Working memory binding of visual object features in older adults.

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Accurate mental representation of visual stimuli requires retaining not only the individual features but also the correct relationship between them. This associative process of binding is mediated by working memory (WM) mechanisms. The present study re-examined reports of WM-related binding deficits with aging. In Experiment 1, 31 older and 31 younger adults completed a visual change detection task with feature-location relations presented either simultaneously or sequentially; the paradigm was also designed specifically to minimize the impact of lengthy retention intervals, elaborative rehearsal, and processing demands of multi-stimulus probes. In Experiment 2, 38 older and 42 younger adults completed a modified task containing both feature-location relations and feature-feature conjunctions. In Experiment 1 although feature-location binding was more difficult with sequential compared with simultaneous presentation, the effect was independent of age. In Experiment 2 while older adults were overall slower and less accurate than young adults, there were no age-specific deficits in WM binding. Overall, after controlling for methodological factors, there was no evidence of an age-related visual WM binding deficit for surface or location features. However, unlike younger adults, older adults appeared less able to restrict processing of irrelevant features, consistent with reported declines with age in strategic capacities of WM.

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**Safety of immune check-point inhibitors in patients with autoimmune conditions and advanced cancer.**


Background: Immune check-point inhibitors (ICI) have revolutionised the treatment of advanced cancer. However, ICI treatment is associated with immune related adverse events (irAEs) leading to patient morbidity and mortality. Safety and efficacy of ICI is not well known in patients with auto-immune (AI) conditions as historically this group has been excluded from clinical trials. The aim of our study was to evaluate the safety and efficacy of primarily anti-PD1 therapy in patients with known AI conditions. Methods: This was a retrospective analysis of patients with advanced cancer treated with ICI at 5 Australian hospitals. Results: 17 patients were identified: melanoma (11), NSCLC (5) and 1 with mRCC. AI conditions: Crohn’s disease (1), Ulcerative colitis (3), rheumatoid arthritis (5 including 1 with common variable immune-deficiency), psoriasis (4) and 4 patients with other AI disease. Treatment received: Nivolumab (7 including 1 with prior Ipilimumab), Pembrolizumab (8) and Ipilimumab (2). 11 patients previously received systemic therapy for their AI condition, 2 had topical therapy and 4 had no previous therapy. Two patients had symptoms of active AI disease at time of starting ICI. Disease flared in 6/17 (35%): 3 with G2 arthritis (2 treated with moderate dose steroids, one with anti-inflammatories), G3 colitis treated with high dose steroids, G3 dyspnoea treated with high dose steroids and G2 psoriatic rash treated with low dose steroids. Nil required steroid sparing agents. irAEs unrelated to AI disease flare: 3 patients with pneumonitis, two G2, one G3 all requiring high dose steroids and one patient with G3 colitis requiring high dose steroids. Response rates: complete (1), partial (7), stable (2) progressive disease (5), non-evaluable (2). Conclusions: Disease flared in 35% of patients with AI conditions undergoing treatment with ICI. Most patients were successfully managed with steroids and treatment was permanently discontinued in only one patient. Although use of ICI in patients with AI conditions seems generally manageable, our data should be interpreted with caution as many patients with AI conditions had no symptoms of active disease at the start of therapy. Response to ICI is similar to historical controls.

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**Bullying in surgery isn’t just Australia’s problem.**

Stamp N, Patterson I.

**Etoposide phosphate hypersensitivity overcome using a desensitisation programme enabling optimal therapy for relapsed Hodgkin lymphoma.**

Polistena P, Tran Q, et al.
An observational study of implicit motor imagery using laterality recognition of the hand after stroke.
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OBJECTIVE: To explore the relationship between laterality recognition after stroke and impairments in attention, 3D object rotation and functional ability.
DESIGN: Observational cross-sectional study.
SETTING: Acute care teaching hospital.
PARTICIPANTS: Thirty-two acute and sub-acute people with stroke and 36 healthy, age-matched controls.
MAIN OUTCOME MEASURES: Laterality recognition, attention and mental rotation of objects. Within the stroke group, the relationship between laterality recognition and functional ability, neglect, hemianopia and dyspraxia were further explored.
RESULTS: People with stroke were significantly less accurate (69% vs 80%) and showed delayed reaction times (3.0 vs 1.9 seconds) when determining the laterality of a pictured hand. Deficits either in accuracy or reaction times were seen in 53% of people with stroke. The accuracy of laterality recognition was associated with reduced functional ability (R(2) = 0.21), less accurate mental rotation of objects (R(2) = 0.20) and dyspraxia (p = 0.03).
CONCLUSION: Implicit motor imagery is affected in a significant number of patients after stroke with these deficits related to lesions to the motor networks as well as other deficits seen after stroke. This research provides new insights into how laterality recognition is related to a number of other deficits after stroke, including the mental rotation of 3D objects, attention and dyspraxia. Further research is required to determine if treatment programmes can improve deficits in laterality recognition and impact functional outcomes after stroke.
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Demonstration of the test-retest reliability and sensitivity of the Lower Limb Functional Index-10 as a measure of functional recovery post burn injury: a cross-sectional repeated measures study design.
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BACKGROUND: Lower limb burns can significantly delay recovery of function. Measuring lower limb functional outcomes is challenging in the unique burn patient population and necessitates the use of reliable and valid tools.
The aims of this study were to examine the test-retest reliability, sensitivity, and internal consistency of Sections 1 and 3 of the Lower Limb Functional Index-10 (LLFI-10) questionnaire for measuring functional ability in patients with lower limb burns over time.

METHODS: Twenty-nine adult patients who had sustained a lower limb burn injury in the previous 12 months completed the test-retest procedure of the study. In addition, the minimal detectable change (MDC) was calculated for Section 1 and 3 of the LLFI-10. Section 1 is focused on the activity limitations experienced by patients with a lower limb disorder whereas Section 3 involves patients indicating their current percentage of pre-injury duties.

RESULTS: Section 1 of the LLFI-10 demonstrated excellent test-retest reliability (intra-class correlation coefficient (ICC) 0.98, 95% CI 0.96-0.99) whilst Section 3 demonstrated high test-retest reliability (ICC 0.88, 95% CI 0.79-0.94). MDC scores for Sections 1 and 3 were 1.27 points and 30.22%, respectively. Internal consistency was demonstrated with a significant negative association (r = -0.83) between Sections 1 and 3 of the LLFI-10 (p < 0.001).

CONCLUSIONS: This study demonstrates that Section 1 and 3 of the LLFI-10 are reliable for measuring functional ability in patients who have sustained lower limb burns in the previous 12 months, and furthermore, Section 1 is sensitive to changes in patient function over time.

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Burns and long-term infectious disease morbidity: A population-based study.

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Background: There is a growing volume of data that indicates that serious injury suppresses immune function, predisposing individuals to infectious complications. With recent evidence showing long-term immune dysfunction after less severe burn, this study aimed to investigate post-burn infectious disease morbidity and assess if burn patients have increased long-term hospital use for infectious diseases. Methods: A population-based longitudinal study using linked hospital morbidity and death data from Western Australia for all persons hospitalised for a first burn (n = 30,997) in 1980-2012. A frequency matched non-injury comparison cohort was randomly selected from Western Australia's birth registrations and electoral roll (n = 123,399). Direct standardisation was used to assess temporal trends in infectious disease admissions. Crude annual admission rates and length of stay for stay for infectious diseases were calculated. Multivariate negative binomial and Cox proportional hazards regression modeling were used to generate adjusted incidence rate ratios (IRR) and hazard ratios (HR), respectively. Results: After adjustment for demographic factors and pre-existing health status, the burn cohort had twice (IRR, 95% confidence interval (CI): 2.04, 1.98-2.22) as many admissions and 3.5 times the number of days in hospital (IRR, 95% CI: 3.46, 3.05-3.92) than the uninjured cohort for infectious diseases. Higher rates of infectious disease admissions were found for severe (IRR, 95% CI: 2.37, 1.89-2.97) and minor burns (IRR, 95% CI: 2.22, 2.11-2.33). Burns were associated with significantly increased incident admissions: 0-30. days (HR, 95%CI: 5.18, 4.15-6.48); 30. days-1. year (HR, 95%CI: 1.69, 1.53-1.87); 1-10 years (HR, 95%CI: 1.40:1.33-1.47); >10. years (HR, 95%CI: 1.16, 1.08-1.24). Respiratory, skin and soft tissue and gastrointestinal infections were the most common. The burn cohort had a 1.75 (95%CI: 1.37-2.25) times greater rate of mortality caused by infectious diseases during the 5-year period after discharge than the uninjured cohort. Conclusions: These findings suggest that burn has long-lasting effects on the immune system and its function. The increase in infectious disease in three different epithelial tissues in the burn cohort suggests there may be common underlying pathophysiology. Further research to understand the underlying mechanisms are required to inform clinical interventions to mitigate infectious disease after burn and improve patient outcomes. Copyright © 2016 Elsevier Ltd and ISBI.

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Burns and long-term infectious disease morbidity: A population-based study.

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Background: There is a growing volume of data that indicates that serious injury suppresses immune function, predisposing individuals to infectious complications. With recent evidence showing long-term immune dysfunction after less severe burn, this study aimed to investigate post-burn infectious disease morbidity and assess if burn patients have increased long-term hospital use for infectious diseases. Methods: A population-based longitudinal study using linked hospital morbidity and death data from Western Australia for all persons hospitalised for a first burn (n = 30,997) in 1980-2012. A frequency matched non-injury comparison cohort was randomly selected from Western Australia's birth registrations and electoral roll (n = 123,399). Direct standardisation was used to assess temporal trends in infectious disease admissions. Crude annual admission rates and length of stay for stay for infectious diseases were calculated. Multivariate negative binomial and Cox proportional hazards regression modeling were used to generate adjusted incidence rate ratios (IRR) and hazard ratios (HR), respectively. Results: After adjustment for demographic factors and pre-existing health status, the burn cohort had twice (IRR, 95% confidence interval (CI): 2.04, 1.98-2.22) as many admissions and 3.5 times the number of days in hospital (IRR, 95% CI: 3.46, 3.05-3.92) than the uninjured cohort for infectious diseases. Higher rates of infectious disease admissions were found for severe (IRR, 95% CI: 2.37, 1.89-2.97) and minor burns (IRR, 95% CI: 2.22, 2.11-2.33). Burns were associated with significantly increased incident admissions: 0-30. days (HR, 95%CI: 5.18, 4.15-6.48); 30. days-1. year (HR, 95%CI: 1.69, 1.53-1.87); 1-10 years (HR, 95%CI: 1.40:1.33-1.47); >10. years (HR, 95%CI: 1.16, 1.08-1.24). Respiratory, skin and soft tissue and gastrointestinal infections were the most common. The burn cohort had a 1.75 (95%CI: 1.37-2.25) times greater rate of mortality caused by infectious diseases during the 5-year period after discharge than the uninjured cohort. Conclusions: These findings suggest that burn has long-lasting effects on the immune system and its function. The increase in infectious disease in three different epithelial tissues in the burn cohort suggests there may be common underlying pathophysiology. Further research to understand the underlying mechanisms are required to inform clinical interventions to mitigate infectious disease after burn and improve patient outcomes. Copyright © 2016 Elsevier Ltd and ISBI.

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http://www.elsevier.com/locate/burns
Modified Vancouver Scar Scale score is linked with quality of life after burn.

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Introduction: This study aimed to determine if a scar quality is associated with quality of life (QoL) at six months post-burn and beyond. Methods: Quantile regression models adjusted for covariates were used to demonstrate the relationship of modified Vancouver Scar Scale (mVSS) total (with and without pigmentation) and the mVSS components, to the Burn Specific Health Scale-Brief (BSHS-B) scores (full scale, Affect and Relations domain, Skin Sensitivity domain). Results: The sample (n = 341) comprised 67% males, 83% with skin grafts with a median age 38 years, total body surface area (TBSA) 4%, length of stay seven days, mVSS total score of five and BSHS-B total score of 153. Between six and 12 months of injury, mVSS total, TBSA and female gender were significantly associated with the BSHS-B, a situation that was not affected by the presence or absence of pigmentation scores. The mVSS components did not individually influence QoL. Discussion: mVSS total score, gender and burn size data may be a useful adjunct to experienced clinical judgment for identifying at risk patients and directing appropriate, timely resource allocation.

Response to Letter to the Editor: ‘Patient opinion of scarring is multidimensional: An investigation of the POSAS with confirmatory factor analysis’.

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Posttraumatic growth after burn in adults: An integrative literature review.

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Posttraumatic growth after burn is a relatively new area of study with only a small number of studies that have examined this phenomenon. It is important to understand the presentation of posttraumatic growth and coping in burn survivors, how it changes over time and the components which influence growth so that we can understand how to promote posttraumatic growth in burn survivors. The aim of this review was to assess these three parameters. Studies were identified through multiple databases with specific search terms to identify posttraumatic growth after burn. From the 813 articles found, 57 were identified as potentially useful, and 8 as eligible for review; three qualitative, one mixed methods, two quantitative, one discussion paper and part of a review which assessed all psychosocial outcomes. Growth presented as realising personal strength, reprioritising, spirituality, humanity, changed relationships, and compassion and altruism. Styles of coping included feelings of gratefulness and downward comparison, humour and planning. Suddenness of the event, and the severity and location of injury might affect the amount of growth experienced. Overall function, quality of life, social support and optimism, hope and new opportunities are influences on growth after burn, all of which have the potential for improvement through targeted intervention strategies. Further research is indicated in many areas related to growth, intervention and measurement.

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Burn leads to long-term elevated admissions to hospital for gastrointestinal disease in a West Australian population based study.

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Background: While the most obvious impact of burn is on the skin, systemic responses also occur after burn, including intestinal inflammation. The objective of this study was to assess if burns are associated with increased long-term admissions for gastrointestinal diseases. Methods: A population-based longitudinal study using linked hospital morbidity and death data from Western Australia was undertaken of adults aged at least 15 years when hospitalized for a first burn (n. = 20,561) in 1980-2012. A frequency matched non-injury comparison cohort was randomly selected from Western Australia's birth registrations and electoral roll (n. = 80,960). Crude admission rates and summed days in hospital for digestive diseases were calculated. Negative binomial and Cox proportional hazards regression modeling were used to generate incidence rate ratios (IRR) and hazard ratios (HR), respectively. Results: After adjustment for demographic factors and pre-existing health status, the burn cohort had 1.54 times (95% confidence interval (CI): 1.47-1.62) as many admissions and almost three times the number of days in hospital with a digestive system diagnosis (IRR, 95% CI: 2.90, 2.60-3.25) than the uninjured cohort. Significantly elevated adjusted post-burn incident rates were identified, with the risk decreasing with increasing time: in the first month (HR, 95% CI: 3.02, 1.89-4.82), from one month to five years (HR, 95% CI: 1.42, 1.31-1.54), and from five to twenty years after burn (HR, 95% CI: 1.13, 1.06-1.20). Conclusions: Findings of increased hospital admission rates and prolonged length of hospital stay for gastrointestinal diseases in the burn cohort provide evidence to support that burns have effects that persist long after the initial injury. Copyright © 2016 Elsevier Ltd and ISBI.

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Mammographic breast density as a predictor of hormone receptor positive breast cancer recurrence: A single centre longitudinal analysis.

Redfern AD, Martin HL, et al.

Mammographic breast density as a predictor of breast cancer recurrence: a single centre longitudinal analysis of women with hormone receptor positive breast cancer Background Mammographic breast density has been associated with risk of development of breast cancer. To date clinical studies examining the use of tamoxifen and fall in mammographic breast density during this treatment have shown reduction in mammographic breast density examining change in mammographic breast density between baseline and a single follow-up mammogram to be predictive for disease recurrence. Aim To examine serial change in mammographic breast density over years to describe the changes which occur with use of aromatase inhibitors and tamoxifen, as well as changes following cessation of this treatment and to determine whether changes observed correlate with outcome. Method Eligible patients were identified from the Royal Perth Hospital breast unit database between January 1994-December 2011. Patient data was prospectively collected through the breast unit database. Additional data regarding endocrine therapy, adherence, weight, height and concomitant medications were obtained from case note review. Recurrence data was obtained from the hospital medical records system, as well as the breast unit database. Mammograms were obtained and mammographic breast density readings undertaken by a single reader using Cumulus. Percentage breast densities were obtained and statistical analysis undertaken to investigate changes in mammographic density on endocrine therapy, at switch of therapy, and cessation of therapy and correlation with disease free and overall survival. Results 1942 eligible patients were identified. 417 were premenopausal at time of diagnosis, 148 perimenopausal, 1328 postmenopausal and the remainder unknown status. 12 declined adjuvant endocrine therapy, 520 received both at least 1 aromatase inhibitor and tamoxifen during follow-up, 1189 tamoxifen only, 56 tamoxifen plus goserelin, and the remainder either aromatase inhibitor only or aromatase inhibitor with ovarian suppression. Over 10,000 mammograms were obtained for analysis. Currently results are available from 4301 mammograms from 689 patients. Mean density change between baseline scan and subsequent imaging after between 11-24 months of patient-reported endocrine adherence was -6.0%, with mean reduction of -11% in patients who were premenopausal at baseline and -4.5% in those who were postmenopausal at baseline. Kaplan Meier analysis showed late separation of overall survival curves favouring those with reduction in mammographic breast density however there was no statistically significant difference in the curves Conclusion Reduction in mammographic breast density was greatest in those who were premenopausal at baseline. Further multivariate analysis and assessment of the additional mammograms in this data set is required to assess the association between mammographic breast density and outcome in this cohort.

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Clinical usefulness of bone turnover marker concentrations in osteoporosis.

Morris HA, Eastell R, et al.

Clinical usefulness of bone turnover marker concentrations in osteoporosis.

Morris HA, Eastell R, et al.
Current evidence continues to support the potential for bone turnover markers (BTM) to provide clinically useful information particularly for monitoring the efficacy of osteoporosis treatment. Many of the limitations identified earlier remain, principally in regard to the relationship between BTM and incident fractures. Important data are now available on reference interval values for CTX and PINP across a range of geographic regions and for individual clinical assays. An apparent lack of comparability between current clinical assays for CTX has become evident indicating the possible limitations of combining such data for meta-analyses. Harmonization of units for reporting serum/plasma CTX (ng/L) and PINP (mg/L) is recommended. The development of international collaborations continues with an important initiative to combine BTM results from clinical trials in osteoporosis in a meta-analysis and an assay harmonization program are likely to be beneficial. It is possible that knowledge derived from clinical studies can further enhance fracture risk estimation tools with inclusion of BTM together with other independent risk factors. Further data of the relationships between the clinical assays for CTX and PINP as well as physiological and pre-analytical factors contributing to variability in BTM concentrations are required.

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Evidence of functional declining and global comorbidity measured at baseline proved to be the strongest predictors for long-term death in elderly community residents aged 85 years: a 5-year follow-up evaluation, the OCTABAIX study.


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OBJECTIVE: To investigate the predictive value of functional impairment, chronic conditions, and laboratory biomarkers of aging for predicting 5-year mortality in the elderly aged 85 years.

METHODS: Predictive value for mortality of different geriatric assessments carried out during the OCTABAIX study was evaluated after 5 years of follow-up in 328 subjects aged 85 years. Measurements included assessment of functional status comorbidity, along with laboratory tests on vitamin D, cholesterol, CD4/CD8 ratio, hemoglobin, and serum thyrotropin.

RESULTS: Overall, the mortality rate after 5 years of follow-up was 42.07%. Bivariate analysis showed that patients who survived were predominantly female (P=0.02), and they showed a significantly better baseline functional status for both basic (P<0.001) and instrumental (P<0.001) activities of daily living (Barthel and Lawton index), better cognitive performance (Spanish version of the Mini-Mental State Examination) (P<0.001), lower comorbidity conditions (Charlson) (P<0.001), lower nutritional risk (Mini Nutritional Assessment) (P<0.001), lower risk of falls (Tinetti gait...
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Cardiovascular Effects of Glucose-Lowering Therapies for Type 2 Diabetes: New Drugs in Perspective.
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Purpose: The purpose of this study was to review the results of clinical trials assessing the cardiovascular effects of drugs for type 2 diabetes and the cardiovascular effects of newer available drugs. Methods: We performed a detailed search of PubMed-listed publications, reports from international meetings, and ongoing studies from clinical trials.gov. Findings: Currently available drugs have neutral or, in some cases, negative effects on cardiovascular outcomes. Modern sulfonylureas appear to be safe, although the biguanide metformin has a slightly better cardiovascular safety profile than the sulfonylureas and is the first choice for monotherapy. The cardiovascular tolerability of thiazolidinediones (glitazones) remains controversial, with particularly adverse effects in patients with cardiac failure. The cardiovascular effects of insulin in type 2 diabetes appear neutral. Newer incretin-based therapies have been closely examined in a large number of clinical trials, some of which are still ongoing. The dipeptidyl peptidase-4 inhibitor (gliptins) trials to date have all found a neutral effect. Of the glucagon-like peptide-1 (GLP-1) agonists, lixisenatide had a neutral effect, whereas li拉glutide and semaglutide had a benefit on outcomes. The results of the sodium-glucose transporter-2 (SGLT-2) inhibitor empagliflozin attracted interest when it was the first to report a strong benefit on cardiovascular mortality. Liraglutide and semaglutide had a neutral effect on cardiac failure admissions, whereas empagliflozin had a benefit. In each of the trials, there was not a clear effect on myocardial infarction and stroke. The mechanism of the cardiovascular benefit is debated, and further studies with other GLP-1 agonists and SGLT-2 inhibitors are awaited. Implications: After 2 decades of disappointment in attempting to control cardiovascular progression in type 2 diabetes with careful glycemic control, there is distinct hope that newer drugs, particularly the GLP-1 agonists and the SGLT-2 inhibitors, will have cardiovascular benefits independent of glycemic control. Copyright © 2016 Elsevier HS Journals, Inc.


Determining reference ranges and optimal thresholds for thyroid stimulating hormone and free thyroxine in older men.
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Context Reference intervals for circulating thyrotrophin (TSH) and free thyroxine (FT4) in adults are provided by assay
manufacturers and local laboratories. These are not stratified by age, despite older adults exhibiting higher TSH concentrations and higher FT4 concentrations being associated with poorer health outcomes in older men. Objectives We sought to define reference intervals for TSH and FT4 in older men based on their distributions generally and in very healthy men, and on their associations with the outcome of all-cause mortality. Participants Community-dwelling men aged 70-89 years. Main outcome measures Baseline TSH and FT4 concentrations were assayed (Elecsys 2010, Roche Diagnostics). Conventional reference intervals were TSH 0.4-4.0 mIU/l and FT4 10-23 pmol/l. Incident deaths were ascertained using data linkage. Reference intervals were formulated based on the entire cohort, the subgroup very healthy men (defined as those self-reporting ‘excellent’ or ‘very good’ health without any history of diabetes, cardiovascular disease, cancer, depression or dementia) and on likelihood of death from any cause. Results Men with thyroid disease or taking thyroid-related medications were excluded. In 3,885 men included in the analysis the 2.5th and 97.5th centiles were TSH 0.64-5.9 mIU/L and FT4 12.1-20.6 pmol/L. In 411 very healthy men defined by excellent or very good self-rated health and absence of major medical comorbidities, 2.5th to 97.5th centiles were TSH 0.67-4.98 mIU/L and FT4 12.1-20.5 pmol/L. In proportional hazards regression TSH was not associated with survival. However, men with FT4 >17.6 pmol/L experienced increased mortality compared to men with FT4 14.1-15.3 pmol/L (adjusted hazard ratio 1.45, 95% confidence interval 1.15-1.85, p=0.002). Applying age-specific reference intervals based on very healthy older men led to reclassification of 310 men (8.0%). Six men with subclinical hyperthyroidism were reclassified as being overtly hyperthyroid. Of previously euthyroid men, five were reclassified as overt hyperthyroidism and 69 as having subclinical hyperthyroidism. Of men previously regarded as having subclinical hypothyroidism we reclassified 212 as euthyroid, and 18 as having overt hypothyroidism. Conclusions In older men, the reference interval for TSH is shifted upwards, while the reference interval for FT4 is compressed compared to the conventional reference ranges. The optimal upper limit for FT4 would be further reduced if based on mortality risk. Applying age-specific reference intervals led to more men being classified as having overt or subclinical hyperthyroidism, and fewer as having subclinical hypothyroidism. Further study is needed to determine whether this approach would improve detection and management of thyroid disease.

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Associations of thyroid hormones with incident prostate, colorectal and lung cancer in the health in men study (HIMS).

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Background Thyroid hormones regulate growth and metabolism in tissues and also activate pro-angiogenic pathways through binding of thyroxine to the integrin alphavbeta3 membrane receptor (1). Despite this the associations of thyroid hormones with incidence of common cancers has not been well explored. Objectives Our aim was to examine the relationship between serum thyroid stimulating hormone (TSH) and free thyroxine (FT4) with incident prostate, colorectal and lung cancer. Methods This was a prospective cohort study involving 4,248 community dwelling men aged 70-89 years. Men with a history of the cancer of interest, and those who were taking thyroid-related medications were excluded. Demographic details, medical co-morbidities and baseline TSH and FT4 levels were measured between 2001-2004. Cancer notifications were obtained through the cancer registry until June 30th 2013. Cox regression models were used to compare hormone levels and cancer outcomes. Results After exclusions, 3,637, 3,888 and 3,990 men were included in the prostate, colorectal and lung cancer analysis respectively. Total follow up time was 28,952, 32,015 and 33,224 person years for prostate, colorectal and lung cancer respectively. During this time, there were 343, 144, and 117 cases of prostate, colorectal and lung cancers. Baseline hormone levels were similar in men who developed prostate and colorectal cancer compared to those who did not. Men who developed lung cancer had higher baseline FT4 levels compared to those who did not (16.4 +/- 2.2 vs 16.0 +/- 2.3 pmol/l, p=0.045). In the age-adjusted Cox proportional hazards regression model, there was a significant association between FT4 and lung cancer (per 1 unit increase FT4 measured as pmol/l, HR 1.10, 95% CI 1.02-1.18; p=0.016). This association was not
significant after accounting for smoking, physical factors and medical comorbidities (adjusted HR 1.06, 95% CI 0.98-1.15; p=0.169). FT4 was not associated with prostate cancer (adjusted HR 1.04, 95% CI 1.00-1.10; p=0.079) or colorectal cancer (adjusted HR 0.96, 95% CI 0.88-1.04; p=0.275). TSH was not associated with either prostate cancer (per 1 unit increase TSH measured as mIU/l, adjusted HR 0.97, 95% CI 0.91-1.05; p=0.555), colorectal cancer (adjusted HR 1.05, 95% CI 0.97-1.14, p=0.208) or lung cancer (adjusted HR 0.90, 95% CI 0.77-1.04; p=0.15). Conclusion In community-dwelling older men, thyroid hormones including TSH and FT4 are not associated with incident prostate, colorectal or lung cancer, after accounting for potential confounders. The apparent association between FT4 and lung cancer appears to be mediated through smoking, and additional physical or comorbid factors.


Australasian evaluation of clinical management intent utilising Ga68-PSMA PET scans in patients with prostate cancer.

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Aim: Conventional imaging has limitations in the accurate evaluation of Prostate cancer (PCa). Ga68-Prostate Specific Membrane Antigen (PSMA) PET scanning is a new imaging technique that has been shown to be more accurate than conventional imaging techniques in many patients. This Australasian multicentre study sought to determine whether the findings of PSMA PET imaging impacts on planned clinical management. Materials: Four centres throughout Australia participated in this prospective study. Local institutional ethics approval was obtained at each site. Prior to undertaking Ga68-PSMA PET imaging, referring medical specialists were required to complete a survey detailing relevant demographic and clinical data as well as the proposed management plan. Once the referring specialist was provided with the Ga68-PSMA PET scan results, they were asked to complete a follow up survey, primarily seeking to determine whether their management plan would change based on the PSMA PET scan finding. Results: For the period between August 2015 and March 2016, 285 patients with PCa had pre- and post-Ga68 PSMA management plans completed by their referring specialists. Scans were performed for primary staging in 22% patients and for a rising PSA following surgery and/or radiotherapy in 78% of patients. On the pre-PSMA management plan, the most common treatment intent was for targeted or localised treatment (66%), followed by systemic therapy (18%) and surveillance (16%). On the post PSMA survey the clinicians indicated that the PSMA scan lead to a change in planned management in 55% of patients. The PSMA-scan revealed disease that was not previously suspected in the prostate bed (30% of patients), locoregional lymph nodes (36% of patients) and distant disease (16% of patients). In those in whom there was no management change, the survey indicated this was most often due to no additional information being provided from the PSMA scan. Conclusions: These preliminary results indicate that PSMA PET scans detect previously unsuspected disease and change planned clinical management in a high proportion of patients with prostate cancer. This demonstrates the potential clinical value of PSMA PET in treatment planning in this patient group.


Introduction There are no evidence-based strategies to improve feed tolerance in gastroschisis. Early commencement of enteral feeds (CEF) is known to improve feed tolerance in preterm infants. It is possible that infants with gastroschisis may also benefit from early CEF. Objectives To conduct a systematic review to evaluate the relationship between time of CEF, and time to reach full enteral feeds (FEF), duration of parenteral nutrition (PN), and duration of hospital stay (HS). Methods PubMed, EMBASE, Cochrane CENTRAL, and relevant conference abstracts were searched in December 2015. Studies of any design reporting on time to CEF and one or more of the outcomes of interest were included. Meta-regression analysis was conducted to find the association between time to CEF and the outcomes of interest. Results There were no randomized controlled trials (RCTs) comparing early (<7 days from birth) versus delayed (>7 days) CEF. Forty-two observational studies on gastroschisis (4,835 infants) where feed-related information was available were included. Meta-regression results indicated that each day delay in CEF was associated with a delay of an additional 1.4 days (95% confidence interval [CI]: 0.95, 1.85) to FEF, 2.05 days (95% CI: 1.50, 2.59) to the duration of PN, and 1.91 days (95% CI: 1.37, 2.45) to the duration of HS. Sensitivity analysis after excluding studies that provided information exclusively on complex gastroschisis continued to show beneficial effects of early CEF. Conclusions Early CEF may be associated with early attainment of FEF in gastroschisis. RCTs comparing early versus delayed CEF are needed urgently. Copyright © 2016, Georg Thieme Verlag KG. All rights reserved.

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Anacetrapib for the treatment of dyslipidaemia: the last bastion of the cholesteryl ester transfer protein inhibitors?


INTRODUCTION: Inhibition of cholesteryl ester transfer protein (CETP) has emerged as a potential way to decrease cardiovascular risk by raising high density lipoprotein (HDL) cholesterol and lowering low density lipoprotein (LDL) cholesterol concentrations. However, high profile withdrawals of several CETP inhibitors have cast doubt over this hypothesis. Despite this concern, anacetrapib appears to be safe, well-tolerated and delivers a substantial increases in HDL cholesterol and reductions in LDL cholesterol as monotherapy and when combined with a statin.

AREAS COVERED: We discuss the role of CETP and HDL cholesterol as therapeutic targets, describe the pharmacokinetics and pharmacodynamics of anacetrapib, as well as report on the recent clinical trials.

EXPERT OPINION: The focus of CETP inhibition has shifted from HDL cholesterol-raising to LDL cholesterol-lowering. Although anacetrapib appears to be safe and is effective in altering lipid-related biochemical parameters of interest, its effect on cardiovascular outcomes remains unknown. Extrapolation of LDL cholesterol lowering to improved cardiovascular outcomes is not possible, because LDL and HDL functionality in the setting of anacetrapib treatment is unclear. The results of the phase III REVEAL randomised controlled trial will be critical for anacetrapib to establish a

**Use of quantitative pharmacology tools to improve malaria treatments.**

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The use of pharmacokinetic (PK) and pharmacodynamic (PD) data to inform antimalarial treatment regimens has accelerated in the past few decades, due in no small part to the stimulus provided by progressive development of parasite resistance to most of the currently available drugs. An understanding of the disposition, interactions, efficacy and toxicity of the mainstay of contemporary antimalarial treatment, artemisinin combination therapy (ACT), has been facilitated by PK/PD studies which have been used to refine treatment regimens across the spectrum of disease, especially in special groups including young children and pregnant women. The present review highlights recent clinically-important examples of the ways in which these quantitative pharmacology tools have been applied to improve ACT, as well as 8-aminoquinoline use and the characterisation of novel antimalarial therapies such as the spiroindolones.


**Pharmacokinetic studies of antimalarials: recent developments.**

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Pharmacokinetic studies are essential for the development of safe and effective antimalarial treatment regimens, but there are clinical situations in which there are limited data on drug disposition. These include very young children, pregnant women, and where drug interactions may alter treatment response. New approaches such as sampling methods involving low volumes and minimal preparation such as dried blood spots, highly sensitive and specific multidrug assays, and population PK analyses which can evaluate the influence of covariates such as age, pregnancy and coadministered therapies, can generate robust data that inform treatment in the most challenging situations in the tropics.


**A Prescription for Resistance: Management of Staphylococcal Skin Abscesses by General Practitioners in Australia.**

OBJECTIVES: We investigated the management of staphylococcal abscesses (boils) by general practitioners (GPs) in the context of rising antibiotic resistance in community strains of Staphylococcus aureus.

DESIGN, SETTING, PARTICIPANTS: We analyzed patient-reported management of 66 cases of uncomplicated skin abscesses from the frequency matched methicillin-resistant S. aureus (MRSA) and methicillin-sensitive S. aureus (MSSA) Community-Onset Staphylococcus aureus Household Cohort (COSAHC) study (Melbourne, Australia, 2008-2012). Susceptibilities in all cases were known: 50/66 abscesses were caused by MRSA. In order to investigate GP-reported management of staphylococcal abscesses, we surveyed a random subset of GPs, from the COSAHC study (41), and of GPs (39) who used the same community-based pathology service (December 2011-May 2012).

MAIN OUTCOME MEASURES: Patient outcomes, antibiotics prescribed, antibiotic resistance profiles of infecting strains, rates of incision and drainage (I&D), and attitudes to ordering microbiological cultures.

RESULTS: MRSA was three times more likely to be cultured from an abscess than MSSA. Patient-reported management revealed 100% were prescribed antibiotics and only 60.6% had I&D. Of those 85% who remembered their prescription(s), 81% of MRSA cases and 23% of MSSA cases initially received inactive antibiotics. Repeat GP visits where antibiotics were changed occurred in 45 MRSA and 7 MSSA cases, although at least 33% of subsequent prescriptions were inactive for the MRSA infections. Patients treated with I&D and antibiotics did no better than those treated with only I&D, regardless of the antibiotic activity. In the GP surveys, 89% reported I&D, with or without antibiotics, to be their preferred management. Only 29.9% of GPs would routinely swab abscesses.

CONCLUSION: The recommended management of uncomplicated Staphylococcus abscesses is I&D without antibiotics to reduce exposure to unnecessary antibiotics. In our study, I&D was performed in only 60.6% of 66 patients, and antibiotics were always prescribed. The prescribed antibiotics were frequently inactive and often changed, and did not appear to affect patient recovery. Our results show that community GPs can confidently reduce their use of antibiotics for patients with skin abscesses and should be aware that MRSA is a much more common in this type of infection.

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Late Strut Fracture Within a Partially Resorbed Bioresorbable Vascular Scaffold: A Possible Cause of Late Scaffold Thrombosis and Acute Coronary Syndrome.

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The Bioresorbable Vascular Scaffold (BVS, Abbott Vascular, Santa Clara, Cal, USA) is an exciting advance in percutaneous coronary intervention providing a temporary drug eluting scaffold resorbed in two to five years. We present two cases of late scaffold thrombosis associated with strut fracture during the period of resorption, at 20 and 24 months following BVS implantation. We propose luminal migration of malapposed struts following strut fracture during resorption as a potential mechanism for late scaffold thrombosis and acute coronary syndrome. Copyright © 2016 Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) and the Cardiac Society of Australia and New Zealand (CSANZ).
Pure small cell carcinoma of the prostate preceded by acute zonal occult outer retinopathy: A case report.


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INTRODUCTION: Pure small cell prostate cancer (SCPC) cases are very rare. Acute zonal occult outer retinopathy (AZOOR) has been described as a non-neoplastic retinopathy. We report the first case of pure SCPC preceded by AZOOR in the literature.

CASE REPORT: A 59 year old gentleman presented with an obstructed infected urinary system. He had a diagnosis of AZOOR 6 months ago that was investigated with full body imaging without any suspicious findings. However, the most recent CT findings demonstrated extensive disease dissemination. The patient underwent rigid cystoscopy and resection that confirmed a diagnosis of pure SCPC.

DISCUSSION: AZOOR is a clinical syndrome of photopsia and rapid zonal field loss. The exact aetiology remains unknown and its association with malignancy remains contentious. Paraneoplastic manifestations of unexplained visual loss in SCPC are rare with only 2 cases reported in the literature. There are no cases demonstrating an association between AZOOR and SCPC.

CONCLUSION: Pure SCPC is an aggressive malignancy with most cases presenting with extensive disease dissemination on diagnosis. Early detection has a role in improving prognosis but is challenging. Further research is required to establish a standard treatment protocol.

An unusual case of asymptomatic non-urothelial bladder tumour.

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INTRODUCTION: Non-urothelial tumours are rare and account for less than 5% of all bladder tumours. Bladder paragangliomas also known as extra-adrenal pheochromocytomas are of the non-urothelial subgroup. We present an unusual case of asymptomatic bladder paraganglioma.

CASE REPORT: A 77 year old lady presented with acute abdominal pain was found to have an incidental enhancing nodule in the bladder. During cystoscopy and transurethral resection the patient experienced significant fluctuations in blood pressure that required anaesthetic adjustments. Review of histology confirmed a diagnosis of bladder paraganglioma.

DISCUSSION: Most bladder paraganglioma cases present with sympathomimetic related symptoms and microscopic haematuria but our patient was asymptomatic which resulted in inadequate pre-operative optimisation and high anaesthetic risk. Majority of paragangliomas are benign but there is a 20-40% chance of malignancy. The management options will predominantly depend on whether disease is localised, regional, metastatic or recurrent in nature.

CONCLUSION: Due to the non-specific nature of disease, variability of presentations and rare incidence, bladder
paragangliomas are often not part of the urologists' differential diagnoses. In our opinion, establishing guidelines should assist to achieve a balance between anaesthetic risks, cystoscopy and follow up.

Florid pustular dermatitis of breast: A case report on a unusual complication from acellular dermal matrix use.

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INTRODUCTION: Idiopathic erythematous reaction of the breast (Red breast syndrome) is a known complication following breast reconstruction with acellular dermal matrix. However pustular dermatitis like presentation is not previously known.

PRESENTATION OF CASE: We present a 42-year-old lady who developed bilateral pustular dermatitis like appearance following breast reconstruction with acellular dermal matrix slings. Though surgical washout was done, both expanders and flex HD could be preserved.

DISCUSSION: Acellular dermal matrix use is the only possible explanation for such a presentation and this can be considered a variant of red breast syndrome.

CONCLUSION: Pustular dermatitis like presentation can be associated with acellular dermal matrix use and should be considered in similar clinical presentations, since this can avoid unnecessary surgical procedures.

Oncologists' estimates of expected survival time and scenarios for survival: Accuracy in the ALTG NITRO trial of 1st line chemotherapy for advanced non-small-cell lung cancer.

Tognela A, Espinoza D, et al.

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Background: We have proposed that best, worst, and typical scenarios for survival, based on simple multiples of an individual's expected survival time (EST) estimated by their oncologist, are a useful way of formulating and explaining prognosis in advanced cancer. The aim of this study was to determine the accuracy and prognostic significance of such estimates in a multicenter, randomized trial. Methods: Oncologists recorded their estimate of the 'expected survival time' at baseline in each of 372 patients recruited in the NITRO trial. We hypothesized that oncologists' estimates of EST would be well-calibrated (~50% of patients living longer or shorter than EST) and imprecise (~< 33% living within 0.75 to 1.33 time their EST), but provide accurate scenarios for survival time (~<10% dying within a quarter of their EST, 10% living longer than 3 times their EST, and 50% living for half to double their EST). We also
hypothesized that oncologists' estimates of EST would be independently significant predictors of survival in a multivariable Cox model adjusting for traditional prognostic factors selected in the first 250 participants recruited, and validated in the remaining 122. Results: Oncologists' estimates of EST were well calibrated (51% of patients lived longer than their EST), but imprecise (24% lived within 0.75 to 1.33 times their EST). Scenarios based on the oncologists' estimates were accurate: 9% of patients died within of their EST, 12% lived longer than 3 times their EST, and 53% lived from half to double their EST. Oncologists' estimates of EST were independently significant predictors of overall survival (HR 0.92, 95% CI 0.88 to 0.96, p = 0.001) in Cox models accounting for ECOG performance status, liver metastases, neutrophil to lymphocyte ratio, and anaemia. Conclusions: Oncologists' estimates of EST were well calibrated, imprecise, and independently significant predictors of survival above and beyond traditional prognostic factors. Best, worst and typical scenarios for survival based on EST were remarkably accurate, and are a good solution to the problem of estimating prognosis in advanced cancer.

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Aim: Whole body therapeutic hypothermia (TH) for hypoxic ischaemic encephalopathy was introduced into clinical practice in New South Wales (NSW) and Australian Capital Territory in 2007. State-wide policy adopting the eligibility criteria and practice based on trial-designs was published in 2009. Methods: The study was conducted by retrospectively reviewing medical records of all TH infants born between 2007 and 2011 in NSW and Australian Capital Territory to examine if eligibility criteria (assessed against evidence-based policy directives) were met. Results: A total of 207 infants received TH, 104 (50%) did not meet the eligibility criteria defined in NSW policy directive. Over the 5-year period, the proportion of infants meeting the eligibility criteria did not change. Seventy percent of infants (73 out of 104) not meeting eligibility criteria did not fulfil the criteria for ‘evidence of asphyxia’, although half of them met ‘moderate or severe encephalopathy criterion’. Adverse events (hypotension, coagulopathy and arrhythmia), were more common in the ‘criteria met’ group than the ‘criteria not met’ group (89 vs. 71%, P=0.001). Similar proportions of infants had TH discontinued before 72h (criteria met: 32 (31%) vs. criteria not met: 27(26%)). Most frequent reason for early cessation was ‘palliation’ (19/32, 59%) in criteria met and ‘clinical improvement’ (16/27, 59%) in criteria not met group. Conclusions: Many TH infants were treated based on clinician judgement, though not meeting the trial-design policy criteria. Early TH cessation (<72h) was common. Future studies are warranted on long-term neurodevelopmental outcomes for all infants receiving TH particularly those with early cessation of therapy. Copyright © 2016 Paediatrics and Child Health Division (Royal Australasian College of Physicians).

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Objective: To describe a family with a newly found ATL1 genetic variant and the associated phenotype. Background: Mutations in the ATL1 gene are known to cause pure early onset autosomal dominant hereditary spastic paraplegia (SPG3A) and ulceromutilating sensory neuropathy, like HSN-1. We describe the detailed clinical and electrophysiological findings in the first family with ulceromutilating sensory neuropathy, along with spastic paraparesis, carrying the p.Ala354Pro likely pathogenic variant in ATL1. Methods: Detailed clinical and electrophysiological studies were performed in affected and at risk family members. Motor and sensory conduction studies, were carried out on upper and lower limbs. Genetic analysis was carried out using a custom designed neurogenic gene panel followed by massively parallel sequencing (MPS). Results: Two affected family members were investigated, as well as one unaffected. Through the family history, 12 patients were found to have had the same phenotype, including three deceased family members. One affected family member was analysed by MPS, with the p.Ala354Pro likely pathogenic variant in ATL1 being the only significant finding. The second affected family member also carried the variant, while the unaffected family member did not. The affected family members had characteristic history of a profound neuropathic pain syndrome, despite relative preservation of superficial sensory modalities. The patients also exhibited spastic paraparesis with hyper-reflexia. This resulted in recurrent painless foot ulcers and osteomyelitis. Nerve Conduction Studies (NCS) showed only a mild sensory neuropathy. Conclusions: This novel ATL1 variant potentially expands the SPG3A phenotype. The combination of severe ulceromutilating neuropathy, a profound neuropathic pain syndrome, and only mild sensory neuropathy on NCS, along with spastic paraparesis, should prompt the screening for ATL1 mutations.

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Effects of the Mediterranean Diet on Cardiovascular Outcomes-A Systematic Review and Meta-Analysis.

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BACKGROUND: A Mediterranean dietary pattern is widely recommended for the prevention of chronic disease. We sought to define the most likely effects of the Mediterranean diet on vascular disease and mortality.

METHODS: We searched MEDLINE, EMBASE and the Cochrane Central Register without language restriction for randomized controlled trials comparing Mediterranean to control diets. Data on study design, patient characteristics, interventions, follow-up duration, outcomes and adverse events were sought. Individual study relative risks (RR) were pooled to create summary estimates.

RESULTS: Six studies with a total of 10950 participants were included. Effects on major vascular events (n = 477), death (n = 693) and vascular deaths (n = 315) were reported for 3, 5 and 4 studies respectively. For one large study (n = 1000) there were serious concerns about the integrity of the data. When data for all studies were combined there was evidence of protection against major vascular events (RR 0.63, 95% confidence interval 0.53-0.75), coronary events (0.65, 0.50-0.85), stroke (0.65, 0.48-0.88) and heart failure (0.30, 0.17-0.56) but not for all-cause mortality (1.00, 0.86-1.15) or cardiovascular mortality (0.90, 0.72-1.11). After the study of concern was excluded the benefit for vascular events (0.69, 0.55-0.86) and stroke (0.66, 0.48-0.92) persisted but apparently positive findings for coronary events (0.73, 0.51-1.05) and heart failure (0.25, 0.05-1.17) disappeared.

CONCLUSION: The Mediterranean diet may protect against vascular disease. However, both the quantity and quality of the available evidence is limited and highly variable. Results must be interpreted with caution.

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Stereological Analysis of Liver Biopsy Histology Sections as a Reference Standard for Validating Non-Invasive Liver Fat Fraction Measurements by MRI.

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BACKGROUND AND AIMS: Validation of non-invasive methods of liver fat quantification requires a reference standard. However, using standard histopathology assessment of liver biopsies is problematical because of poor repeatability. We aimed to assess a stereological method of measuring volumetric liver fat fraction (VLFF) in liver
biopsies and to use the method to validate a magnetic resonance imaging method for measurement of VLFF.

METHODS: VLFFs were measured in 59 subjects (1) by three independent analysts using a stereological point counting technique combined with the Delesse principle on liver biopsy histological sections and (2) by three independent analysts using the HepaFat-Scan technique on magnetic resonance images of the liver. Bland Altman statistics and intraclass correlation (IC) were used to assess the repeatability of each method and the bias between the methods of liver fat fraction measurement.

RESULTS: Inter-analyst repeatability coefficients for the stereology and HepaFat-Scan methods were 8.2 (95% CI 7.7-8.8)% and 2.4 (95% CI 2.2-2.5)% VLFF respectively. IC coefficients were 0.86 (95% CI 0.69-0.93) and 0.990 (95% CI 0.985-0.994) respectively. Small biases (<3.4%) were observable between two pairs of analysts using stereology while no significant biases were observable between any of the three pairs of analysts using HepaFat-Scan. A bias of 1.4+/−0.5% VLFF was observed between the HepaFat-Scan method and the stereological method.

CONCLUSIONS: Repeatability of the stereological method is superior to the previously reported performance of assessment of hepatic steatosis by histopathologists and is a suitable reference standard for validating non-invasive methods of measurement of VLFF.

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**Water First Aid Is Beneficial In Humans Post-Burn: Evidence from a Bi-National Cohort Study.**


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INTRODUCTION: Reported first aid application, frequency and practices around the world vary greatly. Based primarily on animal and observational studies, first aid after a burn injury is considered to be integral in reducing scar and infection, and the need for surgery. The current recommendation for optimum first aid after burn is water cooling for 20 minutes within three hours. However, compliance with this guideline is reported as poor to moderate at best and evidence exists to suggest that overcooling can be detrimental. This prospective cohort study of a bi-national burn patient registry examined data collected between 2009 and 2012. The aim of the study was to quantify the magnitude of effects of water cooling first aid after burn on indicators of burn severity in a large human cohort.

METHOD: The data for the analysis was provided by the Burn Registry of Australia and New Zealand (BRANZ). The application of first aid cooling prior to admission to a dedicated burn service, was analysed for its influence on four outcomes related to injury severity. The patient related outcomes were whether graft surgery occurred, and death while the health system (cost) outcomes included total hospital length of stay and admission to ICU. Robust regression analysis using bootstrapped estimation adjusted using a propensity score was used to control for confounding and to estimate the strength of association with first aid. Dose-response relationships were examined to determine associations with duration of first aid. The influence of covariates on the impact of first aid was assessed.

RESULTS: Cooling was provided before Burn Centre admission for 68% of patients, with at least twenty minutes
duration for 46%. The results indicated a reduction in burn injury severity associated with first aid. Patients probability for graft surgery fell by 0.070 from 0.537 (13% reduction) (p = 0.014). The probability for ICU admission fell by 0.084 from 0.175 (48% reduction) (p<0.001) and hospital length of stay (LOS) fell by 2.27 days from 12.9 days (18% reduction) (p = 0.001). All outcomes except death showed a dose-response relationship with the duration of first aid. The size of burn and age interacted with many of the relationships between first aid and outcome and these are described and discussed.

DISCUSSION & CONCLUSION: This study suggests that there are significant patient and health system benefits from cooling water first aid, particularly if applied for up to 20 minutes. The results of this study estimate the effect size of post-burn first aid and confirm that efforts to promote first aid knowledge are not only warranted, but provide potential cost savings.

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**Molecular Epidemiology of Methicillin-Resistant Staphylococcus aureus Isolated from Australian Veterinarians.**

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This work investigated the molecular epidemiology and antimicrobial resistance of methicillin-resistant Staphylococcus aureus (MRSA) isolated from veterinarians in Australia in 2009. The collection (n = 44) was subjected to extensive molecular typing (MLST, spa, SCCmec, dru, PFGE, virulence and antimicrobial resistance genotyping) and antimicrobial resistance phenotyping by disk diffusion. MRSA was isolated from Australian veterinarians representing various occupational emphases. The isolate collection was dominated by MRSA strains belonging to clonal complex (CC) 8 and multilocus sequence type (ST) 22. CC8 MRSA (ST8-IV [2B], spa t064; and ST612-IV [2B], spa variable,) were strongly associated with equine practice veterinarians (OR = 17.5, 95% CI = 3.3-92.5, P < 0.001) and were often resistant to gentamicin and rifampicin. ST22-IV [2B], spa variable, were strongly associated with companion animal practice veterinarians (OR = 52.5, 95% CI = 5.2-532.7, P < 0.001) and were resistant to ciprofloxacin. A single pig practice veterinarian carried ST398-V [5C2], spa t1451. Equine practice and companion animal practice veterinarians frequently carried multiresistant-CC8 and ST22 MRSA, respectively, whereas only a single swine specialist carried MRSA ST398. The presence of these strains in veterinarians may be associated with specific antimicrobial administration practices in each animal species.

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Pathological relationships involving iron and myelin may constitute a shared mechanism linking various rare and common brain diseases.

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We previously demonstrated elevated brain iron levels in myelinated structures and associated cells in a hemochromatosis Hfe (-/-) xTfr2 (mut) mouse model. This was accompanied by altered expression of a group of myelin-related genes, including a suite of genes causatively linked to the rare disease family 'neurodegeneration with brain iron accumulation' (NBIA). Expanded data mining and ontological analyses have now identified additional myelin-related transcriptome changes in response to brain iron loading. Concordance between the mouse transcriptome changes and human myelin-related gene expression networks in normal and NBIA basal ganglia testifies to potential clinical relevance. These analyses implicate, among others, genes linked to various rare central hypomyelinating leukodystrophies and peripheral neuropathies including Pelizaeus-Merzbacher-like disease and Charcot-Marie-Tooth disease as well as genes linked to other rare neurological diseases such as Niemann-Pick disease. The findings may help understand interrelationships of iron and myelin in more common conditions such as hemochromatosis, multiple sclerosis and various psychiatric disorders.

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Meconium periorchitis - an uncommon cause of perinatal scrotal swelling.

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BACKGROUND: Participation of compatible pairs (CP) in kidney paired donation (KPD) could be attractive to CPs who have a high degree of HLA mismatch, if the CP recipient will gain a better HLA match. Because KPD programs were not designed to help CP, it is important to define allocation metrics that enable CP to receive a better-matched kidney, without disadvantage to incompatible pairs (ICP).

METHODS: Simulations using 46 ICPs and 11 fully HLA-mismatched CPs were undertaken using the Australian KPD matching algorithm. Allocations were performed adding 1 CP at a time or all 11 CPs at once, and with and without exclusion of unacceptable antigens selected to give a virtual calculated panel-reactive antibody ranging 70% to 80% to improve HLA matching in CP recipients.

RESULTS: On average, most CP recipients could be matched and had a lower eplet mismatch (EpMM) with the matched donor (57 +/- 15) than with their own donor (78 +/- 19, P < 0.02). However, only recipients who had an EpMM to own donor greater than 65 achieved a significant reduction in the EpMM with the matched donor. The gain in EpMM was larger when CPs were listed with unacceptable antigens. Furthermore, inclusion of 1 CP at a time increased matching in ICP by up to 33%, and inclusion of all 11 CPs at once increased ICP matching by 50%.

CONCLUSIONS: Compatible pair participation in KPD can increase match rates in ICP and can provide a better immunological profile in CP recipients who have a high EpMM to their own donor when using allocation based on virtual crossmatch. Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

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Elements of cultural competence in an Australian Aboriginal maternity program.

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Background: Pregnancy, labour and neonatal health outcomes for Australian Aboriginal women and their infants are frequently worse than those of the general population. Provision of culturally competent services may reduce these differences by improving access to timely and regular antenatal care. In an effort to address these issues, the Aboriginal Maternity Group Practice Program commenced in south metropolitan Perth, Western Australia, in 2011.

The program employed Aboriginal Grandmothers, Aboriginal Health Officers and midwives working in a partnership model with pre-existing maternity services in the area. Aim: To identify elements of the Aboriginal Maternity Group Practice Program that contributed to the provision of a culturally competent service. Methods: The Organisational Cultural Competence Assessment Tool was used to analyse qualitative data obtained from surveys of 16 program
clients and 22 individuals from partner organisations, and interviews with 15 staff. Findings: The study found that the partnership model positively impacted on the level of culturally appropriate care provided by other health service staff, particularly in hospitals. Two-way learning was a feature. Providing transport, team home visits and employing Aboriginal staff improved access to care. Grandmothers successfully brought young pregnant women into the program through their community networks, and were able to positively influence healthy lifestyle behaviours for clients. Conclusion: Many elements of the Aboriginal Maternity Group Practice Program contributed to the provision of a culturally competent service. These features could be considered for inclusion in antenatal care models under development in other regions with culturally diverse populations. Copyright © 2016 Australian College of Midwives.


Characteristics and outcomes of patients treated with airway pressure release ventilation for acute respiratory distress syndrome: A retrospective observational study.
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Background: The optimal mode of ventilation in acute respiratory distress syndrome (ARDS) remains uncertain. Airway pressure release ventilation (APRV) is a recognized treatment for mechanically-ventilated patients with severe hypoxaemia. However, contemporary data on its role as a rescue modality in ARDS is lacking. The goal of this study was to describe the clinical and physiological effects of APRV in patients with established ARDS. Methods: This retrospective observational study was performed in a 23-bed adult intensive care unit in a tertiary extracorporeal membrane oxygenation (ECMO) referral centre. Patients with ARDS based on Berlin criteria were included through a prospectively-collected APRV database. Patients receiving APRV for less than six hours were excluded. Results: Fifty patients fulfilled the eligibility criteria. Prior to APRV initiation, median Murray Lung Injury Score was 3.5 (interquartile range (IQR) 2.5-3.9) and PaO_2/FiO_2 significantly improved within twenty-four hours post-APRV initiation (ANOVA F(1, 27) = 24.34, P < .005). Two patients (4%) required intercostal catheter insertion for barotrauma. Only one patient (2%) required ECMO after APRV initiation, despite a majority (68%) fulfilling previously established criteria for ECMO at baseline. Hospital mortality rate was 38%. Conclusions: In patients with ARDS-related refractory hypoxaemia treated with APRV, an early and sustained improvement in oxygenation, low incidence of clinically significant barotrauma and progression to ECMO was observed. The safety and efficacy of APRV requires further consideration. Copyright © 2016 Elsevier Inc.

