE). Method In 10 patients and 12 control subjects, transcranial magnetic stimulation (TMS) was used to study long-interval intracortical inhibition (SICI), LICF; post-synaptic GABA A-receptor-mediated and GABA A<sub>B</sub>-mediated respectively) and long-interval intracortical facilitation (LICF; pre-synaptic disinhibition) using transcranial magnetic stimulation. Results While post-synaptic GABA A<sub>B</sub>-mediated inhibition was unchanged in IGE (p = 0.09), LICF was reduced compared to controls (controls: 141 +/- 17% of baseline; untreated patients: 107 +/- 12%, p = 0.2; treated patients: 79 +/- 10%, p = 0.003). GABA A<sub>A</sub>-mediated inhibition was reduced in untreated patients (response amplitude 56 +/- 4% of baseline vs. 26 +/- 6% in controls, p = 0.004) and normalised with treatment (37 +/- 12%, p = 0.5 vs. controls). When measured during LICI, GABA A<sub>A</sub>-mediated inhibition became excitatory in untreated IGE (response amplitude 120 +/- 10% of baseline, p = 0.017), but not in treated patients. Conclusion Pre- and post-synaptic GABA-mediated inhibitory mechanisms are altered in IGE. The findings lend in vivo support to evidence from experimental models and in vitro studies of human epileptic brain tissue that GABA may have a paradoxical excitatory role in ictogenesis.

transient contribution of hematopoietic cells to the healed wound. Further characterisation of the types and extent of wounding
of the response to burn injury.

METHODS: Transgenic mice expressing the LacZ reporter gene in all cells of the hematopoietic lineage underwent a non-severe full-thickness burn injury (80% of total body surface area). Wounds were assessed for LacZ-positive cells at days 7, 14, and 28 post-injury by using whole-mount staining. Cells were also cultured from the wounds at each time point and analysed for expression of fibroblast and myofibroblast markers.

RESULTS: At day 7, positive cells were identified in the wounds representing the inflammatory response. Some dermal cells were also identified at this early stage. At day 14, positive cells were also identified and were cultured from the wound tissue samples. However, by day 28, no positive cells could be detected or cultured from the healed wound tissue. Isolated LacZ-positive cells did not express collagen 1 or alpha-smooth muscle actin proteins, indicating that they had not differentiated into dermal fibroblast-type cells.

CONCLUSIONS: In this model of burn injury, hematopoietic lineage cells were present in the healing wound only transiently and did not appear to contribute to the long-term scar population. This is in contrast with reports demonstrating that fibrocytes contribute a long-term sustained population in scar tissue. This work demonstrates that in a non-severe burn injury model there is a sustained transient contribution of hematopoietic cells to the healed wound. Further characterisation of the types and extent of wounding required to establish a long-term hematopoietic response will be important in determining future cell-based therapies.


Stroke. 2015; 46(9): 2695-8.

**Outcome Following Decompressive Hemicraniectomy for Malignant Cerebral Infarction: Ethical Considerations.**

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Stroke. 2015; 46(1): 279-84.

**Recommendations from the international stroke genetics consortium, part 1: standardized phenotypic data collection.**


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Response to Letter Regarding Article, "Outcome Following Decompressive Hemianciectomy for Malignant Cerebral Infarction: Ethical Considerations".
Honeybul, Stephen. Department of Neurosurgery, Sir Charles Gairdner Hospital and Royal Perth Hospital, Perth, Western Australia, Australia. Ho, Kwok Ming. Department of Intensive Care Medicine and School of Population Health, University of Western Australia, Crawley, Western Australia, Australia. Gillett, Grant. Dunedin Hospital and Otago Bioethics Centre, University of Otago, Dunedin, New Zealand.

Publication Types: Letter


Xiao, Di. Australian e-Health Research Centre, CSIRO. Vignarajan, Janardhan. Australian e-Health Research Centre, CSIRO.
Boyle, Justin. Australian e-Health Research Centre, CSIRO. Zhang, Ming. Australian e-Health Research Centre, CSIRO. Estai, Mohamed R Abdalla. The University of Western Australia. Tennant, Marc. The University of Western Australia. Tay-Kearney, Mei-Ling. Royal Perth Hospital. Kanagasigam, Yogesan. Australian e-Health Research Centre, CSIRO.