Pancreatic neuroendocrine tumor control: Durable objective response to combination 177Lu-octreotide-capecitabine-temozolomide radiopeptide chemotherapy.
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Background/Methods: Thirty patients with advanced progressive grade 1 or 2 pancreatic neuroendocrine tumors (pNETs), treated on a prospective phase II single-center study, were followed up for up to 4 years after 4 cycles of 7.9 GBq <sup>177</sup>Lu-octreotate combined with chemotherapy. Each 8-week cycle of treatment combined radiopeptide therapy with 14 days of capecitabine at 1,500 mg/m<sup>2</sup> and 5 days of temozolomide at 200 mg/m<sup>2</sup>. Results: The overall response rate was 80% (95% CI 66-93), and there was complete remission in 13% (95% CI 4-30) and partial response in 70% (95% CI 52-83) of the cases. No patient manifested progressive disease on treatment. Median progression-free survival was 48 months. Median overall survival had not been reached at a median follow-up of 33 months. No patient was lost to follow-up, all but 1 received 4 cycles of outpatient therapy, and all were evaluated for response and toxicity. No one required hospital admission. The treatment was well tolerated, and no serious dose-limiting toxicities were seen. The commonest toxicity was transient nausea of grade 2 (33%) or 3 (7%). Hematological toxicity was limited to grade 3 thrombocytopenia (10%) and anemia (10%). There were no grade 4 adverse events, and no renal functional impairment was evident. Conclusion: Combined <sup>177</sup>Lu-octreotate-capecitabine-temozolomide radiopeptide chemotherapy is a well-tolerated, highly effective outpatient regimen for control of advanced progressive pNETs, achieving a durable objective response.

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Predictors of moderate to severe fatigue 12 months following admission to hospital for burn: Results from the Burns Registry of Australia and New Zealand (BRANZ) Long Term Outcomes project.

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Introduction Fatigue has been identified as an outcome of concern following burn but is rarely captured in outcomes studies. We aimed to: (i) describe the prevalence, and predictors, of moderate to severe fatigue in the first 12 months following burn, and (ii) establish the association between fatigue and health-related quality of life and work outcomes. Methods Adult burns patients, admitted >24 h, were recruited from five BRANZ sites. Participants were followed-up at 1-, 6-, and 12-months after injury using the Brief Fatigue Inventory (BFI), 36-item Short Form Health Survey (SF-36) and the Sickness Impact Profile (SIP)-work scale. Moderate to severe fatigue was defined as a global BFI score of 4-10. Multivariable mixed effects regression modelling was used to identify demographic, socioeconomic, burn size and severity predictors of moderate/severe fatigue at follow-up. Results The mean +/- SD age of the 328 participants was 42.1 +/- 16.7 years, 70% were male, 47% were flame burns, and the mean +/- SD %TBSA was 8.7 +/- 11.2. The prevalence of moderate/severe fatigue decreased from 37% at 1-month, to 32% at 6-months and 26% at 12-months. The adjusted odds of moderate/severe fatigue were 2.62 (95% CI: 1.27, 5.42) times higher for women compared to men, and 2.64 (95% CI: 1.03, 6.79) times higher in patients with a %TBSA > 20. Compared to patients in major cities, the adjusted odds of reporting moderate/severe fatigue were 2.48 fold higher (95% CI: 1.17, 5.24) for patients residing in inner regional areas, and 3.60 fold (95% CI: 1.43, 9.05) higher for patients living in remote/very remote areas. At
each time point, the physical and mental health summary scores, and each sub-scale score, of the SF-36 were significantly lower in patients reporting moderate/severe fatigue. Patients experiencing moderate to severe fatigue reported higher work-related disability on the SIP work scale at each time point after injury. Discussion and conclusion More than a quarter of participants reported moderate to severe fatigue on the BFI at 12-months and fatigue was strongly associated with poorer health-related quality of life and greater work-related disability. Copyright © 2016 Elsevier Ltd and ISBI PMID:613711942 DOI:http://dx.doi.org/10.1016/j.burns.2016.08.036 http://www.elsevier.com/locate/burns

Assuring the quality of interpretative comments in clinical chemistry.
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The provision of interpretative advice on laboratory results is a post-analytic activity and an integral part of clinical laboratory services. It is valued by healthcare workers and has the potential to prevent or reduce errors and improve patient outcomes. It is important to ensure that interpretative comments provided by laboratory personnel are of high quality: comments should be patient-focused and answer the implicit or explicit question raised by the requesting clinician. Comment providers need to be adequately trained and qualified and be able to demonstrate their proficiency to provide advice on laboratory reports. External quality assessment (EQA) schemes can play a part in assessing and demonstrating the competence of such laboratory staff and have an important role in their education and continuing professional development. A standard structure is proposed for EQA schemes for interpretative comments in clinical chemistry, which addresses the scope and method of assessment including nomenclature and marking scales. There is a need for evidence that participation in an EQA program for interpretative commenting facilitates improved quality of comments. It is proposed that standardizing goals and methods of assessment as well as nomenclature and marking scales may help accumulate evidence to demonstrate the impact of participation in EQA for interpretative commenting on patient outcome. Copyright © 2016 Walter de Gruyter GmbH, Berlin/Boston.
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A binational multicenter pilot feasibility randomized controlled trial of early goal-directed mobilization in the ICU.
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Objectives: To determine if the early goal-directed mobilization intervention could be delivered to patients receiving mechanical ventilation with increased maximal levels of activity compared with standard care. Design: A pilot randomized controlled trial. Setting: Five ICUs in Australia and New Zealand. Participants: Fifty critically ill adults mechanically ventilated for greater than 24 hours. Intervention: Patients were randomly assigned to either early goal-directed mobilization (intervention) or to standard care (control). Early goal-directed mobilization comprised functional rehabilitation treatment conducted at the highest level of activity possible for that patient assessed by the ICU mobility scale while receiving mechanical ventilation. Measurements and Main Results: The ICU mobility scale, strength, ventilation duration, ICU and hospital length of stay, and total inpatient (acute and rehabilitation) stay as well as 6-month post-ICU discharge health-related quality of life, activities of daily living, and anxiety and depression were recorded. The mean age was 61 years and 60% were men. The highest level of activity (ICU mobility scale) recorded during the ICU stay between the intervention and control groups was mean (95% CI) 7.3 (6.3-8.3) versus 5.9 (4.9-6.9), p = 0.05. The proportion of patients who walked in ICU was almost doubled with early goal-directed mobilization (intervention n = 19 [66%] vs control n = 8 [38%]; p = 0.05). There was no difference in total inpatient stay (d) between the intervention versus control groups (20 [15-35] vs 34 [18-43]; p = 0.37). There were no adverse events. Conclusions: Key Practice Points: Delivery of early goal-directed mobilization within a randomized controlled trial was feasible, safe and resulted in increased duration and level of active exercises. Copyright © 2016 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc.

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http://journals.lww.com/ccmj/article/Content/D=emed18a&AN=608968219


Meconium evacuation for facilitating feed tolerance in preterm neonates: A systematic review and meta-analysis.
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Background: A delayed passage of meconium is considered as a risk factor for feed intolerance in preterm neonates. Objectives: The aim of this study was to review the effects of different therapeutic agents for meconium evacuation on feed tolerance in preterm neonates. Methods: A systematic review of randomised controlled trials (RCTs) of different therapeutic agents for meconium evacuation in preterm neonates (gestation <32 weeks and/or birth weight <1,500 g) using the Cochrane systematic review methodology was undertaken. Databases including Google Scholar were searched in January 2016. The primary outcome was the time to reach full feeds (TFF; >120 ml/kg feeds with stoppage of parenteral nutrition >24 h). Secondary outcomes included necrotising enterocolitis (NEC), weight at discharge and adverse effects. The results were summarised as per the GRADE guidelines. Results: Six RCTs (2 each of glycerine suppository and enema, 1 normal saline enema and 1 oral osmotic contrast agent; n = 442) with a low or unclear risk of bias were included. The pooled estimate (random effects model) showed no reduction in TFF [mean difference (MD) -0.03, 95% CI -2.47, 2.41, p = 0.98; level of evidence: low]. No differences in NEC [risk ratio (RR) 1.71, 95% CI 0.63, 4.65, p = 0.30; level of evidence: low] and weight at discharge (MD -0.08, 95% CI -0.30, 0.15, p = 0.50; level of evidence: low) were found. The trial assessing oral osmotic contrast agents reported a trend towards a higher incidence of NEC > stage II. There were no other adverse effects. Conclusion: Limited low-quality evidence indicates that prophylactic glycerine suppository, small volume glycerine/normal saline enema or oral osmotic contrast agents to evacuate meconium did not reduce TFF in preterm neonates. Large, well-designed trials are essential to study this clinically significant issue. Copyright © 2016 S. Karger AG, Basel.

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Summary and recommendations from the Australasian guidelines for the management of pancreatic exocrine insufficiency.

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Background To evaluate the efficacy of treatment with nefiracetam compared to placebo in poststroke apathy.

Methods A parallel group, randomized, placebo-controlled, double-blind two-center trial in patients with recent stroke and apathy was conducted in 2 tertiary teaching hospitals in Perth, Western Australia, between March 2010 and October 2014. Consenting patients hospitalized with stroke were screened for participation at the time of hospitalization and, if diagnosed with apathy 8-36 weeks later, they were randomized to 12 weeks of 900 mg/day nefiracetam or placebo. The primary efficacy parameter was change in apathy at 12 weeks defined by the 14-item Apathy Scale (AS). Results Of 2514 patients screened, only 377 (15%) were eligible for the study after the first screening, 233 declined further participation, and 144 were assessed for apathy at 8-36 weeks post stroke to confirm eligibility. Twenty patients out of 106 with a complete psychiatric assessment had apathy (19%). Of this sample, 13 patients were randomized. Overall, the AS score decreased by a mean of 7.0 points (95% CI = -14.6 to 6), but there was no significant between-group difference at week 12 (mean paired t-tests, P >.14). Conclusions Treatment with nefiracetam did not prove to be more efficacious than placebo in ameliorating apathy in stroke. The main limitation was the very small sample randomized, highlighting the limitations of conducting drug trials for behavioral problems among stroke patients. Pharmacological studies of apathy in stroke will require a large multicenter study and a massive sample of patients. Copyright © 2016 National Stroke Association.
Testing the models using leave one-out cross validation, hold out validation and cross-hold out validation supported the validity of LUR models for PM$_{<10}$, PM$_{<2.5}$ and PM$_{<2.5}$Abs and their corresponding elements in Metropolitan Perth despite the relatively low concentrations. Copyright © 2016 Elsevier Ltd


**Acetabular Version Increases After Closure of the Triradiate Cartilage Complex.**

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**Background:** Although the etiology of primary femoroacetabular impingement (FAI) is considered developmental, the underlying pathogenic mechanisms remain poorly understood. In particular, research identifying etiologic factors associated with pincer FAI is limited. Knowledge of the physiologic growth patterns of the acetabulum during skeletal maturation might allow conclusions on deviations from normal development that could contribute to pincer-related pathomorphologies. 

**Questions/purposes:** In a population of healthy children, we asked if there were any differences related to skeletal maturation with regard to (1) acetabular version; (2) acetabular depth/width ratio; and (3) femoral head coverage in the same children as assessed by MRIs obtained 1 year apart. Methods: We prospectively compared 129 MRIs in 65 asymptomatic volunteers without a known hip disorder from a mixed primary/high school population (mean age, 12.7 years; range, 7-16 years). All participants underwent two MRI examinations separated by a minimum interval of 1 year. Based on the status of the triradiate cartilage complex (open versus closed [TCC]), all hips were allocated to the following groups: "open-open" = open TCC at both MRIs (n = 45 hips [22 bilateral]); "open-closed" = open TCC at initial and closed TCC at followup MRI (n = 26 hips [13 bilateral]); and "closed-closed" group = closed TCC at both MRIs (n = 58 hips [29 bilateral]). We assessed acetabular version in the axial plane at five different locations (5, 10, 15, 20 mm below the acetabular dome and at the level of the femoral head) as well as three-dimensional (3-D) acetabular depth/width ratio and 3-D femoral head coverage on six radial MRI sequences oriented circumferentially around the femoral neck axis. Using analysis of variance for multigroup comparisons with Bonferroni adjustment for pairwise comparisons, we compared the results between the initial and followup MRI examinations and among the three groups. Results: Acetabular version was increased in hips of the "open-closed" group at the followup MRI compared with the initial MRI at 5 mm (-6 +/- 4.6 [95% confidence interval [CI], -7.6 to -3.6] versus -1 +/- 5.0 [95% CI, -3.3 to 0.7]; p < 0.001), 10 mm (0 +/- 4.0 [95% CI, -1.6 to 2.1] versus 7 +/- 4.6 [95% CI, 4.4-8.7]; p < 0.001), and 15 mm (8 +/- 5.0 [95% CI, 6.1-10.2] versus 15 +/- 4.6 [95% CI, 13.3-17.4]; p < 0.001) below the acetabular dome. Acetabular version did not change between the initial and followup MRI in the "open-open" and "closed-closed" groups. Independently of the groups, acetabular version was increased in all hips with a fused TCC compared with hips with an open TCC (mean difference measured at 5 mm below the acetabular dome at initial MRI examination: 2degree +/- 5.9degree [95% CI, 0.2degree-3.4degree] versus -9degree +/- 4.4degree [95% CI, -9.9degree to -7.8degree]; p < 0.001; at followup MRI examination: 1degree +/- 5.7degree [95% CI, 0.1degree-2.7degree] versus -9degree +/- 3.8degree [95% CI, -10degree to -7.6degree]; p < 0.001). Both acetabular depth/width ratio and femoral head coverage did not differ among the groups or between the initial and followup MRI examinations within each group. Conclusions: Although acetabular depth/width ratio and femoral head coverage remain relatively constant, acetabular version increases with advancing skeletal maturity. There seems to be a relatively narrow timeframe near physeal closure of the TCC within which acetabular orientation changes to more pronounced anteverision. Further studies with greater numbers and longer followup periods are required to support these findings and determine whether such version changes may contribute to pincer-type pathomorphologies. Level of Evidence: Level II, prospective study. Copyright © 2016 The Association of Bone and Joint Surgeons

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Erratum to "The implications of endemic IMP-4 carbapenemase for clinical laboratory susceptibility testing" (J. Microbiol. Methods (2016) 124 (10-12) (S0167701216300355) (10.1016/j.mimet.2016.03.001)).
Goire N, Harnett GB, et al.


The publisher regrets that the name of one of the authors of is misspelt as Davild. It should be David and not Davild. The publisher would like to apologise for any inconvenience caused.

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Ampullary Cancers Harbor ELF3 Tumor Suppressor Gene Mutations and Exhibit Frequent WNT Dysregulation.

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Ampullary Cancers Harbor ELF3 Tumor Suppressor Gene Mutations and Exhibit Frequent WNT Dysregulation.
The ampulla of Vater is a complex cellular environment from which adenocarcinomas arise to form a group of histopathologically heterogeneous tumors. To evaluate the molecular features of these tumors, 98 ampullary adenocarcinomas were evaluated and compared to 44 distal bile duct and 18 duodenal adenocarcinomas. Genomic analyses revealed mutations in the WNT signaling pathway among half of the patients and in all three adenocarcinomas irrespective of their origin and histological morphology. These tumors were characterized by a high frequency of inactivating mutations of ELF3, a high rate of microsatellite instability, and common focal deletions and amplifications, suggesting common attributes in the molecular pathogenesis are at play in these tumors. The high frequency of WNT pathway activating mutation, coupled with small-molecule inhibitors of beta-catenin in clinical trials, suggests future treatment decisions for these patients may be guided by genomic analysis.
Objective: Pentoxifylline has previously been shown to increase haemoglobin levels in patients with chronic kidney disease (CKD) and erythropoietin-stimulating agent (ESA)-hyporesponsive anaemia in the HERO multi-centre double-blind, randomized controlled trial. The present study evaluated the effects of pentoxifylline on oxidative stress in ESA-hyporesponsive CKD patients. Methods: This sub-study of the HERO trial compared 15 patients in the pentoxifylline arm (400 mg daily) and 17 in the matched placebo arm on oxidative stress markers: plasma total F2-isoprostanes, protein carbonyls, glutathione peroxidase (GPX), and superoxide dismutase (SOD) activities. Results: Pentoxifylline did not significantly alter total F2-isoprostanes (adjusted mean difference (MD) 35.01 pg/ml, P = 0.11), SOD activity (MD 0.82 U/ml, P = 0.07), GPX activity (MD -6.06 U/l, P = 0.09), or protein carbonyls (MD -0.04 nmol/mg, P = 0.52). Replicating results from the main study, pentoxifylline significantly increased haemoglobin concentration compared with controls (MD 7.2 g/l, P = 0.04). Conclusions: Pentoxifylline did not alter oxidative stress biomarkers, suggesting that alternative mechanisms may be responsible for the agent’s ability to augment haemoglobin levels in CKD patients with ESA-hyporesponsive anaemia. Copyright © 2016 Informa UK Limited, trading as Taylor & Francis Group.


Dysregulation of innate immunity in ulcerative colitis patients who fail anti-Tumor necrosis factor therapy

Basic Study.

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To study the innate immune function in ulcerative AIM To study the innate immune function in ulcerative Submit a Manuscript: http://www.wjgnet.com/esps/ Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx DOI: 10.3748/wjg.v22.i41.9104 WJG www.wjgnet.com 9104 November 7, 2016 Volume 22 Issue 41 World J Gastroenterol 2016 November 7; 22(41): 9104-9116 ISSN 1007-9327 (print) ISSN 2219-2840 (online). ORIGINAL ARTICLE Dysregulation of innate immunity in ulcerative colitis patients who fail anti-Tumor necrosis factor therapy Basic Study Angela C Baird, Dominic Mallon, Graham Radford-Smith, Julien Boyer, Thierry Piche, Susan L Prescott, Ian C Lawrance, Meri K Tulic colitis (UC) patients who fail to respond to anti-Tumor necrosis factor (TNF) therapy. METHODS Effects of anti-TNF therapy, inflammation and medications on innate immune function were assessed by measuring peripheral blood mononuclear cell (PBMC) cytokine expression from 18 inflammatory bowel disease patients pre-And 3 mo post-Anti-TNF therapy. Toll-like receptor (TLR) expression and cytokine production post TLR stimulation was assessed in UC “responders” (n = 12) and “non-responders” (n = 12) and compared to healthy controls (n = 12). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were measured in blood to assess disease severity/activity and inflammation. Pro-inflammatory (TNF, IL-1beta, IL-6), immuno-regulatory (IL-10), Th1 (IL-12, IFNgamma) and Th2 (IL-9, IL-13, IL-17A) cytokine expression was measured with enzyme-linked immunosorbent assay while TLR cellular composition and intracellular signalling was assessed with FACS. RESULTS Prior to anti-TNF therapy, responders and nonresponders had similar level of disease severity and activity. PBMC’s ability to respond to TLR
stimulation was not affected by TNF therapy, patient's severity of the disease and inflammation or their medication use. At baseline, non-responders had elevated innate but not adaptive immune responses compared to responders (P < 0.05). Following TLR stimulation, non-responders had consistently reduced innate cytokine responses to all TLRs compared to healthy controls (P < 0.01) and diminished TNF (P < 0.001) and IL-1β (P < 0.01) production compared to responders. This innate immune dysfunction was associated with reduced number of circulating plasmacytoid dendritic cells (pDCs) (P < 0.01) but increased number of CD4+ regulatory T cells (Tregs) (P = 0.03) as well as intracellular accumulation of IRAK4 in non-responders following TLR-2, -4 and -7 activation (P < 0.001). CONCLUSION Reduced innate immunity in non-responders may explain reduced efficacy to anti-TNF therapy. These serological markers may prove useful in predicting the outcome of costly anti-TNF therapy. Copyright © 2016 Baishideng Publishing Group Inc. All rights reserved.

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**Serum bicarbonate concentration and the risk of cardiovascular disease and death in type 2 diabetes: the Fremantle Diabetes Study.**
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BACKGROUND: Serum bicarbonate is associated with mortality, heart failure (HF) and progression of renal failure in studies of healthy people and patients with chronic kidney disease, but the significance of these observations in unselected patients with diabetes in the general population is unknown. The aim of this study was to determine whether serum bicarbonate was associated with mortality and cardiovascular disease risk in type 2 diabetes.

METHODS: Baseline serum bicarbonate was available for 1283 well-characterized community-based patients (mean +/- SD age 64.1 +/- 11.3 years, 48.7 % males) from the longitudinal observational Fremantle Diabetes Study followed for a mean of 12 years. Associations between serum bicarbonate and mortality, coronary heart disease (CHD) and incident HF were analysed using Cox proportional hazards regression.

RESULTS: Serum bicarbonate was independently and negatively associated with incident CHD. For each 1 mmol/L increase in bicarbonate, the hazard ratio for CHD was 0.95 (95 % confidence interval 0.92-0.99) after adjustment for age as time scale, age at baseline, sex, English fluency, diabetes duration, log<sub>e</sub>(serum triglycerides), log<sub>e</sub>(urinary albumin: creatinine ratio), peripheral sensory neuropathy and peripheral arterial disease. There were no independent associations between serum bicarbonate and all-cause mortality [0.98 (0.95-1.004)] or incident HF [0.99 (0.95-1.03)].

CONCLUSIONS: Serum bicarbonate was a significant independent predictor of incident CHD but not death or HF in community-based patients with type 2 diabetes. This supports intervention trials of bicarbonate replacement in type 2 patients at risk of CHD and who have a low serum bicarbonate concentration.

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**Lung cancer screening in Australia: Progress or procrastination?: There is progress internationally with lung cancer screening but far slower headway in Australia.**
Graft nephrectomy for people with a failed kidney transplant.
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This is a protocol for a Cochrane Review (Intervention). The objectives are as follows: The review aims to look at the immunological and clinical benefits and harms of graft nephrectomy for people with a failed kidney transplant.
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Neuroimaging in psychiatry: an update on neuroimaging in the clinical setting.
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OBJECTIVE: We offered guidance on the role of structural and functional neuroimaging modalities for the general psychiatrist and for trainees in the clinical setting.
METHODS: We outlined the utility of neuroimaging modalities in the clinical setting, specifically with a view to understanding the pathophysiology of manifestations of disease.
RESULTS: Both structural and functional neuroimaging modalities have a clear role in diagnostic evaluation in the spectrum of neurodegenerative disorders.
CONCLUSIONS: Whilst the role of neuroimaging in patients with mood, anxiety and psychotic disorders is less clear, structural and functional imaging modalities have utility in the clinical setting in the form of diagnostic refinement and in understanding the pathophysiology of disorders, towards explaining manifestations and planning treatment.
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Neuroimaging in psychiatry: an update on neuroimaging in the clinical setting.
Redox cycling metals: Pedaling their roles in metabolism and their use in the development of novel therapeutics.

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Essential metals, such as iron and copper, play a critical role in a plethora of cellular processes including cell growth and proliferation. However, concomitantly, excess of these metal ions in the body can have deleterious effects due to their ability to generate cytotoxic reactive oxygen species (ROS). Thus, the human body has evolved a very well-orchestrated metabolic system that keeps tight control on the levels of these metal ions. Considering their very high proliferation rate, cancer cells require a high abundance of these metals compared to their normal counterparts. Interestingly, new anti-cancer agents that take advantage of the sensitivity of cancer cells to metal sequestration and their susceptibility to ROS have been developed. These ligands can avidly bind metal ions to form redox active metal complexes, which lead to generation of cytotoxic ROS. Furthermore, these agents also act as potent metastasis suppressors due to their ability to up-regulate the metastasis suppressor gene, N-myc downstream regulated gene 1. This review discusses the importance of iron and copper in the metabolism and progression of cancer, how they can be exploited to target tumors and the clinical translation of novel anti-cancer chemotherapeutics.

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The role of heparin in a warfarinized patient with mesenteric venous thrombosis.

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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.

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Early postoperative repair status after rotator cuff repair cannot be accurately classified using questionnaires of patient function and isokinetic strength evaluation.


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BACKGROUND: This study investigated if patients with an intact tendon repair or partial-thickness retear early after rotator cuff repair display differences in clinical evaluations and whether early tendon healing can be predicted using these assessments.

METHODS: We prospectively evaluated 60 patients at 16 weeks after arthroscopic supraspinatus repair. Evaluation included the Oxford Shoulder Score, 11-item version of the Disabilities of the Arm, Shoulder and Hand, visual analog scale for pain, 12-item Short Form Health Survey, isokinetic strength, and magnetic resonance imaging (MRI). Independent t tests investigated clinical differences in patients based on the Sugaya MRI rotator cuff classification system (grades 1, 2, or 3). Discriminant analysis determined whether intact repairs (Sugaya grade 1) and partial-thickness retears (Sugaya grades 2 and 3) could be predicted.

RESULTS: No differences (P < .05) existed in the clinical or strength measures. Although discriminant analysis revealed the 11-item version of the Disabilities of the Arm, Shoulder and Hand produced a 97% true-positive rate for predicting partial thickness retears, it also produced a 90% false-positive rate whereby it incorrectly predicted a retear in 90% of patients whose repair was intact. The ability to discriminate between groups was enhanced with up to 5 variables entered; however, only 87% of the partial-retear group and 36% of the intact-repair group were correctly classified.

CONCLUSIONS: No differences in clinical scores existed between patients stratified by the Sugaya MRI classification system at 16 weeks. An intact repair or partial-thickness retear could not be accurately predicted. Our results suggest that correct classification of healing in the early postoperative stages should involve imaging.

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Duration of diabetes and its association with depression in later life: The Health In Men Study (HIMS).

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Objective: To examine if diabetes and duration of diabetes are direct or indirect causes of depression in later life.

Research design and methods: Cross-sectional study of a community-derived sample of 5462 men aged 70-89 years. Men with 'current depression' scored 7 or more on the abbreviated Geriatric Depression Scale (GDS-15), whereas men with 'ever depression' were either currently depressed or reported history or treatment for past depression. The presence of diabetes was established by self-reported history, fasting glucose >7 mmol/L (126 mg/dL), or use of insulin or hypoglycemic drugs. Duration of diabetes relied on self-report. Other measured factors included age, place of birth, education, smoking history, and the FRAIL scale.

Results: Diabetes was associated with increased odds ratio (OR) of ever (OR=1.49, 95%CI=1.25, 1.76) and current depression (OR=1.94, 95%CI=1.15, 2.48). The association between duration of diabetes and risk of current depression was 'J-shaped' with odds ratios of 1.92 (95%CI=1.44, 2.54), 1.56 (95%CI=0.89, 2.75), 2.49 (95%CI=1.16, 5.32) and 3.13 (95%CI=1.28, 7.63) for <10, 10-19.9, 20-29.9 and >30 years of diabetes history compared with older men without diabetes. The strength of these associations was attenuated after the analyses were adjusted for other measured factors, but the shape of the curve did not change. Structural equation modeling showed that frailty mediated some of the association between diabetes and depression (about 15%) and was a strong predictor of depression in the sample.

Conclusions: In older men, the association between time lived with the diagnosis of diabetes and the risk of depression is 'J-shaped'. Frailty mediates some of the association between diabetes and depression, although other unmeasured factors are also likely to play a role. The introduction of strategies that are effective at decreasing diabetes-related complications may also contribute to decrease the risk of depression among older men.

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[Resection at symptomatic cam impingement. Use of a minimally invasive antero-lateral approach].


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Background: Surgical treatment of femoroacetabular impingement (FAI) is nowadays achieved by either open surgical hip dislocation or hip arthroscopy. However, drawbacks of both procedures include the invasiveness of the open procedure and a high learning curve to successfully perform arthroscopic treatment. In our institution, we established a minimally invasive, arthroscopically assisted, antero-lateral approach for the correction of cam type FAI.
OBJECTIVES: The goal of the study was to describe the surgical technique and highlight the short-term clinical outcome in a consecutive series of patients operated between 2011 and 2014 in our institution.

MATERIALS AND METHODS: In total, 77 patients were included in this study. The patients were allocated to two groups (Toennis = 0: Group I; Toennis 1 and 2: Group II). Clinical and radiographic follow up was obtained at 6 and 12 weeks postoperatively. Clinical outcome was assessed using the Hip-Outcome-Score.

RESULTS: The mean age of patients in Group I was 25 (16-48) years and in Group II 38 (17-50) years respectively. Internal rotation (IR) in 90° flexion increased by 11 degrees from pre- to postoperatively in Group I (p<0.001) and by 14 degree in Group II (p<0.001). The Hip Outcome Score revealed the ability to perform sports with reduced pain at three months follow up. Subjectively, all patients benefitted in terms of pain and hip function in both groups (p<0.001). There were no complications with long-term morbidity during the perioperative course.

CONCLUSION: Arthroscopically assisted cam resection using a minimally invasive anterolateral approach is a safe technique for the treatment of FAI. At short term follow up, nearly all operated patients seem to benefit in terms of pain and hip function. The influence of progression of osteoarthritis still has to be shown.

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Maximal exercise does not increase ventilation heterogeneity in healthy trained adults.


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The effect of exercise on ventilation heterogeneity has not been investigated. We hypothesized that a maximal exercise bout would increase ventilation heterogeneity. We also hypothesized that increased ventilation heterogeneity would be associated with exercise-induced arterial hypoxemia (EIAH). Healthy trained adult males were prospectively assessed for ventilation heterogeneity using lung clearance index (LCI), Scond, and Sacinat baseline, postexercise and at recovery, using the multiple breath nitrogen washout technique. The maximal exercise bout consisted of a maximal, incremental cardiopulmonary exercise test at 25 watt increments. Eighteen subjects were recruited with mean +/- SD age of 35 +/- 9 years. There were no significant changes in LCI, Scond, or Sacin at recovery. While there was an overall reduction in SpO2 with exercise (99.3 +/- 1 to 93.7 +/- 3%, P < 0.0001), the reduction in SpO2 was not associated with changes in LCI. Scondor Sacin Ventilation heterogeneity is not increased following a maximal exercise bout in healthy trained adults. Furthermore, EIAH is not associated with changes in ventilation heterogeneity in healthy trained adults.

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Red blood cell transfusion is associated with further bleeding and fresh-frozen plasma with mortality in nonvariceal upper gastrointestinal bleeding.

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BACKGROUND: Blood products are commonly transfused for patients with nonvariceal upper gastrointestinal bleeding (NVUGIB). While concerns exist about further bleeding and mortality in subsets of patients receiving red blood cell (RBC) transfusion, the impact of non-RBC blood products has not previously been systematically investigated. The aim of the study was to investigate the associations between blood products transfusion, further bleeding, and mortality after acute NVUGIB.

STUDY DESIGN AND METHODS: A retrospective cohort study examined further bleeding and 30-day and 1-year mortality in adult patients who underwent gastroscopy for suspected acute NVUGIB between 2008 and 2010 in three tertiary hospitals in Western Australia. Survival analysis was performed.

RESULTS: A total of 2228 adults (63% male) with 2360 hospital admissions for NVUGIB met the inclusion criteria. Median age at presentation was 70 years (range, 19-99 years). Thirty-day mortality was 4.9% and 1-year mortality was 13.9%. Transfusion of 4 or more units of RBCs was associated with greater than 10 times the odds of further bleeding in patients with a hemoglobin level of more than 90 g/L (odds ratio, 11.9; 95% confidence interval [CI], 3.1-45.7; p < 0.001), but was not associated with mortality. Administration of 5 or more units of fresh-frozen plasma (FFP) was associated with increased 30-day (hazard ratio, 2.8; 95% CI, 1.3-5.9; p = 0.008) and 1-year (hazard ratio, 2.6; 95% CI, 1.3-5.0; p = 0.005) mortality after adjusting for coagulopathy, comorbidity, Rockall score, and other covariates.

CONCLUSION: In this large, multicenter study of NVUGIB, RBC transfusion was associated with further bleeding but not mortality, while FFP transfusion was associated with increased mortality in a subset of patients.


Trends in incidence and prevalence of hospitalization for atrial fibrillation and associated mortality in Western Australia, 1995-2010.

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OBJECTIVE: Hospitalization for atrial fibrillation (AF) is a large and growing public health problem. We examined current trends in the incidence, prevalence, and associated mortality of first-ever hospitalization for AF.

METHODS: Linked hospital admission data were used to identify all Western Australia residents aged 35-84 years with prevalent AF and incident (first-ever) hospitalization for AF as a principal or secondary diagnosis during 1995-2010.

RESULTS: There were 57,552 incident hospitalizations, mean age 69.8 years, with 41.4% women. Over the calendar periods, age- and sex-standardized incidence of hospitalization for AF as any diagnosis declined annually by 1.1% (95% CI; 0.93, 1.29), while incident AF as a principal diagnosis increased annually by 1.2% (95% CI; 0.84, 1.50). Incident AF hospitalization was higher among men than women, and 15-fold higher in the 75-84 compared with 35-64 year age group. The age- and sex-standardized prevalence of AF increased annually by 2.0% (95% CI; 1.88, 2.03) over the same period. Comorbidity trends were mixed with diabetes and valvular heart disease increasing, and hypertension, coronary artery disease, heart failure, cerebrovascular disease, and chronic kidney disease decreasing. The 1-year all-cause mortality after incident AF hospitalization declined from 17.6% to 14.6% (trend P<0.001), with an adjusted hazard ratio of 0.86 (95% CI; 0.81, 0.91).

CONCLUSION: This contemporary study shows that incident AF hospitalization is not increasing except for AF as a principal diagnosis, while population prevalence of hospitalized AF has risen substantially. The high 1-year mortality following incident AF hospitalization has improved only modestly over the recent period.

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Moving toward an evidence and consensus based multi-centre enhanced recovery pathway for radical cystectomy: Results of an ANZUP survey.
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Introduction and Objectives: The introduction of an enhanced recovery pathway for radical cystectomy (RC) can safely reduce the high incidence of complications and prolonged length of stay associated with the procedure. However, the lack of a standardised multi-centre protocol has made it difficult to validate any individual interventions within these pathways. In order to best develop a standardised pathway, a consensus on current practice must first be sought.

Method: An online survey was developed by the Bladder Cancer Working Group of the Australian and New Zealand Urogenital and Prostate (ANZUP) cancer trials group and distributed to ANZUP urologists performing RC. The survey included questions about how they currently practiced RC and what their preferences were regarding peri-operative care for RC.

Results: Responses were received from 10 urologists, who performed a median of 10 RCs each year (range 4-25). The majority of respondents did not use bowel preparation (90%) or a nasogastric tube (90%). All respondents used peri-operative antibiotics, with single-agent cephalosporin favored by 89% and continued for at least 24 h by
The majority of respondents used paracetamol (100%), non-steroidal anti-inflammatories (89%) and patient-controlled analgesia (89%) in the postoperative period, with epidurals (56%) and sub-fascial local anaesthetic catheters (25%) being used less commonly. Chewing gum (80%) and metoclopramide (40%) were used for ileus prophylaxis, and only 30% of respondents routinely used gastrointestinal ulcer prophylaxis. Low-molecular weight heparin (80%) was preferred to unfractionated heparin (20%), with 80% of respondents continuing therapy for 4 weeks. Whilst the timing of drain removal was variable, 90% of respondents removed ureteric stents at between 10 and 14 days. Pre-operative nutritional support was variable, with some respondents giving it to none (30%), some (50%) and all (20%) of their patients; nutritional drinks (67%) were used more commonly than carbohydrate loading (38%). Progression of oral intake was variable, although 70% of respondents allowed nourishing fluids by day two and light diet by day three post-operatively. Conclusions: This survey provides useful information on the management of patients undergoing RC in Australia and New Zealand currently. Utilisation of this data in conjunction with a detailed literature review has allowed the development of an enhanced recovery pathway for RC based on evidence and consensus. This has been forwarded to interested institutions with a view to multi-centre introduction of the pathway, a prospective audit of patient outcomes, and a mechanism for testing promising new interventions in subsequent randomised trials.

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Could prompting referral to a urologist on investigation reports improve referral rates for visible haematuria? A case study-based survey.
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Introduction and Objectives: Patients with visible haematuria require urgent assessment in order to exclude urologic malignancy. However, recent research in Western Australia has identified that many of these patients experience significant delays prior to referral to a urologist, with 14% of patients requiring a re-presentation to a GP with recurrent visible haematuria before being referred (1). It was hypothesised that amending mid-stream urine (MSU) and imaging reports may improve the referral of these patients from primary care. Method: Standard and extended MSU and imaging reports were developed, with extended reports containing text in their conclusion that encouraged urologic referral. An online case study-based survey was then developed that randomly issued standard or extended MSU and imaging reports. A link to the survey was included in a Royal Australian College of General Practitioners Western Australia newsletter, as well as on an Australian GP Facebook© forum, resulting in 33 responses. Results: 31% (10/32) of GPs are not confident in managing patients with visible haematuria, and 44% (11/25) refer less than half of patients with visible haematuria to a urologist. GPs issued with extended MSU reports were significantly more likely to refer patients with visible haematuria to a urologist than those issued with standard reports, for both patients with no growth (100% vs. 56%, p = 0.03) or a bacterial growth (54% vs. 0%, p = 0.005). Improved referral with extended imaging reports (67% vs. 55%) did not reach statistical significance, although this may be related to low response rate. Conclusions: Modification of MSU reports to encourage urologic referral may improve the expeditious referral of patients with visible haematuria to a urologist.
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Inconsistent renal cell carcinoma follow up in tertiary cancer centre: Time for a different approach?
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Introduction and Objectives: Follow up of Renal Cancer (RCC) in patients who have undergone curative intent surgical treatment relies on early detection of recurrence or metastasis on the presumption that subsequent treatment at the time of low burden disease is associated with better patient outcomes(1). Follow up of these patients involves clinical examination, blood tests, imaging of the abdomen and chest. Several guidelines exist on optimal follow of patient following treatment of RCC (1,2,3). Our objective was to evaluate the follow up practices after curative intent treatment of RCC in a single Tertiary Centre in Western Australia. Methods: Patients who underwent curative intent treatment, radical nephrectomy (RN) or partial nephrectomy (PN), for RCC between 2005 to 2009 at a single centre were identified to evaluate their follow up. Patient demographics, tumour features, frequency of clinic appointments, type of imaging, blood tests and referral to appropriate specialty team were reviewed. Patients with cytoreductive nephrectomy, metastasis within 6 months of surgery, or second malignancies were excluded. Results: One hundred and five patients underwent either RN or PN for RCC. 71 patients were included in the study population (34 patients excluded), 43 male and 28 female patients, mean age was 58.5 years, mean duration of follow was 47.8 months, Mean timing of first clinic follow up was 5.7 months (range 2-13 months). 64 patients underwent RN and seven patients underwent PN. In terms of staging, 48 patients (67.6%) had T1, 21 patients (29.5%) had T2, nine patients (12.6%) had T3 and the remaining two patients (2.8%) had T4 disease. At the time of first review 17% (12/71) of patients did not have renal function assessment. 21% (15/71) patients have reduced eGFR of <60 with co-morbidities but were not referred for renal physician review. Patients with Furhman Grade > 3 (20), 8 underwent USS abdomen as first mode of imaging (with four patients having eGFR >60) and 12 underwent CT abdomen and pelvis. Of the 27 patients who had high-risk disease (Fuhrman Grade > 3, stage > T3 or positive margins) one patient did not have renal function assessment at time of first review, 10 underwent USS abdomen and remaining CT abdomen Pelvis at the time of first follow up review. Six patients had reduced eGFR but were not referred to renal physicians. Conclusions: Large variation and lack of uniformity in timing of visits, mode of imaging, assessment of renal function and referral to renal physicians was identified for patients with similar stage and grade of RCC. Given these findings our centre has developed a new evidence and consensus based protocol. Following MDT discussion patients are allocated to a high, intermediate or low risk groups for follow-up. This is being trialled as a nurse delivered service.

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The one stop prostate clinic: Evolution of a rapid access diagnostic service.
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Introduction and Objectives: The One Stop Prostate Clinic (OSPC) is for men at high risk of prostate cancer who undergo urological assessment and, if indicated, immediately proceed to TRUS guided prostate biopsy under local anesthesia (1). We report the ongoing experience following recent transition of our service to a new public tertiary hospital with several changes to our practice and patient mix. Method: A prospective analysis was conducted of the first 100 patients to attend the 'new' OSPC between February 2015 and August 2015. Demographic, clinical and histopathologic data was compared to our previously reported data for 200 rural men who attended the previous OSPC between August 2011 and August 2014 (1). The transfer of the OSPC service has resulted in the following changes in our practice and patient mix: 1 Both metropolitan and rural patients are assessed (previously only rural) 2 The service is weekly by two urologists (previously fortnightly by one) 3 The prophylactic antibiotic protocol has been changed to one dose of 500 mg ciprofloxacin (previously six doses over three days). Ertapenem 1 g IV with Asia travel history (unchanged) 4 A biplane side-fire TRUS is utilized (previously end-fire) 5 Histopathology is now reported by Pathwest (previously Uropath) Results: Conclusions: Whilst the OSPC model of care remains effective, this data demonstrates issues requiring attention. Firstly, the increase in the incidence of infective complications since the change in antibiotic prophylaxis, whilst non-significant, will require future re-analysis. Secondly, despite the increased frequency of the clinic, there has been a significant increase in the delay between referral and patient assessment demonstrating the new clinic is under-resourced in comparison to current demand. Finally, the significant difference in pathology between the two cohorts since the change in providers is a cause for concern. Efforts to understand these differences are required as pathology clearly determines subsequent management. A recent further evolution of
this service has been the introduction of prebiopsy multi-parametric MRI that coincides with the OSPC appointment for rural patients, with 'hot' reporting of these studies prior to biopsy. (Table presented).

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**Appropriate investigation and referral of remote patients to Urology with visible haematuria.**

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Introduction and Objectives: Approximately 13% of patients with visible haematuria go on to be diagnosed with a urological malignancy. All adult patients with visible haematuria should therefore be referred to a urologist, and should undergo investigation with cystoscopy and upper tract imaging as a minimum. This prospective study aimed to assess to what extent this occurred in a rural population, and whether age, sex, or indigeneity were predictive of urologic referral. Method: All mid-stream urine samples submitted to a rural hospital pathology laboratory over a three month period with greater than 100 x 10^6/L erythrocytes per high power field were visually inspected by a single clinician. Patients with haematuria that was visible to the naked eye were eligible for inclusion in the study. Relevant information on demographics, referral and investigation were gathered from the patient's medical record and their primary healthcare provider. Three patients were excluded from the study (based on inadequate available information, being aged under sixteen, and haematuria being clearly due to post-partum haemorrhage), resulting in a study population of 27 patients. Results: 41% (11/27) of patients were male, 60% (16/27) were indigenous, and median age was 48 (range 22-81). 67% (18/27) of patients were not referred to a urologist and therefore did not undergo cystoscopy. 81% (22/27) of patients did not undergo any form of upper tract imaging. 41% (11/27) of mid-stream urine samples demonstrated an isolated bacterial growth. Both age (6% [under 50] vs. 64% [over 50], p = 0.003) and sex (64% [male] vs. 6% [female], p = 0.003) were predictive of urologic referral, whereas indigeneity was not (20% [indigenous] vs. 45% [nonindigenous], p = 0.103). Conclusions: This prospective study highlights the apparent inadequate investigation and referral of patients with visible haematuria from a rural Australian population. Patients who are young and/or female appear to be most affected by this problem.

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**A survey of patient attitudes towards the use of smart phone applications by health care professionals for patient care and management.**

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Introduction and Objectives: Optimal communication between health care workers is vital. Many hospitals in WA health still rely on outdated pager system for communication between health care workers and allied health staff. This is despite the growing popularity of use of smart phone and smart phone applications for communication. Studies performed looking at use of smart phones in clinical communication have reported significant benefit through the use of this device for communication (1,2). Despite the potential benefits of using smartphone applications for communication, the department of health WA still prohibits the transfer of clinical information over smart phones for patient care. To date no study has looked at patients' attitude on their information being shared on smart phone applications as part of their clinical management. We aim to explore patients' perspective on the use, by clinicians, of
smart phone applications and the sharing of their clinical information via these devices to assist in their clinical care. Methods: A twelve-item questionnaire was developed to identify patients' willingness to have their information shared between health care workers via smart phone applications. Adults in outpatient Urology clinics were requested to complete the questionnaire. The following factors were evaluated: willingness of patients to have their name, hospital number, body images and radiological images shared for the purpose of treatment decision, teaching, expert opinion and follow up planning. Patients were requested to select from a range of 5 possible options on how willing they were for specific information being shared. Patient demographics; age and gender were recorded. Responder who were 18 years and older and owned a smart phone were included. Incomplete questionnaire were excluded from study. Results: A total 150 participants were surveyed. 10 surveys were excluded. There were 58 (41.4%) male and 82 (58.6%) female responders with age range from 19-83. 88.5% of participants were neutral, agreed or strongly agreed (N/A/SA) to have their name used via smart phone apps for clinical management. Similarly 86.4% were N/A/SA to have their hospital number utilized. 89.2% of participants were N/A/SA that the use of smart phone applications would make their clinical management more efficient and reliable. 91.4% of responders were N/A/SA to the sharing of radiological images between clinicians for patient management. 81.4% of responders were N/A/SA to having clinical images of their abdomen shared however 50.7% of participants disagreed or strongly disagreed to the sharing of clinical images involving the reproductive organs between clinicians. Conclusion: This survey demonstrates widespread consumer support for clinician use of smartphones in patient care. This survey should provide confidence to health care providers and the health department of WA that dedicated smartphone health communication applications is required and has the support of the general public.

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Long term follow up of intravesical botox therapy of neurogenic detrusor overactivity.
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Introduction and Objective: A prospective, randomised, double blinded control trial was conducted in Shenton park Health Campus to investigate the efficacy of intravesical Botox therapy (200 Units vs. 300 Units) in patients with NDO refractory to medical therapy between 2003 to 2005(1). This study demonstrated there were significant reduction in the maximum detrusor pressure (MaxPdet) of overactive contractions, significant increase in reflexic volume and maximum cystometric capacity (MCC) in patient that received Botox therapy. It also demonstrated that these effects were longer lasting with 300 Units of Botox (1). Primary objective was to look at the 10 year follow up of these initial trial patients and evaluate their long term bladder management technique. Secondary objective was to compare the long term urodynamic parameters of patient that continued to receive intravesical Botox therapy for NDO. Methods: A retrospective 10 year follow up study of patients who received intravesical Botox therapy as part of the randomised double blinded Botox trial at Shenton Park Rehab Centre. All patients continued to receive 300 units of Botox even though they may have received 200 units as part of the trial. Of the 32 patients who were included in the initial trial 29 patients were followed up in this study. Of the 3 patient excluded, 1 patient moved interstate and 2 patients passed away prior to 10 year follow up. When comparing urodynamic parameters the most recent urodynamic studies within the last 5 years were used for analysis. Results: 29 patients, 21 male (72.4%) and 8 female (27.6%) were included. 21 had traumatic spinal cord injuries, 3 congenital and 5 others as cause for their NDO. All patients managed their NDO with selfintermittent catherisation (SIMC) at the time of initial trial. At present 21 patients continue with SIMC and 20 of them have regular intravesical Botox injections. 6 patients proceeded to have SPC insertion, 1 patient has long term IDC and 1 patient proceeded to have Memokath insertion. Comparison of most recent urodynamic results to initial pre-Botox urodynamic parameters for patient that continue to manage NDO with SIMC +/- Botox, the mean MCC remained improved 542.3 mL (<0.01), mean MaxPdet remained lower 12.7 cm H2O (<0.01) and mean compliance remained improved 187.6 cm mL/ cm H2O (<0.01). Conclusions: Intravesical Botox therapy is efficacious in the long term for managing NDO that is refractory to medical therapy. Patient in our study who showed good initial response to intravesical Botox injection continued to have sustained benefits from repeated Botox therapy.
Left atrial appendage occlusion with the AMPLATZER Amulet device: An expert consensus step-by-step approach.


Aims: This document aims to describe a standardised methodology for performing left atrial appendage occlusion (LAAO) using the AMPLATZER Amulet device, and to provide useful tips and tricks for operators with different levels of experience. Methods and results: Physicians who are experts in LAAO and had personal clinical experience with the AMPLATZER Amulet device were asked to contribute in the preparation of this consensus document. Twenty-seven physicians (20 interventional cardiologists and 7 electrophysiologists) from 14 different countries reviewed the manuscript. A step-by-step approach, simulating a real case, was followed. Starting with patient selection and planning, related cardiac imaging is discussed, followed by vascular access - transseptal puncture optimisation. Then, angiographic calibration/sizing and the required fluoroscopy views are explained and a device sizing strategy is proposed. Device preparation and de-airing is briefly described, followed by sheath exchange, device deployment steps, evaluation of device stability and decision for final release. The way to recapture and change a device is then shown, together with some additional tips on how to deal with challenging anatomies like "chicken wing" left atrial appendage. Finally, for operators who are switching from AMPLATZER Cardiac Plug to Amulet, the main differences between the two devices with respect to implantation technique are presented. Conclusions: In conclusion, this document reflects a consensus approach by expert implanters on the steps of LAAO technique and best practices for implantation of the AMPLATZER Amulet device, along with some practical tips to minimise the complication rate.

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Warm ischemic time (WIT) measurements do not correlate with early lung allograft function: Analysis from the Australian donation after circulatory death (DCD) lung transplant (LTX) collaborative.

Purpose: The impact and clinical definitions of agonal warm ischemia in controlled DCD LTx are not well described. The lung has unique properties that may protect it from ischemic damage. The relative importance of monitoring agonal, hemodynamic and subsequent ventilatory parameters during the DCD donation process remains unclear. The limits of LTx DCD WIT have been implied from other solid organ DCD transplants. Methods: Since 2006, the Australian DCD LTx Collaborative has recorded DCD donor and recipient data from all 4 LTx centers. WIT measures have been defined as intervals (mean & SD) between multiple time points: Withdrawal (WD), BP systolic 50mmHg (BPs50), asystole (BP0), donor lung ventilation (Vent) and pulmonary artery flush (PAf). Early allograft function is reported as the PO2/FiO2 value closest to 24hrs post-LTx (PF24). WIT intervals were correlated with PF24 using Pearsons Coefficient. Post BP0 stand-off time (2-10mins) and onset of ventilation (2-15mins) varied according to local DCD guidelines and EVLP was not utilized in this cohort. Results: Between May 2006-Oct 2015, WIT data on 227 DCD LTx were reported and analyzed. Mean PF24 was 314+/- 87.9 and there were no significant WIT correlations with PF24 (reported as R2, p= ns for all WIT time intervals). Conclusion: Surprisingly, conventional agonal, hemodynamic and ventilatory measures of warm ischemia do not correlate with early LTx allograft function in our large DCD LTx cohort. Either the clinical timings recorded during controlled LTx DCD donation are significantly short of the tolerable WIT limits, or these parameters do not truly reflect the risk of allograft ischemic damage. These data cautiously encourage the extension of WIT limits for clinical DCD LTx. (Table Presented).

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Maternal obesity and duration of breastfeeding influence the risk of non-alcoholic fatty liver disease in adolescents.

Ayonrinde OT, Oddy WH, et al.

Background and Aims: Non-alcoholic fatty liver disease (NAFLD) in adolescents may have its origins in adiposity gains and nutrition established during childhood. There is a paucity of data regarding the influence of infant nutrition and maternal factors on NAFLD in adolescence. We examined the association of infant nutrition on the subsequent diagnosis of NAFLD at age 17 years in a well-characterised longitudinal pregnancy and birth cohort. Methods: Longitudinally collected data on participants in the cohort study were analysed for associations between maternal prepregnancy and pregnancy characteristics, early life nutrition and subsequent NAFLD. Data included birth, childhood and adolescent characteristics obtained by questionnaires, direct interview, physical examination, blood tests and liver ultrasound. Fatty liver was diagnosed with liver ultrasound. Results: 1170 adolescents aged 17 years had liver ultrasound. NAFLD was diagnosed in 15.2% of the cohort, predominantly female. Birth anthropometry was not associated with NAFLD. Most (94%) of neonates were breastfeeding on leaving hospital. Neonates discharged from hospital breastfeeding had a higher likelihood of still breastfeeding at 6 months when compared with neonates discharged bottle-feeding (59% vs. 3%, p < 0.001). There was a lower prevalence of adolescent NAFLD in neonates discharged home breastfeeding vs. bottle feeding (14.6% vs. 24.3%, p = 0.03) and in infants exclusively breastfeeding for >6 months vs. <6 months (11.3% vs. 17.8%, p = 0.003). There was no difference in the proportion of infants subsequently diagnosed with NAFLD in association with the type of milk consumed at age 1 year, age at introduction of solid foods or maternal age or smoking. Normal range maternal body mass index pre-pregnancy (OR 0.49, 95%CI 0.33-0.72, p < 0.001) and exclusive breastfeeding for >6 months (OR 0.66, 95%CI 0.56-0.95, p < 0.03) were associated with a lower risk of adolescent NAFLD. Breastfeeding beyond 9 months did not further reduce the odds of NAFLD during adolescence (OR 0.73, 95% CI 0.46-1.16, p = 0.18). Conclusions: Normal range BMI at the start of pregnancy
and exclusive breast milk feeding for at least the first 6 months of life may reduce the odds of NAFLD in adolescent offspring by half and one third respectively. These findings suggest a potential benefit of exclusive breastfeeding for >6 months to reduce the odds of a NAFLD diagnosis during adolescence. Other modifiable maternal factors, including obesity, are also associated with NAFLD in adolescents.

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**Infective exacerbation of bronchiectasis due to pasteurella multocida.**
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Case Report: A 25 year old Burmese man presented with a 3 year history of productive cough, mild hemoptysis and wheeze. He denied shortness of breath, fever, night sweats, weight loss and nasal symptoms. He described recurrent childhood chest infections but had no history of whooping cough, measles or tuberculosis. He was not on any medication, had never smoked and did not have any contact with animals. Chest auscultation revealed coarse bi-basal crackles. There was no clubbing or lymphadenopathy. Full blood picture, electrolytes, renal function, liver function test and vasculitic screen were normal. Total IgE was 737 ku/L but Aspergillus-specific IgE was not elevated. Pasteurella multocida was cultured repeatedly from expectorated sputum. CT chest showed significant widespread bronchial wall thickening and cystic bronchiectasis. Treatment with amoxicillin 1g BD for four weeks led to significant improvement of cough and wheeze and complete resolution of hemoptysis. Discussion: Pasteurella multocida is a Gram-negative coccobacillus commonly found in the oral flora of domestic animals and livestock. It is often associated with soft tissue infections following animal bites. Pulmonary involvement can occur in the elderly, patients with impaired host defences and those with underlying lung disease. The spectrum of pulmonary involvement includes airway colonization, bronchitis, pneumonia, lung abscess and empyema. Treatment with penicillins is usually effective. Conclusion: We report an infective exacerbation of bronchiectasis caused by Pasteurella multocida, an uncommon respiratory pathogen associated with animals which usually responds favourably to treatment.

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**Case report: A rare manifestation of idiopathic hypereosinophilic syndrome (HES) with recurrent eosinophilic pleural effusions (EPE).**
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We report the case of Mr RW who presents with an initial diagnostic dilemma of recurrent eosinophilic pleural effusion. He underwent extensive investigation to exclude infection, vasculitis and malignancy on blood tests, imaging with chest CT and PET scans, thoracocentesis, bronchoalveolar lavage, and bone marrow biopsy. Results were negative for all causes sought and he was finally given the diagnosis of exclusion, idiopathic hypereosinophilic syndrome (HES). He was managed successfully with prednisolone, with resolution of pleural effusions, lung infiltrates and peripheral eosinophilia. This case demonstrates the rare manifestation of HES with recurrent eosinophilic pleural effusions and the importance of thorough investigations primarily to rule out malignancy. To the best of our knowledge, there have been very few cases in the literature of this occurrence highlighting the rarity of EPE in HES. Most other cases of reported recurrent EPE have been associated with benign pleural effusions, parapneumonic pleural infections/TB, haematological and solid organ malignancies.

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Skin cancer prevalence in lung transplant recipients in Western Australia.

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Introduction/Aim: Skin cancers are the most common malignancies in solid organ transplantation. A Swedish study in 2013 reported a total number of 251 skin cancers in 6,227 patient years (rate of 0.04 cancers/patient year) in a cohort of 1,012 heart and/or lung transplant recipients. There was a calculated 83-fold increase in total number of skin cancers compared to the general population. Our aim was to calculate the rate and point prevalence of skin cancer in lung transplant recipients in Western Australia, which we hypothesized would be significantly higher given the climate here.