Store-and-forward (S&F) telehealth system has been becoming an increasing application in remote medical consultations. In this paper, we will introduce three novel S&F telehealth systems we developed for ophthalmological, dental and emergency applications. We will explain the general system architecture of the S&F systems. Then we will focus on the specific features and components in each system implemented for meeting their respective clinical requirements. In the final section we will present further implementation details and practices and provide discussions.


Treatment of foregut fistula with biologic plugs.
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Introduction: Enteric fistulas are a recognised complication of various diseases and surgical interventions. Non-operative medical management will result in closure of 60-70% of all fistulas over a six- to eight-week period, those that fail non-operative management will require operative intervention if they are to close. We present a series of upper gastrointestinal fistula managed with endoscopic intervention and insertion of biological fistula plug over a 3-year period across three Hospitals, both public and private, in Western Australia. Methods: Over a three-year period, 14 patients were referred for treatment of acute or persistent foregut fistulas. All fistulas were managed with endoscopic intervention and insertion of a porcine small intestine sub-mucosa plug (Biodesign <sup></sup>Cook medical Inc., Bloomington, IN, USA). No patients with fistula were excluded. Data were collected on patient demographics and underlying diagnosis. The biological plugs were deployed using three different endoscopic techniques (direct deployment via the endoscope, catheter-assisted endoscopic deployment, or a pull through via a guide wire using a rendezvous technique). Results: Fourteen patients with foregut fistula were treated using biological plugs. The age of the fistulas treated ranged from 14 days to 3 years. The fistulas were predominantly gastric in origin (eight cases). Three oesophageal, one gastro-pleural-bronchial, and two jejunal fistulas were also managed using this technique. Of the 14 fistulas treated using this method, 13 resolved following the treatment. Median time to closure of the fistula was 2 days (range 1-120 days). Three patients required more than one intervention to complete closure. Conclusion: Biological plugs offer a further option for management of the traditionally difficult foregut fistula, without major morbidity associated with other treatment modalities. It is limited to the ability to deploy the plug endoscopically.


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Ledowski, Thomas. *Department of Anaesthesia, Royal Perth Hospital +School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia.

When neuromuscular blocking agents (NMBA) were introduced into clinical practice in 1942, the event was called the "second revolution in anaesthesia." Despite some significant side effects, NMBAs have remained in the anesthetists' repertoire, not at least because muscle relaxation has been claimed to allow or facilitate many surgical procedures. Aim of this literature review was to investigate the evidence for the use of NMBA as well as the optimum depth of neuromuscular blockade during laparoscopic surgery. Muscle relaxation may optimize laparoscopic operating conditions by preventing patient movement and achieving more intra-abdominal space for a given intra-abdominal insufflation pressure. In this context, deeper than normally maintained levels of neuromuscular blockade appear to be superior. However, the decision to utilize deeper than standard muscle relaxation should currently be based on a risk-benefit analysis for each individual patient. Thus good communication between surgeon and anesthetist remains crucial to achieve best outcomes.
Thrombosis and Haemostasis. 2015; 114(3): 546-557.
**Association between statin use and plasma d-dimer levels: A systematic review and meta-analysis of randomised controlled trials.**
Sahbeckar A, Serban C, et al.

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D-dimers, specific breakdown fragments of cross-linked fibrin, are generally used as circulating markers of activated coagulation. Statins influence haemostatic factors, but their effect on plasma D-dimer levels is controversial. Therefore, the aim of this meta-analysis was to evaluate the association between statin therapy and plasma D-dimer levels. We searched PubMed, Web of Science, Cochrane Library, Scopus and EMBASE (up to September 25, 2014) to identify randomised controlled trials (RCTs) investigating the impact of statin therapy on plasma D-dimer levels. Two independent reviewers extracted data on study characteristics, methods and outcomes. Meta-analysis of data from nine RCTs with 1,165 participants showed a significant effect of statin therapy in reducing plasma D-dimer levels (standardised mean difference [SMD]: -0.988 mug/ml, 95 % confidence interval [CI]: -1.590 - -0.385, p=0.001). The effect size was robust in sensitivity analysis and omission of no single study significantly changed the overall estimated effect size. In the subgroup analysis, the effect of statins on plasma D-dimer levels was significant only in the subsets of studies with treatment duration >3 months (SMD: -0.761 mug/ml, 95 % CI: -1.163 - -0.360; p< 0.001), and for lipophilic statins (atorvastatin and simvastatin) (SMD: -1.364 mug/ml, 95 % CI: -2.202 - -0.526; p=0.001). Hydrophilic statins (pravastatin and rosuvastatin) did not significantly reduce plasma D-dimer levels (SMD: -0.237 mug/ml, 95 %CI: -1.140-0.665, p=0.606). This meta-analysis of RCTs suggests a decrease of plasma D-dimer levels after three months of statin therapy, and especially after treatment with lipophilic statins. Well-designed trials are required to validate these results.