Methods: We conducted a retrospective cohort study on lung transplant recipients aged > 18 years who were followed up at the state lung transplantation centre as at 31st December 2014. Patients who had not been followed up by our service for 12 months or had not survived past 12 months post-transplant were excluded. Data was collected from medical records and patient databases. Ethics approval was granted by the institution’s Human Research Ethics Committee. Results: 105 patients and 110 transplants (5 redo lung transplants) were included in the data analysis. There were 72 bilateral lung transplants, 28 single lung transplants and 10 heart-lung transplants. The median age at time of transplant was 48 years (mean = 44.6 years). We identified a total of 314 individual skin cancers over 614 patient years (rate of 0.51 cancers/patient year). 46 out of the 105 (43.8%) patients had at least one skin cancer. Of these 46, 29 (63.0%) had at least 3 skin cancers. The point prevalence (percentage of patients living with a current/previous diagnosis of skin cancer) was 39.4%. Median time to first cancer was 21 months (mean = 40 months).

Conclusion: Skin cancers occur frequently in lung transplant recipients in Western Australia. Further research on risk factors and preventative interventions is indicated.

Establishing a new pulmonary rehabilitation program at Fiona Stanley Hospital.

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Introduction: Fiona Stanley Hospital (FSH) is Western Australia’s new flagship tertiary Hospital. The hospital services a local catchment with a wider area for tertiary and quaternary services. Pulmonary rehabilitation (PR) is an evidence-based intervention shown to reduce hospital admissions, improve exercise tolerance and quality of life. The FSH programme is coordinated by senior physiotherapists who have extensive experience in running PR programmes across the continuum of care and have thorough knowledge of the PR programmes run in Perth’s metropolitan area. A key role of these coordinators is to triage referrals and link patients in with the most appropriate level of PR, ideally close to home. Aim: To evaluate the first 6 months of PR programme delivery. To describe the flow of referrals, and identify challenges in the referral processes and subsequent programme uptake. Methods: Retrospective analysis of FSH PR patient database from 2nd February 2015 to 31st July 2015 (n = 61). Patients who transitioned to FSH from Royal Perth or Fremantle Hospital were excluded. Results: Of 61 referrals, 46 (75.4%) were actioned by time of report, and 15 were waiting an appointment. Of those completed 35/46 were assessed at FSH. 15/46 (32.6%) were enrolled at FSH as they required tertiary level care or resided in the local catchment area. 18/46 (39.1%) were referred to a more appropriate secondary hospital or community programme. 13/46 (28.2%) declined, were not medically suitable or deceased. Barriers including parking cost, hospital access and familiarity to other sites impacted on patients’ preference to attend elsewhere. The medical governance model presents a challenge as it restricts referral flow and this impacted on the overall number of referrals received. Conclusion: The FSH PR programme is succeeding in its tertiary hospital requirements of triaging patient referrals and promoting patient care at the most appropriate site.

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Mesenchymal stem cell infusion modulates systemic inflammation in patients with chronic obstructive pulmonary disease (COPD).


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Introduction/Aim: Chronic obstructive pulmonary disease is the most common respiratory disease in the world and is characterized by chronic pulmonary and systemic inflammation. It is a progressive disorder with no effective treatments. Recently, MSC infusions have shown modest success in clinical trials for several inflammatory-driven diseases. Although promising, the reparative mechanisms by MSC and their acute effects post-infusion are poorly characterized, particularly in COPD. MSC possess anti-inflammatory properties, and have been shown to enhance the function of immunosuppressive T regulatory (Tregs) cells. Therefore, we aim to characterize the trafficking of MSC and immunological events occurring after systemic MSC administration. Methods: RadiolabelledMSC were infused intravenously into nine patients with stable COPD and tracked by CT scan across the first week post-fusion. Additionally, peripheral blood was collected across the first week. Systemic inflammatory (sTNFRI, CRP, IL-6, IP-10) and oxidative stress (F2-Isoprostane; F2-IsOP) biomarkers were measured in plasma across 7 days post-infusion by enzyme-linked immunosorbent assay and gas chromatography-mass spectrometry respectively. Proportions of HLA-DR-expressing FoxP3 + CD25+ Tregs were measured by flow cytometry. Results: Mesenchymal stem cell first localized in the lungs from 0-24 h post-infusion and then trafficked to the liver and spleen at day 1-7. Levels of F2-IsOP, IL-6 and IP-10 were significantly lower, while CRP and sTNFR1 significantly increased after MSC infusion. HLA-DR+ Tregs were significantly higher after MSC infusion. Conclusion: We provide novel data showing MSC therapy in COPD patients reduce systemic inflammation within a week of infusion. Further characterization of the systemic immunological changes will provide a deeper understanding of immune regulation during MSC therapy.

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Improving anti-bacterial immune responses in patients with COPD: By blocking inhibitory T-cell receptors.

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Introduction/Aim: Chronic Obstructive Pulmonary Disease (COPD) is the most common respiratory cause of mortality and morbidity worldwide. Notably, acute exacerbations of COPD (AECOPD) are associated with a progressive decline in lung function. AECOPD is usually associated with pulmonary infections but little is known about the mechanisms causing increased susceptibility in COPD. We hypothesize that chronic inflammation in AECOPD patients induces excess T-cell inhibitory molecules (e.g. CTLA-4). This may inhibit anti-bacterial immune responses thus demonstrating a mechanism for increased susceptibility to infections in COPD patients. Methods: Peripheral blood mononuclear cells (PBMC) were isolated from blood samples of AECOPD patients, stable COPD patients and healthy controls. Production of IFNgamma by PBMC was measured by ELISA post-challenge with viable non-typeable Haemophilus influenza (NTHI) or anti-CD3. Bacterial killing was assessed by investigating bacterial viability counts. T-cell expression of CTLA-4 was measured by flow cytometry. Plasma levels of inflammatory biomarkers were measured by ELISA. Results: Acute exacerbations of COPD patients exhibited higher plasma levels of CRP and IL-6 than stable COPD patients (P = 0.07 and P = 0.09, respectively) and healthy controls (P < 0.01 for both). PBMC fromAECOPD patients have lower production of IFNgamma againstNTHI compared to stableCOPD patients and healthy controls, but increased expression of CTLA-4 on CD4+ T-cells (P < 0.05). Blocking of CTLA-4 increased anti-CD3 induced IFNgamma by PBMC.
from COPD and AECOPD patients. However, in response to NTHI challenge, IFN\(\gamma\) responses and bacterial killing were only improved in a subset of patients after CTLA-4 blocking. Conclusion: Increased expression of CTLA-4 could account for the increased frequencies of infections in COPD patients. Blocking multiple antiinflammatory signals could improve anti-bacterial responses to prevent AECOPD.


**Lungscreen WA project-12 months of low dose CT lung cancer screening.**

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Introduction/Aim: Screening high risk current and former smokers with low dose computed tomography (LDCT) can reduce lung cancer deaths, but lung cancer screening is not currently recommended in Australia. Incorporation of risk prediction models to assess eligibility and guide nodule management can improve screening efficiency. The LungScreen WA Project aims to assess the effectiveness and feasibility of community based lung cancer screening in Australia. It is the only on-going lung cancer screening study for smokers in Australia. Methods: This is a prospective cohort study. Current or former smokers aged 55-74 years are self-referred via advertising. The 6-year lung cancer risk is determined by the PLCOM2012 risk calculator. Only participants with >1.5% PLCOM2012 risk are screened with LDCT. Nodule follow-up is determined by Brock malignancy risk score. All participants undergo repeated quality of life assessment and health resource utilization. Results: Seventy-six participants have been recruited, and 51 (67%) were PLCOM2012 risk >1.5% and offered LDCT. Of these 51 participants, the mean age was 65.7 +/- 5.3 (SD) years; 26 (51%) were female, and 23 (45%) were current smokers. The median PLCOM2012 risk was 3.6% (IQR 2.65- 6.05). Currently, 45 (88%) have undergone LDCT screening, 3 (6%) have LDCT pending and 3 (6%) declined further participation. Pulmonary nodules of any size were detected in 26/45 (58%). Indeterminate nodules with amalignancy risk score >6% were detected in 9 (20%). One participant was diagnosed with Stage IB lung adenocarcinoma and treated with resection. Of the current smokers who have completed 2-month follow-up, 2/9 (22%) have quit smoking. Conclusions: Community based LDCT lung cancer screening of high-risk individuals utilizing risk prediction models is feasible. This early data are encouraging and further recruitment with long-term follow-up and healthcare economic data are required.


**Percentage predicted is not superior to absolute six-minute walk distance as a predictor of mortality in pulmonary hypertension.**

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Introduction/Aim: Absolute six-minute walk distance (6MWD) and functional class have been validated as predictors of mortality in patients with pulmonary arterial hypertension and form the basis of PBS (Pharmaceutical Benefits Scheme) funded prescription of pulmonary vasodilator therapies in Australia. Several equations exist for predicting 6MWD in adults from which percentage predicted 6MWD can be calculated. We sought to determine whether percentage predicted 6MWD was a better predictor of mortality than absolute 6MWD in patients with pulmonary hypertension (allWHO groups). Secondary analysis included the impact of baseline WHO functional class and patient
demographics on mortality. Methods: Analysis was conducted from registry data of the Pulmonary Hypertension Society of Australia and New Zealand (PHSANZ) which includes patients with pulmonary hypertension from all five WHO groups. Inclusion criteria were age at diagnosis > 18 years, diagnosis from 2004 and baseline 6MWD within 3 months of diagnostic right heart catheter. Baseline mortality predictors were taken at time of diagnosis. Percentage predicted 6MWD was calculated using Chetta, Jenkins and Enright predictive equations. Survival analysis was performed using cox-proportional hazards model. Results: De-identified data for 2442 registry subjects were reviewed, of which 923 subjects met the inclusion criteria. There were 285 deaths with an annual incidence rate of 9.2%. Mean 6MWD was 308 +/- 136m. Mean duration of follow-up from diagnosis was 3.33 +/- 2.42 years. Absolute 6MWD, percentage predicted 6MWD (all three equations), functional class and age at diagnosis were all significant predictors of mortality (p < 0.001) on univariate analysis. On multivariate analysis, only absolute 6MWD (HR 0.997, 95% CI 0.995-0.998, p < 0.001), functional class (HR 1.965, 95% CI 1.509-2.557, p < 0.001) and age at diagnosis (HR 1.023, CI 1.014-1.032, p < 0.001) remained significant. Conclusion: Percentage predicted is not superior to absolute 6-min walk distance as a predictor of mortality in pulmonary hypertension.

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Anxiety and depression in idiopathic pulmonary fibrosis.

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Introduction: Mood disturbance commonly effects people with IPF. No studies evaluating persistent depression beyond 6 months exist, and there are no longitudinal studies evaluating persistent anxiety in IPF. Aim: Our aim is to determine the frequency and predictors of persistent anxiety and depression in IPF. Methods: Using the Australian IPF Registry (AIPFR), we examined a cohort with persistent anxiety and depression defined as that present at baseline and 12 months follow-up, via the Hospital Anxiety and Depression Scale (HAD-A & D). Univariate and multivariate logistic regression analysis was performed examining associations with demographic features, comorbidities, UCSD shortness of breath questionnaire (UCSD), cough severity (visual analogue scale 0-100mm), oxygen use, hospitalization, spirometry, DLCO, 6MWT and survival. Results: One hundred two of 435 participants in the AIPFR had completed baseline and 12 month follow up HAD-A & D questionnaires: 66 male; mean (+/-SD) age 69.6 +/- 6.9 years. Twenty subjects (21%) had persistent anxiety, and 14 subjects (14%) had persistent depression. Univariate analysis demonstrated persistent anxiety was associated with the degree of baseline dyspnoea (p = 0.008), a trend for association with baseline cough severity (p = 0.07) and oxygen use (p = 0.07). Multivariate analysis demonstrated oxygen use as the only independent predictor of persistent anxiety. Worsening anxiety was associated with worsening cough severity (p = 0.015). Univariate analysis demonstrated persistent depression was associated with the degree of baseline dyspnoea (p = 0.004), cough at baseline (p = 0.003) and had a trend for association with younger age (p = 0.06) and worsening dyspnoea (p = 0.07). Multivariate analysis showed that persistent depression was independently predicted by cough severity (p = 0.015) and confirmed a trend for association with younger age (p = 0.066). Worsening depression was associated with worsening dyspnea (p = 0.047). Conclusions: These data confirm the strong link between mood disturbance and symptom severity. Further research is needed to explore the direction of causality of this link so as to optimize palliative approaches.

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Quality of life of patients with idiopathic pulmonary fibrosis (IPF)-What can the Australian IPF registry tell us?

Glaspole I, Goh N, et al.

Introduction: IPF is a progressive, fibrosing lung disease causing diminished health-related quality of life (HRQoL).

Aim: We sort to determine the principal determinants of HRQoL in IPF.

Methods: Data from the Australian IPF Registry were analysed for demographic features, comorbidities, St George Respiratory Questionnaire (SGRQ), Hospital Anxiety and Depression (HAD-A and D) scale, UCSD Shortness of Breath Questionnaire (UCSD), cough, oxygen use, spirometry, DLco and 6MWT parameters. Linear regression analysis was performed to identify predictors of HRQoL.

Results: Data from 516 patients were available (347 male; mean age 71.3 +/- 8.6 years). Mean FVC 81.3 +/- 22.5%pr, DLco 46.7 +/- 17.4%pr, 6MWD 434 +/- 135 m, resting SpO2 95.1 +/- -3.3%, end-exercise SpO2 84.8 +/- 6.9%. SGRQ score: symptom 47.2 +/- 23.5; activity 61.9 +/- 23.9; impact 37.3 +/- 22.9; total 46.6 +/- 20.9. Symptom scores: UCSD median 38 (17-67); HAD-A score 4 (2-7), 20.3% > 8, HAD-D score 4 (2-7), 17.7% > 8; cough presence 88.5%; cough severity (visual analogue scale 0-100mm): 40.3 +/- 25.8. Significant associations on univariate analysis with HRQoL included: GAP index, smoking, cardiorespiratory comorbidity, oxygen therapy,UCSDSOBQ, HAD-A, HAD-D, cough presence and severity, FEV1, FVC, DLco, 6MWT distance, baseline and end test oxygen saturation and end 6MWT dyspnea score. Multivariate analysis of 109 subjects with complete data demonstrated independent association between SGRQ and UCSDSOBQ (R^2 = 0.76, p < 0.0001), cough severity (R^2 = 0.07, p < 0.0001), HAD-D (R^2 = 0.02, p = 0.003) and age (R^2 = 0.01, p = 0.015).

Conclusions: Cough, dyspnoea and depression are major determinants of HRQoL in IPF. Their treatment may improve HRQoL and should be a focus of future clinical trials.

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Validation and Application of a Dried Blood Spot Assay for Biofilm-Active Antibiotics Commonly Used for Treatment of Prosthetic Implant Infections.


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Dried blood spot (DBS) antibiotic assays can facilitate pharmacokinetic (PK)/pharmacodynamic (PD) studies in situations where venous blood sampling is logistically difficult. We sought to develop, validate, and apply a DBS assay for rifampin (RIF), fusidic acid (FUS), and ciprofloxacin (CIP). These antibiotics are considered active against organisms in biofilms and are therefore commonly used for the treatment of infections associated with prosthetic implants. A liquid chromatography-mass spectroscopy DBS assay was developed and validated, including red cell partitioning and thermal stability for each drug and the rifampin metabolite desacetyl rifampin (Des-RIF). Plasma and DBS concentrations in 10 healthy adults were compared, and the concentration-time profiles were incorporated into
population PK models. The limits of quantification for RIF, Des-RIF, CIP, and FUS in DBS were 15 mug/liter, 14 mug/liter, 25 mug/liter, and 153 mug/liter, respectively. Adjusting for hematocrit, red cell partitioning, and relative recovery, DBS-predicted plasma concentrations were comparable to measured plasma concentrations for each antibiotic (r > 0.95; P < 0.0001), and Bland-Altman plots showed no significant bias. The final population PK estimates of clearance, volume of distribution, and time above threshold MICs for measured and DBS-predicted plasma concentrations were comparable. These drugs were stable in DBSs for at least 10 days at room temperature and 1 month at 4°C. The present DBS antibiotic assays are robust and can be used as surrogates for plasma concentrations to provide valid PK and PK/PD data in a variety of clinical situations, including therapeutic drug monitoring or studies of implant infections.

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**Plasma ferritin concentrations are not associated with abdominal aortic aneurysm diagnosis, size or growth.**

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**BACKGROUND AND AIMS:** Experimental studies using a rodent model have suggested that iron overload may contribute to abdominal aortic aneurysm (AAA) pathogenesis.

**METHODS:** We assessed the association of total body iron, as measured by plasma ferritin, with AAA diagnosis, size and growth in 4024 community-dwelling older men screened for AAA, using logistic regression and linear mixed effects models.

**RESULTS:** Plasma ferritin concentrations were similar in men who did (n = 293) and did not (n = 3731) have an AAA (median [inter-quartile range] concentrations 115.4 [63.0-203.1] and 128.5 [66.1-229.1] ng/mL respectively, p = 0.124). There was no association between plasma ferritin concentration and AAA diagnosis in unadjusted logistic regression (odds ratio (OR) for a 1 standard deviation increase: 0.880 [95%CI: 0.764-1.015]; p = 0.078), or when adjusting for AAA risk factors and factors known to influence circulating ferritin (OR for a 1 standard deviation increase: 0.898 [95% CI: 0.778-1.035]; p = 0.138). Iron overload prevalence (plasma ferritin concentrations >200 ng/mL) was lower in men with an AAA (25.3%) than those without (30.8%; p = 0.048), but was not associated with AAA diagnosis after adjusting as above (OR: 0.781 [95% CI: 0.589-1.035]; p = 0.086). The association of iron overload with AAA growth was investigated in 265 men with small AAAs who received at least 1 repeat ultrasound scan in the 3 years following screening. We saw no difference in AAA growth between men who did and did not have iron overload (n = 65 and 185 respectively, p = 0.164).
CONCLUSIONS: Our data suggest that iron overload is unlikely to be important in AAA pathogenesis.

Pharmacological lactation suppression with D2 receptor agonists and risk of postpartum psychosis: A systematic review.
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BACKGROUND: It has been suggested that D2 receptor agonists commonly used postpartum for the physiological suppression of lactation, such as bromocriptine and cabergoline, may increase the risk of illness onset or relapse in women where there is a predisposition for or history of schizophrenia, bipolar disorder or postpartum psychosis. This is based on two lines of reasoning: current models of psychosis assume episodes are triggered by dysregulation of brain dopaminergic activity and treated by medications that universally have D2 receptor antagonist properties; and limited research suggesting these agents may be associated with psychotic episodes in vulnerable individuals outside of the postpartum period.

AIM: The aim of this study was to examine whether D2 agonists trigger psychosis in previously well mothers, or psychotic relapse or exacerbation of symptoms in mothers with known psychotic illnesses, when used to suppress lactation during the early postpartum period.

MATERIALS AND METHODS: A systematic review of the literature was undertaken of electronic databases, including: MEDLINE, EMBASE and PsychINFO from 1950 to 2015 using keywords.

RESULTS: Eight case reports, three case series and a pharmacovigilance survey were identified.

CONCLUSION: Whilst D2 receptor agonists appear to increase the risk of triggering psychosis in previously well mothers and those previously diagnosed with schizophrenia, bipolar disorder and postpartum psychosis, bromocriptine appears to pose a much greater risk than cabergoline. When considering the use of pharmacological agents to suppress lactation, physicians should carefully screen patients for a history of psychosis and consider alternatives to moderate this risk.

Effects of anaesthesia on paediatric lung function.
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Respiratory adverse events are one of the major causes of morbidity and mortality in paediatric anaesthesia. Aside from predisposing conditions associated with an increased risk of respiratory incidents in children such as concurrent infections and chronic airway irritation, there are adverse respiratory events directly attributable to the impact of
anaesthesia on the respiratory system. Anaesthesia can negatively affect respiratory drive, ventilation/perfusion (V/Q) matching and tidal breathing, all resulting in potentially devastating hypoxaemia. Understanding paediatric respiratory physiology and its changes during anaesthesia will enable anaesthetists to anticipate, recognize and prevent deterioration that can lead to respiratory failure. This review aims to give a comprehensive overview of the effects of anaesthesia on respiration in children. It focuses on the impact of the different components of anaesthesia, patient positioning and procedure-related changes on respiratory physiology.

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Risk of dementia and death in community-dwelling older men with bipolar disorder.
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BACKGROUND: Bipolar disorder has been associated with cognitive decline, but confirmatory evidence from a community-derived sample of older people is lacking.

AIMS: To investigate the 13-year risk of dementia and death in older adults with bipolar disorder.

METHOD: Cohort study of 37 768 men aged 65-85 years. Dementia (primary) and death (secondary), as recorded by electronic record linkage, were the outcomes of interest.

RESULTS: Bipolar disorder was associated with increased adjusted hazard ratio (HR) of dementia (HR = 2.30, 95% CI 1.80-2.94). The risk of dementia was greatest among those with <5 years of history of bipolar disorder or who had had illness onset after 70 years of age. Bipolar disorder was also associated with increased mortality (HR = 1.51, 95% CI 1.28-1.77). Competing risk regression showed that bipolar disorder was associated with increased hazard of death by suicide, accidents, pneumonia or influenza, and diseases of the liver and digestive system.

CONCLUSIONS: Bipolar disorder in later life is associated with increased risk of dementia and premature death.

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The need for effective literature searching for burns research: A timely reminder.

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One world one burn rehabilitation standard.
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According to the World Health Organization (WHO) burns are a huge global health problem resulting in death and devastation to those who survive large burns as they are faced with significant functional limitations that prevent purposeful and productive living. Members of the International Society for Burn Injuries (ISBI) Rehabilitation Committee conducted a needs assessment survey in order to characterize how burn rehabilitation is implemented worldwide and how the international burn rehabilitation community can help improve burn rehabilitation in identified geographic locations which need assistance in rehabilitating burn survivors successfully. The results of this survey indicated that poor and in some cases resource limited environments (RLEs) around the world seem to lack the financial, educational and material resources to conduct burn rehabilitation successfully. It appears that there are vast discrepancies in the areas of education, training and capacity to conduct research to improve the care of burn survivors as evidenced by the variation in responses between the RLEs and developed countries around the globe. In some cases, the problem is not knowledge, skill and ability to practice burn rehabilitation, but rather having the resources to do so due to financial difficulties.

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Discriminant validity of the Hospital Anxiety and Depression Scale, Beck Depression Inventory (II) and Beck Anxiety Inventory to confirmed clinical diagnosis of depression and anxiety in patients with chronic obstructive pulmonary disease.
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The objective of this study was to investigate the discriminant validity of commonly used depression and anxiety screening tools in order to determine the most suitable tool for patients with chronic obstructive pulmonary disease (COPD). COPD patients (n = 56) completed the Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory (BDI-II) and Beck Anxiety Inventory (BAI). These scores were compared to confirmed clinical diagnoses of depression and anxiety using the Mini Neuropsychiatric Interview. HADS depression subscale (HADS-D) sensitivity/specificity was 78/81%; BDI-II 89/77%; HADS anxiety subscale (HADS-A) 71/81%; and BAI 89/62%. HADS-D sensitivity/specificity was improved (100/83%) with the removal of Q4 'I feel as if I am slowed down' and adjusted cut-off (>5). Removal of BDI-II Q21 'Loss of interest in sex' with adjusted cut-off >12 resulted in similar improvement (100/79%). No problematic items were identified for HADS-A or BAI. Previously reported low sensitivity/specificity of the HADS for COPD patients was not replicated. Furthermore, simple modifications of the HADS-D markedly improved sensitivity/specificity for depression. BDI-II, HADS-A and BAI produced acceptable sensitivity/specificity unmodified. Pending further research for COPD patients we recommend continued use of the HADS-A with standard cut-off (>8) and removal of Q4 of the HADS-D with lower cut-off >5.

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Review article: Updated resuscitation guidelines for 2016: A summary of the Australian and New Zealand Committee on Resuscitation recommendations.

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This review paper summarises the key changes made to the resuscitation guidelines used in Australia and New Zealand. They were released by the Australian and New Zealand Committee on Resuscitation in January 2016. These are local adaptations of the evidence previously published in October 2015 by the International Liaison Committee on Resuscitation (ILCOR). They are presented across the main working groups in ILCOR: ALS, BLS, paediatrics, neonates, acute coronary syndromes, first aid and ‘Education, Implementation and Teams’.


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Assessing a doctor you've rarely worked with: The use of workplace-based assessments in a busy inner city emergency department.

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OBJECTIVE: Historically, end-of-term assessments for Junior Medical Officers in our ED have been completed by nominated Consultants based on varying amounts of observation in addition to feedback from other health professionals. Our hypothesis is that this system of assessment is both inconsistent and unreliable. Our objective was to increase the validity of our assessment process using workplace-based assessments linked specifically to the domains set out in the Australian Medical Council intern assessment form.

METHODS: Current practice was established using an online survey. Workplace-based assessments were then performed on each junior doctor throughout the course of a term. A repeat survey at the end of term was used to audit the use of the workplace-based assessments and their effect on the adequacy of the assessments.

RESULTS: Almost three quarters of our Consultants used workplace-based assessments as part of their end-of-term assessment. Overall, 80% of Consultants agreed that the Junior Medical Officers assessment process was improved when using workplace-based assessments as an adjunct.

CONCLUSION: Workplace-based assessments improve the validity of end-of-term assessments for junior doctors in an ED as perceived by those performing the assessment.

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Prominent scapulae mimicking an inherited myopathy expands the phenotype of CHD7-related disease.

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CHD7 variants are a well-established cause of CHARGE syndrome, a disabling multi-system malformation disorder that is often associated with deafness, visual impairment and intellectual disability. Less severe forms of CHD7-related disease are known to exist, but the full spectrum of phenotypes remains uncertain. We identified a de novo missense variant in CHD7 in a family presenting with musculoskeletal abnormalities as the main manifestation of CHD7-related disease, representing a new phenotype. The proband presented with prominent scapulae, mild shoulder girdle weakness and only subtle dysmorphic features. Investigation revealed hypoplasia of the trapezius and sternocleidomastoid muscles and semicircular canal defects, but he did not fulfill diagnostic criteria for CHARGE syndrome. Although the shoulders are often sloping and antverted in CHARGE syndrome, the underlying neuromuscular cause has never been investigated. This report expands the phenotypes associated with CHD7 mutations to include a musculoskeletal presentation, with hypoplasia of the shoulder and neck muscles. CHD7 should be considered in patients presenting in childhood with stable scapular winging, particularly if accompanied by dysmorphic features and balance difficulties.

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Treatment regimens for pregnant women with falciparum malaria.
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INTRODUCTION: With increasing parasite drug resistance, the WHO has updated treatment recommendations for
falciparum malaria including in pregnancy. This review assesses the evidence for choice of treatment for pregnant women.

AREAS COVERED: Relevant studies, primarily those published since 2010, were identified from reference databases and were used to identify secondary data sources. Expert commentary: WHO recommends use of intravenous artesunate for severe malaria, quinine-clindamycin for uncomplicated malaria in first trimester, and artemisinin combination therapy for uncomplicated malaria in second/third trimesters. Because fear of adverse outcomes has often excluded pregnant women from conventional drug development, available data for novel therapies are usually based on preclinical studies and cases of inadvertent exposure. Changes in antimalarial drug disposition in pregnancy have been observed but are yet to be translated into specific treatment recommendations. Such targeted regimens may become important as parasite resistance demands that drug exposure is optimized.

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**Correlation of visceral adipose tissue measured by Lunar Prodigy dual X-ray absorptiometry with MRI and CT in older men.**

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Quantification of abdominal visceral adipose tissue (VAT) is important to understand obesity-related comorbidities. We hypothesized that dual X-ray absorptiometry (DXA) measurements of VAT would correlate with traditional gold standards of magnetic resonance imaging (MRI) and computed tomography (CT) in older men. Deming regression and Bland-Altman plots were used to assess the agreement between VAT measured simultaneously by DXA and MRI (n=95) in a cohort of older males participating in a randomized trial of testosterone replacement for diabetes. We also correlated DXA with single-slice CT (n=102) in a cohort of older males undergoing testosterone deprivation for prostate cancer. Lunar Prodigy DXA scanners using enCORE software was used to measure VAT. DXA VAT volume strongly correlated with MRI VAT volume (r=0.90, P<0.0001) and CT VAT area (r=0.83, P<0.0001). As DXA assesses VAT volume in a smaller compartment than MRI, Bland-Altman analysis demonstrated DXA systematically underestimated VAT by an approximately 30% proportional bias. DXA VAT volume measured by Lunar Prodigy DXA scanners correlate well with gold standard MRI and CT quantification methods, and provides a low radiation, efficient, cost-effective option. Future clinical studies examining the effects of interventions on body composition and regional fat distribution may find DXA an appropriate volumetric method to quantify VAT.

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**Isolation of mecC MRSA in Australia.**

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**Renal denervation for resistant hypertension: closing in on potential confounders.**
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**Progress in the care of common inherited atherogenic disorders of apolipoprotein B metabolism.**
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Familial hypercholesterolaemia, familial combined hyperlipidaemia (FCH) and elevated lipoprotein(a) are common,
inherited disorders of apolipoprotein B metabolism that markedly accelerate the onset of atherosclerotic cardiovascular disease (ASCVD). These disorders are frequently encountered in clinical lipidology and need to be accurately identified and treated in both index patients and their family members, to prevent the development of premature ASCVD. The optimal screening strategies depend on the patterns of heritability for each condition. Established therapies are widely used along with lifestyle interventions to regulate levels of circulating lipoproteins. New therapeutic strategies are becoming available, and could supplement traditional approaches in the most severe cases, but their long-term cost-effectiveness and safety have yet to be confirmed. We review contemporary developments in the understanding, detection and care of these highly atherogenic disorders of apolipoprotein B metabolism.

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**BK virus nephropathy in renal transplant recipients.**
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BK virus nephropathy (BKVN) occurs in up to 10% of renal transplant recipients and can result in graft loss. The reactivation of BK virus in renal transplant recipients is largely asymptomatic, and routine surveillance especially in the first 12-24 months after transplant is necessary for early recognition and intervention. Reduced immunosuppression and anti-viral treatment in the early stages may be effective in stopping BK virus replication. Urinary decoy cells, although highly specific, lack sensitivity to diagnose BKVN. Transplant biopsy remains the gold standard to diagnose BKVN, good surrogate markers for surveillance using quantitative urinary decoy cells, urinary SV40 T immunochemical staining or polyoma virus-Haufen bodies are offered by recent studies. Advanced BKVN results in severe tubulo-interstitial damage and graft failure. Retransplantation after BKVN is associated with good outcomes. Newer treatment modalities are emerging.

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**Interpretative comments specifically suggesting specialist referral increase the detection of familial hypercholesterolaemia.**
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Familial hypercholesterolaemia (FH) is an under-diagnosed inherited condition characterised by elevated low density lipoprotein (LDL)-cholesterol and premature coronary artery disease. The requesting general practitioner of individuals with extremely elevated LDL-cholesterol measured by St John of God Pathology receives an interpretative comment on the lipid results highlighting possible FH. We sought to determine whether specifically recommending referral to the regional Lipid Disorders Clinic (LDC) increased referral and FH detection rates. A prospective case-control study of individuals with LDL-cholesterol >6.5 mmol/L was conducted. All individuals received an interpretative comment highlighting the possibility of FH. The cases comment also suggested LDC referral, and a subset of cases received the LDC’s fax number (fax-cases) in addition. There were 231 individuals with an LDL-cholesterol >6.5 mmol/L: 96 (42%) controls and 135 (58%) cases, of which 99 were fax-cases. Twenty-four (18%) cases were referred to clinic compared with eight (8%) controls (p = 0.035). After specialist review and genetic testing, four probable and four definite FH individuals were detected amongst controls, compared with seven possible, eight probable and nine definite FH amongst cases. Genetic testing was performed in 31 (94%) individuals, 13 (42%) had a causative mutation identified. Interpretative commenting specifically recommending specialist review augments the detection of FH in the community.

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A case of Nocardia mexicana cerebral abscess highlights deficiencies in susceptibility testing and the utility of direct molecular identification.

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CX3CR1 reduces choline-deficient, ethionine-supplemented diet-induced liver injury and liver progenitor cell proliferation.

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CX3CR1 and its cognate ligand, CX3CL1, is elevated in choline-deficient, ethionine-supplemented (CDE) diet-induced liver injury. 1 We assessed the role of CX3CR1 in liver injury and liver progenitor cell (LPC) proliferation by comparing the response of heterozygous CX3CR1<sup>gfp/+</sup> (control) and homozygous CX3CR1<sup>gfp/gfp</sup> (CX3CR1 knockout) mice to the CDE diet after 3 days. Heterozygous CX3CR1<sup>gfp/+</sup> mice exhibited markedly reduced CDE diet-induced LPC proliferation when compared to homozygous CX3CR1<sup>gfp/gfp</sup> mice. Furthermore, liver mRNA expression of the LPC mitogens, TNFalpha and lymphotoxin beta, were also significantly reduced in the homozygous mice. In contrast, levels of IL-6, interferon gamma, HGF, and TWEAK were
not affected. Heterozygous CX3CR1<sup>gfp/+</sup> mice developed less liver injury, steatosis, and inflammation compared to the homozygous CX3CR1<sup>gfp/gfp</sup>, as serum alanine transaminase levels, oil red o staining, and the number of inflammatory cells such as neutrophils and B cells, respectively were reduced. However, the numbers of Kupffer cells and monocyte-derived macrophages were similar in the heterozygous and homozygous mice. In conclusion, CX3CR1 attenuates CDE diet-induced LPC proliferation. This may be a consequence of the reduction in liver injury and accompanying reduced production of the LPC mitogens, TNF and lymphotixin beta.

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Serial mast cell tryptase measurements: Sensitivity and specificity for a diagnosis of anaphylaxis in patients with shock and/or hypoxemia.

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Background: Anaphylaxis is difficult to identify in cases presenting with atypical symptoms. Serial measurements of mast cell tryptase (MCT), looking for changes in MCT levels (delta-MCT) may increase the sensitivity of current diagnostic methods. The usefulness of this approach depends on the ability of delta-MCT to distinguish anaphylaxis from other critical illnesses, which is investigated in this study. Methods: MCT was measured (ImmunoCAP) in serum samples from patients with anaphylaxis (n=85) and non-anaphylactic critical illness (n=120) on at least three occasions: ED arrival, 1-2 hours, 3-4 hours, and 12-24 hours post-arrival where possible. Delta-MCT was calculated as the difference between the highest and lowest values regardless of time point, and analyzed using Receiver Operating Characteristic Curves. A positive delta-MCT was defined as >2.0 ng/mL. Results: 48 (56%) of 85 anaphylaxis cases were positive, compared to 31 (25%) of 120 cases of critical illness (including sepsis, cardiac arrest, trauma and toxicity). Non-anaphylaxis cases had delta-MCT values ranging from 0-22 ng/mL (2 cases had delta-MCT >10), whereas anaphylaxis cases had delta-MCT values ranging from 0-114 ng/mL (22 cases had delta-MCT >10). The diagnostic specificity was 0.74 with a sensitivity of 0.56. Higher cutoff values provided higher specificity but lower sensitivity. Conclusion: The specificity and sensitivity observed in this study indicate that delta-MCT measurements do not perform well in cases where anaphylactic shock has to be differentiated from other critical illnesses, which may also involve some mast cell degranulation. In this situation higher cut-offs are required, however this results in poor sensitivity.

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Mesenchymal stem cell infusion modulates systemic inflammation in patients with chronic obstructive pulmonary disorder (COPD).

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Background: COPD is characterised by chronic pulmonary and systemic inflammation. Recently, MSC infusions have
sound success in clinical trials for improved several aspects of inflammatory-driven diseases including improving repair. Although promising, the reparative mechanisms by MSC and their acute effects post-infusion are poorly characterised, particularly in COPD. MSC possess antiinflammatory properties, and have been shown to enhance the function of immunosuppressive T regulatory (Tregs) cells. Therefore, we hypothesise that MSC infusion will alleviate chronic inflammation in patients with COPD. Aims: 1) To assess trafficking of infused MSC by radiology 2) To evaluate inflammatory biomarkers following MSC infusion. 3) To assess phenotypic changes of Tregs post-infusion Methods: Radiolabelled MSC were infused intravenously into 9 patients with stable COPD and tracked by CT scan across the first week post-infusion. Systemic inflammatory (sTNFR1, CRP, IL-6, IP-10) and oxidative stress (F2-Isoprostane) markers were measured in plasma across 7 days postinfusion by ELISA and GC-MS respectively. HLA-DR+ expressing FoxP3+CD25+ Tregs were quantified by flow cytometry. Results: MSC first localised in the lungs from 0-24 hours post-infusion and then trafficked to the liver and spleen at day 1-7. Levels of F2-isoprostanes, IL-6 and IP-10 were significantly lower, while CRP and sTNFR1 significantly increased after MSC infusion. HLA-DR+ Tregs were significantly higher after MSC infusion. Summary and conclusions: We provide novel data showing MSC therapy in COPD patients modulating systemic inflammation within a week of infusion. Further characterisation of the systemic immunological changes will provide a deeper understanding of immune regulation during MSC therapy.


Improving anti-bacterial immune responses in patients with COPD by blocking inhibitory T-cell receptors.
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Chronic Obstructive Pulmonary Disease (COPD) is the most common respiratory cause of mortality and morbidity worldwide. Notably, acute exacerbations of COPD (AECOPD) accelerates the decline in lung function. AECOPD is usually associated with pulmonary infections but little is known about the mechanisms causing increased susceptibility in COPD. We hypothesize that chronic inflammation in AECOPD patients induces excess T-cell inhibitory molecules (e.g. CTLA-4) that then inhibit antibacterial immune responses in COPD patients. Peripheral blood mononuclear cells (PBMC) were isolated from AECOPD patients, stable COPD patients and healthy controls. Production of IFN gamma by PBMC was measured by ELISA post-challenge with viable non-typeable Haemophilus influenza (NTHI) or anti-CD3. Bacterial killing was assessed by investigating bacterial viability counts. T-cell expression of CTLA-4 was measured by flow cytometry. Plasma levels of inflammatory biomarkers were measured by ELISA. AECOPD patients exhibited higher plasma levels of CRP and IL-6 than stable COPD patients (p=0.07 and p=0.09 respectively) and healthy controls (p<0.01 for both). PBMC from AECOPD patients have lower production of IFN gamma against NTHI compared to stable COPD patients and healthy controls, but increased expression of CTLA-4 on CD4+ T-cells (p<0.05). Blocking of CTLA-4 increased anti-CD3 induced IFN gamma by PBMC from COPD and AECOPD patients. However in response to NTHI challenge, IFN gamma responses and bacterial killing were only improved in a subset of patients after CTLA-4 blocking. Increased expression of CTLA-4 could account for the increased frequencies of infections in COPD patients. Blocking multiple anti-inflammatory signals could improve anti-bacterial responses to prevent AECOPD.


A rare cause for coronary sinus dilation.
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A 29-year-old lady of Indian ethnicity presented with intermittent palpitations. She had an abnormal electrocardiogram with deep asymmetric anteroseptal T wave inversion. Subsequent exercise stress test was negative for ischaemia. Transthoracic echocardiography revealed moderate right ventricular dilatation with preserved systolic function, normal pulmonary pressures (26mmHg) and severe dilatation of the right atrium (RA). Cardiac Computed Tomography (CT) revealed partial anomalous pulmonary venous connection (PAPVC) with left superior (LS) and left inferior (LI) pulmonary veins (PV) draining into a dilated coronary sinus (CS) (Figure) with an intact interatrial septum. Given her paucity of symptoms and desire for pregnancy, cardiac surgery was deferred. (Figure presented) PAPVC is a congenital anomaly involving drainage of some of the PVs into the systemic venous circulation, with an estimated incidence at autopsy of 0.6-0.7% (Healy et al., 1952). The left PV is less commonly involved (16%) (Ammash et al., 1997). Anomalous left PVs drain into superior vena cava (SVC) (59%), RA (12%), RA-SVC (9%) and CS (3%) (Ammash et al., 1997). This case highlights the role of cardiac CT in diagnosis of PAPVC and specifying anatomy for surgical planning.

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**A new technique for improving standardisation and image quality in contrast aortography.**

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Aims: Contrast aortography has been used for more than 50 years however this method remains semi-subjective with high inter-observer variability. We developed a method to determine an Overlap-Free projection which enables standardisation of contrast aortography and improves quantification of aortic regurgitation, particularly useful for para-valvular regurgitation in TAVI. Methods and results: In patients referred for TAVI, a total of 65 computed tomography angiogram (CTA) scans and 19 prospectively collected aortograms were analysed. Using volume rendered three-dimensional reconstruction the Overlap-Free Projection (OFP)-defined as the C-arm angulation with no overprojection of the descending aorta on the aortic root or left ventricle was determined in both right anterior oblique and left anterior oblique orientation. From this data a method was developed to predict the optimal angulation for OFP using information readily available during femoral contrast aortography. In the prospectively collected aortograms there were no cases of overlap when the OFP rule was correctly applied. Conclusions: The OFP rule is an easy to use method to reliably determine a patient specific projection for standardised contrast aortography and will allow for improvements in quantification of aortic regurgitation. Further validation of this method in a larger cohort is currently in progress.

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**Rapid access chest pain clinic (RACPC): Utilisation and outcomes.**

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Rapid Access Chest Pain Clinic (RACPC): Utilisation and outcomes Introduction: Rapid access to chest pain assessment and management potentially improves patient outcomes. Fiona Stanley Hospital commenced an outpatient Rapid Access Chest Pain Clinic (RACPC) accepting referrals from general practitioners (GP) and emergency departments (ED). Referred patients are triaged and reviewed by registrars with on-site cardiologist consultation. Method: We performed a retrospective audit of patients referred to the RACPC from February 2015 to December 2015. We
describe the source of referral, investigations requested and clinical outcomes. Data was collected from the digital medical records. Results: Of 503 patients referred, 56% were male and 62% were under age 65 years. GP referrals accounted for 44%, with ED accounting for 34%. The majority, 57%, of patients were intermediate risk (TIMI score of 2-4). Half of the referred patients were discharged without any invasive investigation, 24% (n=123) were referred for coronary angiogram. The remainder were referred to private cardiologists (4%), did not attend clinic appointment (6%), refused treatment or investigation (2%), were on-referred to other cardiology clinics (10%) or died (<0.5%). Of the patients referred for angiogram 10% had normal angiogram, 30% were medically managed and 60% required percutaneous intervention or coronary artery bypass grafting equating to 1 out of 8 referred patients. Conclusion: We describe the characteristics of a RACPC in a modern tertiary hospital accepting ED and GP referrals. The RACPC potentially allows for efficient outpatient workup and appropriate management avoiding ED presentation or prolonged inpatient admission.

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**Catastrophic ventricular failure secondary to phaeochromocytoma requiring extra-corporeal membrane oxygenation.**
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A normally healthy 58 year old male presented with increasing headache, abdominal and chest pain, with rapidly worsening dyspnoea. His background included longstanding systemic hypertension which had been well controlled. On arrival; he was hypertensive, tachycardic and markedly dyspnoeic. ECG showed sinus tachycardia with 2mm upsloping ST-segment depression, chest X-ray demonstrating bilateral diffuse airspace changes. An urgent CT aortogram showed no aortic dissection. Transthoracic echocardiography revealed severe global left ventricular impairment with no valvular or pericardial pathology, and subsequent urgent coronary angiography showed no obstructive disease. Within an hour of presentation his respiratory condition rapidly deteriorated requiring ventilatory support. Progressive haemodynamic collapse followed despite increasing inotropic support and intra-aortic balloon pump insertion. Veno-arterial extra-corporeal membranous oxygenation (VA-ECMO) was commenced, maintaining adequate perfusion and oxygenation. Over the next 24-hours the patient remained haemodynamically stable, left ventricular function normalised on repeat echocardiography and VA-ECMO and inotropes were weaned. Within 48-hours the patient was extubated with no neurological deficit. Cardiac MRI performed 10 days after initial presentation showed no myocardial abnormality, normal perfusion and calculated left ventricular ejection fraction of 66%. The initial CT aortogram was reviewed in further detail, demonstrating a 23x20mm left-sided adrenal lesion, intensely active on Iodine-123 meta-iodobenzylguanidine scan. Urine and plasma metanephrine levels were consistent with a phaeochromocytoma. The patient was started on phenoxybenzamine, underwent uncomplicated adrenalectomy and remains well at 6 month follow-up. This case demonstrates the importance of prompt escalation of resuscitation measures in patients with undifferentiated cardiogenic shock, and the importance of considering rarer causes.

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**What is the role of emergency transcatheter aortic valve implantation in refractory cardiogenic shock or heart failure due to severe aortic stenosis?**
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Transcatheter aortic valve implantation (TAVI) has been well established for the treatment of high surgical risk patients with severe aortic stenosis. In patients with decompensating severe aortic stenosis with heart failure or shock,
it is unclear whether they are best managed with emergency TAVI (eTAVI) at the time of presentation, or emergency balloon aortic valvuloplasty (eBAV) as a bridge to possible subsequent valve replacement. We performed a retrospective audit of all eTAVI and eBAV at a state wide high risk aortic stenosis service. Cases of severe aortic stenosis presenting in cardiogenic shock or refractory heart failure requiring inotropic support were reviewed. Between 2008 and 2015, 21 eBAV (15 male, mean age 77 years) and 6 eTAVI (5 male, mean age 82 years) were performed. The mean logistic euroscores for eBAV and eTAVI were 64% and 75% respectively. 30-day mortality was 33% for eBAV and 0% for eTAVI. One year mortality was 50% for eBAV and 0% (4/6 cases at 1 year post procedure) for eTAVI. Of the patients treated with eBAV, 4 underwent subsequent TAVI and 3 surgical aortic valve replacement. All survived past 1 year. This audit suggests that eTAVI is a feasible option in high risk, decompensating patients with severe aortic stenosis. eTAVI appears to have a lower perioperative and medium term mortality as compared with eBAV. As demonstrated in previous studies, the medium term mortality following eBAV is high unless patients receive definitive valve treatment. Larger studies would be useful to further assess the role of eTAVI.

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Anticoagulation strategy, bleeding and thrombosis in left ventricular assist device patients.
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Introduction: Patients requiring support with LVAD therapy require anticoagulation therapy. Bleeding and thrombosis result in major morbidity and mortality. Our centre utilises regular patient self-monitoring INR checks (Coaguchek) to assist with optimal anticoagulation therapy. We performed a retrospective review of our anticoagulation strategy and outcome on bleeding and thrombosis within our service. Method: The anticoagulation therapy for all patients implanted with Heartware and Heartmate II LVAD at our centre (n=47) were analysed on a monthly basis from the first month to 13 months post implant. We reviewed INR, antiplatelet therapy and incidence of thrombosis and bleeding. Results: 402 months of therapy were reviewed. Bleeding episodes occurred in 73 months (18%) and thrombotic events occurred in 23 months (6%). INR was within therapeutic range (1.8-3.0) in 307 months (76%). INR <1.8 and > 3.0 in 75 months (19%) and 21 months (5%) respectively. Aspirin therapy was received in 393 months (98%), Clopidogrel therapy 279 months (69%) and dual antiplatelet therapy in 272 months (68%). The incidence of bleeding in patients receiving clopidogrel was lower than in patients receiving aspirin for antiplatelet therapy. Bleeding remained a significant cause of morbidity amongst our patients supported with LVAD despite receiving optimal INR management for the majority of the first 1-13 months post LVAD implant. The use of clopidogrel as an antiplatelet amongst our patients was associated with a lower risk of bleeding compared to aspirin.
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A presentation on lipid and protein markers of instent restenosis.
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Introduction: Instant restenosis (ISR) rates formodern drug eluting stents following percutaneous coronary intervention (PCI) approach 7-13%, with reintervention rates of 4% at 12 months. Predictors of ISR include diabetes, stent length and diameter. Method: We investigated if a protein or lipid profile could identify subjects at risk of ISR. Subjects from the Optima study undergoing PCI, with Optical Coherence Tomography performed immediately post PCI and at one of 3,6,12 or15 months follow-up were included (n=27). ISR was the change in lumen size compared to baseline (Fig1). Baseline serum was analysed for differentially expressed proteins and lipids using iTRAQ discovery platform and qTOF-LCMS. (Figure presented) Results: Diabetic status and direct stenting were associated with ISR. Twelve proteins were associated with ISR (Table 1). Two lipid species correlated with ISR (LPC 18:1 and PS 36:1). Using
multivariate analysis 57.5% of the ISR risk was explained by a model incorporating Diabetes, Maximal balloon diameter and LPC:18:1 and PS 36:1 (Table presented) Conclusion: Lipid species and proteins may be able to identify subjects at greater risk of ISR.

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Atypical presentation of bacterial infective pericarditis in a sixteen-year-old male.

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A sixteen-year-old Indigenous male presented with central pleuritic chest pain. He was treated for left arm cellulitis with oral co-amoxiclav in the preceding week. He was a poorly controlled type 1 diabetic with autoimmune thyroiditis, diagnosed 4 years ago. He was febrile, tachycardic and normotensive. X-ray demonstrated cardiomegaly. Echocardiogram showed a large pericardial effusion with no tamponade. Troponin was 0.28-g/L (normal <0.04), C-reactive protein 293mg/L (normal <5), white cell count normal and no bacterial growth on 3 blood cultures. A diagnosis of myopericarditis was made. He was transferred to a quaternary hospital. He developed increasing dyspnoea, tachypnoea, tachycardia and hypotension. Echocardiography demonstrated tamponade physiology. An apical pericardiocentesis with a drain in situ was performed; ~300ml of straw-coloured transudate was drained with prompt improvement of symptoms. Minimal residual effusion was confirmed on repeat echocardiogram the next day. The pericardial fluid grew methicillin sensitive staphylococcus aureus (MSSA) and intravenous flucloxacillin was commenced despite transudative effusion and absence of leucocytosis given diabetes, recent cellulitis and prior antibiotic use. The patient developed worsening chest pain and tachycardia overnight. Echocardiography showed a loculated pericardial effusion around the right ventricle with tamponade. Straw coloured fluid (~800ml) was drained surgically. The patient developed collapsed lung, consolidation and left-sided pleural effusion requiring ventilation. Intercostal catheter was inserted with ~600ml serous fluid drained which also grew MSSA. MRI did not demonstrate definite evidence of myopericarditis. The patient improved and was discharged on long-term antibiotics. This case demonstrates an atypical presentation of staphylococcus aureus pericarditis in an immunocompromised patient.

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Medical versus surgical management of infective endocarditis in a Western Australia tertiary hospital setting.

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Background: Infective endocarditis (IE) has high inhospital mortality. Well-defined guidelines assist in decision making around medical vs surgical management. We describe in-hospital mortality of IE in 3 tertiary hospitals comparing medical vs surgical management. Methods: Retrospective analysis of IE management during realignment of cardiothoracic surgery services was performed. Between 01/04/14 and 01/10/14, IE cases at 2 hospital sites were identified and following transfer of those services to a new hospital site, IE cases between 01/04/15 and 01/10/15 were identified. 56 patients were included (15 at each site pre-alignment and 26 post-alignment). Indications for surgery were based on the American Heart Association/ American College of Cardiology guidelines. Results: Overall IE mortality was high with 12.5% inhospital death. 21/38 patients meeting surgical criteria underwent operative management, however, the threshold for surgery differed between hospital sites. Those patients meeting surgical criteria had non-significantly higher mortality (18.4% vs 0%, p=0.084). Patients meeting surgical criteria who got surgery versus those who did not get surgery had lower in-hospital mortality (4.8% vs 35.3%, p=0.031). Overall in-hospital mortality was non-significantly lower in the group that received surgery (4.8% vs 17.1%, p=0.237).
In-hospital mortality was lower at sites with higher rates of surgical intervention that followed guidelines. Conclusions: We describe variation in surgical intervention and improved in-hospital mortality outcomes when adherence to indication for surgery guidelines are followed. We recommend cardiology units review their surgical utilisation to optimise IE outcomes.

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Are the benefits of invasive management associated with grace predicted risk modified by age and renal function?

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Introduction: GRACE score, derived from 4 cardiac and 2 non-cardiac components, is validated for objective risk prediction in Acute Coronary syndromes (ACS). While the benefit from invasive management increases with higher GRACE score, these benefits are uncertain when risk is determined largely by the non-cardiac factors of age and renal function. We explored the interaction between GRACE risk and invasive management as a function of the non-cardiac risk components. Methods: Five Australian ACS registries (GRACE, ACACIA, CONCORDANCE, SNAPSHOT, PREDICT[1999-2015]) recorded the GRACE score and 6-month mortality. By using the GRACE score values for age and renal function, we calculated the percentage contribution of these factors to the overall score in each patient (i.e. Age <20%, 20-39%, 40-59%, > 60%; Cr <20%, 20-29%, >30%). The interactions between GRACE score, invasive management, and age or renal function contributions were explored using general estimating equations. Results: In total 17,140 of patients were included, of whom 30.4% were STEMI. An increasing GRACE score was associated with a greater benefit from invasive management. However, a higher contribution of age to the score was associated with a lower impact on mortality from invasive-management. (Relative risk reduction with invasive management: Age% < 20%-82%; 20-39%-66%; 40-59%-54%; 60%-15%, interaction p value <0.001). The benefit from invasive management was constant (no interaction) regardless the contribution of renal function to GRACE score. Conclusion: GRACE score identifies patients benefiting from invasive management. However, with increasing contribution of age to absolute risk, the benefits of invasive management are reduced.

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Myocardial infarction post Kawasaki’s disease: An unfortunate legacy of a childhood disease.

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A 26 year old female presented with chest pain for 3 hours with ST elevation in infero-posterior leads and peak hstroponin I of 33100. The patient had a delayed diagnosis of Kawasaki’s disease at age two and despite intravenous immunoglobulin developed giant coronary artery aneurysms (CAA). She was managed with warfarin and aspirin, which were discontinued at ages 19 and 23. ST elevation myocardial infarction complicating known giant CAA was
diagnosed. Coronary angiography showed proximal occlusion of right coronary artery (RCA) and severe proximal left anterior descending artery (LAD) stenosis with extensive calcification. CT coronary angiography (effective dose 1.0mSv) demonstrated a giant aneurysm (20x19x15mm) of the proximal RCA with thrombotic occlusion of lumen (arrow) and 2 calcified aneurysms in the mid RCA and proximal LAD. Cardiac MRI showed transmural myocardial infarction in RCA territory with viability in other territories. She had coronary artery bypass grafting with LIMA to the LAD and SVG to the PDA with observed functional recovery. Giant CAA (internal diameter >8mm) is associated with poorer prognosis and lower likelihood of regression compared to smaller size aneurysms. Persistent aneurysms result in progressive myointimal proliferation and calcification, increasing risk of stenosis and thrombotic occlusion, which persist into adulthood. Recommended management of giant CAA consist of life-long aspirin and anticoagulation. This raises difficult management challenges, particularly in young female patients wishing to start families.

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1 year outcomes following veno-arterial extracorporeal membrane oxygenation for refractory cardiogenic shock.
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Aim: Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) has been shown to improve short-term outcomes in patients with refractory cardiogenic shock (RCS). However the longer term outcomes are unclear. We examine the course of those patients surviving their initial admission requiring VA-ECMO. Methods: This study was a retrospective, single-centre review of patients who received VA-ECMO for RCS. Baseline patient characteristics, aetiology of RCS, survival as well as cardiovascular and neurological outcomes at hospital discharge and one year were collected. Results: From 2008 to 2015, 37 patients received VA-ECMO for RCS. Mean age was 45 years, 65% were male and median time on VA-ECMO was five days. The aetiology of RCS was acute myocarditis in nine (24%), post-cardiac surgery in seven (19%), post heart/lung transplant in five (14%), acute myocardial infarction in five (14%), decompensated cardiomyopathy in four (11%), and other in seven (19%). Nineteen (51%) patients survived to hospital discharge, of these patients 79% made a full neurological recovery, 47% were medically managed without advanced heart therapies, 31% had received heart transplantation, 16% required left ventricular assist devices (LVAD), and 5% were listed for heart transplantation. At one year, 17 patients remained alive, of these one patient received a heart transplant, one patient progressed from medical therapy to LVAD and one patient was newly listed for transplant. Conclusion: Patients receiving VA-ECMO for RCS who survive to discharge have a favourable medium-term prognosis however a significant proportion require LVAD support or transplantation.