**Genotyping of HLA novel and rare alleles using next generation sequencing on the ion PGM, using a novel group-specific sanger sequencing method as a reference.**
De Santis D, Groeneweg M, et al.

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High resolution genotyping of human leukocyte antigen (HLA) Class I and II alleles is important for successful stem cell transplantation, however it is unknown whether polymorphisms outside exons 2 and 3 are relevant. With the development of Sanger Sequence Based typing (SSBT) methods, a high degree of polymorphism at the HLA loci has been identified. This level of polymorphism makes allele identification challenging. Allele ambiguities frequently occur because of the inability to set phase and the lack of complete genomic sequences in reference databases. With the arrival of Next Generation Sequencing (NGS), it is now possible to sequence the HLA genes clonally, completely and simultaneously. Using newly in-house developed long range PCR on the Ion Torrent PGM, the aim of this study was to confirm and obtain complete gene sequence, on samples identified as novel or rare for HLA alleles by short range SSBT. In addition, the full-length sequences generated by NGS were confirmed using the novel full-length, group-specific sequence based typing (SBT) amplification and complete gene sequencing approach, which results in hemizygous sequences, developed in Maastricht. Analysis of NGS-Ion PGM data identified and confirmed HLA novel and rare alleles reported by short range SSBT. Furthermore, the group-specific sequence based typing results also confirmed data obtained by NGSIon PGM. In addition, a number of novel polymorphisms mainly in intronic sequences were identified by both sequence based typing methods. This study shows the strength of NGS and the continued relevance of SSBT as a reference methodology.

Publication Types: Conference Abstract

HLA typing by next-generation sequencing without the use of PCR for target gene amplification.

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All next generation sequencing methods for HLA typing reported to date are PCR based approaches that are often complicated by PCR-related problems such as: preferential amplification of one allele over another, lack of specificity, PCR chimeras, and PCR incorporation errors and other artefacts. Here we present an innovative alternative to PCR that uses Capture Probes with a proprietary design that enables the detection of all reported alleles and new alleles. Genomic DNA is fragmented, the fragments are repaired and adapters are ligated. The fragments are then enriched and Capture-HLA probes to multiple loci are used to isolate fragments containing HLA specific sequences. These fragments are further enriched and sequenced on a Next Generation DNA Sequencer. The resulting data is then analysed using the AssignTM MPS sequence analysis software. Preliminary testing with Capture Probes to HLA-A, -B and -C only has demonstrated high resolution HLA typing with the identification of novel alleles that have arisen due to nucleotide substitutions. The use of capture probe technology for HLA typing using Next Generation Sequencing technology offers the advantages of simple and rapid sample prep, testing for all loci in a single tube and the ability to add additional probes for other transplant relevant sequences such as the Gamma block SNPs, in addition to removing all PCR associated errors and artefacts. This approach can be used on any of the current popular Next Gen DNA sequencers.

Publication Types: Conference Abstract


A novel assay for the detection of allo-HLA crossreactivity by virus-specific memory T cells.

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We have previously shown that allo-HLA reactivity by virus-specific memory T cells is common. For example, EBV EBN3A specific T cells crossreact against allo-HLA-B*44:02. Here we describe a novel assay suitable for high throughput screening of allo-HLA crossreactivity by virus-specific memory T cells, measuring cytokine production, T cell activation and cytotoxicity all after a single overnight effector-target incubation. EBV EBN3A3 T cell clones were assayed for alloreactivity against a panel of single HLA expressing cell lines (SALs), after overnight co-incubation. Allo-HLA crossreactivity was identified by the increased expression of CD137 on the T cells (T cell activation) and TAD uptake by the SALs (cytotoxicity), and the supernatant from the same experiment was harvested for cytokine analysis. Using this novel assay, we were able to detect specific allo-HLA crossreactivity of EBV EBN3A specific T cells against allo-B*44:02 and B*55:01. Crossreactivity was confirmed by cytokine production, T cell activation and cytolytic function. Interestingly, our EBV EBN3A3 T cell clone also recognised allogeneic HLA-B*44:04:03, when previous studies have shown no cross-reactivity with this molecule. This assay was also suitable to detect allo-HLA crossreactivity by multiple other virus-specific T cells, including CMV and HIV. We describe a novel and highly specific flow cytometry-based assay to screen for allo-HLA crossreactivity by virus-specific memory T cells, with multiple functional markers of crossreactivity measured after a single stimulation. This assay led to discovery of novel patterns of crossreactivity. This technique may have important uses for donor selection, monitoring of transplant recipients and adoptive immunotherapy.