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Right coronary dissection and left anterior thrombus: Dual dilemma in a young cardiac arrest survivor.
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A 22 year old male from Singapore presented to our emergency department as a “STEMI” call after an out of hospital arrest (Fig 1). His parents, both doctors, had run his arrest in a local supermarket with CPR, two DC shocks and adrenaline from an “EpiPen” before achieving ROSC. On retrospective history he was a healthy and active ex-international swimmer. He denied any illicit drug or steroid use and did not drink alcohol. He denied any previous chest pain and there was no family history. His angiogram revealed acute thrombotic occlusion in the mid left anterior descending (LAD) coronary artery (Fig 2). Optical coherence tomography (OCT) was performed pre and post-percutaneous intervention (PCI) and there was no evidence of LAD dissection (Fig 3). His right coronary artery was a dominant vessel, with an appearance suggestive of chronic dissection with a long segment of severe
stenosis involving proximal, mid and distal vessel (Fig 4). Literature review covering young myocardial infarction and spontaneous coronary artery dissection (SCAD) is discussed, covering risk factors, diagnosis and management. This patient did not appear to have any risk factors except his ex-athlete status. The use of OCT as a gold standard for detecting SCAD is also discussed. To our knowledge, this represents the first case report that describes both acute coronary thrombosis and chronic coronary dissection in a young patient without identifiable risk factors. (Graph presented).

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Insights into the use of interventional management in acute coronary syndromes in Australia over the last 15 years.

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Background: Despite the acute coronary syndrome (ACS) evidence base, the use of invasive management within specific risk groups continues to be debated. Our analysis examines the change in the use of invasive management in ACS by patient risk and the associated temporal change in mortality within 5 registries conducted in Australia over the last 15 years. Methods & Results: This study merged multiple ACS registries (ACACIA, CONCORDANCE, GRACE, ACS-Snapshot and PREDICT) with data spanning from 1999-2015. After excluding patients without a final diagnosis of ACS (n=4355) or enrolled outside of Australia (n=1473), 15569 patients were available for analysis. Data was stratified across three time periods (1999-2004; 2005-2009; 2010-2015) to monitor change in practice. Patients were stratified by clinical risk characteristics using age, ACS diagnosis, cardiac biomarker elevation and GRACE score. We observed that the use of invasive management increased over the 15-year period (4073/6863 (59.3%) cases [1999-2009] vs. 6670/8706 (76.6%) cases [2010-2015]), with the greatest improvements in use and outcome seen in the high risk ACS group. Over time our study showed worse outcomes in medical management of ACS compared to interventional management groups (1999-2004 1.55 HR [95% CI 1.36-1.80], p<0.0001 vs. 2010-2015 1.90 HR [95% CI 1.45-2.51], p<0.0001). Conclusions: Clinical practice in ACS has changed over the last 15 years with positive outcomes seen in high risk patients managed with invasive procedures. Unfortunately, a considerable burden of mortality is seen in patients managed medically, highlighting a need for greater focus in research in this group to achieve better outcomes.

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Use of oral anticoagulation combined with single versus dual antiplatelet therapy in acute coronary syndrome patients: An Australian pooled registry analysis.

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Background: Patients with acute coronary syndromes (ACS) requiring concurrent anticoagulation are increasingly frequent. Whether anticoagulation combined with a single antiplatelet agent (double therapy) is as effective but safer
than dual antiplatelet agents (triple therapy) is controversial. Aims and Methods: We reviewed the combined data from 4 ACS registries in Australia spanning 1999 to 2015 of patients requiring long-term anticoagulation for any indication. The endpoints were major bleeding, mortality, myocardial infarction and stroke at six months. Results: Of the 17,812 patients with ACS surviving to discharge, 851 (4.78%) required long-term anticoagulant therapy, including 543 patients on double therapy and 308 on triple therapy. Those discharged on triple therapy were younger (66.4 vs 71.2 years), and were less likely to have a history of prior myocardial infarction (35% vs 43%, p=0.03), diabetes (28% vs 34%, p=0.06), hypertension (64% vs 72%, p=0.008) or dyslipidaemia (56% vs 62%, p=0.07). There was no difference between triple therapy compared to double therapy in terms of mortality (3% [7/215] vs 5% [20/396], p=0.30), myocardial infarction (5% [11/215] vs 4% [16/396], p=0.54), stroke (1% [2/215] vs 1% [3/396], p=0.82), or major bleeding (6% [2/32] vs 2% [1/66], p=0.21). Conclusions: There is no difference in outcomes between patients selected for triple therapy and double therapy when requiring concurrent anticoagulation in this large observational analysis. However the available data are limited, and further randomised trials are required.

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Improving clinical efficiency, timeliness of revascularisation and cost effectiveness among patients with new onset angina; The royal perth hospital experience.

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Background: Managing patients with new onset chest pain continues to place a significant burden on healthcare services. Streamlined pathways, such as a Rapid Access Chest Pain Clinic (RACPC), may improve clinical efficiency, timeliness of revascularisation and provide cost-savings. Methods: We studied patients referred to Royal Perth Hospital, with new onset chest pain, 6-months before and 4-months after the introduction of a RACPC. Comparisons were made between groups; time from referral to (i) clinic assessment, (ii) investigation, (iii) revascularisation as well as unplanned ED presentations. Data expressed as mean (SD) if normally distributed or median (IQR) if skewed. Results: 159 patients (92 pre-RACPC, 67 RACPC) were studied. The cohorts were of similar age (58+/-13.5 vs 58+/-13.5, p=0.85). Compared to pre-RACPC, patients managed in RACPC had a higher incidence of high risk characteristics (diabetes, smoking, hypercholesterolaemia); 81% vs 64%, p<0.05. Among patients managed within the RACPC, time from referral to (i) clinic assessment (5 (3-6) vs 83 (53-111) days, p<0.001), (ii) investigation (14 (5-29) vs 107 (80-147) days, p<0.001) and (iii) revascularisation (12 (8-41) vs 76 (48-104) days, p<0.05) was significantly shorter compared to patients referred in the prior 6-months. Between the time of referral to time seen in clinic, 15 patients from the pre-RACPC group presented to ED compared to none managed within the RACPC. Prevention of unnecessary ED presentations translated to an estimated annual cost-saving of $41,790 (based on ABF costing). Conclusion: Introduction of the RACPC dramatically reduced delays in patients being seen, investigated and revascularised and offered significant cost-savings.

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Long-term persistence on statins following myocardial infarction in a population-cohort: Age and gender perspective.

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Background: The efficacy of statin therapy for secondary prevention is widely accepted but persistence is often sub-optimal. We measured persistence with statins post-myocardial infarction (MI) in a whole-population cohort stratified by age group and gender. Methods: All first MI hospitalisations in WA (35-84 years) for Jan 2003-June 2008 were identified. Among 30-day survivors, the proportion dispensed a statin after discharge was calculated from linked Pharmaceutical Benefits Scheme records for 2003-2011. The Medication Possession Ratio (MPR) at 1 year was calculated for 1 year survivors as the sum of days of statin supply within 1 year, divided by 365 minus days in hospital, with persistence presented as a function of MPR (MPR > 80%). Similarly, the 3 year MPR > 80% was calculated for 3 year survivors. Results: There were 13,011 MI patients (mean age 65 years, males 70%). The proportion of patients dispensed a statin within 30-days of hospital discharge was 80% in men vs 75% in women (p < 0.0001). This proportion was higher in men 35-64 vs 65-84 years (82% vs 78%, p < 0.0001), with a non-significant age group differential in women (77% vs 74% respectively, p = 0.12). Optimal MPR (> 80%) at 1 year post-MI was worse in younger than older men (64% vs 73%, p < 0.0001), and dropped further at 3 years in 35-64 (54%) and 65-84 year olds (68%, p < 0.0001). The pattern was similar in women-MPR > 80% at 3 years was 52% in 35-64 year olds, and 64% in 65-84 year olds (p < 0.0001). Conclusions: Initial dispensing rates of statins early following MI are sub-optimal and long-term optimal persistence is low in both genders, particularly in the younger age groups.

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New hospital, old tricks: Management of atrial fibrillation in the emergency department of a newly opened tertiary hospital.

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Background: Atrial fibrillation (AF) is the most common cardiac arrhythmia presentation to the emergency department (ED). There is a strong evidence base supporting the management of atrial fibrillation including cardiac society guidelines. Objective: To determine the trends in management of AF in the ED of our newly opened tertiary hospital. Method: We performed a retrospective analysis of data utilising the hospital’s electronic coding system. All cases coded for AF in a five-month period were reviewed. The cases of AF as the primary diagnosis were selected for analysis. Data included comorbidities, chronicity, investigations, rate/rhythm strategy, anticoagulation, and follow-up. Results: There were 625 presentations to ED that included a diagnosis of AF. Of these, 114 had AF as the primary diagnosis. 46.5% male, mean age 71 years. 61.5% had guideline indications for anticoagulation but only 34% were on treatment. Of the 70 patients not on anticoagulation, only 41% were commenced on treatment. The choice of treatment varied (75% NOACs vs 25% warfarin). There was no consistency regarding rate slowing or rhythm control agents and choices were not guideline based. The use of rate slowing was higher than rhythm control (83% vs 11%). Cardiology consultation was sought in 63% of cases. 90% of cases were admitted (34% under cardiology, 42% under general medicine). Conclusion: Despite the breadth of evidence available, the management of AF still varies substantially between physicians. We suggest that a cardiologist-supported protocol for the management of AF in the emergency department would be of benefit.

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Voltage-gated potassium channel antibody limbic encephalitis: a case illustrating the neuropsychiatric and PET/CT features with clinical and imaging follow-up.


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OBJECTIVE: To illustrate the neuropsychiatric and imaging findings in a confirmed case of voltage-gated potassium channel antibody limbic encephalitis.

METHOD: Case report and review of the literature.

RESULTS: A 64-year-old man presented with several months’ history of obsessive thoughts and compulsions associated with faciobrachial dystonic seizures. He had no significant past medical and psychiatric history. Physical examinations revealed only mildly increased tone in the left upper limb. Bedside cognitive testing was normal. Positron-emission tomography showed intense symmetrical uptake in the corpus striatum. No underlying malignancy was identified on whole body imaging. Magnetic resonance imaging, lumbar puncture and electroencephalogram were normal. Serum voltage-gated potassium channel antibodies were strongly positive. The patient had a favourable response to antiepileptic drugs, oral steroids and immunotherapy.

CONCLUSIONS: Voltage-gated potassium channel limbic encephalitis characteristically presents with neuropsychiatric symptoms and temporal lobe seizures. Positron-emission tomography-computed tomography can be a useful adjunct to the clinical and biochemical work-up.


Voon K, Silberstein I, et al.

INTRODUCTION: Rehabilitation following burns is integral to improving physical and psychological outcomes. Interactive video game consoles are emerging as therapeutic adjuncts due to their ease of use, affordability, and interactive gameplay. The Xbox KinectTM has advantage over similar consoles, with controller free interaction utilising three dimensional motion capture software. Player movements during gameplay have been shown to be comparable to completing daily tasks and therefore the Xbox KinectTM has potential for use as a rehabilitation tool.

AIM: The objectives of this pilot study were to compare the efficacy of the Xbox KinectTM with conventional physiotherapy as an adjunctive tool to promote activity and, to explore their efficacy in influencing functionality and pain.

METHOD: A randomised controlled clinical trial design was used. Intervention group participants were asked to complete two daily 30min exercise sessions consisting of 15min of self-directed physiotherapy exercise followed by 15min of Xbox KinectTM activities, based on location of burn. Control group participants were asked to complete two daily 30min exercise sessions of self-directed physiotherapy exercises involving two 15min sets of exercises, standardised for location of burn. Participants were recruited for a maximum of 7 days. Outcomes assessed included daily activity time, treatment satisfaction, upper limb disability, pain, and self-reported fear of movement (kinesiophobia).

RESULTS: A sample of 30 burn patients admitted to Royal Perth Hospital was randomised into intervention and control groups. The intervention group demonstrated significantly greater total activity time compared to control group (median 49.4 and 26.7min respectively, p<0.0001), irrespective of total burns surface area (TBSA). Significantly greater satisfaction scores were also demonstrated in the intervention group compared to controls (median 8.53 vs
7.8 respectively, p<0.0001). There was no evidence to support differences between group measures for upper limb disability, pain and fear avoidance of movement.

CONCLUSION: The Xbox KinectTM is a useful tool in increasing rehabilitation exercise time and patient satisfaction compared to conventional physiotherapy without indication of concurrent negative effects on patient recovery.

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Increased admissions for diabetes mellitus after burn.

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BACKGROUND: Currently, limited long-term data on hyperglycaemia and insulin sensitivity in burn patients are available and the data that do exist are primarily related to paediatric severe burns. The aim of this study was to assess if burn is associated with increased post-burn admissions for diabetes mellitus.

METHODS: A population-based longitudinal study using linked hospital morbidity and death data from Western Australia was undertaken of all persons hospitalized for a first burn (n=30,997) in 1980-2012 and a frequency matched non-injury comparison cohort, randomly selected from Western Australia’s birth registrations and electoral roll (n=123,399). Crude admission rates and summed length of stay for diabetes mellitus 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 adjustment for socio-demographic factors and pre-existing health status, the burn cohort had 2.21 times (95% Confidence Interval (CI): 1.36-1.56) as many admissions and almost three times the number of days in hospital with a diabetes mellitus diagnosis (IRR, 95% CI: 2.94, 2.12-4.09) than the uninjured cohort. Admission rates were significantly elevated for those burned during childhood (<18 years, IRR, 95% CI: 2.65, 1.41-4.97) and adulthood (>18 years, IRR, 95% CI: 2.12, 1.76-2.55). Incident admissions were significantly elevated in the burn cohort during the first 5 years post-burn when compared with the uninjured (HR, 95% CI: 1.96, 1.46-2.64); no significant difference was found beyond 5 years post-burn (HR, 95% CI: 1.08, 0.82-1.41).

CONCLUSIONS: Findings of increased hospital admission rates and prolonged length of hospital stay for diabetes mellitus in the burn cohort provide evidence that burns have longer term effects on blood glucose and insulin regulation after wound healing. The first five years after burn discharge appears to be a critical period with significantly elevated incident admissions for diabetes mellitus during this time. Results would suggest prolonged clinical management after discharge and or wound healing to minimise post-burn admissions for diabetes mellitus is required.

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A Randomized Phase IIb Trial of myo-Inositol in Smokers with Bronchial Dysplasia.

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Previous preclinical studies and a phase I clinical trial suggested that myo-inositol may be a safe and effective lung cancer chemopreventive agent. We conducted a randomized, double blind, placebo-controlled phase IIb study to determine the chemopreventive effects of myo-inositol in smokers with bronchial dysplasia. Smokers with >1 site of dysplasia identified by autofluorescence bronchoscopy-directed biopsy were randomly assigned to receive oral placebo or myo-inositol, 9 g once a day for 2 weeks, and then twice a day for 6 months. The primary endpoint was change in dysplasia rate after 6 months of intervention on a per-participant basis. Other trial endpoints reported herein include Ki-67 labeling index, blood and bronchoalveolar lavage fluid (BAL) levels of proinflammatory, oxidant/antioxidant biomarkers, and an airway epithelial gene expression signature for PI3K activity. Seventy-four (n = 38 myo-inositol and n = 36 placebo) participants with a baseline and 6-month bronchoscopy were included in all efficacy analyses. The complete response and the progressive disease rates were 26.3% versus 13.9% and 47.4% versus 33.3%, respectively, in the myo-inositol and placebo arms (P = 0.76). Compared with placebo, myo-inositol intervention significantly reduced IL6 levels in BAL over 6 months (P = 0.03). Among those with a complete response in the myo-inositol arm, there was a significant decrease in a gene expression signature reflective of PI3K activation within the cytologically normal bronchial airway epithelium (P = 0.002). The heterogeneous response to myo-inositol suggests a targeted therapy approach based on molecular alterations is needed in future clinical trials to determine the efficacy of myo-inositol as a chemopreventive agent. Cancer Prev Res; 9(12); 906-14. ©2016 AACR.
Secondary preventive medication use in a prevalent population-based cohort of acute coronary syndrome survivors.


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AIM: Describe the dispensing patterns for guideline-recommended medications during 2008 in people with acute coronary syndrome (ACS) and how dispensing varies by gender and time since last ACS hospitalization.

METHOD: A descriptive cohort spanning 20 years of people alive post-ACS in 2008. We extracted all ACS hospitalizations and deaths in Western Australia (1989-2008), and all person-linked Pharmaceutical Benefits Scheme claims nationally for 2008. Participants were 23,642 men and women (36.8%), alive and aged 65–89 years in mid-2008 who were hospitalized for ACS between 1989 and 2008. Main outcome was the proportion of the study cohort (in 2008) dispensed guideline-recommended cardiovascular medications in that year. Adjusted odds ratios estimating the association between type (and number) of guideline-recommended medications and time since last ACS hospitalization.

RESULTS: Medications most commonly dispensed in 2008 were statins (79.6% of study cohort) and then angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers (ACEi/ARBs) (71.1%), aspirin or clopidogrel (59.4%), and beta-blockers (54.6%). Only 51.8% of the cohort was dispensed three or more of these drug types in 2008. Women with ACS were 18% less likely to be dispensed statins (adjusted odds ratio (OR)=0.82; 95% CI 0.76–0.88). Overall, for each incremental year since last ACS admission, there was an 8% increased odds (adjusted OR=1.08; 95% CI 1.07–1.08) of being dispensed fewer of the recommended drug regimen in 2008.

CONCLUSION: Longer time since last ACS admission was associated with dispensing fewer medications types and combinations in 2008. Interventions are warranted to improve dispensing long term and any apparent gender inequality in the drug class filled.

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Pleural Infections in Intensive Care.

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CONCLUSION: Longer time since last ACS admission was associated with dispensing fewer medications types and combinations in 2008. Interventions are warranted to improve dispensing long term and any apparent gender inequality in the drug class filled.

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Pleural Infections in Intensive Care.

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Incidence and cost of stress ulcer prophylaxis after discharge from the intensive care unit: a retrospective study.

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OBJECTIVE: To describe current patterns in initiation and cessation of proton pump inhibitors (PPIs) for stress ulcer prophylaxis (SUP) in intensive care units, and to assess the costs associated with inappropriate (non-evidence-based) SUP.

DESIGN, SETTING AND PARTICIPANTS: Retrospective observational study in five ICUs in Western Australia. We assessed the medical records of consecutive patients admitted to the ICUs between September 2013 and January 2015. Patients aged < 18 years were excluded.

RESULTS: We included 531 patients in the study. Of the 184 patients in whom PPIs were initiated for SUP in the ICU, 90 (48.9%) were still taking the therapy at the time of discharge from hospital. A documented indication for ongoing therapy was present in only nine patients (10%). We assumed a 10-year life expectancy after ICU discharge and that most patients continued taking a PPI, and calculated an additional cost of $180.20 per patient admitted to the ICU. This was based only on unnecessary PPI costs (ignoring costs of managing additional adverse events). The direct cumulative annual cost to the WA health system of PPIs continued unnecessarily for patients at discharge from hospital is estimated to be $250 800 for each year they continue to receive them.

CONCLUSION: A substantial proportion of patients prescribed SUP in the ICU continue receiving this therapy at hospital discharge despite no clear indication. In addition to potential adverse clinical effects, this is associated with major direct and indirect cost implications.

Evaluation of the posttraumatic growth inventory after severe burn injury in Western Australia: clinical implications for use.

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PURPOSE: Posttraumatic growth (PTG) is “the subjective experience of positive psychological change reported as a result of the struggle with trauma”. Very few studies have explored PTG after burn injury. The Posttraumatic Growth Inventory (PTGI) is a 21-item questionnaire which assesses five domains in which PTG has been found. First, the aim of this study was to assess how PTG presented after a severe burn, and second, whether it could be measured by the PTGI in Australian burn survivors.

METHODS: A mixed method approach was used. Seventeen patients who had a severe burn injury at least 2 years previously were interviewed and completed the PTGI. The interviews were analyzed, then compared to the PTGI responses.

RESULTS: PTG in burn survivors had similarities to PTG arising from other trauma. Burn-specific context such as heat intolerance and functional problems influenced the type of changes made. Barriers to PTG in relationships were related to guilt burden and visible scarring.

CONCLUSION: PTG presents similarly after burn to other trauma types, but has other features to consider when devising intervention strategies. The PTGI is a 5-min screening tool that adequately identifies the presence or absence of PTG in burn survivors in Western Australia, and can guide intervention.

IMPLICATIONS FOR REHABILITATION: The Posttraumatic Growth Inventory is a 5-min screening tool that adequately identifies the degree of PTG in burn survivors in Western Australia. It is a quick and easy tool to use to identify the need for clinical intervention. It will also evaluate the effectiveness of strategies designed to target PTG. A mean score of 2.5 can be used as a threshold to guide intervention strategy.

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Which patients should be transported to the emergency department? A perpetual prehospital dilemma.

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OBJECTIVE: To examine the ability of paramedics to identify patients who could be managed in the community and to identify predictors that could be used to accurately identify patients who should be transported to EDs.

METHODS: Lower acuity patients who were assessed by paramedics in the Perth metropolitan area in 2013 were studied. Paramedics prospectively indicated on the patient care record if they considered that the patient could be treated in the community. The paramedic decisions were compared with actual disposition from the ED (discharge and admission), and the occurrence of subsequent events (ambulance request, ED visit, admission and death) for discharged patients at the scene was investigated. Decision tree analysis was used to identify predictors that were associated with hospital admission.

RESULTS: In total, 57183 patients were transported to the ED, and 10204 patients were discharged at the scene by paramedics. Paramedics identified 2717 patients who could potentially be treated in the community among those who were transported to the ED. Of these, 1455 patients (53.6%) were admitted to hospital. For patients discharged at the scene, those who were indicated as suitable for community care were more likely to experience subsequent events than those who were not. The decision tree found that two predictors (age and aetiology) were associated with hospital admission. Overall discriminative power of the decision tree was poor; the area under the receiver operating characteristic curve was 0.686.

CONCLUSION: Lower acuity patients who could be treated in the community were not accurately identified by paramedics. This process requires further evaluation.


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Diving accidents: a cohort study from the Netherlands.

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BACKGROUND: Diving is, besides professional reasons, an increasingly popular leisure activity. Whilst statistically compared to other sports safe, diving accidents can result in serious complications. In order to treat this specific patient category adequately, early diagnosis is important. In this study, we explore various medical aspects of diving accidents. By sharing our experiences, we intend to create awareness and enhance urgent medical care for this specific category of patients.
METHODS: We conducted a retrospective cohort study using anonymized patient records from the emergency department (ED) of the Admiraal De Ruyter Hospital (ADRZ) and affiliated Medical Centre Hyperbaric Oxygen Therapy (MCHZ1) both in Goes, Netherlands. We evaluated all patients that presented to our ED as a diving accident from 1 November 2011 to 30 August 2015.

RESULTS: In the selected period, 43 patients presented to our ED with complaints after diving; 84 % were male and 49 % older than 40 years, and they came by ambulance or referred by a general practitioner or other medical centres in the area; 70 % presented the same date as their dive, 21 % 1 to 3 days and 9 % later than 3 days after having dived. Pain was the most frequently reported symptom (44 %), followed by constitutional symptoms (42 %). Numbness or paraesthesia was reported in 33 %. Respiratory symptoms, dizziness, a change in mental status (e.g. apathy, confused or restlessess) and problems with coordination were present in 10-21 % of the cases. Symptoms that were apparent in less than 10 % of the cases were cutis marmorata, visual or auditory complaints, muscle weakness, cardiovascular symptoms or a malfunction of the anal sphincter or urinary bladder. Most of our patients exhibited more than one symptom; 70 % of all patients received hyperbaric oxygen recompression therapy.

CONCLUSIONS: The limited number of patients presenting with complaints after a diving incident, the difficulty of recognition and the (potential) huge impact if not recognized and treated adequately make us believe that every diving accident should be discussed with a centre of expertise.

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Remifentanil for labor analgesia: a comprehensive review.

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Japan has seen significant developments in obstetric anesthesia in recent years, including the establishment of the Japanese Society of Obstetric Anesthesia and Perinatology. However, labor pain, which is one of the most important issues in obstetric practice, is still not treated aggressively. The rate of epidural administration for labor analgesia is very low in Japan as compared to other developed countries. Remifentanil has been used for labor analgesia, as part of general anesthesia for cesarean delivery, as well as for various fetal procedures around the world. Intravenous patient-controlled analgesia (IVPCA) with remifentanil is considered to be a reasonable option for labor pain relief. Several studies have demonstrated its efficacy with minimal maternal and neonatal adverse effects. On the other hand, reports of cases of maternal cardiac and respiratory arrest with remifentanil IVPCA within the past couple of years have redirected our attention to its safe use. Remifentanil IVPCA warrants one-to-one nursing monitoring, appropriate education of healthcare providers, continuous maternal oxygen saturation monitoring, end-tidal CO$_2$ monitoring, and availability of both maternal and neonatal resuscitation equipment. This article provides an overview of knowledge and principles of using remifentanil IVPCA for labor analgesia and introduces its potential usage in Japan.

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Characterization of a novel staphylococcal cassette chromosome composite island from community-associated MRSA isolated in aged care facilities in Western Australia.

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BACKGROUND: In Western Australia (WA), clonal complex 5, ST835, community-associated (CA) MRSA is isolated almost exclusively from aged care facilities. In WA four different staphylococcal cassette chromosome (SCC) mec elements have been identified in this ST, indicating high genetic activity in the SCCmec region.
OBJECTIVES: To investigate the SCC region of ST835 CA-MRSA WA MRSA-40 and determine the distribution of an SCCsoritol element found within the region.
RESULTS: The SCC region contained a composite island, SCCmec<sub>WA MRSA-40</sub>-CI, that was composed of three elements, PSISCCCpl, SCCsoritol and SCCmecV<sub>T</sub> (5C2&5). This is the first time that a sorbitol operon has been reported in an SCC element.
CONCLUSIONS: Generation of SCCmec<sub>WA MRSA-40</sub>-CI has involved multiple genetic events and recombination with CoNS has occurred during evolution of the SCC elements. While Staphylococcus aureus is renowned for its ability to utilize mobile genetic elements to disseminate antimicrobial resistance, the SCC region of WA MRSA-40 shows that this clone has also utilized SCC elements to acquire extra virulence and possibly adapt to a niche environment.

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**Strategies for Medical Management of Pediatric Eosinophilic Esophagitis.**

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OBJECTIVE: Eosinophilic esophagitis (EoE) is associated with significant morbidity in children. Strategies for optimizing its outcomes are hence essential. We aimed to review the strategies for medical management of EoE in children.

METHODS: We conducted a systematic review of randomized controlled trials (RCTs) of medical interventions in children with EoE, using the Cochrane methodology. Databases including PubMed, EMBASE, CINAHL, Cochrane Central Library, and Google scholar were searched up to March 2016. Primary outcomes included histological (peak eosinophil count) and symptomatic remission. Secondary outcomes were improvement in endoscopic and other histological parameters and adverse effects.
RESULTS: A total of 5 RCTs (N = 448) with low to unclear risk of bias were included. The interventions included topical oral steroids, swallowed enteral steroids and anti-interleukin (IL)5 agent. Pooling of data from all trials was not possible owing to significant heterogeneity in interventions. Meta-analysis of data (N = 141) from 3 RCTs (oral viscous budesonide: 2, fluticasone: 1) showed significant histological remission in the intervention versus control group participants (risk difference: 10.32 [95% confidence interval: 3.04, 35.03]; P = 0.0002), level of evidence-low. Compared with anti-IL5 agent, the trials assessing steroids reported high rates of clinical remission. Clinical remission did not correlate with histological improvement in any trial. Except for systemic corticosteroids, there were no significant adverse effects related to other interventions.

CONCLUSIONS: Limited low-quality evidence exists on the effects of various interventions in children with EoE. The beneficial effects of swallowed steroid need to be confirmed in large well-designed RCTs.

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Effect of omega-3 fatty acid supplementation on arterial elasticity in patients with familial hypercholesterolaemia on statin therapy.
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BACKGROUND AND AIMS: Increased arterial stiffness is closely linked with raised blood pressure that contributes substantially to enhanced risk of coronary heart disease in high risk individuals with familial hypercholesterolaemia (FH). Omega-3 fatty acid (omega3-FA) supplementation has been demonstrated to lower blood pressure in subjects with a high cardiovascular disease risk. Whether omega3-FA supplementation improves arterial stiffness in FH subjects, on background statin therapy, has yet to be investigated.

METHOD AND RESULTS: We carried out an 8-week randomized, crossover intervention trial to test the effect of 4 g/d omega3-FA supplementation (46% eicosapentaenoic acid and 38% docosahexaenoic acid) on arterial elasticity in 20 adults with FH on optimal cholesterol-lowering therapy. Large and small artery elasticity were measured by pulse contour analysis of the radial artery. omega3-FA supplementation significantly (P < 0.05 in all) increased large artery elasticity (+9%) and reduced systolic blood pressure (-6%) and diastolic blood pressure (-6%), plasma triglycerides (-20%), apoB concentration (-8%). In contrast, omega3-FAs had no significant effect on small artery elasticity. The change in large artery elasticity was not significantly associated with changes in systolic blood pressure or plasma triglyceride concentration.

CONCLUSIONS: omega3-FA supplementation improves large arterial elasticity and arterial blood pressure independent of statin therapy in adults with FH.


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Suicide in older men: The health in men cohort study (HIMS).
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Suicide rates are high in later life, particularly among older men. Mood disorders are known risk factors, but the risk of suicide associated with poor physical health remains unclear. We completed a cohort study of a community representative sample of 38,170 men aged 65-85 in 1996 who were followed for up to 16 years. Data on suicide attempts and completion were obtained from the Western Australia Data Linkage System, as was information about medical and mental health diagnoses. 240 (0.6%) participants had a recorded history of past suicide attempt, most commonly by poisoning (85%). Sixty-nine men died by suicide during follow up (0.3% of all deaths), most often by hanging (50.7%). Age-adjusted competing risk regression showed that past suicide attempt was not a robust predictor of future suicide completion (sub-hazard ratio, SHR=1.58, 95% CI=0.39, 6.42), but bipolar (SHR=7.82, 95% CI=3.08, 19.90), depressive disorders (SHR=2.26, 95% CI=1.14, 4.51) and the number of health systems affected by disease (SHR for 3-4 health systems=6.02, 95% CI=2.69, 13.47; SHR for >5 health systems=11.18, 95% CI=4.89, 25.53) were. The population fraction of suicides attributable to having 5 or more health systems affected by disease was 79% (95% CI=57%, 90%), and for any mood disorder (bipolar or depression) it was 17% (95% CI=3%, 28%). Older Australian men with multiple health morbidities have the highest risk of death by suicide, even after taking into account the presence of mood disorders. Improving the overall health of the population may be the most effective way of decreasing the rates of suicide in later life.

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Interactive patient blood management dashboards used in Western Australia.
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Interactive patient blood management dashboards used in Western Australia.
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The Association Between Broad Antigen HLA Mismatches, Eplet HLA Mismatches and Acute Rejection After Kidney Transplantation.

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BACKGROUND: Epitope matching, which evaluates mismatched amino acids within antigen-antibody interaction sites (eplets), may better predict acute rejection than broad antigen matching alone. We aimed to determine the association between eplet mismatches and acute rejection in kidney transplant recipients.

METHODS: The association between eplet mismatches, broad antigen mismatches and acute rejection was assessed using adjusted Cox proportional hazard regression. Model discrimination for acute rejection was evaluated using the area under receiver operating characteristic curves.

RESULTS: Of the 3,499 kidney transplant recipients from 2006 to 2011, the average (SD) number of broad antigen and eplet mismatches were 3.4 (1.7) and 22.8 (12.2), respectively. Compared with 0 to 2 eplet mismatches, the adjusted hazard ratio (HR) for acute rejection among those with 20 or greater eplet mismatches was 2.16 (95% confidence interval [CI], 1.33-3.52; P = 0.001). The adjusted area under the curve for broad antigen mismatches was 0.58 (95% CI, 0.56-0.61), similar to that for eplet mismatches (HR, 0.59; 95% CI, 0.56-0.61; P = 0.365). In recipients who were considered as low immunological risk (0-2 broad antigen HLA-ABDR mismatch), those with 20 or greater eplet mismatches experienced an increased risk of rejection compared to those with less than 20 mismatches (adjusted HR, 1.85; 95% CI, 1.11-3.08; P = 0.019).

CONCLUSIONS: Increasing number of eplet mismatches is associated with acute rejection in kidney transplant recipients. Consideration of eplet HLA mismatches may improve risk stratification for acute rejection in a selected group of kidney transplant candidates.

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Gastrointestinal ultrasound (GIUS) is an ultrasound application that has been practiced for more than 30 years. Recently, GIUS has enjoyed a resurgence of interest, and there is now strong evidence of its utility and accuracy as a diagnostic tool for multiple indications. The method of learning GIUS is not standardised and may incorporate mentorship, didactic teaching and e-learning. Simulation, using either low- or high-fidelity models, can also play a key role in practicing and honing novice GIUS skills. A course for training as well as establishing and evaluating competency in GIUS is proposed in the manuscript, based on established learning theory practice. We describe the broad utility of GIUS in clinical medicine, including a review of the literature and existing meta-analyses. Further, the manuscript calls for agreement on international standards regarding education, training and indications.

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**In vivo label-free lymphangiography of cutaneous lymphatic vessels in human burn scars using optical coherence tomography.**

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in vivo using optical coherence tomography (OCT). This method corrects for the variation in OCT signal due to the
confocal function and sensitivity fall-off of a spectral-domain OCT system and utilizes a single-scattering model to compensate for A-scan signal attenuation to enable reliable thresholding of lymphatic vessels. A segment-joining algorithm is then incorporated into the method to mitigate partial-volume effects with small vessels. The lymphatic vessel images are augmented with images of the blood vessel network, acquired from the speckle decorrelation with additional weighting to differentiate blood vessels from the observed high decorrelation in lymphatic vessels. We demonstrate the method with longitudinal scans of human burn scar patients undergoing ablative fractional laser treatment, showing the visualization of the cutaneous lymphatic and blood vessel networks.

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Long-term Outcomes of the Western Australian Trial of Screening for Abdominal Aortic Aneurysms: Secondary Analysis of a Randomized Clinical Trial.

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Importance: Mortality from ruptured abdominal aortic aneurysms (AAAs) remains high. The benefit of screening older men for AAAs needs to be assessed in a range of health care settings.

Objective: To assess the influence of screening for AAAs in men aged 64 to 83 years on mortality from AAAs.

Design, Setting, and Participants: This randomized clinical trial performed from April 1, 1996, through March 31, 1999, with a mean of 12.8 years of follow-up (range, 11.6-14.2 years) included a population-based sample from a single metropolitan region in Western Australia identified via the electoral roll. Data analysis was performed from June 1, 2015, to June 1, 2016.

Interventions: Randomization to an invitation to undergo ultrasonography of the abdominal aorta or a control group without invitation.

Main Outcomes and Measures: Surgery for and mortality from AAA.

Results: A total of 49801 men aged 64 to 83 years were identified for the study. Men living too far from screening centers (n=8671) or who died before invitation (n=2650) were excluded, resulting in 19249 men in the invited group and 19231 controls (mean [SD] age, 72.5 [4.6] years; 95% white). Of 19249 men invited for screening, 12203 (63.4%) attended. There were more elective operations (536 vs 414, P<.001) and fewer ruptured AAAs (72 vs 99, P=.04) in the invited group compared with the control group. Overall, there were 90 deaths from AAAs in the invited group (mortality rate, 47.86 per 100000 person-years; 95% CI, 38.93-58.84) and 98 in the control group (52.53 per 100000 person-years; 95% CI, 43.09-64.03) for a rate ratio of 0.91 (95% CI, 0.68-1.21). For men aged 65 to 74 years, the AAA mortality rate in the invited group was 34.52 per 100000 person-years (95% CI, 26.02-45.81) compared with 37.67 per 100000 person-years (95% CI, 28.71-49.44) in the control group for a rate ratio of 0.92 (95% CI, 0.62-1.36). The number needed to invite for screening to prevent 1 death from an AAA in 5 years was 4784 for men aged 64 to 83 years and 3290 for men aged 65 to 74 years. There were no meaningful differences in all-cause, cardiovascular, and other mortality risks.

Conclusions and Relevance: Use of the electoral roll to identify and invite men aged 64 to 83 years for screening for AAAs had no significant effect on the overall mortality from AAAs.

Trial Registration: isrctn.org Identifier: ISRCTN16171472.
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DOI:https://dx.doi.org/10.1001/jamainternmed.2016.6633
INTRODUCTION: Systemic sclerosis (SSc) is a severe and costly multiorgan autoimmune connective tissue disease characterised by vasculopathy and fibrosis. One of the major causes of SSc-related death is pulmonary arterial hypertension (PAH), which develops in 12-15% of patients with SSc and accounts for 30-40% of deaths. In situ thrombosis in the small calibre peripheral pulmonary vessels resulting from endothelial dysfunction and an imbalance of anticoagulant and prothrombotic mediators has been implicated in the complex pathophysiology of SSc-related PAH (SSc-PAH), with international clinical guidelines recommending the use of anticoagulants for some types of PAH, such as idiopathic PAH. However, anticoagulation has not become part of standard clinical care for patients with SSc-PAH as only observational evidence exists to support its use. Therefore, we present the rationale and methodology of a phase III randomised controlled trial (RCT) to evaluate the efficacy, safety and cost-effectiveness of
anticoagulation in SSc-PAH.

METHODS AND ANALYSIS: This Australian multicentre RCT will compare 2.5 mg apixaban with placebo, in parallel treatment groups randomised in a 1:1 ratio, both administered twice daily for 3 years as adjunct therapy to stable oral PAH therapy. The composite primary outcome measure will be the time to death or clinical worsening of PAH. Secondary outcomes will include functional capacity, health-related quality of life measures and adverse events. A cost-effectiveness analysis of anticoagulation versus placebo will also be undertaken.

ETHICS AND DISSEMINATION: Ethical approval for this RCT has been granted by the Human Research Ethics Committees of all participating centres. An independent data safety monitoring board will review safety and tolerability data for the duration of the trial. The findings of this RCT are to be published in open access journals.

TRIAL REGISTRATION NUMBER: ACTRN12614000418673, Pre-results.

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Meconium evacuation for facilitating feed tolerance in preterm neonates—a systematic review.

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Background: Delayed passage of meconium is considered as a risk factor for feed intolerance in preterm neonates. We aimed to review effects of different therapeutic agents for meconium evacuation on feed tolerance in preterm neonates.

Method: A systematic review of randomised controlled trials (RCT) of different therapeutic agents for meconium evacuation in preterm neonates (gestation <32 weeks and/or birth weight <1500 g) using the Cochrane systematic review methodology. Databases including Google scholar were searched in December 2014. Primary outcome was the time to reach full feeds (TFF: >120mL/kg feeds with stoppage of parenteral nutrition >24 h).

Secondary outcomes included necrotising enterocolitis (NEC), weight at discharge and adverse effects. Results were summarised as per GRADE guidelines. Results: A total of 6 RCT (glycerine suppository or enema: 2 each, normal saline enema: 1, oral osmotic contrast agent (OCA): 1, N= 442) were included. These trials had low or unclear risk of bias. The pooled estimate (Random effects model) showed no reduction in TFF (MD: -0.03 (95% CI -2.47, 2.41, P = 0.98). No differences in NEC (RR: 1.71 (95%CI 0.63, 4.65: P = 0.30) and weight at discharge (MD: -0.08 (95% CI -0.30, 0.15, P = 0.50) were found. The trial assessing oral OCA reported a trend towards higher incidence of NEC > Stage II. There were no other adverse effects. Conclusions: Limited low quality evidence indicates that prophylactic glycerine suppository, small volume glycerine/normal saline enema or oral OCA to evacuate meconium did not reduce TFF in preterm neonates. Large well designed trials are essential to study this clinically significant issue.

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Neonatal informatics: Use of electronic medical record in neonatal unit.

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Background and Aim: The quantity of clinical data in Electronic Medical Record (EMR) presents challenges and opportunities to the design of informatics tools that display information to providers. Increasing number of neonatal units is using EMR in Australia. This study was undertaken in a new neonatal unit to evaluate the experience of staff using EMR. Research Method: This study was conducted in a newly opened metropolitan hospital in WA. We used a self-administered quality initiative online questionnaire distributed to staff after 12 months of opening the neonatal
A cross-sectional quantitative analysis was done on the data collected and a qualitative analysis of the free text response. Results: 57 out of 81 staff responded (response rate 71%). One third of respondents were doctors. 89% (72/81) of respondents had not used EMR before. Overall, 22% was highly satisfied, and 75% was satisfied with the use of EMR. EMR was rated 3 out of 5 and 4 out of 5 for ease of entering information and ease of finding patient information, respectively, by more than half respondents. Inability to save entered information and disconnect with other electronic databases was identified to be major areas of concern. Conclusions: EMR has proven highly successful in our neonatal unit. Ongoing background information and technological support is required to refine available patient information datasets, and electronic integration between various databases is paramount to ensure better service and information delivery.

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Randomized double-blind placebo-controlled trial of probiotics in pregnancy (PIP) and its effect on group-B streptococcal colonization-study protocol.
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Background and Aim: Group-B Streptococcal (GBS) colonization in pregnancy is a major public health problem worldwide with up to a quarter of all pregnant women in Australia having GBS colonization. Probiotics have the potential to influence gut and vaginal microbiome during pregnancy. Aim of the study is to determine whether selective probiotic strains given orally to pregnant women reduce the number of women with GBS recto-vaginal colonization at 35-37 weeks, thereby decreasing need for maternal antibiotic administration at time of labour.

Methods and analysis: Study design is a single centre, two arms, double blinded randomized controlled trial. Women will be randomized to receive either probiotics or placebo starting at 24 weeks for 12 weeks. The sample size of 460 (230 per group) will detect a 50% difference in proportion of GBS positive swabs (80% power, alpha 0.05). Data analysis: the active group will be compared with the placebo group by intention to treat analysis, and the primary outcome compared using chi<sup>2</sup> and ORs. Research ethics approval will be obtained from relevant site. Results will be published in peer-reviewed journals and presented to clinicians, policymakers and study participants.

Conclusion: Intrapartum antibiotics have reduced neonatal GBS infection, but there are no scientifically proven strategies to prevent GBS colonization. Such an option, if scientifically tested and proven, will revolutionize the care of women in their pregnancy and for their babies in the neonatal period. PIP trial (funded by Telethon) is being undertaken to study the role of probiotics in reducing GBS colonization.

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Delayed commencement of enteral feeds in gastroschisis results in delay in achieving full enteral feeds: A systematic review and meta regression.
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Background: Gastroschisis is associated with feed intolerance. Some reports have suggested that early commencement of enteral feeds (CEF) may improve feed tolerance. Objectives: To evaluate the association between time of commencement of enteral feeds (CEF) and a. time to reach full enteral feeds (FEF), b. duration of parenteral nutrition (PN) and c. duration of hospital stay (HS). Methods/Design: A systematic review of the literature was
conducted by searching the databases PubMed (1966-2015), EMBASE (1980-2015), Cochrane CENTRAL (May 2015) and Eabstracts of Pediatric academy Societies Conference (2000-2015). Studies that reported on time to CEF feeds and one or more of the following outcomes were included: time to FEF, duration of PN, duration of HS. Values that were given as median and range were converted into mean and 95% confidence intervals (CI) using the formula of Wan et al (Ref: BMC Medical Research Methodology, 14:135, doi:10.1186/1471-2288-14-135). Meta-Regression was conducted to find the association between time to CEF and the outcomes of interest. Results: A total of 41 observational studies (4938 infants with gastroschisis) were included. The results of meta-regression indicate that each day delay in CEF results in a delay of an additional 1.4 days to FEF, 1.8 days to the duration of PN and 1.7 days to duration of HS (Table 1). Conclusions: Delayed commencement of enteral feeds is associated with delayed attainment of full feeds, and prolongation of hospital stay in neonates with gastroschisis. Hence, commencement of enteral feeds as early as feasible needs to be encouraged. (Table Presented).

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Nurses' perception on contextual factors influencing quality care in a neonatal unit.
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Background and Aim: Delivery of safe and effective evidence based quality care to patients is paramount to any health organization. Contextual factors and organizational culture play an important role for continuous quality improvement (CQI) and patient outcomes. The objective of this study was to examine contextual factors that predict the necessary approach in developing a training environment that ensure safe bedside neonatal nursing care.

Research Method: This study was conducted in a newly opened metropolitan hospital in WA. We used a self-administered quality initiative online questionnaire distributed to staff after four months of opening the neonatal unit. A cross sectional quantitative analysis was done on the data collected and a qualitative analysis of the free text response. Results: 71% response rate was achieved. The three most significant contextual factors highlighted from staff were: 'connectedness' of staff to the organisation, which was measured in terms of staff satisfaction to team work and cohesiveness and educational support in the unit; ‘Policies’ that could be adapted to the unique needs of the neonatal unit in an adult tertiary hospital was identified as another major contextual factor; ‘Resources’ in the form of experienced workforce to support up skilling of the team to look after higher acuity patients. 92% (25/27) of nurses felt supported from the current information and education provided in the unit. Conclusions: The results of the study have provided an understanding of contextual factors to support organizations in creating an environment that facilitate effective training and adaptation of neonatal nursing staff.

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Learning needs analysis and nursing education: Perspective from a Newneonatal unit.
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Background and Aim: A needs analysis of employees, preparedness for their required tasks, and identification of knowledge and skill gaps provides an important framework for the strategic provision of suitable educational interventions. Fiona Stanley Hospital is a newly opened major hospital in WA where neonatal nursing staffs have joined the unit from across the globe. Aim of this study was to ascertain the perceptions of nursing staff on their educational needs. Research Method: A cross-sectional survey was performed by sending electronic questionnaire to all the nursing staff after 6months of their joining the unit. Quantitative and qualitative analysis was performed for the
complied responses. Results: Response rate was 71%(26 out of 33). 'Nominal group technique with inclusion' of the staff from varying background and skill levels and 'Individualized learning needs analysis' (ILNA) stood out to be two major themes in the staff perspectives. 20 out of 27 staff (74%) identified to have been benefitted from 'mass intensive orientation' programme led by the unit educators. Targeted training interventions for up-skilling and theoretical evidence based in-service from senior medical staff were recognized as key helpful steps. Conclusions: The educational needs of nurses working in a neonatal unit of newly opened major metropolitan hospital were attained by ILNA within an Adult Learning Theory framework. The method effectively identified their specific learning needs in this context, demonstrating the utility of ‘inclusive learning’ as a part of an educational needs analysis.

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**Birth dose hepatitis b vaccination administration rates in a tertiary Australian hospital.**

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Background: Despite being a vaccine preventable disease, Hepatitis B still contributes to a high public health burden in Australia. Australia’s main preventative strategy against newly acquired Hepatitis B is the infant vaccination schedule, which includes administration of birth dose Hepatitis B vaccine. This audit assessed compliance with administration of birth dose Hepatitis B vaccine prior to discharge from the postnatal ward at Fiona Stanley Hospital.

Method: This retrospective audit was conducted in a tertiary hospital. All neonates discharged from the postnatal ward over a 2-week period in April/May 2015 were included. Neonates were identified from a database record, and case records were interrogated for consent (or declined consent), as well as administration of Hepatitis B vaccine.

Results: Of 71 eligible patients, 60 (84%) received a Hepatitis B vaccine prior to discharge from hospital. Where consent for vaccination was given, there was 100% compliance in administering Hepatitis B vaccine prior to discharge. Of 11 (16%) neonates not vaccinated, 36% had documented ‘do not consent’ for vaccination. Conclusions: While compliance with administration in patients who have consented for vaccination was reassuring, these results suggest there may be a gap in the communication to parents regarding the rationale for Hepatitis B vaccination or in discussing consent for vaccination. Following this study, we are implementing improvements in patient education and informed consent for Hepatitis B vaccination, prior to repeating the audit. This will inform future processes, which may then be applied across Australia, particularly given this is an area lacking national data.

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**Sex differences in vascular endothelial function and health in humans: impacts of exercise.**

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NEW FINDINGS: What is the topic of this review? This brief review discusses potential sex differences in arterial function across the age span, with special emphasis on the effects of oestrogen and testosterone on the vascular endothelium. What advances does it highlight? We discuss the relationship between the impacts of sex hormones on arterial function and health in the context of epidemiological evidence pertaining to the menopause and ageing. Studies performed in humans are emphasized, alongside insights from animal studies. Findings suggest that the combination of exercise and hormone administration should be potentially synergistic or additive in humans. This brief review presents historical evidence for the purported impacts of male and female sex hormones on the vasculature in humans, including effects on macro- and microvascular function and health. Impacts of ageing on hormonal changes and arterial function are considered in the context of the menopause. Physiological data are presented alongside clinical outcomes from large trials, in an attempt to rationalize disparate findings along the bench-to-bedside continuum. Finally, the theoretical likelihood that exercise and hormone treatment may induce synergistic and/or additive vascular adaptations is developed in the context of recent laboratory studies that have compared male and female responses to training. Differences between men and women in terms of the impact of age and cardiorespiratory fitness on endothelial function are addressed. Ultimately, this review highlights the paucity of high-quality and compelling evidence regarding the fundamental impact, in humans, of sex differences on arterial function and the moderating impacts of exercise on arterial function, adaptation and health at different ages in either sex.

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Characteristics and Clinical Course of STEMI Patients who Received no Reperfusion in the Australia and New Zealand SNAPSHOT ACS Registry.
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BACKGROUND: Cohort studies of STEMI patients have reported that over 30% receive no reperfusion. Barriers to greater use of reperfusion in STEMI patients require further elucidation.

METHODS: We collected data on STEMI patients with no reperfusion as part of the SNAPSHOT ACS Registry, which recruited consecutive ACS patients in 478 hospitals throughout Australia and New Zealand during 14-27 May 2012.

RESULTS: Of 4387 patients enrolled, 419 were diagnosed with STEMI. Primary PCI (PPCI) was performed in 160 (38.2%), fibrinolysis was used in 105 (25.1%), and 154 (36.7%) had no reperfusion. Patients with no reperfusion had a mean age of 70.3±15.0 years compared with 63.1±13.5 in the reperfusion group (p<0.0001). There were more females in the no reperfusion group (37.1% vs 23.0% p=0.002) and they were significantly more likely to have prior PCI or CABG, heart failure, atrial fibrillation, chronic kidney disease and other vascular disease, and to be nursing home residents (all p<0.05). Patients without reperfusion had a significantly higher mortality in hospital (11.7% vs 4.9%, p=0.011). In 370 patients who presented within 12 hours, 28 had early angiography without PCI, which was considered an attempt at reperfusion. Therefore reperfusion was attempted in 293 of 370 eligible patients (79.2%).

CONCLUSION: Of consecutive STEMI patients, 36.7% did not receive any reperfusion and they had a higher risk of death in hospital. In eligible patients, reperfusion was attempted in 79.2%. National strategies to encourage earlier
medical contact and greater use of reperfusion in eligible patients may lead to better outcomes.

FibroGENE: A gene-based model for staging liver fibrosis.
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BACKGROUND & AIMS: The extent of liver fibrosis predicts long-term outcomes, and hence impacts management and therapy. We developed a non-invasive algorithm to stage fibrosis using non-parametric, machine learning methods designed for predictive modeling, and incorporated an invariant genetic marker of liver fibrosis risk.

METHODS: Of 4277 patients with chronic liver disease, 1992 with chronic hepatitis C (derivation cohort) were analyzed to develop the model, and subsequently validated in an independent cohort of 1242 patients. The model was assessed in cohorts with chronic hepatitis B (CHB) (n=555) and non-alcoholic fatty liver disease (NAFLD) (n=488). Model performance was compared to FIB-4 and APRI, and also to the NAFLD fibrosis score (NFS) and Forns' index, in those with NAFLD.

RESULTS: Significant fibrosis (F2) was similar in the derivation (48.4%) and validation (47.4%) cohorts. The FibroGENE-DT yielded the area under the receiver operating characteristic curve (AUROCs) of 0.87, 0.85 and 0.804 for the prediction of fast fibrosis progression, cirrhosis and significant fibrosis risk, respectively, with comparable results in the validation cohort. The model performed well in NAFLD and CHB with AUROCs of 0.791, and 0.726, respectively. The negative predictive value to exclude cirrhosis was >0.96 in all three liver diseases. The AUROC of the FibroGENE-DT performed better than FIB-4, APRI, and also to the NAFLD fibrosis score (NFS) and Forns’ index in most comparisons.

CONCLUSION: A non-invasive decision tree model can predict liver fibrosis risk and aid decision making.

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**Novel CT and scintigraphic findings of bone metastasis from invasive lobular breast cancer.**

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INTRODUCTION: The aim of this study is to identify and describe the computed tomography and scintigraphic imaging patterns of osseous metastasis from invasive lobular breast cancer (ILC).

MATERIALS AND METHODS: CT and skeletal scintigraphy (SS) studies of 23 patients with diagnosis of ILC and osseous metastasis on their initial presentation were reviewed.

RESULTS: Osseous metastases in 14 patients (60.8%) appear as uniform small sclerotic lesions (USSL) on CT scan. The SS in these patients were interpreted as negative for metastasis (either normal or with some equivocal findings not typical for metastasis).

CONCLUSION: Osseous metastasis from ILC can have a characteristic imaging pattern on CT and SS. The pattern of USSL on CT scan with negative SS is highly suggestive of osseous metastasis from ILC.

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**Using the Implant Electrode Array to Conduct Real-time Intraoperative Hearing Monitoring During Pediatric Cochlear Implantation: Preliminary Experiences.**

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**OBJECTIVES:** To present the preliminary experiences and findings from a pilot study evaluating a novel technique for monitoring cochlear electrophysiological function during electrode insertion in cochlear implantation surgery.

**STUDY DESIGN:** Prospective pilot cohort study.

**SETTING:** Tertiary academic neuro-otology center.

**PATIENTS:** Pediatric patients with residual hearing undergoing hearing preservation cochlear implant surgery.

**INTERVENTION:** Monitoring of intraoperative cochlear microphonics during cochlear implant surgery.

**MAIN OUTCOME MEASURE:** Intraoperative intracochlear microphonic measurement, preservation of these responses postoperatively and preservation of hearing as measured by audiometry.

**RESULTS:** Intracochlear microphonics could be identified in both patients presented and were preserved during the surgical procedure and postoperatively. The preservation of intracochlear microphonics correlates with preservation of hearing.

**CONCLUSION:** The novel approach using the electrode array to detect and measure intracochlear microphonics during cochlear implantation surgery shows promise as an instrument to alert the operating surgeon to hair cell damage during electrode insertion. Further refinement of the technique is required to better understand the measurements and correlate these with pre- and postoperative hearing and risk of hearing loss from surgery. Improvements in the software algorithm will reduce the time required for each measurement, leading to the development a more real-time monitoring technique.

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DOI:https://dx.doi.org/10.1097/MAO.0000000000000950


**The prognostic impact of CD7 expression of leukaemic blasts in de novo intermediate cytogenetic risk acute myeloid leukaemia.**

Kesavan M, Chuah H, et al.

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PMID:27773218
DOI:https://dx.doi.org/10.1016/j.pathol.2015.12.282

Pathology. 2016; 48 Suppl 1: S68.

**A case of end stage sarcoidosis in an explanted heart.**

Foo T, Dias P, et al.

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Dias, Peter. Department of Cardiology, Fiona Stanley Hospital, WA, Australia.

Sinniah, Raja. Department of Pathology, Fiona Stanley Hospital, WA, Australia.

PMID:27773098
Case series: Two cases of primary retroperitoneal mucinous cystadenoma.

Foo T, Laycock A, et al.

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PMID:27773097
DOI:https://dx.doi.org/10.1016/j.pathol.2015.12.174

A case of acquired high molecular weight kininogen deficiency.

Kesavan M, Chuah H, et al.

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Dixon, Tracy. PathWest Coagulation Laboratory, Fiona Stanley Hospital, Perth, WA, Australia.

PMID:27773017
DOI:https://dx.doi.org/10.1016/j.pathol.2015.12.086

A review and comparison of two commercial molecular methods for detection of respiratory viruses in a new tertiary hospital in Perth.

Chu E, Gibbs T, et al.

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PMID:27772816
DOI:https://dx.doi.org/10.1016/j.pathol.2015.12.299

Prospective longitudinal study of testosterone and incident depression in older men: The Health In Men Study.

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BACKGROUND: Depression in older men has been associated with low circulating testosterone concentration but data from prospective studies are limited.