Publication Types: Conference Abstract


Allo-HLA reactivity by HIV-specific T cells: A potential adjunct to HIV vaccine design?

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The rate of new HIV infections continues to be high, particularly in the developing world. An effective preventative HIV vaccine remains elusive and therefore novel vaccine strategies are urgently required. We have recently reported that allo-HLA crossreactivity by EBV, CMV, VZV and influenza virus-specific T-cells is common, and also that specific allo-HLA stimulation can conversely be used to augment a virus-specific T-cell response. We hypothesized that HIV-specific T-cells can be stimulated by allogeneic HLA molecules. Multiple HIV-1 specific CD8 T-cell clones were generated, using single cell sorting based on HIV peptide/HLA tetrameric staining. The generated T-cell clones were assayed for alloreactivity against a panel of single HLA expressing cell lines (SALs), using cytokine assay, CD137 upregulation and cytotoxicity as readout. HIV-specific T cells do crossreact against allogeneic HLA molecules. A Gag RK9/HLA-A3 specific T-cell clone with TCR Vb23 recognised allogeneic HLA-A*69:01. Two different Gag GL9/HLA-B7 restricted T-cell clones with Vb22 and an unknown Vb usage both recognized allo-HLA-A*33:03. KK10/HLA-B27 restricted T-cell clone with TCR Vb5.1 usage recognized allogeneic HLA-A*33:03 and HLA-B*57:01. Allo-HLA reactivity by HIV-specific T-cells was specific to the HIV target peptide/HLA restriction and Vb usage of the T-cells. Overall 4/25 HIV-specific T-cell clones tested recognized at least one allogeneic HLA molecule. HIV-specific T-cells do crossreact against allogeneic HLA molecules, and therefore allo-HLA stimulation could be a useful adjunct to HIV vaccine design. (Table Presented).

Publication Types: Conference Abstract

Drug induced alloreactivity: A new paradigm for allorecognition.

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Abacavir administration is associated with drug induced hypersensitivity reactions in HIV patients expressing the HLA-B*57:01 allele. However, the immunological effects of abacavir administration in an HLA-B57 mismatched transplantation setting has not been studied. We hypothesised that abacavir exposure would induce de-novo HLA-B57 specific allorecognition. Multiple HIV-specific CD8 T cell clones were generated from HIV infected patients negative for the HLA-B57 antigen, using single cell sorting based on HIV peptide/HLA tetrameric complex staining. The generated T cell clones were assayed for alloreactivity against a panel of single HLA expressing cell lines (SALS), in the presence or absence of abacavir. Cytokine assay, CD137 upregulation and cytotoxicity were used as readout. Abacavir exposure did induce de-novo HLA-B57 allorecognition by HIV-specific T cells. AGAg RK9/HLA-A3 specific T cell clone, from an HLA-B57 negative HIV patient, did recognize allogeneic HLA-B57 but only in the presence of abacavir. Abacavir did not induce recognition of any other allogeneic HLA molecules. Another clone from the same patient with the same specificity, but with different TCR Vb usage, did not recognize allogeneic HLA-B57 in the presence of abacavir, suggesting TCR Vb specificity of the drug induced allorecognition. Results presented here provide the first evidence that administration of a drug could induce specific allorecognition of mismatched allogeneic HLA molecules in the transplant setting. Furthermore, HIV-specific memory T cells themselves may participate in the abacavir induced alloreactivity. We suggest that HIV-positive recipients of a HLA-B57 mismatched graft should not receive abacavir until further studies are completed.

Publication Types: Conference Abstract


Tissue Antigens. 2015; 85 (5): 301.

Increased hospital costs associated with red cell blood transfusion.

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BACKGROUND: Red blood cell (RBC) transfusion is independently associated in a dose-dependent manner with increased intensive care unit stay, total hospital length of stay, and hospital-acquired complications. Since little is known of the cost of these transfusion-associated adverse outcomes our aim was to determine the total hospital cost associated with RBC transfusion and to assess any dose-dependent relationship.