METHODS: We conducted a prospective longitudinal study in a community representative cohort of 3179 older men free of clinically significant depressive symptoms at baseline. The main objective of this study was to determine if low serum testosterone, dihydrotestosterone and estradiol concentrations are associated with the development of depressive symptoms. Incident depression was assessed with the Patient Health Questionnaire and via an electronic health record database (The West Australian Data Linkage System). The main exposures of interest were serum testosterone, dihydrotestosterone and estradiol measured by liquid chromatography-mass spectrometry and calculated free testosterone in baseline blood samples (collected between 2001 and 2004).

RESULTS: One hundred and thirty five men (4.2%) developed depression over a median follow up time of 9.4 years (range 8.4-10.9). Men with incident depression were older (median age 77.7 vs 76.1 years, z=-3.82, p<0.001) and were more likely to have cardiovascular disease (43.0% vs 32.6%, chi(2)=6.32, p=0.012) and diabetes (22.2% vs 13.2%, chi(2)=8.95, p=0.003). Low serum total testosterone (<6.4 nmol/L) was associated with incident depression (HR 2.07, 95%CI 1.17-3.68) and this remained significant after adjustment for relevant potential confounding factors (HR 1.86, 95%CI 1.05-3.31). Low serum dihydrotestosterone, estradiol and calculated free testosterone were not associated with risk of depression.

CONCLUSIONS: Low serum total testosterone, but not calculated free testosterone, was associated with incident depression in this sample of older men.

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The role of liver progenitor cells during liver regeneration, fibrogenesis, and carcinogenesis.

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The growing worldwide challenge of cirrhosis and hepatocellular carcinoma due to increasing prevalence of excessive alcohol consumption, viral hepatitis, obesity, and the metabolic syndrome has sparked interest in stem cell-like liver progenitor cells (LPCs) as potential candidates for cell therapy and tissue engineering, as an alternative approach to whole organ transplantation. However, LPCs always proliferate in chronic liver diseases with a predisposition to...
cancer; they have been suggested to play major roles in driving fibrosis, disease progression, and may even represent tumor-initiating cells. Hence, a greater understanding of the factors that govern their activation, communication with other hepatic cell types, and bipotential differentiation as opposed to their potential transformation is needed before their therapeutic potential can be harnessed.

Evaluating the interstitial lung disease multidisciplinary meeting: a survey of expert centres.

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BACKGROUND: Multidisciplinary meetings (MDM) are the current “gold standard” in interstitial lung disease (ILD) diagnosis and comprise inter-disciplinary discussion of multiple forms of information to provide diagnostic and management outputs. Although bias could be potentially inserted at any step in the discussion process, to date there has been no consensus regarding the appropriate constitution and governance of MDM. We sought to determine the features of ILD MDMs based within ILD centres of excellence around the world.

METHODS: An internet based questionnaire was sent to twelve expert centres in Europe, North America, and Australia seeking information regarding the structure and governance of their MDM. Data was analysed for consistent themes and points of contrast.

RESULTS: Responses were received from 10 out of 12 centres. Similarities were demonstrated with regards to contributing attendees, meeting frequency and case numbers reviewed. Significant heterogeneity in attendee specialty group type, quantity and method of data presentation, approach to diagnosis formulation and documentation, and information provision was apparent.

CONCLUSIONS: The constitution of ILD MDMs differs considerably between expert centres. Such differences may result in discordant outcomes, and emphasise the need for further evidence regarding the appropriate constitution and governance of ILD MDMs.

Screening for the metabolic syndrome in Australia: A national survey of psychiatrists' attitudes and reported practice in patients prescribed antipsychotic drugs.


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Objective: To investigate current reported psychiatric practice in relation to screening for the metabolic syndrome in patients prescribed antipsychotic drugs within Australia. Method: A postal survey of all Fellows of the Royal Australian and New Zealand College of Psychiatrists. A 28-item questionnaire inquired into different aspects of screening and monitoring for metabolic syndrome in patients on antipsychotic medication. Results: Of 3123 questionnaires sent, 955 were returned. Of respondents, 55% had no established metabolic monitoring protocol or guidelines in their workplace, with 13% saying they did not know what to monitor to detect metabolic syndrome. Altogether, 76% reported there was no reliable system in place to remind them when to monitor. Fewer than 50% of respondents routinely check weight, fasting glucose or lipids in their patients on antipsychotics and under than 30% checked blood pressure. Waist circumference was routinely checked in fewer than 7% of patients. Basic monitoring equipment was reported unavailable in more than 50% of clinical settings. However, more than 80% of respondents considered monitoring for metabolic syndrome to be their responsibility and 83% felt they had a medicolegal obligation in this respect. Conclusions: Routine screening for metabolic syndrome in patients on antipsychotic agents, by Australian psychiatrists, is inadequate. Interventions to improve screening rates need to be developed, implemented and evaluated. Copyright © The Royal Australian and New Zealand College of Psychiatrists 2015. PubMed:609233577
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http://apy.sagepub.com/content/by/year


Cardiac (123)I-meta-iodo-benzyl-guanine in a patient with bipolar affective disorder, musical hallucinations and Parkinsonism.

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Conjoint Urological Society of Australia and New Zealand (USANZ) and Urogynaecological Society of Australasia (UGSA) Guidelines on the management of adult non-neurogenic overactive bladder.

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Due to the myriad of treatment options available and the potential increase in the number of patients afflicted with overactive bladder (OAB) who will require treatment, the Female Urology Special Advisory Group (FUSAG) of the...
Urological Society of Australia and New Zealand (USANZ), in conjunction with the Urogynaecological Society of Australasia (UGSA), see the need to move forward and set up management guidelines for physicians who may encounter or have a special interest in the treatment of this condition. These guidelines, by utilising and recommending evidence-based data, will hopefully assist in the diagnosis, clinical assessment, and optimisation of treatment efficacy. They are divided into three sections: Diagnosis and Clinical Assessment, Conservative Management, and Surgical Management. These guidelines will also bring Australia and New Zealand in line with other regions of the world where guidelines have been established, such as the American Urological Association, European Association of Urology, International Consultation on Incontinence, and the National Institute for Health and Care Excellence guidelines of the UK.

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**Soleus Muscle as a Surrogate for Health Status in Human Heart Failure.**
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We propose the hypothesis that soleus muscle function may provide a surrogate measure of functional capacity in patients with heart failure. We summarize literature pertaining to skeletal muscle as a locus of fatigue and present our recent findings, using in vivo imaging in combination with biomechanical experimentation and modeling, to reveal novel structure-function relationships in chronic heart failure skeletal muscle and gait.
PMID:26509482
DOI:https://dx.doi.org/10.1249/JES.0000000000000069

**Diagnosis and management of thrombotic thrombocytopenic purpura (TTP) in Australia: findings from the first 5 years of the Australian TTP/thrombotic microangiopathy registry.**
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BACKGROUND: Thrombotic thrombocytopenic purpura (TTP) is a rare, life-threatening thrombotic microangiopathy (TMA). In 2009, the Australian TTP/TMA registry was established to collect data on patients presenting with TTP/TMA throughout Australia.

AIM: To summarise information on the diagnosis and management of patients with TTP collected in the first 5 years (2009-2014) of the Australian TTP registry.

METHODS: Registry data from June 2009 to October 2014 were reviewed.

RESULTS: Fifty-seven patients were identified with TTP (defined as ADAMTS13 activity <10%), accounting for 72 clinical episodes. ADAMTS13 inhibitor testing was performed in nine out of 57 patients (16%), reflecting the limited availability of accredited testing facilities. Sixty-seven out of 72 episodes were treated with therapeutic plasma exchange (PEx) using cryodepleted plasma (40% of episodes), fresh frozen plasma (36%) or a mixture (22%). Median exposure to plasma products was 55.9L. PEx was commenced >2 days from stated diagnosis in 15% of episodes. Adverse reactions to PEx were common with documented allergic reactions (including life threatening) in 21% of episodes. Adjunctive immunosuppression was documented in 76% of episodes (corticosteroid 71% and rituximab 39%). Platelet transfusion was administered in 15% of episodes.

CONCLUSIONS: Data from the Australian TTP/TMA registry suggest a heterogenous approach to the diagnosis and management of TTP in Australia over the assessed period. These observations highlight areas for improvement and standardisation of practice, including comprehensive diagnostic testing, more immediate access to PEx and a more uniform approach to adjunctive immunosuppression and supportive care.

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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.

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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 (23.7% 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.

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OBJECTIVE: Early childhood psychosocial experiences determine future health and health-care use. Identifying psychosocial predictors in cystic fibrosis may inform intervention strategies that can reduce health-care utilization.

DESIGN: The study was designed as a prospective cohort study.

SETTING: The study was set in the only cystic fibrosis clinic in Western Australia.

PATIENTS: The patients were children up to 6 years diagnosed with cystic fibrosis in Western Australia between 2005 and 2011.

MAIN OUTCOME MEASURES: Psychosocial data collected for each year of life were compared with Australian population data and analysed as predictors of annual hospital, emergency and outpatient visits.

RESULTS: Compared with the Australian population, cystic fibrosis families demonstrated lower socio-economic status and labour supply (P < 0.001), increased residential mobility (P < 0.001) and trends towards increased rates of parental separation (P = 0.066). Marital discord and maternal and child psychological stress significantly predicted increased hospital admissions, emergency and outpatient visits.

CONCLUSIONS: Social gradients may exist for families of young children with cystic fibrosis in Western Australia with potential implications for child health. Family psychological and relationship stress predicted increased child cystic fibrosis-related health-care use.

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Big problem, small incidence, and large registry datasets.
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PMID:26705977
DOI:https://dx.doi.org/10.1016/S2213-2600(15)00519-6
Until recently, the treatment of immune-mediated inflammatory myopathies has largely been empirical with glucocorticoids, steroid-sparing immunosuppressive drugs, and intravenous immunoglobulin. However, a proportion of patients are only partially responsive to these therapies, and there has been a need to consider alternative treatment approaches. In particular, patients with inclusion body myositis are resistant to conventional immunotherapies or show only a transient response, and remain a major challenge. With increasing recognition of the different subtypes of immune-mediated inflammatory myopathies, and improved understanding of their pathogenesis, more targeted treatments are now being trialled. The overall approach to treatment, and novel therapies targeting B cells, T cells, and specific cytokines are discussed in this review.

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DOI:https://dx.doi.org/10.1007/s13311-015-0394-2

The aim of this study was to investigate the hypothesis that chronic widespread pain, (CWP) drawn by patients on a body diagram, could be used as a screening tool for increased pain sensitization, psycho-social load, and utilization of pain management strategies. The triage questionnaires of 144 adults attending a chronic pain outpatients' clinic were audited and the percentage pain surface area (PPSA) drawn on their body diagrams was calculated using the "rule of nines" (RON) method for burns area assessment. Outcomes were measured using the painDETECT Questionnaire (PD-Q) and other indices and compared using a nonrandomized, case-control method. It was found that significantly more subjects with CWP (defined as a PPSA > 20%) reported high (> 19) PD-Q scores (suggesting pain "sensitization" or neuropathic pain) (P = 0.0002), "severe" or "extremely severe" anxiety scores on the Depression, Anxiety and Stress Scale-21 Items Questionnaire (P = 0.0270), > 5 psycho-social stressors (P = 0.0022), > 5 significant life events (P = 0.0098), and used > 7 pain management strategies (PMS) (P < 0.0001), compared to control subjects with a lower PPSA. A Widespread Pain Index score > 7 (OR = 11.36), PD-Q score > 19 (OR = 4.46) and use of > 7 PMS (OR = 5.49) were independently associated with CWP. This study demonstrates that calculating PPSA on a body diagram (using the RON method) is a valid and convenient "snapshot" screening tool to identify patients with an increased likelihood...
of pain sensitization, psycho-social load, and utilizing pain management resources.


Combination of Vancomycin and beta-Lactam Therapy for Methicillin-Resistant Staphylococcus aureus Bacteremia: A Pilot Multicenter Randomized Controlled Trial.

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BACKGROUND: In vitro laboratory and animal studies demonstrate a synergistic role for the combination of vancomycin and antistaphylococcal 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 1.5 g intravenously twice daily and were randomly assigned (1:1) to receive intravenous flucloxacillin 2 g every 6 hours for 7 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, 41%-102%; P = .06) that in the standard therapy group. There was no difference in the secondary end points of 28- and 90-day mortality, metastatic infection, nephrotoxicity, or hepatotoxicity.

CONCLUSIONS: Combining an antistaphylococcal beta-lactam with vancomycin may shorten the duration of MRSA bacteremia. Further trials with a larger sample size and objective clinically relevant end points are warranted.


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Lung cancer screening in Australia: progress or procrastination?
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PMID:26349552

The Healthy Heart-Mind trial: melatonin for prevention of delirium following cardiac surgery: study protocol for a randomized controlled trial.
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BACKGROUND: Delirium is a common occurrence in patients undergoing major cardiac surgery and is associated with a number of adverse consequences for the individual, their family and the health system. Current approaches to the prevention of delirium include identifying those at risk together with various non-pharmacological and pharmacological strategies, although the efficacy of these is often modest. Emerging evidence suggests that melatonin may be biologically implicated in the development of delirium and that melatonin supplementation may be beneficial in reducing the incidence of delirium in medical and surgical patients. We designed this trial to determine whether melatonin reduces the incidence of delirium following cardiac surgery compared with placebo.

METHODS/DESIGN: The Healthy Heart-Mind trial is a randomized, double-blind, placebo-controlled clinical trial of 3 mg melatonin or matching placebo administered on seven consecutive days for the prevention of delirium following cardiac surgery. We will recruit 210 adult participants, aged 50 and older, undergoing elective or semi-elective cardiac surgery with the primary outcome of interest for this study being the difference in the incidence of delirium between the groups within 7 days of surgery. Secondary outcomes of interest include the difference between groups in the severity and duration of delirious episodes, hospital length of stay and referrals to mental health services during admission. In addition, we will assess differences in depressive and anxiety symptoms, as well as cognitive performance, at discharge and 3 months after surgery.

DISCUSSION: The results of this trial will clarify whether melatonin reduces the incidence of delirium following cardiac surgery.
TRIAL REGISTRATION: The trial is registered with the Australian Clinical Trials Registry, trial number ACTRN12615000819527 (10 August 2015).
Lipoprotein lipase deficiency presenting with neonatal perianal abscesses.
Akesson LS, Burnett JR, et al.

Lipoprotein lipase (LPL), a member of the triglyceride lipase gene family, is synthesised by parenchymal cells of the heart, skeletal muscle and adipose tissues before being transported to luminal surfaces of vascular endothelial cells to exert its main physiological function to hydrolyse plasma lipoproteins. LPL deficiency is a rare autosomal recessive disorder, resulting in severe hypertriglyceridaemia from birth. The effect of marked hypertriglyceridaemia on the immune function in children has not been described. We present a case of a neonate with LPL deficiency and grossly elevated plasma triglyceride levels, presenting with recurrent and recalcitrant perianal abscesses suggestive of underlying immunodeficiency. With reduced levels of plasma triglycerides, the recurrent perianal infections resolved. This case report reviews evidence for potential deleterious effects of hypertriglyceridaemia on immune function, however, underlying mechanisms are poorly understood. Whether hypertriglyceridaemia contributes to immune dysfunction in this context is unknown. If there is a pathophysiological link, this may have implications for hypertriglyceridaemia management.

Outcomes of open partial nephrectomies performed by Australian trainees.
Tucker PE, Rukin NJ, et al.

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 31mm. Mean operative time was 157min, with a mean cold ischaemic time of 27min. Mean pre- and post-operative creatinine levels were equivalent (77μmol/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.

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A Toll-like receptor-1 variant and its characteristic cellular phenotype is associated with severe malaria in Papua New Guinean children.

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Genetic factors are likely to contribute to low severe malaria case fatality rates in Melanesian populations, but association studies can be underpowered and may not provide plausible mechanistic explanations if significant associations are detected. In preparation for a genome-wide association study, 29 candidate single-nucleotide polymorphisms (SNPs) with minor allele frequencies >5% were examined in a case-control study of 504 Papua New Guinean children with severe malaria. In parallel, an immunological substudy was performed on convalescent
peripheral blood mononuclear cells (PBMCs) from cases and controls. Following stimulation with a Toll-like receptor (TLR) 1/2 agonist, effector cytokines and chemokines were assayed. The only significant genetic association observed involved a nonsynonymous SNP (TLR1rs4833095) in the TLR1 gene. A recessive (TT) genotype was associated with reduced odds of severe malaria of 0.52 (95% confidence interval (0.29-0.90), P=0.006). Concentrations of pro-inflammatory cytokines interleukin-1beta and tumour necrosis factor alpha were significantly higher in severe malaria cases compared with healthy controls, but lower in children with the protective recessive (TT) genotype. A genetic variant in TLR1 may contribute to the low severe malaria case fatality rates in this region through a reduced pro-inflammatory cellular phenotype.

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Lifetime depression history and depression risk in type 2 diabetes: A case-control study.
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AIMS: To assess whether a personal history of depression assists in risk prediction for depression in type 2 diabetes.
METHODS: Age- and sex-matched participants with and without diabetes from the Busselton Health Survey were assessed for current and previous depression using the 9-item Patient Health Questionnaire and the Brief Lifetime Depression Scale (BLDS). In the diabetic participants, the temporal relationship between first depression episode and diabetes onset was also explored.

RESULTS: In 184 paired participants (age 70.2+/-10.1years, 50% female), those with diabetes had a higher prevalence of any current depression (12.5% vs 4.3%, P<0.01) and lifetime history of major depression (30.6% vs 21.1%, P=0.06) compared to those without diabetes. After adjustment, lifetime major depression history was independently associated with any current depression in the combined sample (odds ratio (95% CI): 5.55 (3.09-9.98), P<0.001), in those with diabetes (4.17 (2.00-8.71), P<0.001), in those without diabetes (8.29 (3.24-21.23), P<0.001) and in diabetes whether sub-divided by depression first occurring before or after diabetes onset (before: 3.16 (1.38-7.24), P=0.007; after: 2.77 (1.00-7.70), P=0.051).

CONCLUSIONS: Obtaining a lifetime history of major depression using the BLDS assists in depression risk prediction in type 2 diabetes regardless of whether depression preceded diabetes onset or not.
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Australian trends in the distribution of intravenous immunoglobulin to chronic lymphocytic leukemia patients with acquired hypogammaglobulinaemia and severe and/or recurrent infections from 2008-2013.
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Aim: To describe the distribution of Intravenous Immunoglobulin (IVIg) within Australia to chronic lymphocytic leukemia (CLL) patients with acquired hypogammaglobulinaemia and severe and/or recurrent infections from 2008-2013. Method: We obtained retrospective data from the Australian Red Cross Blood Service’s IVIg registries (STARS and Legacy Databases) of CLL patients with acquired hypogammaglobulinaemia and severe and/or recurrent infections from 2008-2013. A trend analysis was performed to determine if there were differences in the national distribution of IVIg to these patients according to month, season, year or the geographical location of these CLL patients. Results: A total of 48,870 treatment episodes of IVIg were distributed to 2,734 individual CLL patients with acquired hypogammaglobulinaemia and severe and/or recurrent infections from 2008 to 2013. Male patients received 56% of the total number of IVIg treatment episodes despite a 3:2 male predominance possibly in keeping with longer female survival. The average age for a patient to receive their first dose of IVIg was 74 +/- 11 years. There were 6 different IVIg products available during this period, with the domestically manufactured, Intragram P, accounting for almost 90% of the product distributed. The distribution of IVIg to CLL patients increased 5.5% per annum despite the number of new CLL patients being commenced on IVIg remaining reasonably stable. There did not appear to be recurrent monthly peaks in the distribution of IVIg; however there was consistently more product distributed during spring season. Approximately one third of individual CLL patients lived in NSW (32.8%) whilst a little over a fifth lived in either Victoria (23.1%) or Queensland (21.8%). Not surprisingly, more than 80% of the national IVIg was distributed to the CLL patients who lived in one of these three most populous states. There was a marked increase in the distribution of IVIg to the small proportion of CLL patients who lived in the ACT (41.4%). Furthermore, CLL patients in Queensland, Tasmania and the ACT received more treatment episodes of IVIg per 1,000 capita than the Australian average. This may partially be explained by the demographic characteristics of these regions, but may also reflect the prescribing preferences of treating physicians. Conclusion: The demographic characteristics of Australian CLL patients who receive IVIg for acquired hypogammaglobulinaemia with severe and/or recurrent infections appear to be similar to international cancer registries. The national distribution of IVIg to these patients appears to have a recurrent seasonal peak in spring with a steady annual increase from 2008 to 2013. More than 80% of the IVIg was distributed to CLL patients who lived in NSW, Victoria and Queensland; however, there was a disproportionately high distribution of IVIg to CLL patients who lived in Queensland, Tasmania and the ACT which could not be explained by the demographic characteristics alone, suggesting that the prescribing preferences of treating physicians was substantial.

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Divergent Inflammatory, Fibrogenic, and Liver Progenitor Cell Dynamics in Two Common Mouse Models of Chronic Liver Injury.
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Complications of end-stage chronic liver disease signify a major cause of mortality worldwide. Irrespective of the underlying cause, most chronic liver diseases are characterized by hepatocellular necrosis, inflammation, fibrosis, and proliferation of liver progenitor cells or ductular reactions. Vast differences exist between experimental models that mimic these processes, and their identification is fundamental for translational research. We compared two common murine models of chronic liver disease: the choline-deficient, ethionine-supplemented (CDE) diet versus thioacetamide (TAA) supplementation. Markers of liver injury, including serum alanine transaminase levels, apoptosis, hepatic fat loading, and oxidative stress, as well as inflammatory, fibrogenic and liver progenitor cell responses, were assessed at days 3, 7, 14, 21, and 42. This study revealed remarkable differences between the models. It identified periportal injury and fibrosis with an early peak and slow normalization of all parameters in the CDE regimen, whereas TAA-treated mice had pericentral patterns of progressive injury and fibrosis, resulting in a more severe hepatic injury phenotype. This study is the first to resolve two different patterns of injury and fibrosis in the CDE and TAA model and to indisputably identify the fibrosis pattern in the TAA model as driven from the pericentral vein region. Our data provide a valuable foundation for future work using the CDE and TAA regimens to model a variety of human chronic liver diseases.

Surgical Results and Outcomes After Reimplantation for the Management of Anomalous Aortic Origin of the Right Coronary Artery.

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BACKGROUND: Anomalous aortic origin of the right coronary artery (AAORCA) has been reported to cause myocardial ischemia, leading to angina, dyspnea, and decreased exercise tolerance. Reimplantation is a repair technique devised to exclude the abnormal intramural portion of the anomalous artery and avoid the known late attrition of saphenous vein grafts. Our study aims to evaluate the medium-term clinical outcomes with this technique.

METHODS: A retrospective review was made of patients who underwent repair of AAORCA by reimplantation between 2002 and 2014 in two institutions in Western Australia. Follow-up computed tomography coronary angiography was used to assess the status of the reimplanted right coronary artery (RCA). Data on survival, freedom from symptoms, cardiac events, and cardiac interventions were also analyzed.

RESULTS: Of the 16 patients (aged 17 to 70 years old), 14 (88%) were symptomatic before surgery, with angina (50%) and exertional dyspnea (56%) being the most common symptoms. Surgical reimplantation was successful in 15 patients (94%) without operative mortality. One patient required saphenous vein bypass grafting of the RCA intraoperatively after presumed failed repair and difficulty weaning from cardiopulmonary bypass. All patients who had successful reimplantation of AAORCA were symptom-free after surgery, and none had subsequent cardiac events attributable to the RCA or required further interventions. Ten patients (67%) had computed tomography coronary angiography...
angiography after surgery; none had stenosis, kinking, or compression of the RCA by the pulmonary artery. Two further patients (including the patient who underwent saphenous vein grafting for presumed failed reimplantation) underwent conventional angiography, which demonstrated patent reimplantations.

CONCLUSIONS: To the best of our knowledge, this is the largest reported series of anomalous RCA managed by surgical reimplantation. Our results suggest that this technique is safe and has excellent medium to long-term results regarding symptom-free survival.

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Diverse impacts of the rs58542926 E167K variant in TM6SF2 on viral and metabolic liver disease phenotypes.


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UNLABELLED: A genome-wide exome association study has identified the transmembrane 6 superfamily member 2 (TM6SF2) rs58542926 variant encoding an E167K substitution as a genetic determinant of hepatic steatosis in nonalcoholic fatty liver disease (NAFLD). The roles of this variant across a spectrum of liver diseases and pathologies and on serum lipids comparing viral hepatitis to NAFLD and viral load in chronic viral hepatitis, as well as its intrahepatic molecular signature, have not been well characterized. We undertook detailed analyses in 3260 subjects.
with viral and nonviral liver diseases and in healthy controls. Serum inflammatory markers and hepatic expression of TM6SF2 and genes regulating lipid metabolism were assessed in a subset with chronic hepatitis C (CHC). The rs58542926 T allele was more prevalent in 502 NAFLD patients than controls (P = 0.02) but not different in cohorts with CHC (n = 2023) and chronic hepatitis B (n = 507). The T allele was associated with alterations in serum lipids and hepatic steatosis in all diseases and with reduced hepatic TM6SF2 and microsomal triglyceride transfer protein expression. Interestingly, the substitution was associated with reduced CHC viral load but increased hepatitis B virus DNA. The rs58542926 T allele had no effect on inflammation, impacted >F2 fibrosis in CHC and NAFLD assessed cross-sectionally (odds ratio = 1.39, 95% confidence interval 1.04-1.87, and odds ratio = 1.62, 95% confidence interval 1.03-2.52, respectively; P < 0.03 for both), but had no effect on fibrosis progression in 1174 patients with CHC and a known duration of infection.

CONCLUSION: The TM6SF2 E167K substitution promotes steatosis and lipid abnormalities in part by altering TM6SF2 and microsomal triglyceride transfer protein expression and differentially impacts CHC and chronic hepatitis B viral load, while effects on fibrosis are marginal. (Hepatology 2016;64:34-46).


Comparison of the quick mild cognitive impairment (qmci) screen to the montreal cognitive assessment (moca) in an australian geriatrics clinic.


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Introduction The Montreal Cognitive Assessment (MoCA) accurately differentiates mild cognitive impairment (MCI) from mild dementia and normal controls (NC). While the MoCA is validated in multiple clinical settings, few studies compare it with similar tests also designed to detect MCI. We sought to investigate how the shorter Quick Mild Cognitive Impairment (Qmci) screen compares with the MoCA. Methods Consecutive referrals presenting with cognitive complaints to a teaching hospital geriatric clinic (Fremantle, Western Australia) underwent a comprehensive assessment and were classified as MCI (n = 72) or dementia (n = 109). NC (n = 41) were a sample of convenience. The Qmci and MoCA were scored by trained geriatricians, in random order, blind to the diagnosis. Results Median Qmci scores for NC, MCI and dementia were 69 (+/-19), 52.5 (+/-12) and 36 (+/-14), respectively, compared with 27 (+/-5), 22 (+/-4) and 15 (+/-7) for the MoCA. The Qmci more accurately identified cognitive impairment (MCI or dementia), area under the curve (AUC) 0.97, than the MoCA (AUC 0.92), p = 0.04. The Qmci was non-significantly more accurate in distinguishing MCI from controls (AUC 0.91 vs 0.84, respectively = 0.16). Both instruments had similar accuracy for differentiating MCI from dementia (AUC of 0.91 vs 0.88, p = 0.35). At the optimal cut-offs, calculated from receiver operating characteristic curves, the Qmci (<57) had a sensitivity of 91% and specificity of 93% for cognitive impairment, compared with 87% sensitivity and 80% specificity for the MoCA (<23). Conclusion While both instruments are accurate in detecting MCI, the Qmci is shorter and arguably easier to complete, suggesting that it is a useful instrument in an Australian geriatric outpatient population. Copyright © 2016 John Wiley & Sons, Ltd.
(PsycINFO Database Record (c) 2016 APA, all rights reserved)
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Response to the Letter to the Editor regarding “A pilot study investigating basic fibroblast growth factor for the repair of chronic tympanic membrane perforations in pediatric patients”.
Cauda equina syndrome: an uncommon cause of urinary retention in a young woman.

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Interdisciplinary Management of Complex Regional Pain Syndrome of the Face.

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BACKGROUND AND PURPOSE: Orofacial pain disorders are relatively uncommon and pose a substantial diagnostic challenge. This case report documents the diagnosis and management of hemifacial pain in a patient who was referred to an interdisciplinary pain medicine unit. The purpose of this case report is twofold. First, it presents complex regional pain syndrome (CRPS) as a potential differential diagnosis in cases of facial pain. Second, it describes the successful adaption of contemporary management approaches for distal-extremity CRPS to treat people with CRPS of the facial region.

CASE DESCRIPTION: The patient had hemifacial pain and concomitant motor and autonomic symptoms after a small laceration of the eyelid. Extensive specialist medical evaluations were undertaken to exclude an underlying structural pathology. After detailed clinical assessments by a physical therapist, pain physician, and clinical psychologist, a
A diagnosis of CRPS involving the face was made.

OUTCOMES: The patient's pain was largely unresponsive to pharmacological agents. A modified graded motor imagery program, together with desensitization and discrimination training, was commenced by the physical therapist and clinical psychologist. A positive clinical response was indicated by a decrease in allostynia, normalization of motor control, and regained function in activities of daily living.

DISCUSSION: Complex regional pain syndrome is an infrequently reported differential diagnosis that can be considered in patients with persistent facial pain. This case report highlights how careful examination and clinical decision making led to the use of an innovative therapeutic strategy to manage a challenging condition.


Controlled moderate hypovolaemia in healthy volunteers is not associated with the development of oxidative stress assessed by plasma F2-isoprostanes and isofurans.

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Hypovolaemia can be associated with substantial morbidity, particularly when it occurs in the setting of trauma and in patients with comorbid diseases. Hypovolaemia and inflammation such as occur in the setting of trauma and surgery, are associated with systemic oxidative stress and free-radical injury. Free-radical injury that results from hypovolaemia-induced organ reperfusion may further augment inflammatory processes. It is unknown exactly what proportion of free-radical injury is associated with isolated hypovolaemia as opposed to the contribution from inflammation from surgery or trauma. In the first human study of its kind, we exposed 8 adult male volunteers to venesection-induced hypovolaemia in progressive aliquots of 5% of total blood volume until 20% had been removed. This blood was subsequently reinfused. Plasma F2-isoprostanes and isofurans, markers of in vivo lipid oxidation, were measured by gas chromatography-mass spectrometry at each 5% aliquot venesected and at each 5% reinfused. Between baseline and maximal blood loss there was a minor fall in haemoglobin concentration from 143.9g/l to 138.8g/l (p=0.004, 95% CI 2.2, 8.0g/L). No significant change from baseline occurred in the concentrations of either plasma F2-isoprostanes or isofurans during venesection (p=0.116 and p=0.152, respectively) or blood reinfusion (p=0.553 and p=0.736, respectively). We can conclude that in healthy adult volunteers, isolated hypovolaemia to 20% total blood volume loss is not associated with detectable systemic oxidative stress. The free-radical injury identified in surgical and trauma patients may represent the effects of tissue damage and inflammation, with an uncertain contribution from tissue ischemia as may occur with hypovolaemia.


Human mesenchymal stem cells attenuate early damage in a ventilated pig model of acute lung injury.

Acute lung injury/acute respiratory distress syndrome (ALI/ARDS) is a major cause of global morbidity and mortality. Mesenchymal stem cells (MSC) have shown promise in treating inflammatory lung conditions. We hypothesised that human MSC (hMSC) can improve ALI/ARDS through their anti-inflammatory actions. We subjected pigs (n=6) to intravenous oleic acid (OA) injury, ventilation and hMSC infusion, while the controls (n=5) had intravenous OA, ventilation and an infusion vehicle control. hMSC were infused 1h after the administration of OA. The animals were monitored for additional 4h. Nuclear translocation of nuclear factor-light chain enhancer of activated B cells (NF-kappaB), a transcription factor that mediates several inflammatory pathways was reduced in hMSC treated pigs compared to controls (p=0.04). There was no significant difference in lung injury, assessed by histological scoring in hMSC treated pigs versus controls (p=0.063). There was no difference in neutrophil counts between hMSC-treated pigs and controls. Within 4h, there was no difference in the levels of IL-10 and IL-8 pre- and post-treatment with hMSC. In addition, there was no difference in hemodynamics, lung mechanics or arterial blood gases between hMSC treated animals and controls. Subsequent studies are required to determine if the observed decrease in inflammatory transcription factors will translate into improvement in inflammation and in physiological parameters over the long term.
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INTRODUCTION: Malignant pleural effusions (MPEs) can complicate most cancers, causing dyspnoea and impairing quality of life (QoL). Indwelling pleural catheters (IPCs) are a novel management approach allowing ambulatory fluid drainage and are increasingly used as an alternative to pleurodesis. IPC drainage approaches vary greatly between centres. Some advocate aggressive (usually daily) removal of fluid to provide best symptom control and chance of spontaneous pleurodesis. Daily drainages however demand considerably more resources and may increase risks of complications. Others believe that MPE care is palliative and drainage should be performed only when patients become symptomatic (often weekly to monthly). Identifying the best drainage approach will optimise patient care and healthcare resource utilisation.

METHODS AND ANALYSIS: A multicentre, open-label randomised trial. Patients with MPE will be randomised 1:1 to daily or symptom-guided drainage regimes after IPC insertion. Patient allocation to groups will be stratified for the cancer type (mesothelioma vs others), performance status (Eastern Cooperative Oncology Group status 0-1 vs >2), presence of trapped lung (vs not) and prior pleurodesis (vs not). The primary outcome is the mean daily dyspnoea score, measured by a 100 mm visual analogue scale (VAS) over the first 60 days. Secondary outcomes include benefits on physical activity levels, rate of spontaneous pleurodesis, complications, hospital admission days, healthcare costs and QoL measures. Enrolment of 86 participants will detect a mean difference of VAS score of 14 mm between the treatment arms (5% significance, 90% power) assuming a common between-group SD of 18.9 mm and a 10% lost to follow-up rate.

ETHICS AND DISSEMINATION: The Sir Charles Gairdner Group Human Research Ethics Committee has approved the study (number 2015-043). Results will be published in peer-reviewed journals and presented at scientific meetings.

TRIAL REGISTRATION NUMBER: ACTRN12615000963527; Pre-results.

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Improving healthcare for Aboriginal Australians through effective engagement between community and health services.


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BACKGROUND: Effectively addressing health disparities between Aboriginal and non-Aboriginal Australians is long overdue. Health services engaging Aboriginal communities in designing and delivering healthcare is one way to tackle the issue. This paper presents findings from evaluating a unique strategy of community engagement between local Aboriginal people and health providers across five districts in Perth, Western Australia. Local Aboriginal community members formed District Aboriginal Health Action Groups (DAHAGs) to collaborate with health providers in designing culturally-responsive healthcare. The purpose of the strategy was to improve local health service delivery for Aboriginal Australians.

METHODS: The evaluation aimed to identify whether the Aboriginal community considered the community engagement strategy effective in identifying their health service needs, translating them to action by local health services and increasing their trust in these health services. Participants were recruited using purposive sampling. Qualitative data was collected from Aboriginal participants and health service providers using semi-structured interviews or yarning circles that were recorded, transcribed and independently analysed by two senior non-Aboriginal researchers. Responses were coded for key themes, further analysed for similarities and differences between districts and cross-checked by the senior lead Aboriginal researcher to avoid bias and establish reliability in interpreting the data. Three ethics committees approved conducting the evaluation.

RESULTS: Findings from 60 participants suggested the engagement process was effective: it was driven and owned by the Aboriginal community, captured a broad range of views and increased Aboriginal community participation in decisions about their healthcare. It built community capacity through regular community forums and established DAHAGs comprising local Aboriginal community members and health service representatives who met quarterly and were supported by the Aboriginal Health Team at the local Population Health Unit. Participants reported health services improved in community and hospital settings, leading to increased access and trust in local health services.

CONCLUSION: The evaluation concluded that this process of actively engaging the Aboriginal community in decisions about their health care was a key element in improving local health services, increasing Aboriginal people’s trust and access to care.

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A cross sectional evaluation of an alcohol intervention targeting young university students.

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BACKGROUND: Hazardous drinking has been found to be higher among young university students compared to their non-university peers. Although young university students are exposed to new and exciting experiences, including greater availability and emphasis on social functions involving alcohol there are few multi strategy comprehensive interventions aimed at reducing alcohol-related harms.

METHODS: Random cross sectional online surveys were administered to 18-24 year old students studying at the main campus of a large metropolitan university in Perth, Western Australia. Prior to the completion of the second survey an alcohol intervention was implemented on campus. Completed surveys were received from 2465 (Baseline; T1) and 2422 (Post Year 1: T2) students. Students who consumed alcohol in the past 12 months were categorised as low risk or hazardous drinkers using the Alcohol Use Disorders Identification Test (AUDIT). Due to the cross sectional nature of the two samples two-tailed two-proportion z-test and two sample t-tests were employed to determine statistical significance between the two time periods for categorical and continuous variables respectively.

RESULTS: At T1 and T2 89.1 % and 87.2 % of the total sample reported drinking alcohol in the past month respectively. Hazardous levels of alcohol consumption reduced slightly between T1 (39.7 %) and T2 (38 %). In both time periods hazardous drinkers reported significantly higher mean scores for experienced harm, second-hand harm and witnessed harm scores compared to low risk drinkers (p <0.001). Hazardous drinkers were significantly more likely to experience academic problems due to their alcohol consumption and to report more positive alcohol expectations than low risk drinkers at both time periods (p <0.001).

CONCLUSIONS: Harms and problems for students who report hazardous drinking are of concern and efforts should be made to ensure integrated and targeted strategies reach higher risk students and focus on specific issues such as driving while intoxicated and alcohol related unplanned sexual activity. However there is also a need for universal strategies targeting all students and low risk drinkers as they too are exposed to alcohol harms within the drinking and social environment. Changing the culture of the university environment is a long term aim and to effect change a sustained combination of organisational actions, partnerships and educational actions is required.

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**Optimal use of plasma and urine BK viral loads for screening and predicting BK nephropathy.**


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BACKGROUND: BK virus is a polyoma virus causing renal allograft nephropathy. Reduction of immunosuppression with the early recognition of significant BK viral loads in urine and plasma can effectively prevent BKV associated nephropathy (BKVN), however the optimal compartment and frequency of BK viral load measurement post renal transplantation are undetermined. Our purpose was to examine time to detection and viral loads in urine compared to plasma, and establish viral load cut-offs associated with histological BKVN.
METHODS: We performed a retrospective analysis of the BKV screening frequency and compartment(s) of 277 adult renal transplant recipients (RTR).

RESULTS: BKVN was histologically diagnosed in 17 (6.1 %) RTR. In cases where both urine and plasma were tested fortnightly for 6 months (n=53), BKV was detected in the urine 29 days earlier than plasma. Fortnightly (n=72) versus 3-monthly (n=78) testing demonstrated that BKV was detected in the urine significantly earlier (median 63 versus 97 days, p=0.001) and at a lower level (median 3.27 versus 6.71 log10 c/mL, p<0.001) with more frequent testing, but this difference was not evident in plasma first detection (80 versus 95 days, p=0.536) or first positive viral load (3.18 versus 3.30 log10 c/mL, p=0.603). The optimum cut-off BK viral load for histological diagnosis of BKVN was 4.10 log10 c/mL for the first positive urine, 3.79 log10 c/mL for the first positive plasma, 9.24 log10 c/mL for the peak urine, and 4.53 log10 c/mL for the peak plasma.

CONCLUSIONS: Frequent urinary BK viral load screening for the prevention of BKVN is suggested due to its high sensitivity and earlier detection.

An updated view of plasmid conjugation and mobilization in Staphylococcus.


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The horizontal gene transfer facilitated by mobile genetic elements impacts almost all areas of bacterial evolution, including the accretion and dissemination of antimicrobial-resistance genes in the human and animal pathogen Staphylococcus aureus. Genome surveys of staphylococcal plasmids have revealed an unexpected paucity of conjugation and mobilization loci, perhaps suggesting that conjugation plays only a minor role in the evolution of this genus. In this letter we present the DNA sequences of historically documented staphylococcal conjugative plasmids and highlight that at least 3 distinct and widely distributed families of conjugative plasmids currently contribute to the dissemination of antimicrobial resistance in Staphylococcus. We also review the recently documented “relaxase-in trans” mechanism of conjugative mobilization facilitated by conjugative plasmids pWBG749 and pSK41, and discuss how this may facilitate the horizontal transmission of around 90% of plasmids that were previously considered non-mobilizable. Finally, we enumerate unique sequenced S. aureus plasmids with a potential mechanism of mobilization and predict that at least 80% of all non-conjugative S. aureus plasmids are mobilizable by at least one
mechanism. We suggest that a greater research focus on the molecular biology of conjugation is essential if we are to recognize gene-transfer mechanisms from our increasingly in silico analyses.

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**Five-year plans and once-in-a-decade interventions: Need to move from filling gaps to bridging chasms in mental health care in India.**
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**Laparoscopic kidney transplant by extra peritoneal approach: Two years follow up.**
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Introduction: Recently, we have applied an innovative laparoscopic technique for kidney transplant via extra peritoneal approach. The aim of this study is to report its outcomes over two years follow up. Materials and Methods: The study patient was a 49-year-old male and received the kidney that was transplanted by laparoscopic technique via extra peritoneal approach. The details of the technique were reported elsewhere in the past[1]. Briefly, a Pfannenstiel incision (7 cm) was made for delivery of the kidney graft to the right iliac fossa. The renal artery and renal vein was anastomosed to the side of external iliac artery and vein by laparoscopic technique. The control patient was a 66-year-old gentleman received the contralateral kidney that was transplanted by open surgery. Results and Discussion: The surgery was successful for both patients. Both kidneys experienced delayed graft function but the kidneys started function on day 6 post transplant. The recovery of kidney graft function by laparoscopic transplantation is the same as the kidney from open transplant. The creatinine level is stable (109 vs 107 umol/L) over two years follow up. The incision is much less visible on study patient (Figure 1). There is no surgical complication over two years follow up. Conclusion: This report has shown that the kidney graft function is satisfactory when transplanted by laparoscopic technique. The benefit for the patient is a smaller incision, less pain and better cosmetic appearance. There was no adverse effect seen from laparoscopic surgery. (Figure Presented).
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**Central nervous system involvement by multiple myeloma: A multi-institutional retrospective study of 172 patients in daily clinical practice.**
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The multicenter retrospective study conducted in 38 centers from 20 countries including 172 adult patients with CNS MM aimed to describe the clinical and pathological characteristics and outcomes of patients with multiple myeloma (MM) involving the central nervous system (CNS). Univariate and multivariate analyses were performed to identify
prognostic factors for survival. The median time from MM diagnosis to CNS MM diagnosis was 3 years. Thirty-eight patients (22%) were diagnosed with CNS involvement at the time of initial MM diagnosis and 134 (78%) at relapse/progression. Upon diagnosis of CNS MM, 97% patients received initial therapy for CNS disease, of which 76% received systemic therapy, 36% radiotherapy and 32% intrathecal therapy. After a median follow-up of 3.5 years, the median overall survival (OS) from the onset of CNS involvement for the entire group was 7 months. Untreated and treated patients had median OS of 2 and 8 months, respectively (P<0.001). At least one previous line of therapy for MM before the diagnosis of CNS disease and >1 cytogenetic abnormality detected by FISH were independently associated with worse OS. The median OS for patients with 0, 1 and 2 of these risk factors were 25 months, 5.5 months and 2 months, respectively (P<0.001). Neurological manifestations, not considered chemotherapy-related, observed at any time after initial diagnosis of MM should raise a suspicion of CNS involvement. Although prognosis is generally poor, the survival of previously untreated patients and patients with favorable cytogenetic profile might be prolonged due to systemic treatment and/or radiotherapy. Am. J. Hematol. 91:575-580, 2016. © 2016 Wiley Periodicals, Inc.


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BACKGROUND: Thyroid nodules may be incidentally detected on (18) F-FDG-positron emission tomography (PET) scans. Previous reports suggest a high incidence of malignancy in FDG-avid nodules. The aims of this study were to examine the incidence of malignancy in a large cohort and to report on the histological features. The findings suggest that poor prognostic histologic features are often associated with FDG-avid thyroid nodules and this may have clinical implications.

METHODS: A retrospective review of prospectively collected data was conducted. A database containing all patients who underwent PET scanning at a single tertiary referral centre from January 2006 to January 2013 was searched to identify those with incidental PET-positive thyroid nodules. Patients with known preexisting thyroid disease were excluded from analysis. The demographics, fine-needle aspiration (FNA) biopsy result and operative histopathology were analysed.

RESULTS: A total of 27 851 FDG-PET scans were performed of which 221 found incidental PET-positive thyroid nodules (incidence 0.8%). Fifty-three patients went on to have further investigation and 21 of these were found to have malignant disease (incidence 39.6%). Histopathological examination of 12 malignant nodules revealed an expected rate of poor prognostic features, including poorly differentiated subtype (8.3%), lymphovascular invasion (16.7%), perineural invasion (8.3%) and extrathyroid extension (33.3%).

CONCLUSION: Our data indicate that PET-positive thyroid nodules are associated with a high incidence of malignancy. This finding provides strong support for further investigation including FNA biopsy in all surgically suitable patients.


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UNLABELLED: The purpose of this study was to investigate the relationship between mental health and self-reported itch in patients with burns across a 6 month time period and to test the hypothesis that poorer mental health outcomes are associated with increased severity of itch.

METHOD: A quantitative study with three time points for data collection was conducted. Participants (232) completed assessments at 1 month, 3 months, and 6 months after burn injury. The Patient and Observer Scar Assessment Scale (POSAS) was used to report itch and the Short Form Health Survey (SF-36) provided an assessment of mental health across time. Only data from the itch and mental health subscales were used in the analysis. To analyze the data a quantile regression model was used.

RESULTS: Mental health is significantly associated with itch after adjusting for variation in itch over time (p=0.001). The regression coefficient indicates that as mental health increases by one unit, itch decreases by 0.03. Of importance, the relationship remained significant after adjusting for total burn surface area (p<0.001).

CONCLUSION: These findings suggest there is a relationship between mental health and itch. Given the powerful impact itch can have on an individual's wellbeing health professionals can begin to further investigate itch from a bio-psychosocial perspective. Further research to investigate causal relationships between mental health and itch is important.

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Lipoprotein metabolism in an apoB-80 familial hypobetalipoproteinemia heterozygote.
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OBJECTIVE: Familial hypobetalipoproteinemia (FHBL) is characterized by mutations in APOB, the majority of these causing protein truncations, and low plasma levels of apolipoprotein (apo) B. The hypobetalipoproteinemia may be due to enhanced clearance and possibly reduced production of apoB-containing lipoproteins; the mechanism may
depend on the length of the apoB truncation. We studied fasting lipoprotein metabolism in an FHBL subject heterozygous for a mutation causing a truncated apoB, apoB-80.

DESIGN AND METHODS: Very low density lipoprotein (VLDL)-, intermediate density lipoprotein (IDL)-, and low density lipoprotein (LDL)-apoB kinetics were determined in the fasting state using stable isotope methods and compartmental modeling.

RESULTS: Compared with lean normolipidemic controls the apoB-80 FHBL subject had an elevated VLDL-apoB fractional catabolic rate and lower LDL production. ApoB production rates and IDL- and LDL-apoB fractional catabolic rates were not different.

CONCLUSION: FHBL subjects heterozygous for a mutation truncating apoB to 80% of full-length are able to produce VLDL-apoB normally, but have rapid clearance of these particles, resulting in low levels of circulating apoB.

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Metabolic memory and all-cause death in community-based patients with type 2 diabetes: the Fremantle Diabetes Study.

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AIMS: To validate the findings, in a usual care setting, of glycaemic intervention trials, which have shown that tight control in patients with recently diagnosed type 2 diabetes protects against death during post-study monitoring, but that it may be deleterious in long-duration diabetes with vascular complications.

METHODS: A subset of 531 patients with type 2 diabetes from the community-based observational Fremantle Diabetes Study Phase 1, who attended >5 annual reviews (mean follow-up 15.9 years), were categorized by baseline diabetes duration [<1 year (Group 1); 1 to <5 years (Group 2); and >5 years (Group 3)]. Glycated haemoglobin (HbA1c) trajectories over the first 5 years were determined [low, medium and high; equivalent to mean HbA1c <6.6% (<49 mmol/mol), 6.7-8.0% (50-64 mmol/mol) and >8.0% (>64 mmol/mol), respectively]. Kaplan-Meier analysis was used to assess survival by duration and HbA1c trajectory. Cox proportional hazards modelling identified predictors of all-cause death.

RESULTS: There was greater mortality in patients with a medium versus those with a low trajectory in Group 1: hazard ratio (HR) 1.99 [95% confidence interval (CI) 1.003-3.94; p = 0.049], and in patients with a high versus a low trajectory in Group 2: HR 2.02 (95% CI 1.11-3.71; p = 0.022). In Group 3, both medium [HR 0.57 (95% CI 0.35-0.92; p = 0.022)] and high [HR 0.56 (95% CI 0.32-0.96); p = 0.035] trajectories were independently and inversely associated with death.

CONCLUSIONS: In community-based patients with newly or recently diagnosed type 2 diabetes, poor glycaemic control was an adverse prognostic indicator. Tight control was independently associated with death in patients with diabetes duration >5 years. These data parallel intervention trial findings and support individualization of HbA1c targets.

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Cerebral arterial gas embolism after pre-flight ingestion of hydrogen peroxide.
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Cerebral arterial gas embolism (CAGE) is a feared complication of ambient depressurisation and can also be a complication of hydrogen peroxide ingestion. We present an unusual case of CAGE in a 57-year-old woman exposed to both of these risk factors. We describe her subsequent successful treatment with hyperbaric oxygen, despite a 72-hour delay in initial presentation and diagnosis, and discuss the safety of aero-medical transfer following hydrogen peroxide ingestions.

Cochlear implantation in children with congenital unilateral deafness: Mid-term follow-up outcomes.
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OBJECTIVES: Although cochlear implantation is widely used to treat unilateral deafness in adults, very little literature exists on its use and effects on the paediatric population. This report adds to the literature showing the mid-term follow-up outcomes achieved by these children.
MATERIAL AND METHODS: Three children with congenital unilateral deafness were studied after implantation. Speech perception in noise, and sound localization ability were evaluated using age-appropriate materials.
RESULTS: The preliminary data of our small group of 3 children with congenital unilateral profound hearing loss revealed that up to 3 years post-implantation, congenitally deaf children who received a cochlear implant after 4 years of age do not demonstrate binaural hearing benefits.
CONCLUSION: Early intervention in the prelingual phase may be crucial for the development of binaural hearing.

Perianal CD assessment surgery.
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PMID:26991526
DOI:https://dx.doi.org/10.1111/jgh.13354

Magnetic resonance imaging of perianal Crohn's disease.
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Crohn's disease imaging in the emergency department.
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A pilot study of the utility of choline PET-CT in prostate cancer biochemical relapse following radical prostatectomy.
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INTRODUCTION: To evaluate the detection rate of positive choline PET-CT and its clinical role in assisting with management decisions and the correlation between positive choline PET-CT and clinical/pathological parameters in prostate cancer patients with biochemical relapse following radical prostatectomy.

METHODS: This was a longitudinal observational pilot study of 34 patients who received choline PET-CT scans with biochemical relapse after radical prostatectomy. Variables including peak PSA, PSA doubling time (DT), Gleason score, age, initial PSA at diagnosis, use of ADT prior to PET and initial clinical staging were statistically analysed to assess for independent predictive factors for positive PET findings.

RESULTS: Choline PET-CT was positive in 38.2% of patients (13/34). The only statistically significant predictor for positive PET-CT was the use of ADT prior to PET-CT, with OR 18.7 (95% CI, 2.87-122.45), P < 0.01. Mean peak PSA for patients with positive PET-CT was 5.5 +/- 4.8 ng/mL. Patients with positive PET-CT had a mean PSA DT of 5.1 +/- 3.8 months and mean total Gleason of 7.6 +/- 0.8. Although these variables were not statistically significant, they showed a tendency towards significance. At Receiver Operator Characteristics (ROC) analysis, a peak PSA value of 1.65 ng/mL and PSA DT of 4.4 months were determined to be the optimal cut-off values predicting positive PET-CT.
CONCLUSION: Choline PET-CT has its potential as a diagnostic modality enabling the detection of occult prostate cancer recurrence and to differentiate localised disease from systemic disease thus guiding management. Use of ADT prior to PET-CT is a significant predictor of positive PET-CT. Patients with a short PSA DT, high-peak PSA and high Gleason score should also be considered for choline PET-CT.


Sunitinib as Neoadjuvant Chemotherapy in the Management of Metastatic Renal Cell Carcinoma Mimicking a Glomus Vagale Tumor in the Head and Neck: A Case Report and Review of Literature.

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Background Metastatic renal cell carcinoma (RCC) of the head and neck with intracranial extension is rare and may pose difficulties to the diagnosis and management. Method We describe a unique case of a 76-year-old man with a metastatic RCC to the neck and lateral skull base with intracranial extension presenting with Collet-Sicard syndrome 8 years after initial diagnosis. The radiologic features were consistent with the diagnosis of a glomus vagale tumor on the basis of clinical and radiologic features. Results Despite radiotherapy, the intracranial extension progressed in size, resulting in early hydrocephalus. Sunitinib, a novel tyrosine kinase inhibitor, was instituted to treat the glomus vagale tumor with a marked reduction in tumor volume and resolution of the early hydrocephalus. The surgical resection of the tumor with its intracranial extension was achieved without additional postoperative morbidity. The histopathologic diagnosis surprisingly demonstrated metastatic RCC. Conclusion We present a case of metastatic RCC to the head and neck region mimicking a glomus vagale tumor and describe the first use of sunitinib as a neoadjuvant chemotherapy to achieve a single-stage radical en bloc resection of the tumor mass.


Opportunistic adolescent health assessment in the child protection unit.

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AIM: Adolescent health assessments are recommended to identify health-risk behaviours. Adolescents who experience maltreatment are more likely to engage in such behaviours. This study (i) describes the frequency of
health-risk behaviours amongst adolescents attending a hospital-based child protection unit (CPU) and (ii) determines whether use of a health assessment questionnaire increases the identification of these behaviours.

METHODS: A retrospective audit was performed of case notes of adolescents (aged >12 years) presenting to the CPU over 5 years (2007-2011). Data regarding health-risk behaviours were extracted. In 2012, following the introduction of a standardised HEADSS-based four-page questionnaire, health-risk data were collected prospectively over 18 months. The proportion of subjects reporting health-risk behaviours, before and after questionnaire introduction, was analysed.

RESULTS: Two hundred fifty-eight subjects, median age 13 (range 12-18) years, 78% female, were included in the pre-questionnaire period; and 85 subjects, median age 14 (range 12-17) years, 86% female, were included following introduction of the questionnaire. Questionnaire use was associated with an increase in the frequency of health-risk behaviours identified in the following domains: Education (odds ratio 4.48 [confidence interval 2.56-7.96] P<0.001), Activities (16.18 [6.70-42.74] P<0.001), Drugs/alcohol (4.00 [2.23-7.16] P<0.001) and Suicidality (8.27 [4.59-14.92] P<0.001). Participants reported higher rates of health-risk behaviours than the national population.

CONCLUSION: Adolescents attending a hospital-based CPU report high rates of health-risk behaviours. A standardised questionnaire results in increased identification of such behaviours.


Malignant pleural mesothelioma: an update on diagnosis and treatment options.
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Malignant pleural mesothelioma (MPM) represents a significant diagnostic and therapeutic challenge and is almost always a fatal disease. Imaging abnormalities are common, but have a limited role in distinguishing mesothelioma from metastatic pleural disease. Similarly, minimally invasive biomarkers have shown promise but also have limitations in the diagnosis of mesothelioma. In experienced centers, cytology and immunohistochemistry are now sufficient to diagnose the epithelioid subtype of mesothelioma, which can reduce the need for more invasive diagnostic investigations. Prognosis of MPM is modestly impacted by oncological treatments. Chemotherapy with cisplatin and pemetrexed is considered the standard of care, though the addition of bevacizumab to the platinum doublet may be the new standard of care. New targeted therapies have demonstrated some promise and are being addressed in clinical trials. This review focuses on the current data on the diagnostic and therapeutic issues of MPM.

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Herpetic cranial polyneuritis mimicking brain stem infarction-an atypical presentation of Ramsay Hunt syndrome.