STUDY DESIGN AND METHODS: A retrospective cohort study of all multiday acute care inpatients discharged from a five hospital health service in Western Australia between July 2011 and June 2012 was conducted. Main outcome measures were incidence of
When thoracic organ recipients become abdominal organ donors: sharing the risks and benefits of transplantation: a case report.


Penicillium marneffei infection in a lung transplant recipient.

Stathakis A, Lim KP, et al.

Penicillium marneffei is a thermally dimorphic fungus that can cause severe opportunistic infections in endemic regions of Southeast Asia, particularly in individuals infected with human immunodeficiency virus-1, but has rarely been reported in solid organ transplant recipients. Herein, we report the first case, to our knowledge, of P. marneffei infection in a lung transplant recipient, occurring in a 41-year-old woman 28 months post lung transplantation, after recent travel to Vietnam. We have reviewed the literature to derive some management principles for this rare infection in this clinical context. The number of P. marneffei infections in transplant recipients may increase, as a result of increasing rates of transplantation and travel to endemic areas.


Translational Psychiatry. 2015; 4(12).

A combination of physical activity and computerized brain training improves verbal memory and increases cerebral glucose metabolism in the elderly.


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Physical exercise interventions and cognitive training programs have individually been reported to improve cognition in the healthy elderly population; however, the clinical significance of using a combined approach is currently lacking. This study evaluated whether physical activity (PA), computerized cognitive training and/or a combination of both could improve cognition. In this nonrandomized study, 224 healthy community-dwelling older adults (60-85 years) were assigned to 16 weeks home-based PA (n = 64), computerized cognitive stimulation (n = 62), a combination of both (combined, n = 51) or a control group (n = 47). Cognition was assessed using the Rey Auditory Verbal Learning Test, Controlled Oral Word Association Test and the CogState computerized battery at baseline, and 16 weeks post intervention. Physical fitness assessments were performed at all time points. A subset (total n = 45) of participants underwent [18F] fluorodeoxyglucose positron emission tomography scans at 16 weeks (postintervention). One hundred and ninety-one participants completed the study and the data of 172 participants were included in the final analysis. Compared with the control group, the combined group showed improved verbal episodic memory and significantly higher brain glucose metabolism in the left sensorimotor cortex after controlling for age, sex, premorbid IQ, apolipoprotein E (APOE) status and history of head injury. The higher cerebral glucose metabolism in this brain region was positively associated with improved verbal memory seen in the combined group only. Our study provides evidence that a specific combination of physical and mental exercises for 16 weeks can improve cognition and increase cerebral glucose metabolism in cognitively intact healthy older adults.


RBC transfusion and mean inpatient hospital costs.

RESULTS: Of 89,996 multiday, acute care inpatient discharges, 4805 (5.3%) were transfused at least 1 unit of RBCs. After potential confounders were adjusted for, the mean inpatient cost was 1.83 times higher in the transfused group compared with the nontransfused group (95% confidence interval, 1.78-1.89; p < 0.001). The estimated total hospital-associated cost of RBC transfusion in this study was AUD $77 million (US $72 million), representing 7.8% of total hospital expenditure on acute care inpatients. There was a significant dose-dependent association between the number of RBC units transfused and increased costs after adjusting for confounders.

CONCLUSION: RBC transfusions were independently associated with significantly higher hospital costs. The financial implication to hospital budgets will assist in prioritizing areas to reduce the rate of RBC transfusions and in implementing patient blood management programs. Copyright © 2014 AABB.

CONCLUSIONS: These donations illustrate the interrelated risks and benefits for transplant recipients who themselves can become unintended, but effective donors. Crown Copyright 2015. Published by Elsevier Inc. All rights reserved.

TRIAL REGISTRATION: The MERINO trial is registered under the Australian New Zealand Clinical Trials Register (ANZCTR), reference number: NCT02176122 (registered 24 June 2014).


ACKNOWLEDGMENTS: This study is supported by the National Health and Medical Research Council (Grant 1034133). The authors thank Ms. Samantha Chua and Dr. Paul Peleg for providing the study concept.


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text articles in English or with English translation were assessed for relevance to the topic before being included in the review.