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An elderly man presented with severe right ear pain and discharge, hoarseness and dysphagia causing significant
involuntary weight loss. Extensive investigations by varied specialties only highlighted right vocal cord palsy and right parotid lymphadenitis. Reassessment on transfer to a rehabilitation ward noted clinically subtle right Ramsay Hunt syndrome with multiple lower cranial nerve involvement. We illustrate a case of varicella zoster virus cranial polyneuritis with bulbar symptoms mimicking bulbar stroke, requiring percutaneous endoscopic gastrostomy feeds, with significant clinical and radiological recovery over 1 year.

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Simultaneous Coronary and Pulmonary Angiography to Diagnose Critical Left Main Coronary Artery Stenosis Secondary to Dilated Pulmonary Artery.

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Estimating eligibility for lung cancer screening in an Australian cohort, including the effect of spirometry.

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OBJECTIVES: To estimate the proportion of ever-smokers who are eligible for lung cancer screening in an Australian cohort, and to evaluate the effect of spirometry in defining chronic obstructive pulmonary disease (COPD) when assessing screening eligibility.

DESIGN: Cross-sectional study of 3586 individuals aged 50-68 years who live in the Busselton Shire of Western Australia.

OUTCOMES: Proportion of ever-smokers eligible for lung cancer screening based on United States Preventive Services Task Force (USPSTF) criteria, and PLCoM2012 lung cancer risk > 1.5%. The effect of using self-reported COPD, symptoms consistent with COPD, or spirometry to define COPD for screening eligibility according to the PLCoM2012 criteria.

RESULTS: Of ever-smokers aged 55-68 years, 254 (20.1%) would be eligible for screening according to USPSTF criteria; fewer would be eligible according to PLCoM2012 criteria (225, 17.9%; P = 0.004). This is equivalent to 8.9-10.0% of the total population aged 55-68 years, which suggests about 450 000 individuals in Australia may be eligible for lung cancer screening. The proportions of eligible participants were not significantly different whether spirometry results or symptoms consistent with COPD were used to determine PLCoM2012 risk.

CONCLUSIONS: The proportion of ever-smokers in this population who were eligible for lung cancer screening was 17.9-20.1%. Using symptoms to define COPD is an appropriate surrogate measure for spirometry when determining the presence of COPD in this population. There are significant challenges for policy makers on how to identify and
recruit these eligible individuals from the wider population.

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**Australian Group on Antimicrobial Resistance Australian Staphylococcus aureus Sepsis Outcome Programme annual report, 2014.**

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From 1 January to 31 December 2014, 27 institutions around Australia participated in the Australian Staphylococcal Sepsis Outcome Programme (ASSOP). The aim of ASSOP 2014 was to determine the proportion of Staphylococcus aureus bacteraemia (SAB) isolates in Australia that are antimicrobial resistant, with particular emphasis on susceptibility to methicillin and to characterise the molecular epidemiology of the isolates. Overall, 18.8% of the 2,206 SAB episodes were methicillin resistant, which was significantly higher than that reported in most European countries. The 30-day all-cause mortality associated with methicillin-resistant SAB was 23.4%, which was significantly higher than the 14.4% mortality associated with methicillin-sensitive SAB (P <0.0001). With the exception of the beta-lactams and erythromycin, antimicrobial resistance in methicillin-sensitive S. aureus remains rare. However in addition to the beta-lactams, approximately 50 of methicillin-resistant S. aureus (MRSA) were resistant to erythromycin and ciprofloxacin and approximately 15% were resistant to co-trimoxazole, tetracycline and gentamicin. When applying the European Committee on Antimicrobial Susceptibility Testing breakpoints, teicoplanin resistance was detected in 2 S. aureus isolates. Resistance was not detected for vancomycin or linezolid. Resistance to non-beta-lactam antimicrobials was largely attributable to 2 healthcare-associated MRSA clones; ST22-IV [2B] (EMRSA-15) and ST239-III [3A] (Aus-2/3 EMRSA). ST22-IV [2B] (EMRSA-15) has become the predominant healthcare associated clone in Australia. Sixty per cent of methicillin-resistant SAB were due to community-associated (CA) clones. Although polyclonal, almost 44% of community-associated clones were characterised as ST93-IV [2B] (Queensland CA-MRSA) and ST1-IV [2B] (WA1). CA-MRSA, in particular the ST45-V [SC285] (WA84) clone, has acquired multiple antimicrobial resistance determinants including ciprofloxacin, erythromycin, clindamycin, gentamicin and tetracycline. As CA-MRSA is well established in the Australian community it is important that antimicrobial resistance patterns in community and
healthcare-associated SAB is monitored as this information will guide therapeutic practices in treating S. aureus sepsis.

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From 1 January to 31 December 2014, 27 institutions around Australia participated in the Australian Enterococcal Sepsis Outcome Programme (AESOP). The aim of AESOP 2014 was to determine the proportion of enterococcal bacteraemia isolates in Australia that were antimicrobial resistant, and to characterise the molecular epidemiology of the Enterococcus faecium isolates. Of the 952 unique episodes of bacteraemia investigated, 94.4% were caused by either E. faecalis (54.9%) or E. faecium (39.9%). Ampicillin resistance was detected in 0.6% of E. faecalis and in 89.4% of E. faecium. Vancomycin non-susceptibility was reported in 0.2% and 46.1% of E. faecalis and E. faecium respectively. Overall 51.1% of E. faecium harboured vanA or vanB genes. For the vanA/B positive E. faecium isolates, 81.5% harboured vanB genes and 18.5% vanA genes. The percentage of E. faecium bacteraemia isolates resistant to vancomycin in Australia is significantly higher than that seen in most European countries. E. faecium consisted of 113 pulsed-field gel electrophoresis pulsotypes of which 68.9% of isolates were classified into 14 major pulsotypes containing 5 or more isolates. Multilocus sequence typing grouped the 14 major pulsotypes into clonal cluster 17, a major hospital-adapted polyclonal E. faecium cluster. The geographical distribution of the 4 predominant sequence types (ST203, ST796, ST555 and ST17) varied with only ST203 identified across most regions of Australia. Overall 74.7% of isolates belonging to the four predominant STs harboured vanA or vanB genes. In conclusion, the AESOP 2014 has shown enterococcal bacteraemias in Australia are frequently caused by polyclonal ampicillin-resistant high-level gentamicin resistant vanA or vanB E. faecium, which have limited treatment options.

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The Australian Group on Antimicrobial Resistance performs regular period-prevalence studies to monitor changes in antimicrobial resistance in selected enteric Gram-negative pathogens. The 2014 survey was the second year to focus on bloodstream infections. During 2014, 5,798 Enterobacteriaceae species isolates were tested using commercial automated methods (Vitek 2, BioMerieux; Phoenix, BD) and results were analysed using the Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (January 2015). Of the key resistances, non-susceptibility to the third-generation cephalosporin, ceftriaxone, was found in 9.0%/9.0% of Escherichia coli (CLSI/EUCAST criteria) and 7.8%/7.8% of Klebsiella pneumoniae, and 8.0%/8.0% K. oxytoca. Non-susceptibility rates to ciprofloxacin were 10.4%/11.6% for E. coli, 5.0%/7.7% for K. pneumoniae, 0.4%/0.4% for K. oxytoca, and 3.5%/6.5% in Enterobacter cloacae. Resistance rates to piperacillin-tazobactam were 3.2%/6.8%, 4.8%/7.2%, 11.1%/11.5%, and 19.0%/24.7% for the same 4 species respectively. Fourteen isolates were shown to harbour a carbapenemase gene, 7 blaIMP-4, 3 blaKPC-2, 3 blaVIM-1, 1 blaNDM-4, and 1 blaOXA-181-lke.

PMID:27522134


The index of TWIST.

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Case 1 A 25-year-old, P1 + 6 , with previous emergency caesarean section (CS) for acute abruption at 32 weeks of gestation, was for birthing at 39 weeks by elective Caesarean section (CS). She had a past history of six miscarriages, bilateral pulmonary embolism and laparoscopic gastric banding. She was on Insulin for gestational diabetes, prophylactic Enoxaparin and serial ultrasound scan (USS) surveillance in the index pregnancy. She had a category 1 CS for acute abdominal pain and antepartum haemorrhage (APH) at 32+5 weeks. The baby had Apgar scores of 91, 95. Placental histology showed hypercoiling of cord (4-5/10 cm), early acute choioamnionitis and eccentric insertion of the cord. Case 2 A 23-year-old, P1, with a previous vaginal birth at term was on serial USS surveillance for foetal unilateral multicystic dysplastic kidney detected at anomaly scan, was for birthing by elective CS at term. She had a category 1 CS for irregular tightenings and APH at 34<sup>+</sup>+4</sup> weeks. The baby was born in poor condition and had neonatal death. Placental histology showed hypercoiling of cord (6-8/10 cm) with retroplacental haemorrhage over 80% of surface, central insertion of cord and no choioamnionitis. Discussion Umbilical cord has two arteries and one vein running a spiral course. These helices may be clockwise (dextral) or anticlockwise (sinistral) in a ratio of 1:6. Coiling is a complete 360degree spiral course of umbilical blood vessels around Wharton's jelly. This occurs from distension of the vessels with blood. Foetal movement contributes to cord twists and length. The chirality is independent of the viewing end and helices are detectable on USS in the first trimester. Umbilical coiling index (UCI) may be defined as the number of complete coils per 10 cm cord length (normally between 2 and 3). Greater than 3 coils per 10 cm (UCI > 90th centile) is termed hypercoiling and has association with adverse pregnancy outcomes (Table 1). USS detection does not form part of routine antenatal assessment as sonographic determination
has poor sensitivity (40%) with postpartum examination. Most studies are retrospective with weak antenatal associations. Hence sending placenta for histology should be a routine practice after all perinatal morbidity and mortality. (Table Presented).

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DOI:http://dx.doi.org/10.1111/1471-0528.14101


PIVOT: Patient information videos on operations trial. A single blinded randomised controlled study.
Zimmermann E, Gordon E, et al.

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Introduction Whilst patients are always explained the key risks and complications of any elective surgical intervention, they often feel unprepared for both the hospital stay and the postoperative period. An educational video outlining key points of the operation and postoperative period allows 24/7 delivery of concise information that can be shared with relatives and/or carers. Research question Does the additional use of multimedia provide a more effective means of educating the patient on risks and benefits of a common elective surgical procedure as well as reduce overall pre-operative anxiety? Methods We performed a single centre single-blinded randomised controlled study. National ethics approval was obtained via IRAS (Ref 12/EM/0212). Two rapid sequence animation videos (RSAV) were created explaining (i) elective caesarean section (LSCS) and (ii) transobturator/transvaginal tape (TVT/TOT). Participants were block-randomised in groups of 10 to either control (no video) or intervention (video). Two questionnaires were completed at baseline (preoperative assessment, stage 1) and immediately preoperatively (stage 2). These questionnaires assessed anxiety (Stait Trait Anxiety Inventory) and preoperative knowledge. Target recruitment was 60 patients for elective LSCS and 60 for TVT/TOT. Data entry was performed by a dedicated research nurse blinded to participant allocation, and statistics was performed by our trust statistician. Results Recruitment target was achieved for the LSCS group between September 2014 and April 2015. Recruitment to the TVT/TOT group was limited (n = 12) by reduction in the anticipated number of procedures within the project time frame, precluding meaningful analysis in this group. Within the LSCS group, anxiety scores decreased in the intervention arm and increased in the control arm (-5.8% versus +3.6%, P = 0.03, CI 95%). Whilst knowledge scores increased in both groups from baseline to immediately preoperatively, the intervention arm demonstrated a comparably significant increase in score (6.7% versus 14.8%, P = 0.002, CI 95%) Conclusion Our study demonstrated that the use of a RSVA resulted in a significant reduction in preoperative anxiety and significant increase in knowledge for women undergoing elective LSCS. This suggests that RSVA may be an inexpensive and effective way to enhance patients’ surgical experience. We recommend multimedia use be incorporated in patient information delivery for the elective surgical patient and suggest more videos be created in order to assess transferability of our results to other surgical procedures.

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SSRI and SNRI use during pregnancy is associated with both obstetric and neonatal complications.

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Background Selective serotonin inhibitors (SSRIs) and serotonin noradrenaline reuptake inhibitors (SNRIs) are commonly prescribed for depression. SSRIs/SNRIs have been associated with an increased risk of pregnancy and labour complications including rates of stillbirth, preterm birth and fetal growth restriction. In addition, these medications have been associated with problems in neonatal transition. Our aim was to determine the rates of complications in women and the neonatal transition at King Edward Memorial Hospital, Perth, Australia. Methods Retrospective review of all pregnancies at KEMH between 07/2005 and 06/2010 using midwifery and neonatal databases and case records. Analysis using univariate and multivariate models correcting for antenatal factors. Results 28,517 livebirths over this period. Neonatal data from 295 mothers treated with SSRIs and 91 with SNRIs compared with mothers prescribed neither. Rates of threatened abortion were 2.0% in mothers not receiving SSRI/SNRI, 4.7% in the SSRI group and 1.1% in the SNRI group P = 0.007. Gestational hypertension was seen in 2.6%, 2.7% and 9.6% respectively P = 0.001. Transient hypertension during labour 0.9% 1.0% and 4.4% P = 0.011. Meconium staining of the liquor 9.3% 14.7% and 12.1% P = 0.005. No effect was detected on preterm birth SSRI [Adj OR 1.16 (0.85-1.58) P = 0.35] SNRI [1.28 (0.69-2.40) P = 0.44. 75 babies of mothers prescribed multiple psychiatric medications excluded. Nursery admission rates for no antidepressant, SSRI, SNRI were 24.8%, 31.2% [Adj OR 1.38 (0.96-1.99) P = 0.08], 41.8% [2.05 (1.13-3.73) P = 0.019]. Need for any resuscitation SSRI [Adj OR 2.20 (1.67-2.89) P < 0.001] SNRI [1.80(1.16-2.79) P = 0.009]. A dose response effect for high, intermediate and low doses of SSRI and SNRI was noted. Conclusion Maternal SSRI/SNRI dosage should be kept as low as practical. The use of these medications may increase the rate of some antenatal and labour complications. In each case the risk versus benefit needs to be assessed prior to and during pregnancy. In terms of neonatal outcomes, our recommendation is for a skilled resuscitator attend each delivery.

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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), point-of-care (Radiometer ABL800 Flex) and laboratory (Abbott CellDyne SapphireTM) 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.

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Endocrine therapy is an established and effective treatment strategy for hormone receptor positive metastatic breast cancer. The clinical utility of endocrine therapy is lost over time due to evolving changes in tumor biology and the development of endocrine resistance. Many agents targeting the intracellular signaling pathways associated with endocrine resistance are in development. Following our systematic review of treatments with established benefits in this supplement, we review some of the more promising new strategies for overcoming endocrine resistance, looking at the impact on disease control and quality of life for women with hormone receptor positive, HER2 negative breast cancer. We also examine the biomarkers that may guide selection of the best therapy for the individual.

Endocrine therapy for the treatment of hormone receptor positive, HER2 negative, metastatic breast cancer is continually evolving. We systematically reviewed phase 2 and 3 randomized controlled trials (RCTs) of agents used in this setting to assess the effectiveness and safety of these agents for postmenopausal women. Across the 32 studies in more than 10,000 patients, the greatest improvement in progression-free survival (PFS) was seen with the addition of a cyclin-dependent kinase (CDK)4/6 inhibitor to standard endocrine therapy. Treatment with a mammalian target of rapamycin (mTOR) inhibitor, phosphoinositol-3-kinase (PI3K) inhibitor, vascular endothelial growth factor (VEGF) inhibitor and with a selective estrogen receptor degrader (SERD) also showed benefit in PFS for selected trials. Overall survival (OS) improved with the use of mTOR inhibitors and a SERD; however, studies were not powered for an OS endpoint. Encouraging results from early studies of histone deacetylase (HDAC) and B-cell lymphoma (BCL2) inhibitors are yet to be confirmed in phase III clinical trials. Study discontinuation rates and toxicity-related deaths were highest with VEGF inhibitors in combination with endocrine therapy, limiting their use in hormone receptor positive breast cancer. CDK4/6 inhibitors and mTOR inhibitors appeared to have activity in both first and second line settings, but required additional monitoring for common toxicities. The activity of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors was limited to the first-line setting and treatment discontinuation rates were higher than with mTOR inhibitors and SERDs. Overall, PFS benefit appears to be greatest when agents acting on CDK4/6, mTOR and PI3K pathways, and SERDs are added to standard endocrine therapy. If these early results persist in further
studies, these data are likely to change the way we treat hormone receptor positive, HER2 negative metastatic breast cancer. In the follow-up article to this review, we will consider the potential future treatment options for these patients.

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Sporadic inclusion body myositis: A review of recent clinical advances and current approaches to diagnosis and treatment.

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Sporadic inclusion body myositis is the most frequent acquired myopathy of middle and later life and is distinguished from other inflammatory myopathies by its selective pattern of muscle involvement and slowly progressive course, and by the combination of inflammatory and degenerative muscle pathology and multi-protein deposits in muscle tissue. This review summarises the findings of recent studies that provide a more complete picture of the clinical phenotype and natural history of the disease and its global prevalence and genetic predisposition. Current diagnostic criteria, including the role of electrophysiological and muscle imaging studies and the recently identified anti-5'-nucleotidase (anti-cN1A) antibody in diagnosis are also discussed as well as current trends in the treatment of the disease.

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Ridgeon E, Bellomo R, et al.

OBJECTIVE: Trials in critical care have previously used unvalidated systems to classify cause of death. We aimed to provide initial validation of a method to classify cause of death in intensive care unit patients.

DESIGN, SETTING AND PARTICIPANTS: One hundred case scenarios of patients who died in an ICU were presented online to raters, who were asked to select a proximate and an underlying cause of death for each, using the ICU Deaths Classification and Reason (ICU-DECLARE) system. We evaluated two methods of categorising proximate cause of death (designated Lists A and B) and one method of categorising underlying cause of death. Raters were ICU specialists and research coordinators from Australia, New Zealand and the United Kingdom.

MAIN OUTCOME MEASURES: Inter-rater reliability, as measured by the Fleiss multirater kappa, and the median proportion of raters choosing the most likely diagnosis (defined as the most popular classification choice in each case).

RESULTS: Across all raters and cases, for proximate cause of death List A, kappa was 0.54 (95% CI, 0.49-0.60), and for proximate cause of death List B, kappa was 0.58 (95% CI, 0.53-0.63). For the underlying cause of death, kappa was 0.48 (95% CI, 0.44-0.53). The median proportion of raters choosing the most likely diagnosis for proximate cause of death, List A, was 77.5% (interquartile range [IQR], 60.0%-93.8%), and the median proportion choosing the most likely diagnosis for proximate cause of death, List B, was 82.5% (IQR, 60.0%-92.5%). The median proportion choosing the most likely diagnosis for underlying cause was 65.0% (IQR, 50.0%-81.3%). Kappa and median agreement were similar between countries. ICU specialists showed higher kappa and median agreement than research coordinators.

CONCLUSIONS: The ICU-DECLARE system allowed ICU doctors to classify the proximate cause of death of patients who died in the ICU with substantial reliability.

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Structured and Modular Training Pathway for Robot-assisted Radical Prostatectomy (RARP): Validation of the RARP Assessment Score and Learning Curve Assessment.


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BACKGROUND: Use of robot-assisted radical prostatectomy (RARP) for prostate cancer is increasing. Structured surgical training and objective assessment are critical for outcomes.

OBJECTIVE: To develop and validate a modular training and assessment pathway via Healthcare Failure Mode and Effect Analysis (HFMEA) for trainees undertaking RARP and evaluate learning curves (LCs) for procedural steps.

DESIGN, SETTING, AND PARTICIPANTS: This multi-institutional (Europe, Australia, and United States) observational prospective study used HFMEA to identify the high-risk steps of RARP. A specialist focus group enabled validation. Fifteen trainees who underwent European Association of Urology robotic surgery curriculum training performed RARP and were assessed by mentors using the tool developed. Results produced LCs for each step. A plateau above score 4 indicated competence.

OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: We used a modular training and assessment tool (RARP Assessment Score) to evaluate technical skills. LCs were constructed. Multivariable Kruskal-Wallis, Mann-Whitney U, and kappa coefficient analyses were used.

RESULTS AND LIMITATIONS: Five surgeons were observed for 42 console hours to map steps of RARP. HFMEA identified 84 failure modes and 46 potential causes with a hazard score >8. Content validation created the RARP Assessment Score: 17 stages and 41 steps. The RARP Assessment Score was acceptable (56.67%), feasible (96.67%), and had educational impact (100%). Fifteen robotic surgery trainees were assessed for 8 mo. In 426 RARP cases (range: 4-79), all procedural steps were attempted by trainees. Trainees were assessed with the RARP Assessment Score by their expert mentors, and LCs for individual steps were plotted. LCs demonstrated plateaus for anterior bladder neck transection (16 cases), posterior bladder neck transection (18 cases), posterior dissection (9 cases), dissection of prostatic pedicle and seminal vesicles (15 cases), and anastomosis (17 cases). Other steps did not plateau during data collection.

CONCLUSIONS: The RARP Assessment Score based on HFMEA methodology identified critical steps for focused RARP training and assessed surgeons. LCs demonstrate the experience necessary to reach a level of competence in technical skills to protect patients.

PATIENT SUMMARY: We developed a safety and assessment tool to gauge the technical skills of surgeons performing robot-assisted radical prostatectomy. Improvement was monitored, and measures of progress can be used in future to guide mentors when training surgeons to operate safely.

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Associations of demographic and behavioural factors with glycaemic control in young adults with type 1 diabetes mellitus.

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BACKGROUND: Despite recognised benefits of optimal glycaemic control in patients with type 1 diabetes mellitus (T1DM), good control is still difficult to achieve, particularly for adolescents and young adults. Recognition of factors that may assist early optimisation of glycaemic control is therefore important.

AIMS: We explored associations of demographic, social and behavioural factors with glycosylated haemoglobin (HbA1c) levels in participants with T1DM aged 18-25 years.

METHODS: A cross-sectional analysis was performed on young adults attending a dedicated multidisciplinary clinic at Fremantle Hospital, Western Australia from January to August 2014.

RESULTS: Data from 93 participants were analysed. Mean age was 21.4 +/- 2.3 years, and 39.8% of the cohort were female. Longer duration of diabetes was associated with higher HbA1c (r=0.25, P=0.04). Men had lower HbA1c than women (8.2 +/- 1.6 vs 9.2 +/- 2.0%, P=0.01). Increased frequency of clinic attendance was associated with lower HbA1c (r=-0.27, P=0.02). Those engaged in work or study had better HbA1c compared with those who were not (8.9 +/- 2.1 vs 10.5 +/- 2.1%, P=0.03). Socioeconomic disadvantage, risk-taking behaviour, insulin pump use and distance travelled to clinic were not associated with differences in HbA1c.

CONCLUSION: In young adults with T1DM, geographical separation, socioeconomic disadvantage and risk-taking behaviours did not influence glycaemic control. Longer duration of diabetes identifies young adults at higher risk of poor control, while attendance at a multidisciplinary clinic and engagement in work or study was associated with better glycaemic control. Additional studies are warranted to clarify the role of behavioural interventions to improve diabetes management in young adults.

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Epidemiological and Mendelian Randomization Studies of Dihydrotestosterone and Estradiol and Leukocyte Telomere Length in Men.

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CONTEXT: Advancing age is accompanied by an accumulation of ill health and shortening of chromosomal telomeres signifying biological aging. T is metabolized to DHT by 5alpha-reductase (SRD5A2) and to estradiol (E2) by aromatase (CYP19A1). Telomerase preserves telomeres, and T and E2 regulate telomerase expression and activity in vitro.

OBJECTIVE: The objective of the study was to establish whether circulating T or its metabolites, DHT or E2, and single-nucleotide polymorphisms in SRD5A2 or CYP19A1 associate with leucocyte telomere length (LTL) in men.

PARTICIPANTS AND METHODS: Early-morning serum T, DHT, and E2 were assayed using mass spectrometry, and SRD5A2 and CYP19A1 single-nucleotide polymorphisms and LTL analyzed by PCR in 980 men from the Western Australian Busselton Health Survey who participated in the study. LTL was expressed as the T/S ratio.

RESULTS: Men were aged (mean +/- SD) 53.7 +/- 15.6 years. LTL decreased linearly with age, from the T/S ratio of 1.89 +/- 0.41 at younger than 30 years to 1.50 +/- 0.49 at 70 to younger than 80 years (r = -0.225, P < .0001). After adjustment for age, DHT and E2 were positively correlated with LTL (DHT, r = 0.069, P = .030; E2, r = 0.068, P = .034). The SRD5A2 rs9282858 polymorphism was associated with serum DHT but not with LTL. Three dominant alleles of CYP19A1 were each associated with lower serum E2 and shorter LTL: rs2899470 T (E2, 59.3 vs 68.6 pmol/L, P < .0001; T/S ratio, 1.54 vs 1.62, P = .045), rs10046 C (60.5 vs 68.1 pmol/L, P = .0005, 1.54 vs 1.62, P = .035), and rs700518 A (59.9 vs 68.9 pmol/L, P < .0001, 1.54 vs 1.63, P = .020). A single-copy haplotype C/T/I/A/T rs10046/rs2899470/rs11575899/rs700518/rs17703883 (52% prevalence) was associated with both lower E2 and shorter LTL.

CONCLUSIONS: In men, serum DHT and E2 correlate with LTL independently of age. Aromatase gene polymorphisms include three dominant alleles that are associated with both lower serum E2 and shorter LTL. E2 influences telomere length in vivo, thus warranting further studies to examine whether hormonal interventions might slow biological aging in men.

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En Bloc Resection of Desmoplastic Neurotropic Melanoma with Perineural Invasion of the Intracranial Trigeminal and Intraparotid Facial Nerve: Case Report and Review of the Literature.
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Background Desmoplastic neurotropic melanoma (DNM) is a rare, highly malignant, and locally invasive form of cutaneous melanoma with a tendency for perineural invasion (PNI). Methods We report a case of a 61-year-old man presenting with right-sided trigeminal neuralgia and progressive facial paresis due to the PNI of the intracranial trigeminal nerve and the intraparotid facial nerve from DNM. We also present a review of the literature with six cases of DNM with PNI of the intracranial trigeminal nerve identified. Results The combined transtemporal-infratemporal fossa approach was performed to achieve total en bloc resection of the tumor mass followed by postoperative radiotherapy (PORT). After 24 months of follow-up, the patient remains disease free with no signs of recurrence on magnetic resonance imaging. Conclusion We recommend the en bloc resection of the tumor mass followed by PORT for the management of DNM with PNI. A high index of suspicion for PNI as a cause of cranial neuropathies is essential for the early detection and treatment of patients with known melanoma.

Modeling anxiety in Parkinson's disease.

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BACKGROUND: The aim of this work was to construct a model for anxiety in PD and compare the relative contributions of PD-specific and -nonspecific general population risk factors for anxiety in this model.

METHODS: Structural equation modeling of associations of risk factors with the anxiety outcome using a cross-sectional data set of 342 patients with PD were used.

RESULTS: A model with acceptable to good fit was generated that explained 65% of the variance in anxiety scores. A previous history of depression and the severity of the depressive symptoms scored on the Hamilton Depression Rating Scale were the only nonspecific variables with a direct effect on anxiety. The presence of motor fluctuations and disease-related decline in activities of daily living were PD-specific markers of anxiety. Nonspecific risk factors had a greater influence in the model than PD-specific risk factors. Standardized regression coefficients suggested that the Hamilton Depression Rating Scale score was the most important contributor to the variation in anxiety. A post-hoc analysis showed that the effects of the following variables on anxiety levels were fully mediated by depression: sex; family history of depression; previous history of anxiety; cognitive status; difficulties in non-disease-specific activities of daily living; and severity of motor signs.

CONCLUSION: In this cross-sectional study, we showed that nonspecific general population risk factors are more important markers for anxiety than PD-specific risk factors. Depression was the most prominent marker. PD-specific markers for anxiety appear to be more situational and related to off periods and disease-specific disturbances of activities of daily living.

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AIM: The Fish oils and Aspirin in Vascular access OUtcomes in REnal Disease (FAVOURED) trial investigated whether 3 months of omega-3 polyunsaturated fatty acids, either alone or in combination with aspirin, will effectively reduce primary access failure of de novo arteriovenous fistulae. This report presents the baseline characteristics of all study participants, examines whether study protocol amendments successfully increased recruitment of a broader and more representative haemodialysis cohort, including patients already receiving aspirin, and contrasts Malaysian participants with those from Australia, New Zealand and the United Kingdom (UK).
METHOD: This international, randomized, double-blind, placebo-controlled trial included patients older than 19 years with stage 4 or 5 chronic kidney disease currently receiving, or planned within 12 months to receive haemodialysis.
RESULTS: Participants (n=568) were overweight (28.6+/-7.3kg/m(2)), relatively young (54.8+/-14.3 years), and predominantly male (63%) with a high prevalence of diabetes mellitus (46%) but low rate of ischaemic heart disease (8%). Sixty one percent were planned for lower arm arteriovenous fistula creation. Malaysian participants (n=156) were younger (51.8+/-13.6 years vs 57.1+/-14.2 years, P<0.001) with a higher prevalence of diabetes mellitus (65% vs 43%, P<0.001), but less ischaemic heart disease (5% vs 14%, P<0.01) compared with the combined Australian, New Zealand and UK cohort (n=228). Protocol modifications allowing for inclusion of patients receiving aspirin increased the prevalence of co-morbidities compared with the original cohort.
CONCLUSIONS: The FAVOURED study participants, while mostly similar to patients in contemporary national registry reports and comparable recent clinical trials, were on average younger and had less ischaemic heart disease. These differences were reduced as a consequence of including patients already receiving aspirin.
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Impact of a Patient Blood Management Program and an Outpatient Anemia Management Protocol on Red
Cell Transfusions in Oncology Inpatients and Outpatients.
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BACKGROUND: Patient blood management (PBM) programs are associated with reduced transfusion usage, reduced hospital costs, and improved patient outcomes. The application of PBM principles in patients with malignant disease might achieve similar results. However, this population presents unique challenges. The aim of the present study was to investigate the impact of a PBM program on blood usage and patient outcomes in cancer patients, particularly in the setting of restricted use of erythropoiesis-stimulating agents (ESAs).

MATERIALS AND METHODS: A retrospective observational study was performed of patients admitted with a primary diagnosis of malignancy treated at Eastern Maine Medical Center as inpatients or outpatients, or both, from January 2008 through July 2013.

RESULTS: The proportion of inpatients and outpatients receiving ESAs decreased from 2.9% in 2008 to 1.1% in 2013 (p < .001). During the same period, an increase occurred in the mean dose of intravenous (IV) iron from 447 mg (95% confidence interval [CI], 337-556) to 588 mg (95% CI, 458-718). The mean red blood cell (RBC) units transfused per inpatient and outpatient episode decreased from 0.067 to 0.038 unit (p < .001). In inpatients, significant increases occurred in the proportion of single-unit RBC transfusions (p < .001) and patients infused with IV iron (p = .02), and significant decreases in the mean pretransfusion hemoglobin (p = .02) and RBC transfusion rate (p = .04). In-hospital mortality and length of stay did not change significantly during this period.

CONCLUSION: Despite the decreased use of ESA therapy, the implementation of a PBM program and outpatient anemia management protocol in cancer patients at our medical center was associated with significant reductions in RBC usage.


Successful Treatment of Congenital Erythroleukemia With Low-Dose Cytosine Arabinoside.
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BACKGROUND: There is a paucity of data on mortality and causes of death (CoDs) in patients with sporadic inclusion body myositis (sIBM), a rare, progressive, degenerative, inflammatory myopathy that typically affects those aged over 50 years.

OBJECTIVE: Based on patient records and expertise of clinical specialists, this study used questionnaires to evaluate physicians' views on clinical characteristics of sIBM that may impact on premature mortality and CoDs in these patients.

METHODS: Thirteen physicians from seven countries completed two questionnaires online between December 20, 2012 and January 15, 2013. Responses to the first questionnaire were collated and presented in the second questionnaire to seek elaboration and identify consensus.

RESULTS: All 13 physicians completed both questionnaires, providing responses based on 585 living and 149 deceased patients under their care. Patients were reported to have experienced dysphagia (60.2%) and injurious falls (44.3%) during their disease. Over half of physicians reported that a subset of their patients with sIBM had a shortened lifespan (8/13), and agreed that bulbar dysfunction/dysphagia/oropharyngeal involvement (12/13), early-onset disease (8/13), severe symptoms (8/13), and falls (7/13) impacted lifespan. Factors related to sIBM were reported as CoDs in 40% of deceased patients. Oropharyngeal muscle dysfunction was ranked as the leading feature of sIBM that could contribute to death. The risk of premature mortality was higher than the age-matched comparison population.

CONCLUSIONS: In the absence of data from traditional sources, this study suggests that features of sIBM may contribute to premature mortality and may be used to inform future studies.

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Genomic analyses identify molecular subtypes of pancreatic cancer.


Genomic analyses identify molecular subtypes of pancreatic cancer.


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Integrated genomic analysis of 456 pancreatic ductal adenocarcinomas identified 32 recurrently mutated genes that aggregate into 10 pathways: KRAS, TGF-beta, WNT, NOTCH, ROBO/SLIT signalling, G1/S transition, SWI-SNF, chromatin modification, DNA repair and RNA processing. Expression analysis defined 4 subtypes: (1) squamous; (2) pancreatic progenitor; (3) immunogenic; and (4) aberrantly differentiated endocrine exocrine (ADEX) that correlate with histopathological characteristics. Squamous tumours are enriched for TP53 and KDM6A mutations, upregulation of the TP63N transcriptional network, hypermethylation of pancreatic endodermal cell-fate determining genes and have a poor prognosis. Pancreatic progenitor tumours preferentially express genes involved in early pancreatic development (FOXA2/3, PDX1 and MNX1). ADEX tumours displayed upregulation of genes that regulate networks involved in KRAS activation, exocrine (NR5A2 and RBPJL), and endocrine differentiation (NEUROD1 and NKX2-2). Immunogenic tumours contained upregulated immune networks including pathways involved in acquired immune suppression. These data infer differences in the molecular evolution of pancreatic cancer subtypes and identify opportunities for therapeutic development.

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n-3 Fatty Acid Supplementation and Leukocyte Telomere Length in Patients with Chronic Kidney Disease.

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DNA telomere shortening associates with the age-related increase cardiovascular disease (CVD) risk. Reducing oxidative stress, could modify telomere erosion during cell replication, and CVD risk in patients with chronic kidney disease (CKD). The effect of n-3 fatty acids and coenzyme Q10 (CoQ) on telomere length was studied in a double-blind placebo-controlled trial in CKD. Eighty-five CKD patients were randomized to: n-3 fatty acids (4 g); CoQ (200 mg); both supplements; or control (4 g olive oil), daily for 8 weeks. Telomere length was measured in neutrophils and peripheral blood mononuclear cells (PBMC) at baseline and 8 weeks, with and without correction for cell counts. Main and interactive effects of n-3 fatty acids and CoQ on telomere length were assessed adjusting for baseline values. F2-isoprostanes were measured as markers of oxidative stress. There was no effect of n-3 fatty acids or CoQ on peripheral blood mononuclear cell (PBMC) telomere length. However, telomere length corrected for neutrophil count was increased after n-3 fatty acids (p = 0.015). Post-intervention plasma F2-isoprostanes were negative predictors of post-intervention telomere length corrected for neutrophil count (p = 0.025). The effect of n-3 fatty acids to increased telomere length corrected for neutrophil count may relate to reduced oxidative stress and increased clearance of neutrophils with shorter telomeres from the circulation. This may be a novel mechanism of modifying CVD risk in CKD patients.
CAMERA2 - combination antibiotic therapy for methicillin-resistant Staphylococcus aureus infection: study protocol for a randomised controlled trial.
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BACKGROUND: Methicillin-resistant Staphylococcus aureus (MRSA) bacteraemia is a serious infection resulting in 20-50 % 90-day mortality. The limitations of vancomycin, the current standard therapy for MRSA, make treatment difficult. The only other approved drug for treatment of MRSA bacteraemia, daptomycin, has not been shown to be superior to vancomycin. Surprisingly, there has been consistent in-vitro and in-vivo laboratory data demonstrating synergy between vancomycin or daptomycin and an anti-staphylococcal beta-lactam antibiotic. There is also growing clinical data to support such combinations, including a recent pilot randomised controlled trial (RCT) that demonstrated a trend towards a reduction in the duration of bacteraemia in patients treated with vancomycin plus flucloxacillin compared to vancomycin alone. Our aim is to determine whether the addition of an anti-staphylococcal penicillin to standard therapy results in improved clinical outcomes in MRSA bacteraemia.
METHODS/DESIGN: We will perform an open-label, parallel-group, randomised (1:1) controlled trial at 29 sites in Australia, New Zealand, Singapore, and Israel. Adults (aged 18 years or older) with MRSA grown from at least one blood culture and able to be randomised within 72 hours of the index blood culture collection will be eligible for inclusion. Participants will be randomised to vancomycin or daptomycin (standard therapy) given intravenously or to standard therapy plus 7 days of an anti-staphylococcal beta-lactam (flucloxacillin, cloxacillin, or cefazolin). The primary endpoint will be a composite outcome at 90 days of (1) all-cause mortality, (2) persistent bacteraemia at day 5 or...
beyond, (3) microbiological relapse, or (4) microbiological treatment failure. The recruitment target of 440 patients is based on an expected failure rate for the primary outcome of 30% in the control arm and the ability to detect a clinically meaningful absolute decrease of 12.5%, with a two-sided alpha of 0.05, a power of 80%, and assuming 10% of patients will not be evaluable for the primary endpoint.

DISCUSSION: Key potential advantages of adding anti-staphylococcal beta-lactams to standard therapy for MRSA bacteremia include their safety profile, low cost, and wide availability.


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**The hundred most cited publications in orthopaedic hip research - a bibliometric analysis.**

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BACKGROUND: The aim of this study was to identify the 100 most cited classics in the field of hip research analysing their qualities and characteristics.

METHODS: Hip joint related articles were identified and the hundred most cited selected for subsequent analysis of citation count, current citation rate, citation density (citations/article age), authorship, geographic origin institution, and level of evidence (LOE).

RESULTS: In a total of 121 journals, 1,311,851 articles were published between 1945 and 2013, of which 1,287 (0.1%) possessed 250 citations or more. Total citations per article for the 100 most-cited ranged from 290 to 3,144 citations. The most common areas of research were degenerative disease and arthroplasty, followed by hip preserving surgery for which the leading authors were William H. Harris and Reinhold Ganz respectively. All articles were published in 8 journals and originated from 9 countries. 10 institutes published 48/100 of the articles. There was a significant negative correlation between both citation rate, citation density and article age. Total citation count was highest for articles published in the decade of 1970. Although 5% (2,103 articles) of hip literature comprised randomised trials (RCTs), only 1 (1%) of the citation classics was an RCT.

CONCLUSIONS: The study provides intellectual milestones in hip research, reflecting on the qualities and characteristics of the research. Degenerative hip disease and arthroplasty research take up the greatest proportion of citations, followed by hip preserving research. LOE was low and there was only one RCT amongst the classics, emphasising that high LOE is not a prerequisite for a high citation count.

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**Does the presence of an after hours physiotherapy service affect frequency of respiratory intervention for**
intubated adults with community acquired pneumonia? A national survey.
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Introduction: Community acquired pneumonia (CAP) is a common reason for ICU admission for intubation.
Physiotherapy practice for intubated patients with CAP is observed to be variable regarding the type, duration and
frequency of intervention delivered to facilitate sputum clearance, gas exchange and functional recovery. The
physiotherapy literature regarding the management of intubated, critically ill patients with CAP is scant and therefore
little guidance exists for clinical practice. Study Objectives: The aim of this study was to explore factors which
influenced the delivery of respiratory physiotherapy intervention for critically ill patients with CAP during the acute
intubated period. Methods: A cross-sectional, mixed methods online survey of 104 senior ICU physiotherapists from
Australian public and private hospitals was developed and piloted to explore current clinical practice and clinical
reasoning for intubated patients with CAP. Quantitative and qualitative data were collected using categorical and
Likert scale responses. Open-ended responses were also collected for each item. Data were collected regarding ICU
physiotherapy service provision and the presence and nature of an afterhours (AH) physiotherapy service. Results:
Response rate was 72% (n=75). Respiratory physiotherapy intervention was provided once or twice a day (88% of
respondents). Intervention frequency was determined by treatment response (100% of respondents), sputum volume
(93% of respondents), cough effectiveness (92% of respondents) and sputum viscosity (90% of respondents). An AH
physiotherapy service was not universally available (54% respondents), with onsite AH physiotherapist presence
limited (22% respondents). A combination of onsite and on-call physiotherapy was provided in 19% of cases.
Treatment response (83% of respondents) was the biggest factor including patients for AH intervention. Conclusion:
Respiratory physiotherapy intervention is not commonly provided AH for intubated patients with CAP, however the
majority of facilities included did not provide an AH service. The optimal intervention dosage and frequency
impacting patient outcomes is unknown.

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Donor-recipient ABO compatibility independently influences survival after allogeneic HSCT: Outcomes of 281
patients from a single centre.
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We have previously shown that ABO compatibility influences red cell and platelet transfusion burden during the 12
months following haematopoietic stem cell transplantation (HSCT). We investigated whether ABO compatibility also
influences transplant outcomes in 281 patients undergoing first allogeneic HSCT at our centre between January 2004
and January 2015. Grafts with minor and bidirectional ABO incompatibility were plasma-depleted prior to infusion.
Patient characteristics are described in the Table. Median age at transplant was 43 years (range 17 - 67) and median
follow-up was 40 months (range 2 - 10). Overall survival (OS) at 4 years was 46 +/- 3% and was inferior for recipients
of minor ABO incompatible donors (Figure). Refined DRI was also associated with OS (34 +/- 5% for high/very high
compared to 54 +/- 5% for low/intermediate rDRI, p < 0.001), while recipient age, donor type (related vs unrelated),
CMV match, stem cell source and conditioning regimen intensity were not. On multivariate analysis, both minor ABO
incompatibility [hazard ratio (HR) 1.77, 95% confidence interval (CI) 0.14 - 2.76, p = 0.012] and high/very high rDRI
(HR 1.79, 95% CI 1.22 - 2.63, p = 0.003) were independently associated with OS. Differences in overall survival were
reflected in higher risk of relapse for recipients of minor ABO compatible donors, adjusted forrDRI (HR 2.00, 95% CI
1.28 - 3.54, p = 0.018). PBSC recipients were then analysed separately to investigate a possible effect of graft
processing on survival. Recipients of plasma depleted PBSC grafts had a higher risk of mortality on univariate analysis
(p = 0.038), and on multivariate analysis adjusted for rDRI (HR 1.68, 95%CI 1.09 - 2.58, p = 0.018), although not when also adjusted for ABO compatibility (HR 1.71, 95% CI 0.74 - 3.98, p = 0.212). Differences in survival and relapse according to ABO compatibility may reflect manipulation of the graft prior to infusion with subsequent effects on T-cell numbers or function. In this study population, it is difficult to differentiate the effects of graft processing from ABO compatibility as the two were closely linked. Alternatively, the presence of minor ABO mismatch may modify immune restoration in vivo and alter graft-vs-malignancy effect. These results warrant replication and further investigation to determine whether ABO incompatibility influences outcome of allogeneic HSCT and the mechanism by which this occurs. (figure present).

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Patient reported symptoms compared to documented clinician findings in the assessment of chronic graft versus host disease.
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Topic Significance & Study Purpose/Background/Rationale: Comprehensive assessment of chronic graft versus host disease (cGVHD) is critical to patient care after allogeneic haematopoietic progenitor cell transplantation (HPCT). To improve cGVHD assessment, our centre recently developed a GVHD screening questionnaire based on published recommendations (Carpenter et al, Blood, 2011). Methods, Intervention, & Analysis: We compared questionnaire responses with findings documented in the medical record (MR) to assess the utility of the questionnaire as well as the adequacy of cGVHD assessment and documentation in the MR. From May to September 2015, 36 allogeneic HPCT recipients completed the questionnaire once each (median 2.5 years post-transplant, range 6 months - 11 years). Findings & Interpretation: Dry eyes (44%), dry mouth (38%), alopecia (36%), muscle cramps (36%), respiratory symptoms (dyspnoea, cough or wheeze, 31%) and dry skin (30%) were commonly reported by questionnaire. Of 14 (39%) respondents who were sexually active, 7 (50%) had genital symptoms during sexual activity. An assessment of cGVHD was documented in the MR in most (86%) cases. The most common areas assessed were skin, mouth and eyes. Questionnaire responses correlated well with the MR in 7 cases (19%), usually in patients with no cGVHD. Of the remainder, symptoms reported by questionnaire correlated partly (10 cases, 28%) or poorly (19 cases, 47%) with the MR. Of the group that correlated poorly, 52% were on immunosuppression. Disparity between questionnaire and MR was particularly evident in patients reporting musculoskeletal symptoms (incidence 36% versus 11%) and sexual symptoms (50% versus 21%). In 9 cases, symptoms reported by questionnaire were attributed to a cause other than cGVHD in the MR. In one case, no symptoms were reported by questionnaire despite the presence of oral cGVHD documented in the MR. Discussion & Implications: The screening questionnaire was useful for identifying cGVHD symptoms in almost all cases in which it was subsequently documented in the MR. Furthermore, patients usually reported more symptoms than were recorded during the clinical encounter. While some reported symptoms were likely not due to cGVHD, it appears that musculoskeletal, respiratory and sexual symptoms of cGVHD may be underestimated in the clinic. These systems will be prioritised in ongoing attempts to improve assessment and documentation of cGVHD at our centre.

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"Slow and steady" cyclosporine initiation is not associated with increased risk of acute graft versus host disease-12 years' experience from a single centre.
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Introduction: There is much variation in clinical practice and little literature regarding the optimal dose and timing of
cyclosporine (CsA) initiation for acute graft versus host disease (aGHVD) prophylaxis. Material (or patients) and methods: To guide the development of consensus guidelines for CsA initiation at our centre, we reviewed information from consecutive recipients of allogeneic HSCT at our centre who received methotrexate and CsA GVHD prophylaxis and achieved neutrophil recovery between January 2004 and August 2015. Methotrexate was given at 15 mg/m² on day +1 and 10 mg/m² on day +3, +6 and +11. CsA was commenced at 1.5 mg/kg twice daily as an IV infusion and titrated to achieve a target trough level of 200-300 mug/L, with routine levels taken every Monday, Wednesday and Friday. Results: A total of 207 recipients of myeloablative (n = 171) and reduced intensity (n = 36) allogeneic HSCT were included. CsA was commenced on transplant day -1 (n = 93) or earlier (n = 109, 5 cases missing data) depending on physician preference. Antifungal prophylaxis was with fluconazole alone (n = 171) or another agent (n = 30, 6 cases missing data). Trough CsA levels are summarised in the Table. CsA levels (<100 mug/L) were achieved in 12% of patients by day +3 and 42% of patients by day +5, while 26% had low CsA levels (<100 mug/L) by day +3 and 5% by day +5. The type of antifungal prophylaxis used did not correlate with the achievement of target CsA levels at any of the time points measured (Fisher’s exact test). The cumulative incidence of grade II-IV aGVHD was 56% by day 180 (95% confidence interval (CI) 49-62%). Neither the timing of CsA initiation (day -1 versus earlier) nor the CsA level by day +3 or day +5, nor time to achieve target CsA levels were associated with the risk of aGVHD (Cox regression). Interestingly, patients with low (<100 mug/L) CsA levels by day +3 had a lower risk of grade II-IV aGVHD (HR 0.60, 95% CI 0.38-0.95, P = 0.029). On multivariate analysis adjusting for donor type (related versus unrelated) and conditioning regimen intensity, early CsA level <100 mug/L was independently associated with a lower risk of aGVHD (HR 0.61, 95% CI 0.38-0.97, P = 0.035). Conclusion: At a uniform starting dose of 1.5 mg/kg twice daily IV, target CsA levels were only reached after a median 8 days of therapy. However, earlier achievement of target CsA levels did not infer a lower risk of aGVHD. Rather, patients with low CsA levels very early after transplant had a lower risk of aGVHD, independent of conventional GVHD risk factors. While this observation requires replication and further investigation, our analysis provides no rationale for more intensive initiation of CsA after allogeneic HSCT. (Table Presented).


Androgens and cardiovascular risk.

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Ageing is accompanied by a reduction in circulating testosterone (T), and progressive accumulation of medical morbidities. There is ongoing debate as to whether low T contributes to ill-health, particularly to increased risk of cardiovascular disease, as opposed to being a biomarker for its presence. Despite this uncertainty, prescriptions for T are rising on a background of concern over potential adverse effects. Observational studies show lower risk of cardiovascular events in older men with higher T concentrations. In longitudinal analyses from the Western Australian Health In Men Study (HIMS) we have shown that optimal circulating T predicts survival in older men, and that higher T concentrations are independently associated with reduced incidence of stroke. Furthermore, in HIMS men with higher concentrations of the more potent androgen dihydrotestosterone (DHT) experienced lower mortality from ischaemic heart disease. Concern has been raised following the Testosterone in Older Men with Mobility Limitations (TOM) trial, which was terminated due to excess cardiovascular adverse events reported in the T treatment arm. However, no such signal was seen in a comparable study of T in intermediate-frail and frail older men. Of note, these and other randomised controlled trials (RCTs) of T supplementation have been underpowered for the outcome of cardiovascular events. Recent metaanalyses generally have not shown an excess of cardiovascular adverse events to be associated with T therapy. Retrospective studies of prescription databases have produced controversial and conflicting results. Thus additional RCTs are required to clarify the role of T supplementation to modulate cardiovascular risk in older men in the absence of pituitary or testicular disease. T replacement therapy should be considered in androgen deficient men, with evaluation of potential benefits and risks.

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**Differential associations of ferritin and 25-hydroxyvitamin D with fasting glucose and diabetes risk in community dwelling older men.**

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Aims: High ferritin and low vitamin D concentrations are associated with an increased incidence and prevalence of diabetes mellitus but the strength and nature of the association in older adults remains unclear. We examined the roles of ferritin and 25-hydroxyvitamin D as independent predictors of glycaemia in older men. Methods:
Cross-sectional analysis of a population-based cohort study of 4248 community dwelling older men aged 70-89 years in Perth, Western Australia. Plasma ferritin, 25-hydroxyvitamin D and glucose were assayed. Diabetes was ascertained from self-report, medication usage and fasting glucose concentrations. Multivariate analyses adjusted for age, smoking, BMI, waist: hip ratio, physical activity, hypertension, lipids, creatinine, CRP and medical comorbidity. Results: There were 588 men with diabetes (13.9%). Ferritin was associated with fasting glucose in non-diabetic men (0.05 mmol/L per 1 SD increase in ferritin, p = 0.01). 25-hydroxyvitamin D was inversely associated with fasting glucose in non-diabetic men (-0.08 mmol/L per 1 SD, p < 0.001). Ferritin was not associated with prevalent diabetes (highest vs. lowest quartile; > 225 vs < 65.5 ng/mL: adjusted odds ratio [OR] 0.91, 95% confidence interval [CI], 0.70-1.18, p = 0.47). Higher vitamin D was associated with a decreased odds of prevalent diabetes (highest vs lowest quartile; > 81.6 nmol/L vs < 52.9 nmol/L: adjusted OR = 0.58, 95% CI = 0.44-0.75, p < 0.001). There was no interaction between ferritin and vitamin D on diabetes risk. The results were similar after exclusion of diabetic men using insulin. Conclusions: In older men, increased ferritin is associated with increased plasma fasting glucose concentrations; however it is not a predictor of overall diabetes risk. Higher 25-hydroxyvitamin D concentrations are independently associated with lower fasting glucose levels and reduced risk of diabetes. In older adults manipulation of plasma ferritin may not alter diabetes risk, whereas interventional studies are required to determine whether vitamin D supplementation reduce the incidence of diabetes as vitamin D levels are associated with other health indices.

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Introduction and aims: Undercarboxylated osteocalcin (ucOC) modulates insulin secretion and sensitivity in mice, and higher ucOC is associated with lower diabetes risk in men (1). Diabetes is associated with cardiovascular risk, but the influence of ucOC on incidence of cardiovascular events is unclear. We examined associations of ucOC and other bone turnover markers with incidence of myocardial infarction (MI) and stroke in older men. Participants and methods: This was a longitudinal study of communitydwelling men aged 70-89 years resident in Perth, Western Australia. 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 immunoassay, and ucOC by hydroxyapatite binding. The ratio ucOC/TOC was calculated. Hospital admissions and deaths from myocardial infarction (MI) and stroke were ascertained. Results: There were 3384 men followed for 7.0 years during which 293 experienced an MI, 251 stroke and 2840 neither. In multivariate analyses, higher ratio of ucOC/TOC (expressed as %) was associated with lower incidence of MI (quartiles Q2-4, > 49% vs Q1, < 49%, hazard ratio [HR] = 0.70, 95% confidence interval [CI] = 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 mug/L vs Q1, < 28.2 mug/L HR = 1.45, 95% CI = 1.06-1.97), but not of stroke (0.94, 0.70-1.26). CTX was not associated with incident MI or stroke. These results were unchanged following exclusion of men experiencing MI within the first year of follow-up. Conclusions: A reduced proportion of ucOC relative to TOC, or higher P1NP, is 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.

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Response to Kottek and Kilpatrick, 'Estimating Occupational Exposure to Asbestos in Australia'.


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Modulation of Kinin B2 Receptor Signaling Controls Aortic Dilatation and Rupture in the Angiotensin II-Infused Apolipoprotein E-Deficient Mouse.

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OBJECTIVE: Abdominal aortic aneurysm (AAA) is an important cause of mortality in older adults. Activity of the local kallikrein-kinin system may be important in cardiovascular disease. The effect of kinin B2 receptor (B2R) agonist and antagonist peptides on experimental AAA was investigated.

APPROACH AND RESULTS: AAA was induced in apolipoprotein E-deficient mice via infusion of angiotensin II (1.0 μg/kg per minute SC). B2R agonists or antagonists were given via injection (2 mg/kg IP) every other day. The B2R agonist (B9772) promoted aortic rupture in response to angiotensin II associated with an increase in neutrophil infiltration of the aorta in comparison to controls. Mice receiving a B2R/kinin B1 receptor antagonist (B9430) were relatively protected from aortic rupture. Neutrophil depletion abrogated the ability of the B2R agonist to promote aortic rupture. Progression of angiotensin II-induced aortic dilatation was inhibited in mice receiving a B2R antagonist (B9330). Secretion of metalloproteinase-2 and -9, osteoprotegerin, and osteopontin by human AAA explant was reduced in the presence of the B2R antagonist (B9330). B2R agonist and antagonist peptides enhanced and inhibited, respectively, angiotensin II-induced neutrophil activation and aortic smooth muscle cell inflammatory phenotype. The B2R antagonist (B9330; 5 μg) delivered directly to the aortic wall 1 week post-AAA induction with calcium phosphate in a rat model reduced aneurysm growth associated with downregulation of aortic metalloproteinase-9.

CONCLUSIONS: B2R signaling promotes aortic rupture within a mouse model associated with the ability to stimulate inflammatory phenotypes of neutrophils and vascular smooth muscle cells. B2R antagonism could be a potential therapy for AAA.
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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 <80nmol/L (P<0.05) and >80nmol/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.
and morphologically variable entity which accounts for approximately 12% of cases of Sweet’s Syndrome. We present two similar and very unusual clinical presentations of localised drug-induced Sweet’s Syndrome following subcutaneous azacitidine injection in two patients - one with myelodysplastic syndrome and one with acute erythroid leukaemia. Clinically the lesions were dusky circular purpuric plaques composed of numerous concentric rings, suggesting Sweet’s Syndrome lesions with subcutaneous red cell extravasation or vascular dilation. Histopathology in both cases demonstrated a dense neutrophilic infiltrate consistent with Sweet’s Syndrome. Bacterial and fungal cultures were negative. Both patients demonstrated excellent response to oral prednisolone and their condition rapidly resolved leaving only residual bruising within 1 week. There are a handful of reported cases in the literature of azacitidine induced Sweet’s Syndrome. Unless a careful history is taken, a drug induced aetiology may not be recognised in these patients as haematological malignancy is also an independent cause for Sweet’s. The cases we present are of particular interest given their unique morphology.