Dickman E.
(Dickman) Update in Clinician-Performed Echocardiography Jorge Rabat Surgery, Fremantle Hospital, Bolivar, Venezuela
E. Dickman, Update in Clinician-Performed Echocardiography Jorge Rabat Surgery, Fremantle Hospital, Bolivar, Venezuela
The use of ultrasound has developed over the last 50 years into an indispensable first-line test for the cardiac evaluation of symptomatic patients. Echocardiography is a very important tool in emergency department offering vital clues in early diagnosis and also very useful in assisting therapeutic procedures. The fact that echocardiography is a portable rapid, noninvasive technology which can be repeated when required makes it highly useful in emergency department. Hence all physicians managing critically ill patients should learn the skill of echocardiographic examination in a focused Echocardiography has shown to be an essential diagnostic tool in the critically ill patient's manner. This skill adds to the clinical acumen towards a correct diagnosis and treatment assessment. In this scenario the initial fluid therapy, such as it is recommended in the actual clinical guidelines, not always provides the desired results and maintains a considerable incidence of cardiorespiratory insufficiency. Echocardiography can counsel us on these patients' clinical handling, not only the initial fluid therapy but also on the best-suited election of the vasoactive/inotropic treatment and the early detection of complications. It contributes as well to improving the etiological diagnosis, allowing one to know the heart performance with more precision. The parameters that are evaluated cardiac function, ejection fraction, and Cardiac Output index, systolic volume. The Pre-load: Ventricular size, diameter of the inferior vena cava (IVC). Post-load: Peripheral Vascular Resistance Anatomy: pericardial fluid with or without tamponade. Probably is the time that hemodinamic monitoring guided by Ultrasound be generalized in all ICUs.


Orthotopic neobladder reconstruction.
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Department of Surgery, University of Melbourne, Victoria; Ludwig Institute for Cancer Research, Austin Hospital, Melbourne, Victoria; Department of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia.
Orthotopic neobladder reconstruction is becoming an increasingly common urinary diversion following cystectomy for bladder cancer. This is in recognition of the potential benefits of neobladder surgery over creation of an ileal conduit related to quality of life (QoL), such as avoiding the need to form a stoma with its cosmetic, psychological and other potential complications. The PubMed database was searched using relevant search terms for articles published electronically between January 1994 and April 2014. Full-text articles in English or with English translation were assessed for relevance to the topic before being included in the review. Patients with neobladders have comparable or better post-operative sexual function than those with ileal conduits. They also have comparable QoL to those with ileal conduits. Orthotopic neobladder is a good alternative to ileal conduit in suitable patients who do not want a stoma and are motivated to comply with neobladder training. However, the selection of a neobladder as the urinary diversion of choice requires that patients have good renal and liver functions and are likely to be compliant with neobladder training and the early detection of complications. It contributes as well to improving the etiological diagnosis, allowing one to know the heart performance with more precision. The parameters that are evaluated cardiac function, ejection fraction, and Cardiac Output index, systolic volume. The Pre-load: Ventricular size, diameter of the inferior vena cava (IVC). Post-load: Peripheral Vascular Resistance Anatomy: pericardial fluid with or without tamponade. Probably is the time that hemodinamic monitoring guided by Ultrasound be generalized in all ICUs.


Orthotopic neobladder reconstruction.
Chang DT, Lawrentschuk N.
Department of Urology, Fremantle Hospital and Health Service, Fremantle, WA, Australia (Lawrentschuk) Department of Surgery, University of Melbourne, Austin Hospital, 210 Burgundy St., Heidelberg, VIC 3084, Australia (Lawrentschuk) Ludwig Institute for Cancer Research, Austin Hospital, Melbourne, VIC, Australia (Lawrentschuk) Department of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia.
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**Interventional primary patency** was calculated as 100%, 100%, 88.4% and 32.8% at 1, 6, 9 and 12 months, respectively. The post-

**Primary technical success** regarding access was achieved in all patients. There were no peri-procedural complications. The post-

**RESULTS:** Primary technical success (residual stenosis <30%) was achieved in all cases where angioplasty was performed. A 4-French (Fr) micropuncture kit was used to access the radial artery and then subsequently upgraded to a 5-Fr

**METHOD:** From June 2012 to February 2013, 30 patients with end-stage renal failure were evaluated for transradial vascular access intervention. Based on colour-coded Duplex scan and/or photoelectric plethysmography, all access-site arteries showed normal perfusion;

**BACKGROUND:** Percutaneous interventional procedures for vascular access are usually performed using the draining cephalic or basilic vein. The transradial approach, which has been extensively investigated for coronary angiography and intervention, could be an attractive new technique for peri-anastomotic arteriovenous fistula stenosis.

**METHOD:** From June 2012 to February 2013, 30 patients with end-stage renal failure were evaluated for transradial vascular access intervention. A 4-French (Fr) micropuncture kit was used to access the radial artery and then subsequently upgraded to a 5-Fr sheath. Fourteen patients required an upgrade to a 6-Fr sheath for the final intervention.

**RESULTS:** Primary technical success (residual stenosis <30%) was achieved in all cases where angioplasty was performed. Technical success regarding access was achieved in all patients. There were no peri-procedural complications. The post-interventional primary patency was calculated as 100%, 100%, 88.4% and 32.8% at 1, 6, 9 and 12 months, respectively. The post-interventional primary assisted patency was calculated as 100%, 100%, 100% and 63.3% at 1, 6, 9 and 12 months, respectively.

**CONCLUSION:** The transradial approach for vascular access endovascular interventions is technically feasible and safe. It allows simultaneous treatment of peri-anastomotic lesions in fistulas with complex venous anatomy as well as lesions in the arterial inflow and central outflow.

**Five winters of pneumococcal serotype replacement in UK carriage following PCV introduction.**

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The seven-valent pneumococcal conjugate vaccine (PCV7) was added to the UK national immunisation programme in September 2006. PCV13 replaced PCV7 in April 2010. As carriage precedes disease cases this study collected carried pneumococci from children each winter from 2006/7 to 2010/11 over PCV introduction. Conventional microbiology and whole genome sequencing were utilised to characterise pneumococcal strains. Overall prevalence of pneumococcal carriage remained stable. Vaccine serotypes (VT) decreased (p<0.0001) with concomitant increases in non-vaccine serotypes (NVT). In winter 2010/11 only one isolate of PCV7 VT was observed (6B). PCV13 unique VTs decreased between winters immediately preceding and following PCV13 introduction (p=0.04). Significant decreases for VTs 6B, 19F, 23F (PCV7) and 6A (PCV13) and increases for NVT 21, 23B, 33F and 35F were detected. The serotype replacement was accompanied by parallel changes in genotype prevalence for associated sequence types with clonal expansion contributing to replacement. By winter 2010/11, serotype coverage of PCV7 and PCV13 was 1% and 11% respectively. VT replacement was observed for PCV7 and PCV13 serotypes. Conjugate vaccine design and use requires continuous monitoring and revision.

**Transradial approach for challenging vascular access interventions.**


BACKGROUND: Percutaneous interventional procedures for vascular access are usually performed using the draining cephalic or basilic vein. The transradial approach, which has been extensively investigated for coronary angiography and intervention, could be an attractive new technique for peri-anastomotic arteriovenous fistula stenosis.

METHOD: From June 2012 to February 2013, 30 patients with end-stage renal failure were evaluated for transradial vascular access intervention. A 4-French (Fr) micropuncture kit was used to access the radial artery and then subsequently upgraded to a 5-Fr sheath. Fourteen patients required an upgrade to a 6-Fr sheath for the final intervention.

RESULTS: Primary technical success (residual stenosis <30%) was achieved in all cases where angioplasty was performed. Technical success regarding access was achieved in all patients. There were no peri-procedural complications. The post-interventional primary patency was calculated as 100%, 100%, 88.4% and 32.8% at 1, 6, 9 and 12 months, respectively. The post-interventional primary assisted patency was calculated as 100%, 100%, 100% and 63.3% at 1, 6, 9 and 12 months, respectively.

CONCLUSION: The transradial approach for vascular access endovascular interventions is technically feasible and safe. It allows simultaneous treatment of peri-anastomotic lesions in fistulas with complex venous anatomy as well as lesions in the arterial inflow and central outflow.

**Exercise-associated hyponatremic encephalopathy in an endurance open water swimmer.**

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EXERCISE-ASSOCIATED HYponatRemic ENCEPHALOPATHY IN AN ENDURANCE OPEN WATER SWIMMER.
Exercise-associated hyponatremia and its more serious form, known as exercise-associated hyponatremic encephalopathy, are recognized as some of the most important medical problems seen in a variety of different forms of endurance exercise. We describe a case of exercise-associated hyponatremic encephalopathy presenting as altered conscious state and seizures in a woman who had completed a 20-km open ocean swim. Her serum sodium measured approximately 1 hour after her seizure was 119 mmol/L on point-of-care testing. With ongoing critical care support and the use of hypertonic saline, she was able to be extubated the next day, neurologically intact, and ultimately was discharged from hospital without neurological sequelae. This case emphasizes both the importance of considering exercise-associated hyponatremic encephalopathy as a cause of neurological impairment in all athletes and the pivotal role of hypertonic saline in the treatment of this condition. Copyright © 2015 Wilderness Medical Society.