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**A 62-year-old man with papular granulomatous dermatitis of uncertain aetiology mimicking leprosy.**
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We present the case of a 62-year-old man of Burmese descent who presented with a 3 month history of multiple skin coloured papules on his limbs and trunk, which were itchy at times. There were no hypopigmented patches, although there was a thickened ulnar nerve. The only significant medical history was a Burkholderia pseudomallei infection of the prostate 2 years prior, which had been treated successfully. Initial skin biopsies showed superficial perivascular and periadnexal granulomatous dermatitis. Stains for acid fast bacilli and M.leprae were negative. Extensive investigation did not show any definite evidence of sarcoidosis, tuberculosis or any other cause of granulomatous dermatitis. However, as the granulomas were suggestive of tuberculoid leprosy he was commenced on treatment, with no improvement in his condition. Subsequent skin biopsies also failed to show any evidence of an infective agent, and the working diagnosis was changed to a probable hypersensitivity reaction to Burkholderia pseudomallei. However electron microscopy of tissue specimens did not show any definite evidence of Burkholderia and whole body imaging did not show any foci of infection. Based on the working diagnosis of immune mediated cutaneous granulomas he was commenced on oral prednisolone 25 mg daily, with regression of the lesions. Oral azathioprine and UV phototherapy have been introduced, with successful slow weaning of the oral prednisolone. This case is presented to highlight the difficulty in identifying the cause of granulomas in some cases of granulomatous dermatitis. We propose an algorithm for investigating cases of cutaneous granulomas of uncertain aetiology.

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**Calcinosis cutis, symptom or disease? A unique case of calcinosis universalis.**
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Calcinosis cutis is a rare condition involving the cutaneous deposition of insoluble calcium and phosphate salts. Historically, it has been classified into four major subsets based on the suspect aetiology of cutaneous calcification: dystrophic, metastatic, iatrogenic and idiopathic. We report a case of a 51-year-old male, who presented with a 10 year history of small, hard nodules in the buttocks and fingertips. There was no preceding history of dermatomyositis or any other autoimmune disease. He had normal biochemical parameters with a normal serum calcium level (2.41 mmol/L) and a normal phosphate level (1.38 mmol/L). His renal function, vitamin D level, thyroid and parathyroid function were found to be normal. Histopathology of multiple lesions confirmed the presence of
widespread focal areas of calcification within the dermis. On the basis of clinical, laboratory and histological findings, the patient was diagnosed with calcinosis universalis in the absence of a known systemic metabolic disorder. On several occasions limited surgical excisions of buttock lumps of calcinosis were performed, but the disease has been progressing slowly. He is currently on diltiazem with out any significant improvement. This case is presented to discuss the complex processes of cutaneous calcium deposition and the challenges a clinician may face in identifying the cause of disease. We propose a clinical algorithm to assist in the assessment and management of a patient with calcified cutaneous nodules.

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**Escherichia coli cellulitis and myonecrosis in a patient with Hepatitis B.**

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Cellulitis is an acute spreading infection of the skin and subcutaneous tissue. It usually occurs secondary to a cutaneous portal of entry, with the commonest organisms being Streptococcus pyogenes and Staphylococcus aureus. Cellulitis due to Escherichia coli is rare and is typically only seen in immunocompromised patients, including those with cirrhosis. In these patients the cellulitis may be secondary to E.coli bacteraemia and can present with bullae, abscesses and myonecrosis. We present a case of E. coli cellulitis of the left leg with myonecrosis in a 49-year-old man who denied significant past medical history and current comorbidities. There was no history of any preceding injury to the leg. There was no icterus or other clinical evidence of liver disease. Culture from the tissue biopsy showed a growth of E. coli susceptible to Piperacillin-Tazobactam. Subsequently, further history revealed a recent diagnosis of Hepatitis B infection. Investigations did not reveal any other causes of immunosuppression. Aggressive treatment with systemic antibiotic therapy, drainage of pus, wound debridement and skin grafting resulted in improvement. This is the first reported case of E.coli cellulitis and myonecrosis associated with Hepatitis B infection, without overt cirrhosis.  
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**Clearance of an extramammary paget's disease lesion with milk weed latex (Euphorbia peplus): A case report.**

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Extramammary Paget's disease (EMPD) is a distinct, relatively rare skin neoplasm. Recurrence rates can be high, despite aggressive surgery and patients are at risk of developing invasive adenocarcinoma. <sup>1</sup> We present the case of an 85-year-old man with EMPD in the pubic and umbilical areas. The initial lesion in the pubic region was surgically excised. Screening revealed an adenocarcinoma of the ascending colon, which was surgically resected. Five months after the removal of the EMPD on the pubic region he developed a new plaque at the umbilicus. A skin biopsy of this lesion also revealed EMPD. The patient refused surgical resection therefore, was prescribed Imiquimod cream topical application. Instead, on his own accord he topically applied the latex of milkweed (Euphorbia peplus, active ingredient ingenol mebutate) from his backyard, every 2 weeks for 4 months. This application was associated with severe inflammation and vesicle formation in the treated area. On two occasions the patient used the latex of another plant, later identified as Euphorbia terracina. That too caused a similar inflammatory response. Five months after finishing the application of the milkweed latex, the lesion had clinically resolved, with some superficial scarring of the skin. There had not been any major side effects other than severe inflammation at the treated site, similar to the effects of commercially available ingenol mebutate gel. We record for the first time the clearance of an EMPD lesion with the latex of Euphorbia peplus latex. A study using ingenol mebutate for EMPD is
Painful leg ulceration in a hypertensive diabetic woman - A report of a martorell ulcer with serial photographs.

Didan A, Malhi H, et al.

Martorell ulcer is a form of lower limb ulceration, preceded by a small area of excruciating pain. It often appears as a solitary lesion on the outer aspect of the lower limb, and is primarily associated with poorly controlled hypertension and sometimes with diabetes mellitus. Treatment of the ulcer involves awareness and early correct diagnosis, adequate control of blood pressure, management of infection and wound care. We describe a 77-year-old diabetic and hypertensive woman presenting with excruciating pain on her right lower lateral leg leading to a necrotic ulcer. A differential diagnosis of calciphylaxis, pyoderma gangrenosum and atypical infections were also considered. Based on the history, clinical features, skin biopsy and the evolution of the ulcer a diagnosis of Martorell ulcer was made. Serial photographs of evolution of the lesion and eventual healing of the ulcer are presented. This case emphasizes the importance of considering Martorell ulcer in patients presenting with an ulcer on a background of poorly controlled hypertension and disproportionate excruciating pain in the ischemic area prior to ulceration.

An unusual presentation of pyoderma gangrenosum leading to circulatory shock.


Introduction: We report an atypical presentation of Pyoderma Gangrenosum (PG) in a 26-year-old Pakistani male who had a negative septic screen. The patient required ICU admission for vasopressor support. We believe the cause of circulatory shock in this patient is an overwhelming cytokine reaction secondary to extensive PG. Case description: The patient presented with multiple large ulcers, the largest being 4 cm on the central chest. He developed fevers and shock preceding his ICU admission. Microbiological specimens including blood cultures and wound swabs were negative for any growth (bacterial, fungal, TB). No infective focus could be identified for the cause of haemodynamic instability. During this admission, the patient’s condition (Figure presented) was complicated by multi-organ dysfunction and debridement was deemed necessary. Histopathology showed abundant neutrophils but could not confirm an infective process. Overall, he made an impressive recovery and serial photos show almost complete healing of all lesions following oral prednisolone. The patient had a history of ulcerative colitis and a similar presentation with facial lesions which also necessitated ICU admission 3 years prior. Discussion: A review of literature revealed one case, of a 76-year-old female with lower leg ulcers who developed circulatory shock and required amputation1. Lesions continued to appear despite antibiotics and surgical treatment. Microbial specimens were negative and she was subsequently diagnosed with PG. Interestingly, the patient rapidly recovered after steroid therapy. Our patient had an atypical but severe presentation of PG with circulatory shock. We hypothesize the haemodynamic compromise was predominantly due to a cytokine reaction secondary to PG lesions.
Necrobiotic xanthogranuloma initially presenting as urticaria.

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A 41-year-old female presented with a 2-week history of urticaria-like waxing and waning pruritic rash and swelling of face that developed overnight. There were no obvious triggers other than application of a new sunscreen the previous evening. The initial pruritus and swelling settled down with oral prednisolone and anti-histamines but she subsequently developed thick infiltrated yellowish plaques and nodules on her eyelids, lips, buccal mucosa and cheeks. She has been on fluoxetine for several years and has history of easy bruising with trauma. She also gives history of ductal carcinoma-in-situ of breast. She gives family history of coeliac disease, inflammatory bowel disease, multiple malignancies, hypothyroidism and juvenile diabetes mellitus. The differential diagnoses considered included oro-facial granulomatosis, sarcoidosis, angioedema, connective tissue diseases and necrobiotic xanthogranuloma (NXG) and she was evaluated accordingly. Histopathology showed features consistent with a diagnosis of NXG. Hematologic evaluation showed no evidence of paraproteinemia. She had an abnormal platelet aggregation in response to arachidonic acid and collagen. There were no features supporting any of the other differentials considered. The patient is on close follow-up for any evolving hematologic abnormality. We are reporting this case because of the atypical initial clinical presentation as urticaria. The patient had no paraproteinemia that is often associated with NXG. Hematologic malignancies are reported in association with NXG but the significance of a platelet aggregation abnormality and easy bruising is unclear.

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A curious case of inguinal keratotic lesions posing a diagnostic dilemma.

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A 28-year-old female presented with scaly, inflammed, fissured, hyperkeratotic, non-pruritic, erythematous plaques over her groins, inner thighs, perilabial and perianal areas of 7 months’ duration. The rash had started 1 month before delivery and continued post-partum. Her general practitioner had tried topical steroid anti-fungal combinations and flucloxacillin. She had no history of drug allergies. She had one episode of psoriasis several years back. She was otherwise well. Her baby’s birth was uneventful. Her father was diagnosed to have cyclical inguinal keratoderma with histology similar to pityriasis rubra pilaris and it responded to acitretin. The differential diagnoses considered included seborrhoeic dermatitis, fungal infections, inverse psoriasis, Hailey-Hailey disease, pemphigus vegetans, Darier’s disease, acanthosis nigricans, zinc deficiency, amino acid deficiency, necrolytic migratory erythema, contact dermatitis, congenital keratodermas, cyclical inguinal keratoderma and granular parakeratosis. The patient was investigated accordingly. The fungal and bacterial studies and relevant biochemical studies were negative. Histopathology was consistent with a diagnosis of granular parakeratosis and not supportive of any other differentials considered. The patient showed moderate response to topical steroids but the rash persisted. A therapeutic trial of Augmentin was given and the patient showed a clear and dramatic response to the drug and the rash never recurred. We are presenting this case of granular parakeratosis limited to inguinal region because of the atypical therapeutic response to amoxicillin-clavulanic acid combination (Augmentin) despite being bacterial culture negative. We further highlight the diagnostic dilemma posed by inguinal keratotic lesions and discuss the various differential diagnoses.

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Cutaneous pyogenic granuloma treated with intralesional triamcinolone injection: A case and review.
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Pyogenic granuloma is a rapidly developing, non-neoplastic vascular proliferation. It characteristically presents as a friable, verrucous polypoid tumour, with a tendency to bleed, and association with hormonal factors and minor trauma. Conventional treatment of pyogenic granuloma is with surgical techniques such curettage and cautery or imiquimod therapy. We present this case of a 58-year-old man on haemodialysis with a pyogenic granuloma over the anterior chest wall. The location of the lesion, adjacent to a Hickman line, and a palpable deeper component, proved problematic for routine surgical excision. An alternative approach was taken, and the lesion treated with intralesional steroid injection, a method infrequently described for cutaneous pyogenic granuloma. We aim to review the treatment options of pyogenic granulomas, discuss implications for surgically challenging PG lesions and present our results with intralesional triamcinolone.

Patient presentation patterns at the dermatological clinics of three major teaching hospitals in Western Australia.
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Background: Dermatological conditions comprise a significant proportion of disease burden in the community. Dermatological disease pattern at the major public hospitals are important for health care planning and dermatological training. In the past 20 years, only a few studies have been conducted to document the epidemiology of dermatological diseases in the region. Aims: To determine the disease presentation pattern at the dermatological clinics at the three major teaching hospitals of Western Australia. Methods: Over a six-week period, patients with their first presentation at the dermatological clinics in three Western Australian tertiary hospitals were recorded for basic demographic data and their presenting dermatological condition, as diagnosed by their attending physician. Results: Over the study period, 182 patients’ diagnoses were recorded. Overall, the most common condition for clinic attendance was malignant tumours(28.6%), followed by benign tumours(15.4%), solar keratosis(8.2%) and psoriasis(5.5%). Out of the malignant tumours, the most common tumour was basal cell carcinoma(14.3%) followed by squamous cell carcinoma(7.1%). Discussion: The proportions of presentations were compared to a similar prospective study performed in 1992 at the same three hospitals. Some of the differences observed included a rise in the number of malignant and benign tumour presentations, whilst inversely, a fall in the number of psoriasis and leg ulcer presentations. The possible causes for these changing trends are discussed. Conclusions: Amongst new presentations at dermatology clinics, the most commonly seen conditions are malignant skin tumours followed by benign tumours. The pattern of patient presentation can provide insight into planning and improving future dermatology services.

Making sense of acquired macular hyperpigmentation of uncertain aetiology.
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Macular pigmentation of the skin without an identifiable cause (macular pigmentation of uncertain aetiology/MPUA) is not an uncommon dilemma in clinical dermatology. Visible patches of hyperpigmentation can be distressing to the patient. It is more obvious in the Fitzpatrick skin Types III-V. Ashy dermatosis, erythema dyschromicum perstans, lichen planus pigmentosus, idiopathic eruptive macular pigmentation and Riehl’s melanosis are some terms that have been used to describe these cases. However the literature is confusing as there has not been a consensus on the use of the terms. One of the main problems is that the histopathology is rather nonspecific with dermal melanophages (give rise to the ashy grey colour) and sparse dermal lymphocytic infiltrates. Interface dermatitis is seen in some cases, but not in all. The histopathology can be indistinguishable from post inflammatory hyperpigmentation, burnt out lichen planus, graft versus host reactions, fixed drug eruptions and several other conditions. It is very important to rule out various forms of drug induced hyperpigmentations, frictional melanoses, macular amyloidosis, endocrine causes etc. in diffuse and patchy acquired pigmentation. It is best to consider various causes that can lead to macular pigmentation of uncertain aetiology(MPUA) in a rational way before labelling as ashy dermatosis, LPP, EDP, Riehl’s melanosis or IEMP. Various causes of acquired patchy pigmentation and a rational approach to diagnosing and managing these difficult cases will be discussed.

Survey of Australian dermatological postoperative patient information leaflets: Are we consistent in the guidance we provide.
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Introduction: Patient information leaflets (PIL) are commonly given to patients after skin surgery to provide guidance and reassurance once they return home. Evidence from the United Kingdom suggests that the advice provided in these PILs is highly varied. This survey aimed to evaluate the guidance specified in dermatological postoperative PILs across Australia. Method: All 40 Australian teaching dermatology departments/clinics were asked to provide their postoperative PILs on sutured wound care or excision biopsy (September - October 2015). Ten preselected parameters were evaluated for each leaflet. Results: 28/40 (70%) of departments/clinics responded, of these 11/28 (39.3%) specified that they did not use PILs. Of the 17 that provided postoperative leaflets, 6/17 (35.3%) specified a minimum dressing duration of 48 h, with an equal number stating 24 h. 12 leaflets advised regarding the time to press on a bleeding wound, with 10mins and 20mins (both 3/12) being the mode guidance. 14 leaflets advised on analgesia, with the most common suggestion advocating Paracetamol only and avoiding Aspirin (4/14, 28.6%). 11/17 (64.7%) leaflets described =2 signs of infection, 7/17 (41.2%) advised petroleum jelly application to the wound, 16/17 (94.1%) highlighted the contact for postoperative problems, 5/17 (29.4%) mentioned scarring, and 3/17 (17.6%) PILs advised against smoking. Only 8/17 (47.1%) of leaflets provided advice regarding active excise, with the most common advice being to avoid until suture removal (2/8). Conclusion: The advice provided in postoperative dermatological patient information leaflets is highly varied. Consensus guidelines would be of benefit to make advice to patients more consistent. 
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Is the four point pusher scale a reliable and valid assessment tool for measuring lateropulsion and/or pushing behaviour in adults following stroke?
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Background: Pushing behaviour (PB) is a postural control disorder observed in some patients following stroke. Two scales have been validated to assess PB: the Burke Lateropulsion Scale (BLS) and the Scale for Contraversive Pushing
(SCP). However, the BLS can take 10 minutes to administer and the SCP may not detect mild PB; factors which may compromise the uptake of these scales by clinicians. The Four Point Pusher Scale (4PPS) has been described as a brief and simple scale, however its reliability and validity have not been published. Question: Is the Four Point Pusher Scale a reliable and valid scale for measuring lateropulsion and/or pushing behaviour in adults following stroke? Methods: Patients who had experienced a stroke were invited to participate within 48 hours of admission to an inpatient rehabilitation ward. Intra-rater reliability of the 4PPS was determined by examining scores assigned to the same patient by the same physiotherapist. Inter-rater reliability of the 4PPS was determined by examining scores assigned to the same patient by two different physiotherapists. Concurrent validity of the 4PPS was determined by examining associations with the BLS, SCP and functional scales. Results: 74 participants who were (median [interquartile range]) 13 [9 to 22] days post-stroke completed this study. Intra- and inter-rater reliability were k<inf>w</inf>=0.98 (pw=0.95), SCP (r<inf>s</inf>=0.96), Berg Balance Scale (r<inf>s</inf>=0.76), Chedoke-McMaster Postural Control Scale (r =-0.75) and Functional Independence Measure mobility sub-score (r<inf>s</inf>=-0.66) (all p Conclusion: The 4PPS is a reliable and valid scale to assess PB in patients following stroke in an inpatient rehabilitation setting. (Figure Presented).

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Comparison of clinical cut-points and treatment targets for urine NTX and plasma betaCTX-I in osteoporosis.

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OBJECTIVE: We undertook to identify levels for plasma beta isomerised carboxy-terminal telopeptides of type I collagen (p-betaCTX-I) that are comparable to currently used urine amino-terminal telopeptides of type I collagen (u-NTX) cut-points and treatment targets in osteoporosis.

DESIGN AND METHODS: Fasting morning samples were collected from patients attending tertiary hospitals and clinics for investigation of metabolic bone disease. Patients with Paget’s disease or <20 years of age were excluded. Second void spot urine for NTX and plasma (EDTA) samples were utilised. Urine was analysed routinely and plasma stored at -20°C until analysis by enzyme-linked immunosorbent assay (ELISA) (Immunodiagnostic Systems plc), E170 (Roche Diagnostics) and IDS-iSYS (Immunodiagnostic Systems plc) methods. The relationship of u-NTX with each p-betaCTX-I method’s results was assessed by Passing and Bablok regression, and p-betaCTX-I levels equivalent to u-NTX cut-points and targets were interpolated.

RESULTS: One hundred and forty six patients were included. Spearman correlation coefficients ranged from 0.71 to 0.75 for the three betaCTX-I assays. The equivalent betaCTX-I concentrations for NTX/Cr values of 21 (fracture risk reduction target following risedronate therapy), 27 (healthy pre-menopausal women’s mean value), and 38 (threshold for reduction of BMD on calcium alone) nmol BCE/mmol were 230, 312 and 462ng/L for the automated Roche assay and 271, 395 and 624ng/L for the automated IDS i-SYS assay respectively.

CONCLUSIONS: The p-betaCTX-I equivalent to the only available fracture outcome based absolute treatment threshold of 21nmol BCE/mmol established for u-NTX, is close to 250ng/L but will vary between p-betaCTX-I assays. Copyright © 2015 The Canadian Society of Clinical Chemists. Published by Elsevier Inc. All rights reserved. PMID:26680567

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The Efficacy of Earplugs as a Sleep Hygiene Strategy for Reducing Delirium in the ICU: A Systematic Review and Meta-Analysis.
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OBJECTIVE: A systematic review and meta-analysis to assess the efficacy of earplugs as an ICU strategy for reducing delirium.
DATA SOURCES: MEDLINE, EMBASE, and the Cochrane Central Register of controlled trials were searched using the terms “intensive care,” “critical care,” “earplugs,” “sleep,” “sleep disorders,” and “delirium.”
STUDY SELECTION: Intervention studies (randomized or nonrandomized) assessing the efficacy of earplugs as a sleep hygiene strategy in patients admitted to a critical care environment were included. Studies were excluded if they included only healthy volunteers, did not report any outcomes of interest, did not contain an intervention group of interest, were crossover studies, or were only published in abstract form.
DATA EXTRACTION: Nine studies published between 2009 and 2015, including 1,455 participants, fulfilled the eligibility criteria and were included in the systematic review. Studies included earplugs as an isolated intervention (n = 3), or as part of a bundle with eye shades (n = 2), or earplugs, eye shades, and additional sleep noise abatement strategies (n = 4). The risk of bias was high for all studies.
DATA SYNTHESIS: Five studies comprising 832 participants reported incident delirium. Earplug placement was associated with a relative risk of delirium of 0.59 (95% CI, 0.44-0.78) and no significant heterogeneity between the studies (I² = 39%; p = 0.16). Hospital mortality was reported in four studies (n = 481) and was associated with a relative risk of 0.77 (95% CI, 0.54-1.11; I² = 0%; p < 0.001). Compliance with the placement of earplugs was reported in six studies (n = 681). The mean per-patient noncompliance was 13.1% (95% CI, 7.8-25.4) of those assigned to receive earplugs.
CONCLUSIONS: Placement of earplugs in patients admitted to the ICU, either in isolation or as part of a bundle of sleep hygiene improvement, is associated with a significant reduction in risk of delirium. The potential effect of cointerventions and the optimal strategy for improving sleep hygiene and associated effect on patient-centered outcomes remains uncertain.
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Naphthoquine: An Emerging Candidate for Artemisinin Combination Therapy.

Naphthoquine: An Emerging Candidate for Artemisinin Combination Therapy.
Papua New Guinea.
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Naphthoquine is a 4-aminoquinoline antimalarial drug first synthesised in China in 1986 but which was not developed for clinical use until the late 1990s. Early in vitro parasite sensitivity and in vivo efficacy data, together with a long terminal elimination half-life (up to 23 days), suggested that it could be used as monotherapy for uncomplicated falciparum and vivax malaria, but is now marketed as a single-dose, fixed co-formulation with artemisinin in a milligram per kilogram ratio of 1:2.5. This form of artemisinin combination therapy (ACT) has also shown high cure rates, especially in two randomised trials in which, consistent with World Health Organization recommendations for all ACTs, it was administered daily for 3 days rather than as single dose for Plasmodium falciparum and P. vivax infections (28-day adequate clinical and parasitological response >98.4 %). Although detailed safety monitoring has been performed in a minority of subjects, >4000 healthy volunteers and patients with malaria have been exposed to naphthoquine without any documented significant toxicity. As with other 4-aminoquinolines, naphthoquine is associated with prolongation of the electrocardiographic QT interval but not with cardiac or neurological events. It has been administered to children as young as 4 months of age but, due to a lack of pharmacokinetic, efficacy and toxicity data in young infants and in pregnant/lactating women, it should not be used in these vulnerable patient groups. With the emergence of parasite resistance to other ACTs, naphthoquine partnered with a potent artemisinin derivative may prove a viable alternative treatment for uncomplicated malaria.
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The use of biochemical markers of bone turnover in the clinical management of primary and secondary osteoporosis.
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The purpose of the present study was to examine of the current role of bone turnover markers (BTMs) in the management of osteoporosis. Perusal of the literature examines the available evidence for the utility of BTMs for decision to treat and for the monitoring of treatment for osteoporosis. There is no evidence for the use of BTMs for fracture risk calculation, decision to treat or for treatment selection. A very abnormal BTM value may be a clue to the presence of bone pathology other than uncomplicated osteoporosis. Whilst changes to BTMs following various osteoporosis treatments are well defined, their utility in monitoring individual patients has been less well established. Some fracture outcome-based data exist for the use of u-NTX target of <21 nmol BCE/mmol for antiresorptive therapy; the equivalent s-CTX level is ~250 ng/L. Suboptimal BTM response to treatment may indicate non-compliance or the presence of secondary causes of osteoporosis which may need addressing. Studies are needed to establish treatment targets based on fracture outcomes for commonly used BTMs for each established osteoporosis therapy.
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A Human Variant of Glucose-Regulated Protein 94 That Inefficiently Supports IGF Production.

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IGFs are critical for normal intrauterine and childhood growth and sustaining health throughout life. We showed previously that the production of IGF-1 and IGF-2 requires interaction with the chaperone glucose-regulated protein 94 (GRP94) and that the amount of secreted IGFs is proportional to the GRP94 activity. Therefore, we tested the hypothesis that functional polymorphisms of human GRP94 affect IGF production and thereby human health. We describe a hypomorphic variant of human GRP94, P300L, whose heterozygous carriers have 9% lower circulating IGF-1 concentration. P300L was found first in a child with primary IGF deficiency and was later shown to be a noncommon single-nucleotide polymorphism with frequencies of 1%-4% in various populations. When tested in the grp94(-/-) cell-based complementation assay, P300L supported only approximately 58% of IGF secretion relative to wild-type GRP94. Furthermore, recombinant P300L showed impaired nucleotide binding activity. These in vitro data strongly support a causal relationship between the GRP94 variant and the decreased concentration of circulating IGF-1, as observed in human carriers of P300L. Thus, mutations in GRP94 that affect its IGF chaperone activity represent a novel causal genetic mechanism that limits IGF biosynthesis, quite a distinct mechanism from the known genes in the GH/IGF signaling network.

The CRUSADE score is useful in stratifying risk of major bleeding and death following STEMI PCI.

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Aims: To determine if the CRUSADE bleeding risk score, developed for NSTEMI, is discriminating for bleeding and mortality risk in patients with STEMI undergoing PCI. Methods and results: All patients with PCI-treated STEMI admitted to Western Australian public hospitals between 2000 and 2005 were identified from the hospital admissions database of the Western Australian Data Linkage System. STEMI was identified from the International Classification of Diseases 10th edition (ICD-10) code in the principal diagnosis field. The sample represented 98.6% of STEMI PCI cases in Western Australia. Hospital admissions and mortality data (from the Western Australian Data Linkage System) were linked with procedural and transfusion databases obtained electronically from the hospitals. Major bleeding was defined as admissions for GI bleeds, intracranial haemorrhage, or other major bleeds not elsewhere classified, within 30 days and 1 year from PCI, or a haemoglobin drop >2 AND transfusion of >1 unit of packed red cells within 7 days of PCI. The calculated CRUSADE score has a range of 1 to 100 and was stratified into its 5 risk categories (<20, 21-30, 31-40, 41-50, >50). Associations with major bleeding and mortality at 30 days and 1 year were assessed using the Cochran-Armitage trend test and logistic regression (unadjusted and age-adjusted models). The c-statistic from the logistic regression models was used to assess the model discrimination (values >0.7 indicate reasonable discrimination; >0.8 indicate strong model discrimination). We identified 2,308 patients with mean age 60 years (range 24-91) and 76.4% were male. Mortality at 30 days and 1 year was 3.6% (n=83) and 5.9% (n=136), respectively. The major bleeding rates at 30 days and 1 year were 4.3% (n=99) and 5.4% (n=124), respectively. There was a significant increasing trend across CRUSADE risk strata for all outcomes (p<0.0001) which persisted after adjusting for age. The age-adjusted odds ratio for 30-day death increased rapidly with CRUSADE risk stratum, from 1.0 (very low risk stratum: score <20) to 6 (95% CI: 2-22) for low risk stratum, 17 (95% CI: 5-59) for moderate risk stratum, 51 (95%
CI: 14-177) for high risk stratum, and 118 (95% CI: 33-420) for the very high risk stratum (score >50). For 1-year death, the odds ratio increased from 1.0 (very low risk) to 40 (95% CI: 18-90) for the very high risk stratum. Corresponding odds ratios for 30-day major bleeding were 1.0 (very low risk), 3 (95% CI: 1-6) for the low risk stratum, 5 (95% CI: 2-11) for moderate risk, 8 (95% CI: 4-19) for high risk, and 9 (95% CI: 4-24) for the very high risk stratum. For 1-year major bleeding, the odds ratio increased to 7 (95% CI: 3-15) for the very high risk stratum. The c-statistic was 0.84 for the age-adjusted logistic regression model for outcome of 30-day death and 0.75 for 30-day major bleeding (the CRUSADE study had a c-statistic of 0.7 for major bleeding). Conclusions: The CRUSADE score has strong associations with 30-day and 1-year death and bleeding in STEMI PCI, and can be used for stratifying both bleeding and mortality risks in these patients.


Medium-term outcomes after pulmonary valve replacement with the Freestyle valve for congenital heart disease: a case series.

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OBJECTIVES: The Freestyle valve may be used for pulmonary valve replacement (PVR). Whether its stentless design and anticalcification treatment improve durability relative to alternative bioprostheses, however, is unknown and long-term data are lacking.

METHODS: We performed a retrospective review of all Freestyle PVRs performed by a single surgeon in two institutions. All patients were contacted for follow-up to establish survival, New York Heart Association class and reintervention. Up to date, echocardiography was obtained to assess valve function. Perioperative factors associated with structural valve dysfunction (SVD) were assessed using Cox regression.

RESULTS: Between 2000 and 2014, PVR with a Freestyle valve was performed in 114 patients with congenital heart disease. There were 70 males and 44 females. The median age was 21 years (interquartile range 11-35 years). The median clinical and echocardiographic follow-up was 62 months (interquartile range 35-115 months, n = 110) and 58 months (interquartile range 30-93 months, n = 107), respectively. Follow-up was complete for 107 of 114 patients (94%). The survival rate was 95% at 5 years and 91% at 10 years. The rate of freedom from SVD at 5 years was 82%, and at 10 years was 61%. The reintervention-free survival rate was 85% at 5 years, and 71% at 10 years.

CONCLUSION: The Freestyle valve in the pulmonary position in a congenital population is associated with low medium-term incidences of SVD and reintervention. It performs equally well to the homograft when a conduit is required and can be considered a valid alternative to stented bioprostheses when PVR alone is required.

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Medium-term outcomes in patients post VA-ECMO.
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Purpose: Venous-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) has been shown to improve short-term outcomes in patients with refractory cardiogenic shock (RCS). However the medium-term outcomes are unclear. We aim to examine the course of those patients surviving their initial admission requiring VA-ECMO. Methods: This study was a retrospective, single-centre review of patients who received VA-ECMO for RCS. Baseline patient characteristics, aetiology of RCS, survival as well as cardiovascular and neurological outcomes both at hospital discharge and at 1 year were collected by review of medical records. Results: From 2008 to 2014, 34 patients received VA-ECMO for RCS. Mean age was 43 years (+ 19), 65% were male and total time on VA-ECMO was 6 days (+ 4.3). The aetiology of RCS was acute myocarditis in 9 (25%), post-cardiac surgery in 6 (18%), post heart/lung transplant in 5 (15%), acute myocardial infarction in 4 (12%), decompensated cardiomyopathy in 4 (12%), right heart failure in 3 (9%) and other in 3 (9%). 18 (53%) patients survived to hospital discharge, of whom 14 (41%) made a full neurological recovery. 8 (24%) patients were medically managed without advanced therapy, 6 (18%) required heart transplantation, 3 (9%) required left ventricular assist devices (LVAD) and 1 patient (3%) was listed for heart transplantation. At 1 year, 14 patients (44%) were still alive. 5 (16%) patients were medically managed. 6 (19%) patients had required heart transplantation. 2 (6%) patients required LVAD support and 1 (3%) was listed for transplant. During this time, 1 patient was newly listed for transplant, 1 patient had progressed from medical therapy to LVAD and 1 patient progressed from LVAD to transplant. Conclusion: Patients receiving VA-ECMO for RCS who survive to discharge have a favourable medium-term prognosis however a significant proportion will require LVAD support or transplantation. A minority of patients survive to 1 year without advanced therapy highlighting the need for all ECMO survivors to have close follow-up by a heart failure/transplant unit. (Figure Presented).
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**Sternal cables are not superior to traditional sternal wiring for preventing deep sternal wound infection.**

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OBJECTIVES: Deep sternal wound infection is a devastating complication of cardiac surgery. In the current era of increasing patient comorbidity, newer techniques must be evaluated in attempts to reduce the rates of deep sternal wound infection.

METHODS: A randomized controlled trial comparing sternal closure with traditional sternal wires in figure-8 formation with the Pioneer cabling system from Medigroup after adult cardiac surgery was performed.

RESULTS: A total of 273 patients were enrolled with 137 and 135 patients randomized to sternal wires and cables group, respectively. Baseline characteristics between the two groups were well balanced. Deep sternal wound infection occurred in 0.7% of patients in the wires group and 3.7% of patients in the cables group (absolute risk difference = -3.0%, 95% confidence interval: -7.7 to 0.9%; P = 0.12). Patients in the cables group were extubated slightly earlier than those in the sternal wires group postoperatively (9.7 vs 12.8 h; P = 0.03). There was, however, no significant difference in hospital and follow-up pain scores or analgesia requirements.

CONCLUSIONS: The Pioneer sternal cabling system appears to facilitate early extubation after adult cardiac surgery, but it does not reduce the rate of deep sternal infection.Australian New Zealand Clinical Trials Registry: ANZCTR-ACTRN12615000973516.


**Adverse metabolic phenotype of adolescent girls with non-alcoholic fatty liver disease plus polycystic ovary syndrome compared with other girls and boys.**

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BACKGROUND AND AIMS: Non-alcoholic fatty liver disease (NAFLD) and polycystic ovary syndrome (PCOS) share risk associations of adiposity and insulin resistance. We examined the impact of a PCOS diagnosis on the metabolic phenotype of adolescent girls with NAFLD and compared this to girls without PCOS or NAFLD and to age-matched boys.

METHODS: Community-based adolescents from the Raine Cohort participated in assessments for NAFLD (572 girls and 592 boys) and PCOS (244 girls). One hundred and ninety-nine girls attended both assessments.

RESULTS: Amongst the 199 girls, PCOS was diagnosed in 16.1% and NAFLD in 18.6%. NAFLD was diagnosed in 10.1% of the boys. NAFLD was more prevalent in girls with PCOS than girls without PCOS (37.5% vs 15.1%, P=0.003). Girls with NAFLD plus PCOS had greater adiposity (waist circumference, body mass index, suprailiac skinfold thickness [SST], serum androgens, high-sensitivity C-reactive protein, ferritin, homeostasis model assessment for insulin resistance (HOMA-IR), and lower serum sex hormone binding globulin levels than girls with NAFLD without a PCOS diagnosis (all P<0.05). Girls with NAFLD plus PCOS had similar adiposity, HOMA-IR, and adiponectin levels to boys with NAFLD, but more adiposity, serum leptin and HOMA-IR than both girls and boys without NAFLD. PCOS (odds ratios 2.99, 95% confidence intervals 1.01-8.82, P=0.048) and SST (odds ratios 1.14, 95% confidence intervals 1.08-1.20, P<0.001) independently predicted NAFLD in adolescent girls, however, serum androgens and HOMA-IR levels did not.

CONCLUSIONS: Adolescent girls with NAFLD plus PCOS have a similar metabolic phenotype to boys with NAFLD. Increasing SST and pre-existing PCOS independently predict NAFLD in adolescent girls.

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This guideline is endorsed by the specialty associations involved in the care of head and neck cancer patients in the UK. This paper summarises the current imaging modalities in use for head and neck cancer evaluation. It highlights their role in the management with recommendations on modality choice for each cancer subsite. Recommendations * Offer appropriate radiological imaging, based on tumour extent, site and local expertise, to stage tumours and plan treatment for patients diagnosed with head and neck cancer. (G) * Consider positron emission tomography combined with computed tomography (PET-CT) imaging if conventional cross-sectional imaging identifies no primary site. (R) * Offer PET-CT imaging 12 weeks after non-surgical treatment to detect residual disease. (R).

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Investigations into methods to improve the antibacterial activity of Acticoat.


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Multiple studies have shown that the antibacterial dressing Acticoat can inhibit growth of bacteria but is unable to completely clear a wound of infection, which could leave patients vulnerable to sepsis. Agar inoculated with four different Staphylococcus aureus strains and overlaid with Acticoat showed growth inhibition beneath and within a 1 mm perimeter of the dressing after 24 h. When lifted from inoculated agar and briefly blotted onto fresh agar plates, Acticoat transferred viable bacteria. Scanning electron microscopy of the surface of Acticoat that overlaid meticillin-resistant S. aureus for 24, 48 and 72 h showed dense clusters of apparently undamaged bacteria distributed across the mesh. The number of bacteria growing on inoculated pig skin, underneath and on the surface of Acticoat, was lower than on controls for the first 8 h, but after 24 h the number of bacteria on the skin was 2.3-fold greater than the untreated controls. In contrast, after 24 h the number of bacteria surviving on the surface of the Acticoat was 11.9% of controls. Acticoat moistened with 10% glycerol plus antimicrobial peptides (AMPs) mel12-26 or bac8c (50 μg ml⁻¹) reduced the numbers of bacteria on the dressing and on the skin underneath to below 10% and 0.01% of the controls, respectively. When lysozyme (1 mg ml⁻¹) was added to Acticoat wetted with glycerol and the AMP bac8c, the dressing was able to prevent the survival of bacteria on densely inoculated pig skin and on the surface of Acticoat for up to 24 h. In effect, biocompatible solvents and AMPs significantly enhance the bactericidal efficacy of Acticoat.

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Temporal flux in beta-lactam resistance among Klebsiella pneumoniae in Western Australia.

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Our aim was to identify long-term beta-lactam resistance trends in local Klebsiella pneumoniae isolates, which are a common cause of sepsis in Western Australia. We studied three collections of K. pneumoniae isolates from Western Australia between 1977 and 2015 comprising contemporary blood culture (n=98), multiresistant (n=21) and historical (n=50) isolates. Antimicrobial resistance was determined by Clinical and Laboratory Standards Institute agar dilution methods. PCR DNA sequencing identified beta-lactamase variants and porin mutations contributing to beta-lactam resistance. Isolates were genotyped by PFGE, multilocus sequence typing and a variable number tandem repeat method. From 1989 onwards, we detected the SHV-2a extended-spectrum beta-lactamase (ESBL) in ceftriaxone-resistant isolates, and in ceftazidime- and aztreonam-resistant isolates from 1993. Ceftriaxone, ceftazidime and aztreonam resistance persisted, with bla<inf>CTX-M</inf> types becoming the dominant ESBLs by 2010. CTX-M-15 was encountered in both multiresistant and blood culture isolates. Meropenem resistance was detected for the first time in 2011 in a locally isolated bla<inf>IMP-4</inf>-positive K. pneumoniae. We found sequence types ST23 and ST86 that occurred in multiple isolates from invasive infections. ST86 was the most common and maintained a high degree (90%) of similarity by PFGE since 1977. Cefazidime-resistant K. pneumoniae sequence types have caused invasive infections in Western Australia since 1993. Invasive isolates producing CTX-M-14 and CTX-M-15
appeared in Western Australia during the last decade, before the appearance of carbapenemases. The diversity of beta-lactam resistance and beta-lactamase resistance mechanisms in Western Australian K. pneumoniae has increased since ESBLs were first described locally. Copyright © 2016 The Authors Printed in Great Britain.

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The implications of endemic IMP-4 carbapenemase for clinical laboratory susceptibility testing.

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A local predominance of carbapenemase producing Enterobacteriaceae with low minimum inhibitory concentrations (MIC) to meropenem prompted a review of methods available for carbapenemase detection. We report on results using two selective media, temocillin discs, CarbaNP test, GeneXpert Carba-R assay and an in-house PCR assay. Crown Copyright © 2016. Published by Elsevier B.V. All rights reserved.
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Scientific Advances in Lung Cancer 2015.

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Lung cancer continues to be a major global health problem; the disease is diagnosed in more than 1.6 million new patients each year. However, significant progress is underway in both the prevention and treatment of lung cancer. Lung cancer therapy has now emerged as a “role model” for precision cancer medicine, with several important therapeutic breakthroughs occurring during 2015. These advances have occurred primarily in the immunotherapy
field and in treatments directed against tumors harboring specific oncogenic drivers. Our knowledge about molecular mechanisms for oncogene-driven tumors and about resistance to targeted therapies has increased quickly over the past year. As a result, several regulatory approvals of new agents that significantly improve survival and quality of life for patients with lung cancer who have advanced disease have occurred. The International Association for the Study of Lung Cancer has gathered experts in different areas of lung cancer research and management to summarize the most significant scientific advancements related to prevention and therapy of lung cancer during the past year.

Efficacy and toxicity of treatment with the anti-CTLA-4 antibody ipilimumab in patients with metastatic melanoma after prior anti-PD-1 therapy.

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BACKGROUND: Recent phase III clinical trials have established the superiority of the anti-PD-1 antibodies pembrolizumab and nivolumab over the anti-CTLA-4 antibody ipilimumab in the first-line treatment of patients with advanced melanoma. Ipilimumab will be considered for second-line treatment after the failure of anti-PD-1 therapy.

METHODS: We retrospectively identified a cohort of 40 patients with metastatic melanoma who received single-agent anti-PD-1 therapy with pembrolizumab or nivolumab and were treated on progression with ipilimumab at a dose of 3mgkg(-1) for a maximum of four doses.

RESULTS: Ten percent of patients achieved an objective response to ipilimumab, and an additional 8% experienced...
prolonged (>6 months) stable disease. Thirty-five percent of patients developed grade 3-5 immune-related toxicity associated with ipilimumab therapy. The most common high-grade immune-related toxicity was diarrhoea. Three patients (7%) developed grade 3-5 pneumonitis leading to death in one patient.

CONCLUSIONS: Ipilimumab therapy can induce responses in patients who fail the anti-PD-1 therapy with response rates comparable to previous reports. There appears to be an increased frequency of high-grade immune-related adverse events including pneumonitis that warrants close surveillance.

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Carotid sheath 'intubation' during an emergency surgical cricothyroidotomy.
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Perinatal maternal depression and cortisol function in pregnancy and the postpartum period: a systematic literature review.
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BACKGROUND: Perinatal depression has a significant impact on both mother and child. However, the influence of hormonal changes during pregnancy and the postpartum period remains unclear. This article provides a systematic review of studies examining the effects of maternal cortisol function on perinatal depression.

METHOD: A systematic search was conducted of six electronic databases for published research on the relationship between cortisol and perinatal depression. The databases included; MEDLINE complete, PsychINFO, SCOPUS, Psychology and Behavioural Sciences, Science Direct and EBSCO, for the years 1960 to May 2015. Risk of bias was assessed and data extraction verified by two investigators.

RESULTS: In total, 47 studies met criteria and studies showed considerable variation in terms of methodology including sample size, cortisol assays, cortisol substrates, sampling processes and outcome measures. Those studies identified as higher quality found that the cortisol awakening response is positively associated with momentary mood states but is blunted in cases of major maternal depression. Furthermore, results indicate that hypercortisolism is linked to transient depressive states while hypocortisolism is related to chronic postpartum depression.

DISCUSSION AND CONCLUSION: Future research should aim to improve the accuracy of cortisol measurement over time, obtain multiple cortisol samples in a day and utilise diagnostic measures of depression. Future studies should also consider both antenatal and postnatal depression and the differential impact of atypical versus melancholic depression on cortisol levels, as this can help to further clarify the relationship between perinatal depression and maternal cortisol function across pregnancy and the postpartum period.

**Novel APOB missense variants, A224T and V925L, in a black South African woman with marked hypocholesterolemia.**


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**BACKGROUND:** One genetic cause of markedly low plasma concentrations of apolipoprotein (apo) B and low density lipoprotein (LDL)-cholesterol is familial hypobetalipoproteinemia.

**OBJECTIVE:** We aimed to determine the molecular basis for the marked hypocholesterolemia consistent with heterozygous familial hypobetalipoproteinemia in a black female subject of Xhosa lineage.

**METHODS:** Coding regions of APOB, MTTP, PCSK9, ANGPTL3, SAR1B and APOC3 were sequenced, and APOE was genotyped. COS-7 cells were transfected with plasmids containing apoB variants. Western blotting was used to detect cellular and secreted apoB, and co-immunoprecipitation performed to assess binding with the microsomal triglyceride transfer protein (MTP).

**RESULTS:** Sequence analysis of the APOB gene revealed her to be heterozygous for two novel variants, c.751G>A (A224T) and c.2854G>C (V925L). She was also homozygous for the APOEpsilon2 allele, and did not carry a PCSK9 loss-of-function mutation. Although Ala(224) is within the postulated MTP binding region in apoB, it is not conserved among mammalian species. Subsequent genotyping showed that Ala224Thr is found in a southern African population (n=654) with an allele frequency of 1.15% and is not associated with plasma lipid levels. Val(925), like Ala(224), is within the N-terminal 1000 amino acids required for lipoprotein assembly, but was not found in the population screen. However, in vitro studies showed that apoB V925L did not affect apoB48 production or secretion nor have a deleterious effect on MTP interaction with apoB.

**CONCLUSION:** Taken together, this suggests that the hypocholesterolemia in our case may be a result of being homozygous for APOEpsilon2 with a low baseline cholesterol.

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**Can femoral venous pressure be used as an estimate for standard vesical intra-abdominal pressure measurement?**

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Intra-abdominal hypertension (IAH) is highly prevalent in critically ill patients admitted to the intensive care unit and is associated with an increased morbidity and mortality. The present study investigated whether femoral venous pressure (FVP) can be used as a surrogate parameter for intra-abdominal pressure (IAP) measured via the bladder in IAH grade II (IAP <20 mmHg) or grade III (IAP >20 mmHg). This was a single-centre prospective study carried out in a tertiary adult intensive care unit. IAP was measured via the bladder with a urinary catheter with simultaneous recording of the FVP via a femoral central line. If the IAP was <20 mmHg external weight to a maximum of 10 kg was applied to the abdomen with subsequent measurements of IAP and FVP. Eleven patients were enrolled into the study. IAH (IAP >12 mmHg) was identified in five patients (42%) and abdominal compartment syndrome (ACS, IAP >20 mmHg with new onset organ failure) in two (18%) with all-cause study mortality of 18%. The mean Acute Physiology and Chronic Health Evaluation (APACHE) II score was 21 +/- 5, Simplified Acute Physiology (SAPS 2) score 49 +/- 8, and Sequential Organ Failure Assessment (SOFA) score 9 +/- 3. At baseline the bias between IAP and FVP was 3.2 with a precision of 3.63 mmHg (limits of agreement [LA] -4.1, 10.4). At 5 kg and 10 kg, the bias was 2.5 with a precision of 3.92 mmHg (LA -5.4, 10.3) and 2.26 mmHg (LA -2.1, 7.0) respectively. A receiver operating characteristic analysis for FVP to predict IAH showed an area under the curve of 0.87 (95% confidence interval 0.74-0.94, P=0.0001). FVP cannot be recommended as a surrogate measure for IAP even at IAP values above 20 mmHg. However, an elevated FVP was a good predictor of IAH.

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Not all ductal carcinoma in situ is created equal: can we avoid surgery for low-risk ductal carcinoma in situ?
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Nanocrystalline silver dressings significantly influence bioimpedance spectroscopy measurements of fluid volumes in burns patients.
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Bioimpedance spectroscopy (BIS) is a tool utilized in health care to investigate body composition and fluid
distribution. Limited research has addressed the clinical use of BIS in burns. This study aimed to examine the effects of silver dressings on BIS measurements in burns patients. BIS measurements were collected during two dressing conditions: no dressing (ND), and Acticoat dressing (AD). Wilcoxon sign-ranks tests determined if there were any significant differences in BIS measures between the dressing conditions. Multilevel mixed-effects linear regressions examined the effect of %TBSA and body mass on BIS variables across the dressing conditions. The mean age of the patients (n=31) was 34.90 years; with a median TBSA of 15%. There was a significant increase in extracellular fluid (ECF) (p<0.001), intracellular fluid (ICF) (p<0.001) and total body water (TBW) (p<0.001) when AD was in place. There were significant interactions between dressing condition, %TBSA and body mass, whereby the difference in ECF, ICF and TBW between the ND and AD conditions were increased as %TBSA and body mass increased. Algorithms were developed subsequently to adjust BIS outputs for use when AD is in place. Clinician's may continue to use BIS in real-time using the predictive algorithms established during this study.
One of the many parameters that can affect cochlear implant (CI) users’ performance is the site of presentation of electrical stimulation, from the CI, to the auditory nerve. Evoked compound action potential (ECAP) measurements are commonly used to verify nerve function by stimulating one electrode contact in the cochlea and recording the resulting action potentials on the other contacts of the electrode array. The present study aimed to determine if the ECAP amplitude differs between the apical, middle, and basal region of the cochlea, if double peak potentials were more likely in the apex than the basal region of the cochlea, and if there were differences in the ECAP threshold and recovery function across the cochlea. ECAP measurements were performed in the apical, middle, and basal region of the cochlea at fixed sites of stimulation with varying recording electrodes. One hundred and forty one adult subjects with severe to profound sensorineural hearing loss fitted with a Standard or FLEX\textsuperscript{SOFT} electrode were included in this study. ECAP responses were captured using MAESTRO System Software (MED-EL). The ECAP amplitude, threshold, and slope were determined using amplitude growth sequences. The 50% recovery rate was assessed using independent single sequences that have two stimulation pulses (a masker and a probe pulse) separated by a variable inter-pulse interval. For all recordings, ECAP peaks were annotated semi-automatically. ECAP amplitudes were greater upon stimulation of the apical region compared to the basal region of the cochlea. ECAP slopes were steeper in the apical region compared to the basal region of the cochlea and ECAP thresholds were lower in the middle region compared to the basal region of the cochlea. The incidence of double peaks was greater upon stimulation of the apical region compared to the basal region of the cochlea. This data indicates that the site and intensity of cochlear stimulation affect ECAP properties.

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**Dose-response relationship between statin therapy and glycaemia in community-based patients with type 2 diabetes: the Fremantle Diabetes Study.**

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Although statins may increase glycaemia in type 2 diabetes, available data are from single-dose intervention trials or studies with no adjustment for concomitant changes in blood glucose-lowering therapy. To provide real-life data covering common statin types and doses, glycated haemoglobin (HbA1c) data from patients in the Fremantle Diabetes Study phases I (FDS1) and II (FDS2) and data on stable diabetes treatment before and after statin initiation were analysed. Intensity of statin therapy was categorized as low, moderate or high based on within-group dose
regimens with similar serum LDL cholesterol-lowering effects. In pooled analyses of 335 eligible patients in FDS1 and FDS2, there was no change in HbA1c in the low-intensity group (0.04% or 0.4 mmol/mol; n=159; p=.40), but a mean increase of 0.22% (2.4 mmol/mol) in the moderate-intensity group (n=185; p=.022) and a larger mean increase of 1.05% (11.5 mmol/mol) increase in the high-intensity group (n=11; p=.023). These real-life data suggest a dose-response relationship between statin treatment intensity and glycaemia that has potential clinical implications.


Asymptomatic CMV infections in long-term renal transplant recipients are associated with the loss of FcRgamma from LIR-1+ NK cells.

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While it is established that cytomegalovirus (CMV) disease affects NK-cell profiles, the functional consequences of asymptomatic CMV replication are unclear. Here, we characterize NK cells in clinically stable renal transplant recipients (RTRs; n = 48) >2 years after transplantation. RTRs and age-matched controls (n = 32) were stratified by their CMV serostatus and the presence of measurable CMV DNA. CMV antibody or CMV DNA influenced expression of NKG2C, LIR-1, Nkp30, Nkp46, and FcRgamma, a signaling adaptor molecule, on CD56(dim) NK cells. Phenotypic changes ascribed to CMV were clearer in RTRs than in control subjects and affected NK-cell function as assessed by TNF-alpha and CD107a expression. The most active NK cells were FcRgamma(-) LIR-1(+) NKG2C(-) and displayed high antibody-dependent cell cytotoxicity responses in the presence of immobilized CMV glycoprotein B reactive antibody. However, perforin levels in supernatants from RTRs with active CMV replication were low. Overall we demonstrate that CMV can be reactivated in symptom-free renal transplant recipients, affecting the phenotypic, and functional profiles of NK cells. Continuous exposure to CMV may maintain and expand NK cells that lack FcRgamma but express LIR-1.

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Intravenous iron or placebo for anaemia in intensive care: the IRONMAN multicentre randomized blinded trial: A randomized trial of IV iron in critical illness.

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PURPOSE: Both anaemia and allogenic red blood cell transfusion are common and potentially harmful in patients admitted to the intensive care unit. Whilst intravenous iron may decrease anaemia and RBC transfusion requirement, the safety and efficacy of administering iron intravenously to critically ill patients is uncertain.

METHODS: The multicentre, randomized, placebo-controlled, blinded Intravenous Iron or Placebo for Anaemia in Intensive Care (IRONMAN) study was designed to test the hypothesis that, in anaemic critically ill patients admitted to the intensive care unit, early administration of intravenous iron, compared with placebo, reduces allogeneic red blood cell transfusion during hospital stay and increases the haemoglobin level at the time of hospital discharge.

RESULTS: Of 140 patients enrolled, 70 were assigned to intravenous iron and 70 to placebo. The iron group received 97 red blood cell units versus 136 red blood cell units in the placebo group, yielding an incidence rate ratio of 0.71 [95 % confidence interval (0.43-1.18), P = 0.19]. Overall, median haemoglobin at hospital discharge was significantly higher in the intravenous iron group than in the placebo group [107 (interquartile ratio IQR 97-115) vs. 100 g/L (IQR 89-111), P = 0.02]. There was no significant difference between the groups in any safety outcome.

CONCLUSIONS: In patients admitted to the intensive care unit who were anaemic, intravenous iron, compared with placebo, did not result in a significant lowering of red blood cell transfusion requirement during hospital stay. Patients who received intravenous iron had a significantly higher haemoglobin concentration at hospital discharge. The trial was registered at http://www.anzctr.org.au as # ACTRN12612001249842.

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Dysregulated Erythropoietin, Hepcidin, and Bone Marrow Iron Metabolism Contribute to Interferon-Induced Anemia in Hepatitis C.
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Anemia is a complication of interferon-containing hepatitis C treatments. We characterized effects of interferon-based therapy on hepcidin and erythropoietin (EPO) production, iron metabolism, hemolysis, and hematopoiesis. Standard hemopoiesis [reticulocyte hemoglobin (Hb), reticulocyte production index (RPI), free Hb, and haptoglobin], iron biochemistry, hepcidin, and EPO levels were measured in 10 subjects over 12 weeks. There was a rapid decline in Hb during treatment, from a mean pretreatment (t=0 weeks) Hb of 158.6 to 125.2g/L at week 4 (P=0.003) and 122.8g/L at week 12 (P=0.005). Paradoxically, the RPI (a measure of bone marrow responsiveness to EPO) decreased on initiation of hepatitis C virus treatment from 0.78% to 0.53% (P=0.04). Despite worsening anemia, there was no significant increase in EPO levels. Hepcidin levels increased to >20nM in 3 subjects from 5.8 to 27.5nM (P=0.009) compared with 9.6 to 12.3nM (P=0.5) for the remainder of subjects. Hepcidin levels peaked at week 1 before returning to baseline levels at week 4. Subjects who responded with a rise in serum hepcidin levels to >20nM had a significantly greater drop in Hb (27.2g/L, P=0.008) and reticulocyte Hb (-1.4g/L, P=0.013) compared with the subjects who did not exhibit any change in hepcidin production. In conclusion, 30% of subjects treated with interferon exhibited significant transient increase in serum hepcidin levels, which was associated with more extreme anemia and decreased iron availability as evidenced by decreased reticulocyte Hb. In addition, there was a failure to upregulate EPO production in response to anemia and hemolysis (https://clinicaltrials.gov trial NCT01726400).

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Phylogenetic diversity, antimicrobial susceptibility and virulence characteristics of phylogroup F Escherichia coli in Australia.