**Efficacy of moxifloxacin-based sequential therapy for first-line eradication of Helicobacter pylori infection in gastrointestinal disease.**

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AIM: To evaluate the efficacy of 14-d moxifloxacin-based sequential therapy as first-line eradication treatment of Helicobacter pylori (H. pylori) infection. METHODS: From December 2013 to August 2014, 161 patients with confirmed H. pylori infection randomly received 14 d of moxifloxacin-based sequential group (MOX-ST group, n = 80) or clarithromycin-based sequential group (CLA-ST group, n = 81) therapy. H. pylori infection was defined on the basis of at least one of the following three tests: a positive (13)C-urea breath test; histologic evidence of H. pylori by modified Giemsa staining; or a positive rapid urease test (CLOtest; Delta West, Bentley, Australia) by gastric mucosal biopsy. Successful eradication therapy for H. pylori infection was defined as the negative (13)C-urea breath test four weeks after the end of eradication treatment. Compliance was defined as good when drug intake was at least 85%. H. pylori eradication rates, patient compliance with drug treatment, adverse event rates, and factors influencing the efficacy of eradication therapy were evaluated. RESULTS: The eradication rates by intention-to-treat analysis were 91.3% (73/80; 95% CI: 86.2%-95.4%) in the MOX-ST group and 71.6% (58/81; 95% CI: 65.8%-77.4%) in the CLA-ST group (P = 0.014). The eradication rates by per-protocol analysis were 93.6% (73/78; 95% CI: 89.1%-98.1%) in the MOX-ST group and 75.3% (58/77; 95% CI: 69.4%-81.8%) in the CLA-ST group (P = 0.022). Compliance was 100% in both groups. The adverse event rates were 12.8% (10/78) and 24.6% (19/77) in the MOX-ST and CLA-ST group, respectively (P = 0.038). Most of the adverse events were mild-to-moderate in intensity; there was none serious enough to cause discontinuation of treatment in either group. In multivariate analysis, advanced age (> = 60 years) was a significant independent factor related to the eradication failure in the CLA-ST group (adjusted OR = 2.13, 95% CI: 1.97-2.29, P = 0.004), whereas there was no significance in the MOX-ST group. CONCLUSION: The 14-d moxifloxacin-based sequential therapy is effective. Moreover, it shows excellent patient compliance and safety compared to the 14-d clarithromycin-based sequential therapy.


**Boceprevir early-access for advanced-fibrosis/ cirrhosis in Asia-pacific hepatitis C virus genotype 1 non-responders/ relapers.**

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AIM: To examined the efficacy and safety of treatment with boceprevir, PEGylated-interferon and ribavirin (PR) in hepatitis C virus genotype 1 (HCVGT1) PR treatment-failures in Asia. METHODS: The Boceprevir Named-Patient Program provided boceprevir to HCVGT1 PR treatment-failures. Participating physicians were invited to contribute data from their patients: baseline characteristics, on-treatment responses, sustained virological response at week 12 (SVR12), and safety were collected and analysed. Multivariate analysis was performed to determine predictors of response. RESULTS: 150 patients were enrolled from Australia, Malaysia, Singapore and Thailand (Asians = 86, Caucasians = 63). Overall SVR12 was 61% (Asians = 59.3%, Caucasians = 63.5%). SVR12 was higher in relapers (78%) compared with non-responders (34%). On-treatment responses predicted SVR, with undetectable HCVRNA at week 4, 8 and 12 leading to SVR12s of 100%, 87%, and 82% respectively, and detectable HCVRNA at week 4, 8 and 12, leading to SVR12s of 58%, 22% and 6% respectively. Asian patients were similar to Caucasian patients with regards to on-treatment responses. Patients with cirrhosis (n = 69) also behaved in the same manner with regards to on-treatment responses.
Those with the IL28B CC genotype (80%) had higher SVRs than those with the CT/TT (56%) genotype (P = 0.010). Multivariate analysis showed that TW8 and TW12 responses were independent predictors of SVR. Serious adverse events occurred in 18.6%: sepsis (2%), decompensation (2.7%) and blood transfusion (14%). Discontinuations occurred in 30.7%, with 18.6% fulfilling stopping rules. CONCLUSION: Boceprevir can be used successfully in PR treatment failures with a SVR12 > 80% if they have good on-treatment responses; however, discontinuations occurred in 30% because of virological failure or adverse events.