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Unlike Escherichia coli strains belonging to phylogroup B2, the clinical significance of strains belonging to phylogroup F is not well understood. Here we report on a collection of phylogroup F strains recovered in Australia from faeces and extra-intestinal sites from humans, companion animals and native animals, as well as from poultry meat and water samples. The distribution of sequence types was clearly non-random with respect to isolate source. The antimicrobial resistance and virulence trait profiles also varied with the sequence type of the isolate. Phylogroup F strains tended to lack the virulence traits typically associated with phylogroup B2 strains responsible for extra-intestinal infection in humans. Resistance to fluoroquinolones and/or expanded-spectrum cephalosporins was common within ST648, ST354 and ST3711. Although ST354 and ST3711 are part of the same clonal complex, the ST3711 isolates were only recovered from native birds being cared for in a single wildlife rehabilitation centre,
whereas the ST354 isolates were from faeces and extra-intestinal sites of dogs and humans, as well as from poultry meat. Although ST354 isolates from chicken meat in Western Australia were distinct from all other ST354 isolates, those from poultry meat samples collected in eastern Australia shared many similarities with other ST354 isolates from humans and companion animals.


**Brain iron accumulation affects myelin-related molecular systems implicated in a rare neurogenetic disease family with neuropsychiatric features.**


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The ‘neurodegeneration with brain iron accumulation’ (NBIA) disease family entails movement or cognitive impairment, often with psychiatric features. To understand how iron loading affects the brain, we studied mice with disruption of two iron regulatory genes, hemochromatosis (Hfe) and transferrin receptor 2 (Tfr2). Inductively coupled plasma atomic emission spectroscopy demonstrated increased iron in the Hfe<sup>-/-</sup> x Tfr2<sup>mut</sup> brain (P=0.002, n >5/group), primarily localized by Perls’ staining to myelinated structures. Western immunoblotting showed increases of the iron storage protein ferritin light polypeptide and microarray and real-time reverse transcription-PCR revealed decreased transcript levels (P<0.04, n >5/group) for five other NBIA genes, phospholipase A2 group VL fatty acid 2-hydroxylase, ceruloplasmin, chromosome 19 open reading frame 12 and ATPase type 13A2. Apart from the ferroxidase ceruloplasmin, all are involved in myelin homeostasis; 16 other myelin-related genes also showed reduced expression (P<0.05), although gross myelin structure and integrity appear unaffected (P>0.05). Overlap (P<0.0001) of differentially expressed genes in Hfe<sup>-/-</sup> x Tfr2<sup>mut</sup> brain with human gene co-expression networks suggests iron loading influences expression of NBIA-related and myelin-related genes co-expressed in normal human basal ganglia. There was overlap (P<0.0001) of genes differentially expressed in Hfe<sup>-/-</sup> x Tfr2<sup>mut</sup> brain and post-mortem NBIA basal ganglia. Hfe<sup>-/-</sup> x Tfr2<sup>mut</sup> mice were hyperactive (P<0.0112) without apparent cognitive impairment by IntelliCage testing (P>0.05). These results implicate myelin-related systems involved in NBIA.
neuropathogenesis in early responses to iron loading. This may contribute to behavioral symptoms in NBIA and hemochromatosis and is relevant to patients with abnormal iron status and psychiatric disorders involving myelin abnormalities or resistant to conventional treatments.

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Rare variants in SQSTM1 and VCP genes and risk of sporadic inclusion body myositis.

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Genetic factors have been suggested to be involved in the pathogenesis of sporadic inclusion body myositis (sIBM). Sequestosome 1 (SQSTM1) and valosin-containing protein (VCP) are 2 key genes associated with several neurodegenerative disorders but have yet to be thoroughly investigated in sIBM. A candidate gene analysis was conducted using whole-exome sequencing data from 181 sIBM patients, and whole-transcriptome expression analysis was performed in patients with genetic variants of interest. We identified 6 rare missense variants in the SQSTM1 and VCP in 7 sIBM patients (4.0%). Two variants, the SQSTM1 p.G194R and the VCP p.R159C, were significantly overrepresented in this sIBM cohort compared with controls. Five of these variants had been previously reported in patients with degenerative diseases. The messenger RNA levels of major histocompatibility complex genes were upregulated, this elevation being more pronounced in SQSTM1 patient group. We report for the first time potentially pathogenic SQSTM1 variants and expand the spectrum of VCP variants in sIBM. These data suggest that defects in neurodegenerative pathways may confer genetic susceptibility to sIBM and reinforce the mechanistic overlap in these neurodegenerative disorders.


Treatment and outcomes in necrotising autoimmune myopathy: An Australian perspective.
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Necrotising Autoimmune Myopathy (NAM) presents as a subacute proximal myopathy with high creatine kinase levels. It is associated with statin exposure, 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) antibody, connective tissue diseases, signal recognition particle (SRP) antibody and malignancy. This case series presents our Western Australian NAM patient cohort: comparing the subgroup presentations, biopsy appearance and treatment outcomes. We retrospectively collected data on patients diagnosed with NAM at the Western Australian Neuroscience Research Institute between the years 2000 and 2015. We identified 20 patients with Necrotising Autoimmune Myopathy: 14 with anti-HMGCR antibodies; two with anti-SRP antibodies; three with connective tissue disease; two as yet unspecified. Median creatine kinase level was 6047 units/L (range 1000-17000). The statin naïve patients with HMGCR antibodies and patients with SRP antibodies were the most severely affected subgroups, with higher creatine kinase
levels, and were more resistant to immunotherapy. Two or more immunotherapy agents were required in 90%; eight patients required IVIG and rituximab. Steroid weaning commonly precipitated relapses. Four patients had complete remission, and the remaining patients still require immunotherapy. Necrotising Autoimmune Myopathy is a potentially treatable myopathy, which can be precipitated by statin therapy and requires early, aggressive immunotherapy, usually requiring multiple steroid sparing agents for successful steroid weaning.

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Bone marrow transplantation (BMT) has been performed as a successful life-saving treatment for hematological and neoplastic diseases. Despite the predictable long-term survival rates in BMT, pulmonary complications reduce the survival rates significantly mainly because of chronic graft-versus-host disease (GVHD). This report briefly discusses a successful lung transplantation case for severe lung GVHD after allograft for acute lymphoblastic leukemia. This case report supports the scarce evidence in the literature for the importance of lung transplantation as a therapeutic option for patients who develop respiratory failure secondary to BMT.

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Current practices of Asia-Pacific cardiologists in the utilization of bioresorbable scaffolds.

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BACKGROUND & AIMS: Although Absorb Bioresorbable Vascular Scaffolds (A-BVS) are routinely used in the Asia-Pacific, there is little information on patient selection or deployment technique here. This document investigates the experiences of leading interventional cardiologists from the Asia-Pacific region with a focus on patient characteristics, deployment techniques and management.

METHODS AND RESULTS: A detailed questionnaire was distributed to 28 highly-experienced interventional cardiologists ('Authors') from 13 Asia-Pacific countries. The results were discussed at a meeting on patient selection, technical consideration, deployment practices and patient management. Potential patient benefits of Absorb compared to metallic DES, the learning curve for patient selection and preparation, device deployment, and subsequent patient management approaches are presented.

CONCLUSIONS: Current practices are derived from guidelines optimized for European patients. Differences in approach exist in the Asia-Pacific context, including limited access to imaging and frequency of occurrence of complex lesions. Nevertheless, the use of the Absorb BVS ('Absorb') in certain Asia-Pacific countries has flourished and practices here are continuing to mature.

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Management of adverse events related to new cancer immunotherapy (immune checkpoint inhibitors).

Bourke JM, O'Sullivan M, et al.

New immunotherapies have significantly improved survival in certain advanced cancers in recent years, particularly metastatic melanoma and lung cancer. The most effective of these therapies are the immune checkpoint inhibitors (ICIs) such as ipilimumab, nivolumab and pembrolizumab. The use of ICIs will continue to increase in the coming years as evidence of their benefit in a range of other cancers builds. ICIs are associated with novel immune-related adverse events (irAEs), which can involve a wide range of organs. The most common irAEs involve the skin (rash, pruritus), gastrointestinal tract (diarrhoea, colitis) and endocrine system (thyroid, pituitary). While severity is generally mild, life-threatening complications can occur if not recognised and treated promptly. Due to the diverse manifestations of irAEs, patients may present to doctors who are not familiar with these drugs, which creates the potential for delays in management. Management of irAEs depends on severity and the organ affected. Systemic steroids are often required and ICI therapy may be withheld or discontinued. Additional immunosuppressive medications may be necessary in steroid-refractory cases. This review provides an overview of the potential toxicities and their management for general clinicians. Broader awareness of these issues among medical professionals will hopefully reduce unnecessary delays in diagnosis and treatment. Patient and carer education regarding irAEs is extremely important; patients and carers should be advised to seek urgent medical attention if required.


Investigation of optical coherence micro-elastography as a method to visualize micro-architecture in human axillary lymph nodes.

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BACKGROUND: Evaluation of lymph node involvement is an important factor in detecting metastasis and deciding whether to perform axillary lymph node dissection (ALND) in breast cancer surgery. As ALND is associated with potentially severe long term morbidity, the accuracy of lymph node assessment is imperative in avoiding unnecessary ALND. The mechanical properties of malignant lymph nodes are often distinct from those of normal nodes. A method to image the micro-scale mechanical properties of lymph nodes could, thus, provide diagnostic information to aid in the assessment of lymph node involvement in metastatic cancer. In this study, we scan axillary lymph nodes, freshly excised from breast cancer patients, with optical coherence micro-elastography (OCME), a method of imaging micro-scale mechanical strain, to assess its potential for the intraoperative assessment of lymph node involvement.

METHODS: Twenty-six fresh, unstained lymph nodes were imaged from 15 patients undergoing mastectomy or breast-conserving surgery with axillary clearance. Lymph node specimens were bisected to allow imaging of the internal face of each node. Co-located OCME and optical coherence tomography (OCT) scans were taken of each sample, and the results compared to standard post-operative hematoxylin-and-eosin-stained histology.

RESULTS: The optical backscattering signal provided by OCT alone may not provide reliable differentiation by inspection between benign and malignant lymphoid tissue. Alternatively, OCME highlights local changes in tissue strain that correspond to malignancy and are distinct from strain patterns in benign lymphoid tissue. The mechanical contrast provided by OCME complements the optical contrast provided by OCT and aids in the differentiation of malignant tumor from uninvolved lymphoid tissue.

CONCLUSION: The combination of OCME and OCT images represents a promising method for the identification of malignant lymphoid tissue. This method shows potential to provide intraoperative assessment of lymph node involvement, thus, preventing unnecessary removal of uninvolved tissues and improving patient outcomes.

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Efficacy of brief behavioral counselling by allied health professionals to promote physical activity in people with peripheral arterial disease (BIPP): study protocol for a multi-center randomized controlled trial.
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BACKGROUND: Physical activity is recommended for people with peripheral arterial disease (PAD), and can improve walking capacity and quality of life; and reduce pain, requirement for surgery and cardiovascular events. This trial will assess the efficacy of a brief behavioral counselling intervention delivered by allied health professionals to improve physical activity in people with PAD.

METHODS: This is a multi-center randomised controlled trial in four cities across Australia. Participants (N=200) will be recruited from specialist vascular clinics, general practitioners and research databases and randomised to either the control or intervention group. Both groups will receive usual medical care, a written PAD management information sheet including advice to walk, and four individualised contacts from a protocol-trained allied health professional over 3 months (weeks 1, 2, 6, 12). The control group will receive four 15-min telephone calls with general discussion about PAD symptoms and health and wellbeing. The intervention group will receive behavioral counselling via two 1-h face-to-face sessions and two 15-min telephone calls. The counselling is based on the 5A framework and will promote interval walking for 3x40 min/week. Assessments will be conducted at baseline, and 4, 12 and 24 months by staff blinded to participant allocation. Objectively assessed outcomes include physical activity (primary), sedentary behavior, lower limb body function, walking capacity, cardiorespiratory fitness, event-based claudication index, vascular interventions, clinical events, cardiovascular function, circulating markers, and anthropometric measures. Self-reported outcomes include physical activity and sedentary behavior, walking ability, pain severity, and health-related quality of life. Data will be analysed using an intention-to-treat approach. An economic evaluation will assess whether embedding the intervention into routine care would likely be value for money. A cost-effectiveness analysis will estimate change in cost per change in activity indicators due to the intervention, and a cost-utility analysis will assess change in cost per quality-adjusted life year. A full uncertainty analysis will be undertaken, including a value of information analysis, to evaluate the economic case for further research.

DISCUSSION: This trial will evaluate the efficacy and cost-effectiveness of a brief behavioral counselling intervention for a common cardiovascular disease with significant burden.

TRIAL REGISTRATION: ACTRN 12614000592640 Australian New Zealand Clinical Trials Registry. Registration Date 4 June 2014.

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Mycobacterium chimaera colonisation of heater-cooler units (HCU) in Western Australia, 2015: investigation of possible iatrogenic infection using whole genome sequencing.
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Following the reported link between heater-cooler unit (HCU) colonisation with Mycobacterium chimaera and endocarditis, mycobacterial sampling of all HCUs in use in Western Australia was initiated from August 2015, revealing M. chimaera colonisation in 10 of 15 HCUs. After M. chimaera was isolated from a pleural biopsy from a cardiothoracic patient who may have been exposed to a colonised HCU, a whole genome sequencing investigation was performed involving 65 specimens from 15 HCUs across five hospitals to assess if this infection was related to the HCU. Genetic relatedness was found between the 10 HCU M. chimaera isolates from four hospitals. However the M. chimaera isolate from the cardiothoracic patient was not genetically related to the HCU M. chimaera isolates from that hospital, nor to the other HCU isolates, indicating that the HCUs were not the source of the infection in this patient.


**Familial combined hyperlipidemia and hyperlipoprotein(a) as phenotypic mimics of familial hypercholesterolemia: Frequencies, associations and predictions.**

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BACKGROUND: A significant proportion of index cases presenting with phenotypic familial hypercholesterolemia (FH)
are not found to have a pathogenic mutation and may have other inherited conditions.

OBJECTIVES: Familial combined hyperlipidemia (FCHL) and elevated lipoprotein(a) [Lp(a)] may mimic FH, but the frequency and correlates of these disorders among mutation-negative FH patients have yet to be established.

METHODS: The frequency of FCHL and elevated Lp(a) was investigated in 206 FH mutation-negative index cases attending a specialist lipid clinic. An FCHL diagnostic nomogram was applied to each index case; a positive diagnosis was made in patients with a probability score exceeding 90%. Plasma Lp(a) concentration was measured by immunoassay, with an elevated level defined as >0.5 g/L. Clinical characteristics, including coronary artery disease (CAD) events, were compared between those with and without FCHL and hyper-Lp(a).

RESULTS: Of mutation-negative FH patients, 51.9% had probable FCHL. These patients were older (P = .002), had a higher BMI (P = .019) and systolic (P = .001) and diastolic blood pressures (P = .001) compared with those without FCHL. Elevated Lp(a) was observed in 44.7% of cases, and there were no significant differences in clinical characteristics with Lp(a) status. The presence of elevated Lp(a) (P = .002), but not FCHL, predicted CAD events. This association was independent of established CAD risk factors (P = .032).

CONCLUSION: FCHL and elevated Lp(a) are common disorders in patients with mutation-negative FH. Among such patients, FCHL co-expresses with components of the metabolic syndrome, and elevated Lp(a) is the major contributor to increased CAD risk.

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Grip and Muscle Strength Dynamometry Are Reliable and Valid in Patients With Unhealed Minor Burn Wounds.

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Small burns are common and can cause disproportionate levels of disability. The ability to measure muscle impairment and consequent functional disability is a necessity during rehabilitation of patients. This study aimed to determine the reliability and validity of grip and muscle strength dynamometry in patients with unhealed, minor burn wounds. Grip and muscle strength were assessed three times on each side. Assessment occurred at presentation for the initial injury and again every other day (or every 5 days beyond 10 days post injury) until discharge from the service. Reliability was assessed using intraclass correlation. Minimum detectable differences were calculated for each muscle group. Validity was assessed using regression analysis, incorporating appropriate burn severity measures and patient demographics. Thirty patients with TBSA <15% were assessed. Both grip and muscle strength demonstrated very good reliability (intraclass correlation coefficient: 0.85-0.96). Minimum detectable differences ranged from 3.8 to 8.0kg. Validity of both forms of dynamometry was confirmed through associations with gender for all muscle groups (P < .001). In addition, grip strength was associated with the dominant hand (P = .002) and time to assessment (P < .001). Strength was seen to improve over time in all muscle groups. Grip and muscle strength dynamometry are reliable and valid assessments of strength and are applicable for clinical use in patients who have unhealed, minor burn wounds.

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The contribution of routine follow-up to the detection of breast cancer recurrence after treatment for early disease.

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Aims: With increasing incidence and rising survival, there is a growing population of breast cancer survivors in Australia. Cancer Australia guidelines recommend a minimum follow-up incorporating seven visits over the first 5 years, based on level IV evidence, making this a substantial consumer of medical resources. Accepted components include regular histories, examination and annual mammography. We have assessed the value of these individual elements of follow-up through a review of relapse detection mechanisms. Methods: We examined the method of detection and mode of recurrence for 241 women (12.5%) relapsing from an initial observed population of 1942 patients with estrogen receptor positive early breast cancer. Data were obtained from a multidisciplinary breast service database with further information accrued from medical records and death certification. Results: Relapses included 44 local, 20 regional, 51 contralateral (likely new primary) and 168 distant events. 147 (60%) patients recurred within 5 years, 75 (31%) between 5 and 10 years and 21 (9%) after 10 years. Mode of recurrence detection was available on 195 cases and included 21 (11%) detected in routine clinics, 113 (58%) by patient self-detection and early presentation, and 45 (23%) by routine mammography. 64%, 88% and 0% of such cases involved metastatic disease at first relapse. Eight clinic-detected events involved symptom investigation and 13 were locoregional recurrences found on examination, with five of the latter surviving. Initial treatment was endocrine in 55%, chemotherapeutical in 36% and radiotherapeutical in 7%. 2% of patients received best supportive care alone. In seven of the 195 cases, relapse detection at an advanced stage potentially limited therapy. Conclusions: Overall, only one in 10 recurrences was detected by routine follow-up processes, the majority of relapses being diagnosed following selfpresentation with symptoms or through mammography. For the purposes of relapse detection, systems of routinemammographic surveillance and patient-driven symptom investigation should take precedence over routine clinic visits.

PMID:613440452


Toxicity and adherence to adjuvant antiestrogens and the utility of switching to second-line agents.

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Aim: To assess reported endocrine treatment toxicity and consequent adherence in a cohort of women with hormone receptor positive breast cancer treated at a single center, including the success of antiestrogen switching due to toxicity

Methods: This was a single center study at Royal Perth Hospital. Patients with hormone receptor positive breast cancer treated with curative intent were identified from the Breast Unit database. Patient-reported treatment toxicity and adherence were obtained from case notes and clinic letters for endocrine therapy used. Outcome data were also obtained. Results: 1921 patients were identified from the database from 1994 to 2011. 62% received tamoxifen as initial endocrine therapy, 13% letrozole, 18% anastrazole and 5% ovarian suppression plus and aromatase inhibitor or tamoxifen. At last follow-up, 31% were continuing on their first-line endocrine therapy, 20% had ceased as a result of completion of first-line therapy, 11% had ceased as a result of a planned switch of therapy, 5% had ceased as a result of development of metastatic disease and 26% had ceased as a result of treatment-related toxicity. The most frequently listed toxicity resulting in treatment cessation was hot flushes with this given as the main reason for cessation for 27% of those who ceased endocrine therapy. Of the 490 patients who ceased first-line endocrine therapy as a result of treatment toxicity, 316 (64%) trialled a second line of endocrine therapy. Of those, 160 (51%) were recorded as able to tolerate second-line treatment sufficiently to continue treatment to completion, last recorded follow-up or development of further breast cancer-related event. Conclusion: A significant proportion of patients ceased first-line endocrine therapy as a result of treatment toxicity. Trial of a second line of endocrine therapy where the first is ceased as a result of intolerance is worthwhile in this population.

PMID:613440415
A comparison of daily versus intermittent consultant medical oncology ward round: Does daily consultant ward rounds improve length of stay and early discharges?

Lam WS, Chan T, et al.

Background: There is an increasing evidence that daily consultant ward rounds improve length of stay. As a result, there is pressure from administration to implement daily consultant ward rounds. The evidence is strong for acute medical units; however, there is limited evidence in medical specialities including medical oncology. We assessed the length of stay and rate of early discharges in two ward round models, a daily consultant ward round versus an intermittent ward round, during the same period of time. Patients and Methods: Inpatients from Fiona Stanley Hospital from February 2015 to October 2015 were reviewed. Patients who were initially admitted to nononcological units were excluded. 184 episodes of care were identified in the daily ward round team, while 174 episodes of care were identified in the intermittent ward round team. Results: The average length of stay was 7.2 days for the daily consultant ward round team and 7.8 days for the intermittent ward round team. There was a difference of 0.6 days, which was not statistically significant (P = 0.5479). Total amount of patients discharged before 12 pm was 31 for the daily consultant ward round team and 32 from the intermittent ward round team, which was not statistically significant (P = 0.3187). Conclusion: Daily consultant ward rounds did not impact length of stay or early discharges. Other processes may need to be explored to improve efficiencies in inpatient medical oncology services.

Mammographic breast-density change as a predictor of outcome in hormone receptor positive breast cancer.

Martin HL, Yap F, et al.

Aim: To investigate the association between mammographic breast-density (MBD) change and disease-free survival in hormone receptor positive breast cancer during antiestrogen therapy. Methods: This was a single center study performed at Royal Perth Hospital. Patients were identified from the hospital breast unit database with hormone receptor positive breast cancer planned for curative treatment between 1994 and 2011. Demographic, pathology, treatment and outcome data were obtained from the unit database, case notes, clinic letters, electronic radiology and pathology systems and the Western Australian Cancer Registry. Mammograms were obtained from the hospital radiology archives and Breastscreen Western Australia. Film mammograms were scanned to obtain digital images. MBD was read by single reader using Cumulus software. Percentage change in MBD was compared between groups. The mammogram taken at diagnosis and the first mammogram taken in the 9-18-month period post-diagnosis were compared. Results: A total of 1921 patients were identified. At diagnosis, 22% were premenopausal, 8% perimenopausal and 69% postmenopausal. 62% received tamoxifen as initial endocrine therapy, 13% letrozole, 18% anastrazole and 5% ovarian suppression plus and aromatase inhibitor or tamoxifen. Interim univariate analysis of 921 patients gave a disease-free survival hazard ratio of 0.45 (95%CI 0.25-0.8; P = 0.006) for those with MBD reduction of >20% relative to those with MBD reduction of <0%. MBD measurement has now been completed on the remaining mammograms and analysis of the full cohort will be presented. Conclusion: Interim analysis shows that a greater reduction in MBD during antiestrogen therapy is associated with improved breast cancer outcome. Measurement of MBD change has the potential to allow tailoring of adjuvant endocrine therapy.

Use of positron emission tomography (PET) scan in breast cancer—a single center study.

Agarwal V, Martin H.
Background: The role of positron emission tomography (PET scan) in breast cancer is not yet clearly defined. PET scan has been shown to have potential for utility for management of breast cancer patients in a variety of settings, particularly with reference to metastatic disease. The aim of this project is to summarize current clinical practice at a single center regarding the use of PET-CT for breast cancer and assess its utility in patient management.

Method: All PETs performed at FSH were screened to identify those requested for patients known to have breast cancer. Details of the request indication, requesting clinician and other investigations ordered prior or following the imaging request were also recorded. The PET reports were also screened for any new findings that directly led to change of management.

Results: A total of 16 scans were done during the study period, eight were ordered by Medical Oncologist, five by general practitioners and three by other clinicians. Three were performed for patients with localized disease to investigate for potential metastatic disease, and 12 for patients with known metastatic disease. Eight scans resulted in findings that altered patient management subsequently. These findings included a suspicious ovarian lesion, subsequently diagnosed to be ovarian cancer, and progression of disease not seen on other modalities of imaging. Of the eight scans that showed new findings, which altered management, five were generated by Oncologist. Conclusion: PET is being used, but infrequently for patients with breast cancer. For 50% of the patients, the PET scan results altered subsequent patient management. This imaging modality should be considered in selected cases, with further prospective research required.

PMID:613440233

Impact of tumour infiltrating lymphocytes (TILs) & tumour regression in primary cutaneous melanoma on response to immune checkpoint inhibitor (ICI) therapy.

Introduction: Immune checkpoint inhibitors (ICIs) have revolutionized melanoma treatment. However, only one third of patients achieve durable disease control and long-term survival. Treatment is costly and associated with novel immune related adverse events. Therefore, there is an urgent need for predictive biomarkers to better select patients most suited to treatment with ICIs. Tumor infiltrating lymphocytes (TILs) is a favorable prognostic marker in different tumour types. We therefore evaluated the predictive significance of TILs and regression in primary cutaneous melanoma and correlated it with response to ICI therapy.

Patients & Methods: Patients treated with ICI therapy between Feb 2015- June 2016 for advanced melanoma were identified from institutional database. Data was collected from electronic medical records and Cancer Registry with a censor date of 1st June 2016. Survival was calculated through Kaplan-Meir analysis. Overall survival (OS) and progression free survival (PFS) was calculated from start of therapy till date of death/last follow up & date of progression/death respectively. Results: 35 patients were identified that fulfilled selection criteria. Regression and TILs were reported in the primary pathology of 21 patients. Patients with TILs in their primary pathology had a trend towards improved outcome with ICI for both PFS (6m vs 2.5m, log-rank P=0.052) and OS (NR vs 3m, p=0.2) compared to those with no TILs. There was no difference in PFS or OS for those with or without regression. Conclusion: TILs in primary cutaneous melanoma could be a useful predictor of response to ICI therapy and needs to be further evaluated prospectively in larger studies.

PMID:613440118

Linen facilities - What's under the sheets?

Introduction: Auditing laundry facilities, laundry transportation vehicles, and storage of linen is a key component of
NSQHS Standard 3, however, it is an integral hospital service that can be overlooked, especially when the service is provided by an external contractor. A new linen provider was reviewed in October 2015, and it was apparent that there were a number of areas that did not meet infection prevention and management (IP&M) standards and required significant advice and input. The infrastructure of the facility, coupled with poor work and IP&M practices at the initial audit were concerning to find.

Method: A baseline audit was undertaken with a new provider. This revealed a failure to comply with the AS/NZS 4146:2000 with a result of only 21.6% compliance to the standard. The ‘new’ contractor currently held the linen contract for all of Western Australia (WA) Health’s major public hospitals. All failed audit components were identified along with the expected action to be implemented to ensure the facility and its practices met the standard.

Results: The implementation of a detailed action plan to improve laundry standards resulted in a compliance rate of 91% over 8 weeks to ensure patient and staff safety which remains paramount.

Conclusion: Fiona Stanley (FSH) recommendations are now the benchmark for the linen service across WA. These new operating standards for the laundry facility have reduced the risk for patients state-wide. FSH has played a major role in enforcing and lifting standards of linen services across all health care facilities in WA.

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Achieving hand hygiene benchmarks in a greenfield hospital: The challenge, the journey and the outcomes to date.

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Introduction: In 2015 a greenfield hospital opened with high expectations of being innovative, developing a new culture and delivering patient and staff safety. Infection Prevention (IP) and Hand Hygiene (HH) were at the forefront. New workflows, technology and transitioning staff from varying facilities contributed to initial HH results being 61.3%. Re-establishing HH as a priority and increasing compliance was imperative to mitigate potential increases in Hospital Associated Infections, ensuring patient and staff safety.

Methods: Multiple targeted methodologies were employed across the organisation engaging the inter-professional workforce and empowering instigation of change. This incorporated:* Providing real time feedback to clinicians at ward level* Weekly hospital wide feedback including areas requiring improvement and acknowledging areas of success* Face to face education* Rewarding high achievers* Engaging consumers: “It’s ok to ask” campaign* Significant executive buy in assisted with:* Building of culture* Reinforcing patient centred care* Adhering to CARE values

Increased daily auditing (utilising the Hand Hygiene Australia standardised audit tool) enabled a greater visual presence of IP staff and establishing strong relationships with clinicians.

Results: A 20.5% increase in Compliance with the 5 moments for HH was achieved over a 1 year period (Audit 1 2016 result: 82.8%), exceeding national benchmarks reflecting staff engagement and commitment to excellence.

Conclusion: Various factors will influence staff compliance with standard practices including the 5 moments for HH. Through carefully targeted strategies and interprofessional engagement it has been demonstrated that HH rates can be increased to above benchmark levels.

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First-in-human clinical study with a novel drug-filled stent: 9-month clinical, angiographic, IVUS, and OCT outcomes from the revolution study.

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BACKGROUND The novel polymer-free drug-filled stent (DFS, Medtronic) is formed from a multi-layered wire (cobalt chromium outer, tantalum inner) with the core removed to create a continuous lumen within the stent structure. Sirolimus is loaded within this lumen. Small, abluminal laser-drilled holes (~20 mum) on the stent surface determine the rate of drug elution. Preclinical studies show drug release kinetics and drug tissue levels comparable to durable polymer DES and with peri-strut inflammation scores comparable with bare metal stents. By eliminating the need for a polymer matrix on the stent surface, DFS may provide more uniform drug delivery and avoid polymer-associated adverse vascular responses, thereby improving healing and potentially allowing for shorter duration of dual antiplatelet therapy. METHODS RevElution is an investigational study of DFS that enrolled 101 subjects with de novo lesions at 15 international sites. Subjects were divided into 2 cohorts (50 subjects each) in which angiography, intravascular ultrasound (IVUS), and clinical outcomes are measured at 9 months (“9-month” cohort) or 24 months (“24-month” cohort). Healing by optical coherence tomography (OCT) is evaluated in 60 subjects (30 in each cohort): the 9-month cohort undergoes OCT at baseline, either 1 or 3 months, and 9 months, and the 24-month cohort undergoes OCT at baseline, either 2 or 6 months, and 24 months. The powered primary endpoint is late lumen loss at 9 months compared with a historical control (durable polymer Resolute ZES). All patients are followed annually to 5 years. RESULTS At 1 month, median stent strut coverage was 91.4%, and median 0.3% (mean 1.5+/–2.3%) stent struts were malapposed. The 9-month clinical, angiographic, and IVUS outcomes in the 9-month cohort (N=50), as well as OCT at 1 (N=13), 3 (N=15), and 9 months (N=30) post implantation will be available at TCT 2016. CONCLUSION DFS implantation resulted in a high degree of stent strut coverage and a low rate of malapposition at 1 month, indicative of a favorable early healing profile. Complete 9-month imaging and clinical data will be presented at the meeting, providing a comprehensive intermediate-term assessment of DFS performance.

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(HL) plays in HDL metabolism and to better understand LPL- and HL-deficiency states.

METHODS: We examined the apolipoprotein (apo) A-I-, A-II-, A-IV-, C-I-, C-III-, and E-containing HDL subpopulation profiles, assessed by native 2-dimensional gel-electrophoresis and immunoblotting, in 6 homozygous and 11 heterozygous LPL-deficient, 6 homozygous and 4 heterozygous HL-deficient, and 50 control subjects.

RESULTS: LPL-deficient homozygotes had marked hypertriglyceridemia and significant decreases in LDL-C, HDL-C, and apoA-I. Their apoA-I-containing HDL subpopulation profile was shifted toward small HDL particles compared to controls. HL-deficient homozygotes had moderate hypertriglyceridemia, modest increases in LDL-C and HDL-C level, but normal apoA-I concentration. HL-deficient homozygotes had a unique distribution of apoA-I-containing HDL particles. The normally apoA-I:A-II, intermediate-size (alpha-2 and alpha-3) particles were significantly decreased, while the normally apoA-I only (very large alpha-1, small alpha-4, and very small prebeta-1) particles were significantly elevated. In contrast to control subjects, the very large alpha-1 particles of HL-deficient homozygotes were enriched in apoA-II. Homozygous LPL- and HL-deficient subjects also had abnormal distributions of apo C-I, C-III, and E in HDL particles. Values for all measured parameters in LPL- and HL-deficient heterozygotes were closer to values measured in controls than in homozygotes.

CONCLUSIONS: Our data are consistent with the concept that LPL is important for the maturation of small discoidal HDL particles into large spherical HDL particles, while HL is important for HDL remodeling of very large HDL particles into intermediate-size HDL particles.


Kimberley Indigenous mental health: An examination of metabolic syndrome risk factors.
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OBJECTIVE: There is an increased risk of physical health comorbidities in people with a mental illness. This paper examines the metabolic syndrome parameters for the general population, indigenous Australians and people with a mental illness, and compares them to a sample of predominantly indigenous adults with mental health problems.

DESIGN: A longitudinal (24 month) audit of patient medical records was conducted between February 2011 and March 2013.

SETTING: The Kimberley Mental Health and Drug Service in Broome, Western Australia.

PARTICIPANTS: Largely indigenous adults with a mental illness. Sample numbers increased from 56 at baseline (80% indigenous) to 136 at 18 months (70% indigenous).

MAIN OUTCOME MEASURES: Waist circumference, blood pressure, fasting lipids, and fasting blood glucose.

RESULTS: Preliminary assessment of the data indicates a high percentage of abnormalities at baseline and at the 18 month period on all four parameters, yet not all patients were assessed on a regular basis.

CONCLUSIONS: Abnormalities in metabolic profiles consistent with the non-Indigenous mental health population were found. There are considerable challenges to implementing regular monitoring of physical and metabolic profiles of indigenous people in rural and remote communities.
Active surveillance is suitable for intermediate term follow-up of renal oncocytoma diagnosed by percutaneous core biopsy.

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OBJECTIVES: To evaluate the intermediate outcome of conservative management in patients with biopsy-proven oncocytoma.

PATIENTS AND METHODS: Patients with oncocytoma diagnosed on percutaneous core biopsy between January 2000 to December 2014 were identified from the renal biopsy database of a large specialist urologic pathology laboratory. After review of patient clinical records, the study cohort comprised only of patients enrolled in active surveillance. Clinicopathological and follow-up details were reviewed for each case, in particular: type and interval of surveillance imaging, tumour growth, definitive intervention and reason for intervention. Where possible, correlation was made between the final surgical and the initial biopsy specimens.

RESULTS: Fifty three patients diagnosed with oncocytoma on core biopsy were initially placed on active surveillance with median follow-up of 34 months (range 6-109). The median age at diagnosis was 65 years (range 20-85) and median tumour size was 30 mm (range 13-87). Mean average tumour growth was 1.4 mm per annum (median 0 mm/year) with the majority (36 of 53, 68%) exhibiting minimal growth (less than 2 mm per annum) or partial regression. Forty seven of the 53 patients remained on active surveillance with no significant progression. Six patients elected to undergo definitive intervention (five surgical excision, one ablation). Renal oncocytoma was confirmed in all five patients who underwent surgical excision of their lesions.

CONCLUSIONS: The majority of oncocytomas in this study showed minimal growth rate or regression. Patients with biopsy proven oncocytoma can be conservatively managed with active surveillance.
Bone Marrow Transplantation. 2016; 51(10): 1400-1403.

**All is not lost in accelerated phase/blast crisis and after tyrosine kinase inhibitors fail in chronic myeloid leukaemia: a retrospective study of allogeneic stem cell transplant outcomes in Australia and New Zealand.**


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**$^{68}$Ga DOTATATE PET/CT of Non-FDG-Avid Pulmonary Metastatic Hemangiopericytoma.**

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We present the FDG and Ga DOTATATE PET/CT findings of a 68-year-old woman with pulmonary metastases 28 years after her initial diagnosis of central nervous system hemangiopericytoma. The largest of the pulmonary lesions showed prominent Ga DOTATATE uptake with comparatively minimal FDG avidity. Hemangiopericytoma is a rare mesenchymal tumor that arises from malignant pericytes, cells that form the walls of capillaries and postcapillary venules. This case demonstrates the potential of radiolabeled somatostatin analogs as a therapeutic option in the setting of widespread metastatic disease.

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**The authors reply.**

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DOI:https://dx.doi.org/10.1097/CCM.0000000000001973


**Determinants of Urinary Output Response to IV Furosemide in Acute Kidney Injury: A Pharmacokinetic/Pharmacodynamic Study.**

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OBJECTIVES: This study assessed the determinants of urinary output response to furosemide in acute kidney injury; specifically, whether the response is related to altered pharmacokinetics or pharmacodynamics.

DESIGN: Prospective cohort.

SETTING: Tertiary ICU.

PATIENTS: Thirty critically ill patients with acute kidney injury without preexisting renal impairment or recent diuretic exposure.

INTERVENTION: A single dose of IV furosemide.

MEASUREMENTS AND MAIN RESULTS: Baseline markers of intravascular volume status were obtained prior to administering furosemide. Six-hour creatinine clearance, hourly plasma/urinary furosemide concentrations, and hourly urinary output were used to assess furosemide pharmacokinetics/pharmacodynamics parameters. Of 30 patients enrolled, 11 had stage-1 (37%), nine had stage-2 (30%), and 10 had stage-3 (33%) Acute Kidney Injury Network acute kidney injury. Seventy-three percent were septic, 47% required norepinephrine, and 53% were mechanically ventilated. Urinary output doubled in 20 patients (67%) following IV furosemide. Measured creatinine clearance was strongly associated with the amount of urinary furosemide excreted and was the only reliable predictor of the urinary output after furosemide (area under the receiver-operating-characteristic curve, 0.75; 95% CI, 0.57-0.93). In addition to an altered pharmacokinetics (p < 0.01), a reduced pharmacodynamics response to furosemide also became important when creatinine clearance was reduced to less than 40mL/min/1.73 m (p = 0.01). Acute kidney injury staging and markers of intravascular volume, including central venous pressure, brain-natriuretic-peptide concentration, and fractional urinary sodium excretion were not predictive of urinary output response to furosemide.

CONCLUSIONS: The severity of acute kidney injury, as reflected by the measured creatinine clearance, alters both pharmacokinetics and pharmacodynamics of furosemide in acute kidney injury, and was the only reliable predictor of the urinary output response to furosemide in acute kidney injury.

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**Tigecycline use in the outpatient parenteral antibiotic therapy setting.**

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In the context of globally increasing antimicrobial resistance, tigecycline appears to be a useful therapeutic option. The need for prolonged courses for complex infections has prompted consideration of its use via outpatient parenteral antibiotic therapy (OPAT) programmes, although clinical outcomes when used in this setting remain unknown. We retrospectively reviewed the patient characteristics and outcomes of 11 patients who received tigecycline, most commonly delivered as 100 mg once daily, via OPAT at three tertiary Australian hospitals. Rates of
co-morbidity and prior antibiotic use were high. Patients had a wide range of infections including bone and/or joint (n=5), intra-abdominal (n=3), lower respiratory tract (n=2) and parapharyngeal abscess (n=1). Mycobacterial species (n=5) were the most frequent pathogen, and multi-resistant organisms were common (n=4). The median OPAT duration was 14 days (IQR 6-30). Nausea was encountered in 45 % of cases. At completion of OPAT, 1 patient (9 %) was cured, 2 (18 %) had improved and 8 (73 %) failed therapy. Failure occurred due to either progression or non-response of infection (n=4), re-admission (n=3), premature cessation of tigecycline due to nausea (n=3) or death (n=1). Whilst OPAT delivery of tigecycline is a therapeutic option, when used as second-line therapy for complex, often multi-resistant infections in patients with multiple comorbidities, high rates of clinical failure, readmissions and adverse effects, especially nausea, should be anticipated.

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Antifungal susceptibilities of non-Aspergillus filamentous fungi causing invasive infection in Australia: support for current antifungal guideline recommendations.

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Antifungal susceptibilities of non-Aspergillus filamentous fungal pathogens cannot always be inferred from their identification. Here we determined, using the Sensititre® YeastOne® YO10 panel, the in vitro activities of nine antifungal agents against 52 clinical isolates of emergent non-Aspergillus moulds representing 17 fungal groups in Australia. Isolates comprised Mucorales (n=14), Scedosporium/Lomentospora spp. (n=18) and a range of hyaline hyphomycetes (n=9) and other dematiaceous fungi (n=11). Excluding Verruconis gallopava, echinocandins demonstrated poor activity (MICs generally >8mg/L) against these moulds. Lomentospora prolificans (n=4) and Fusarium spp. (n=6) demonstrated raised MICs to all antifungal drugs tested, with the lowest being to voriconazole and amphotericin B (AmB), respectively (geometric mean MICs of 3.4mg/L and 2.2mg/L, respectively). All Scedosporium apiospermum complex isolates (n=14) were inhibited by voriconazole concentrations of <0.25mg/L, followed by posaconazole and itraconazole at <1mg/L. Posaconazole and AmB were the most active agents against
the Mucorales, with MIC90 values of 1mg/L and 2mg/L, respectively, for Rhizopus spp. For dematiaceous fungi, all isolates were inhibited by itraconazole and posaconazole concentrations of <0.5mg/L (MIC90, 0.12mg/L and 0.25mg/L, respectively), but voriconazole and AmB also had in vitro activity (MIC90, 0.5mg/L and 1mg/L, respectively). Differences in antifungal susceptibility within species and between species within genera support the need for testing individual patient isolates to guide therapy. The Sensititre() YeastOne() offers a practical alternative to the reference methodology for susceptibility testing of moulds.

Differences in antifungal susceptibility within species and between species within genera support the need for testing individual patient isolates to guide therapy. The Sensititre() YeastOne() offers a practical alternative to the reference methodology for susceptibility testing of moulds.

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Mental health nurses’ contributions to community mental health care: An Australian study.

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Australian mental health policy is focused on providing mental health care in the community setting and community mental health teams provide services to clients in a shared model with primary care. The historical literature reports that community mental health nurses’ experience high levels of stress and are often allocated the most complex and challenging clients managed by the team. Yet information on their specific roles remains limited. This paper reports on research conducted at one Australian public mental health service to identify the components of the community mental health nursing role and to quantify the time nurses spent in each component during the study period. Six focus groups were conducted with community mental health nurses to identify their perceived role within the team. Data analysis identified 18 components of which 10 were related to direct clinical contact with clients and eight covered administrative and care coordination activities. A data collection tool based on the findings of the focus groups was designed and nurses recorded workload data on the tool in 15-min intervals over a 4-week period. Seventeen nurses collected 1528 hours of data. Internal coordination of care was identified as the top workload item followed by clinical documentation and national data collection responsibilities supporting the complexity of the community mental health nursing role. The high rating attached to the internal coordination of care role demonstrates an important contribution that community mental health nurses make to the functioning of the team and the delivery of quality mental health care.

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Should women with incontinence and prolapse do abdominal curls?

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INTRODUCTION AND HYPOTHESIS: Urinary incontinence (UI) and pelvic organ prolapse (POP) occur in 30-50 % of
women. It is proposed that increases in intra-abdominal pressure (IAP) caused by high-intensity activities may contribute to symptoms of pelvic floor dysfunction. There is a lack of consensus as to the type of activity restrictions that may be necessary in this population. The objective was to determine the change in IAP (cm H20) during abdominal curl and cough in patients with UI and POP attending urodynamic evaluation.

METHODS: In this exploratory descriptive study, 30 women with diagnosed POP and/or UI were recruited. IAP was measured by multichannel cystometry whilst participants performed three abdominal curls and three maximal coughs.

RESULTS: Participants were aged 29-80 (mean 56.2) years, and mean +/- standard deviation (SD) body mass index (BMI) was 29.9 (5.2) kg/m(-2). All participants had UI and 12 had POP in addition to UI. IAP increased significantly from rest to abdominal curl and cough (19.6-50.3 and 78.4, respectively; p<0.001). Greater pressures were generated in the women with POP than in those with UI only (p=0.02). There were large variations in change in pressure between participants (1.67-159.66 for cough; 4-81.67 for abdominal curl).

CONCLUSION: The large variability in IAP generated during abdominal curl and cough suggests some current recommendations may be unnecessarily restrictive in some women but important in others. Advice for women with pelvic floor dysfunction undertaking tasks that increase IAP needs to be individualized.

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Day-of-Surgery Mobilization Reduces the Length of Stay After Elective Hip Arthroplasty.

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BACKGROUND: To determine the effect of mobilization on the day of surgery on the readiness for discharge and length of stay after elective total hip arthroplasty (THA).

METHODS: We devised a randomized control trial with concealed allocation and intention-to-treat analysis. Overall, 126 patients who underwent THA and met the criteria for mobilization on the day of surgery were randomly allocated into 2 groups; the intervention group was mobilized on the day of surgery, n = 58 and the control group was mobilized on the day after surgery, n = 68. Apart from timing of mobilization, both groups received the same postoperative management. The primary outcome measures were length of hospital stay and time to readiness for discharge.

RESULTS: The early mobilization group was ready for discharge 63 hours (standard deviation [SD] = 15 hours) after surgery, compared to 70 hours (SD = 18 hours) for the control group (P = .03, 95% CI, 0.7-12.8). There was no significant difference in hospital stay in the early mobilization group (77 hours [SD = 30 hours]), compared to the control group (87 hours [SD = 35 hours]; P = .11, 95% CI, -2.1 to 21.6). Despite this at any point in time after the surgery, the intervention group was 1.8 times (P = .003, 95% CI, 1.2-2.7) more likely to have been discharged.

CONCLUSION: Mobilization on the day of THA surgery significantly increases the probability of discharge at any singular point in time compared with mobilization on the day after surgery and decreases the time to readiness for discharge.

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omega-3 Fatty Acid Ethyl Esters Diminish Postprandial Lipemia in Familial Hypercholesterolemia.

Chan DC, Pang J, et al.
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CONTEXT: Impaired postprandial chylomicron metabolism induces hypertriglyceridemia and may increase the risk of atherosclerotic cardiovascular disease. Omega-3 fatty acid ethyl ester (omega-3 FAEE) supplementation decreases plasma triglycerides. However, its effect on postprandial chylomicron metabolism in familial hypercholesterolemia (FH) has not yet been investigated.

OBJECTIVE: We aimed to examine the effect of omega-3 FAEE supplementation on postprandial responses in plasma triglycerides, very-low-density lipoprotein (VLDL) apolipoprotein B (apoB)-100, and apoB-48 in FH patients receiving standard cholesterol-lowering treatment.

DESIGN, SETTING, AND PATIENTS: We carried out an 8-week open-label, randomized, crossover intervention trial to test the effect of oral supplementation with 4 g/d omega-3 FAEE (46% eicosapentaenoic acid and 38% docosahexaenoic acid) on postprandial triglyceride, VLDL-apoB-100, and apoB-48 responses in FH patients after ingestion of an oral fat load.

OUTCOMES MEASURES: Plasma total and incremental triglyceride, VLDL-apoB-100, and apoB-48 0- to 10-hour area under the curve (AUC).
RESULTS: omega-3 FAEE supplementation significantly (P < .05 in all) reduced concentrations of fasting plasma triglyceride (-20%), apoB (-8%), VLDL-apoB-100 (-26%), and apoB-48 (-36%); as well as systolic blood pressure (-6%) and diastolic blood pressure (-6%). Postprandial triglyceride and VLDL-apoB-100 total AUCs (-19% and -26%, respectively; P < .01) and incremental AUCs (-18% and -35%, respectively; P < .05), as well as postprandial apoB-48 total AUC (-30%; P < .02) were significantly reduced by omega-3 FAEE supplementation.

CONCLUSION: Supplementation with omega-3 FAEs improves postprandial lipemia in FH patients receiving standard care; this may have implications for further reducing atherosclerotic cardiovascular disease in this high-risk patient group.

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Efficacy and safety of grazoprevir + ribavirin for 12 or 24 weeks in treatment-naive patients with hepatitis C virus genotype 1 infection.

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Grazoprevir (GZR) is a second-generation hepatitis C virus NS3/4A protease inhibitor. The aim of this study was to evaluate GZR plus ribavirin (RBV) in patients with HCV GT1 infection. Noncirrhotic, IL28B CC patients with HCV genotype 1 infection were randomized to GZR 100 mg once daily and RBV for 12 or 24 weeks. Patients in the 12-week arm with detectable HCV RNA at treatment week 4 (TW4) had treatment extended to 24 weeks (response-guided therapy, RGT). The primary endpoint was sustained virologic response (SVR12) at follow-up week 12 (HCV RNA <25 IU/mL) in the per-protocol (PP) population (excluding patients with important protocol deviations). Twenty-six patients were randomized and 22 were included in the PP population. SVR12 was 58.3% (7 of 12) and 90% (9 of 10) in the RGT and 24-week arms, respectively. Seven PP patients had virologic failure, including one patient in the 24-week arm who relapsed after follow-up week 12. All three breakthrough patients had wild-type (WT) virus at baseline and developed breakthrough at TW6 or TW12 with Y56H, A156T and D168A/N mutations. Of the five relapse patients, four had WT at baseline (at relapse three had WT and one had V55A and D168A), and one had S122A/T at baseline and S122T at relapse. There were no serious adverse events (AEs), discontinuations due to AEs or grade 3/4 elevations in total and/or direct bilirubin. Grazoprevir plus RBV was associated with a rapid and sustained suppression of HCV RNA. These results support further evaluation of grazoprevir-based regimens (NCT01716156; protocol P039).

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Emu Oil Combined with LyprinolTM Reduces Small Intestinal Damage in a Rat Model of Chemotherapy-Induced Mucositis.

Chemotherapy-induced mucositis is characterized by inflammation and ulcerating lesions lining the alimentary tract. Emu Oil and LyprinolTM have independently demonstrated their therapeutic potential in intestinal inflammatory disorders, including mucositis. We investigated Emu Oil and LyprinolTM in combination for their further potential to alleviate chemotherapy-induced mucositis in rats. Rats were gavaged with (1 ml) water, Olive Oil, Emu Oil + Olive Oil, LyprinolTM + Olive Oil or Emu Oil + LyprinolTM from Days 0 to 7, injected with saline (control) or 5-Fluorouracil (5-FU) on Day 5 and euthanized on Day 8. Myeloperoxidase (MPO) activity (indicative of acute inflammation), histological severity scores, and intestinal architecture were quantified. Myeloperoxidase activity was significantly increased in the jejunum and ileum following 5-FU, compared to saline controls. Both Olive Oil and Emu Oil + LyprinolTM significantly reduced jejunal MPO levels (1.8-fold and 1.7-fold, respectively), whereas only Emu Oil + LyprinolTM significantly decreased ileal MPO levels, relative to 5-FU controls. All oil treatments decreased histological severity scores in the jejunum and ileum, and normalized crypt depth in the mid small intestine, relative to 5-FU controls. Emu Oil combined with LyprinolTM partially reduced acute small intestinal inflammation. Isolating bioactive constituents of these naturally sourced oils could provide a more targeted strategy to protect against intestinal mucositis.

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BACKGROUND AND OBJECTIVE: The systemic responses triggered by burns and resuscitative measures may cause pulmonary damage and edema in the acute phase. These effects may occur in the absence of inhalation injury. Currently, there is a paucity of data on the recovery of the respiratory system postburn. This study aimed to examine 10-year hospital service use for respiratory morbidity in children with cutaneous burns and no smoke inhalation injury.

METHODS: A population-based longitudinal study with 10-year follow-up using linked hospital and death from Western Australia for children <5 years when hospitalized for a first burn injury (n = 5290) between 1980 and 2012 and a frequency matched noninjury comparison cohort, randomly selected from Western Australia’s birth registrations (n = 27061). Multivariate negative binomial and Cox proportional hazards regression models were used to generate adjusted incidence rate ratios (IRR) and hazard ratios, respectively.

RESULTS: After adjustment for demographic factors and preexisting health status, the burn cohort had higher rates of admissions for influenza and viral pneumonia (IRR, 1.78; 95% confidence interval [CI], 1.10–2.87), bacterial pneumonia (IRR, 1.34; 95% CI, 1.06–1.70), and other respiratory infections (IRR, 1.65; 95% CI, 1.43–1.90). No significant difference was found for other upper respiratory tract conditions (IRR, 1.10; 95% CI, 0.98–1.23) or chronic lower respiratory diseases (IRR, 0.99; 95% CI, 0.80–1.23) compared with the uninjured cohort.

CONCLUSIONS: These findings demonstrated increased respiratory infection admissions after burns. These outcomes suggest that immune changes triggered by a burn injury may persist in some children for at least 10 years after wound healing.

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Wide-field optical coherence micro-elastography for intraoperative assessment of human breast cancer margins.
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Incomplete excision of malignant tissue is a major issue in breast-conserving surgery, with typically 20 - 30% of cases requiring a second surgical procedure arising from postoperative detection of an involved margin. We report advances in the development of a new intraoperative tool, optical coherence micro-elastography, for the assessment of tumor margins on the micro-scale. We demonstrate an important step by conducting whole specimen imaging in
intraoperative time frames with a wide-field scanning system acquiring mosaicked elastograms with overall dimensions of ~50 x 50 mm, large enough to image an entire face of most lumpectomy specimens. This capability is enabled by a wide-aperture annular actuator with an internal diameter of 65 mm. We demonstrate feasibility by presenting elastograms recorded from freshly excised human breast tissue, including from a mastectomy, lumpectomies and a cavity shaving.

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The impact of non-severe burn injury on cardiac function and long-term cardiovascular pathology.

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Severe burn injury significantly affects cardiovascular function for up to 3 years. However, whether this leads to long-term pathology is unknown. The impact of non-severe burn injury, which accounts for over 80% of admissions in developed countries, has not been investigated. Using a rodent model of non-severe burn injury with subsequent echocardiography we showed significantly increased left ventricular end systolic diameter (LVESD) and ventricular wall thickness at up to 3 months post-injury. Use of propranolol abrogated the changes in cardiac measures observed. Subsequently we investigated changes in a patient cohort with non-severe injury. Echocardiography measured at baseline and at 3 months post-injury showed increased LVESD at 3 months and significantly decreased posterior wall diameter. Finally, 32 years of Western Australian hospital records were used to investigate the incidence of cardiovascular disease admissions after burn injury. People who had experienced a burn had increased hospital admissions and length of stay for cardiovascular diseases when compared to a matched uninjured cohort. This study presents animal, patient and population data that strongly suggest non-severe burn injury has significant effects on cardiovascular function and long-term morbidity in some burn patients. Identification of patients at risk will promote better intervention and outcomes for burn patients.

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Observational studies - should we simply ignore them in assessing transfusion outcomes?

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BACKGROUND: As defined by evidence-based medicine randomized controlled trials rank higher than observational studies in the hierarchy of clinical research. Accordingly, when assessing the effects of treatments on patient outcomes, there is a tendency to focus on the study method rather than also appraising the key elements of study design. A long-standing debate regarding findings of randomized controlled trials compared with those of observational studies, their strengths and limitations and questions regarding causal inference, has recently come into focus in relation to research assessing patient outcomes in transfusion medicine.

DISCUSSION: Observational studies are seen to have limitations that are largely avoided with randomized controlled trials, leading to the view that observational studies should not generally be used to inform practice. For example, observational studies examining patient outcomes associated with blood transfusion often present higher estimates of adverse outcomes than randomized controlled trials. Some have explained this difference as being a result of observational studies not properly adjusting for differences between patients transfused and those not transfused. However, one factor often overlooked, likely contributing to these variances between study methods is different exposure criteria. Another common to both study methods is exposure dose, specifically, measuring units transfused during only a part of the patient’s hospital stay. When comparing the results of observational studies with randomized controlled trials assessing transfusion outcomes it is important that one consider not only the study method, but also the key elements of study design. Any study, regardless of its method, should focus on accurate measurement of the exposure and outcome variables of interest. Failure to do so may subject the study, regardless of its type, to bias and the need to interpret the results with caution.


Leiomyosarcoma of great saphenous vein localised to the calf.
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We present the case of a 76-year-old man with a 2-month history of mildly tender swelling in the right calf for which he had an initial excision and then a wide local excision followed by a split skin graft because the initial histopathology confirmed that there was a Grade I leiomyosarcoma of great saphenous vein. A simple lump in the lower limb could be a malignant vascular tumour and should always be considered in the list of differential diagnosis of a lump in the lower limb.

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A randomized, double-blind, placebo-controlled study of bimagrumab in patients with sporadic inclusion body myositis.
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Background/Purpose: Bimagrumab (BYM338) is a novel fully human monoclonal antibody that binds competitively to activin type II receptors with greater affinity than natural inhibitory ligands such as activin and myostatin, thereby inducing skeletal muscle hypertrophy. This study examined efficacy and safety of bimagrumab on physical function, muscle strength and muscle mass in patients with sporadic inclusion body myositis (sIBM). Methods: RESILIENT was a multicenter, randomized, double-blind, placebo-controlled, dose-finding study (clinicaltrials.gov NCT01925209). Eligible participants were randomized (1:1:1:1) to receive i.v. infusions of bimagrumab 10, 3, 1 mg/kg or placebo every 4 weeks for at least 48 weeks. Change from baseline to Week 52 in 6-minute walk distance test (6MWD; primary outcome), quadriceps quantitative muscle testing (QMT), sIBM physical functioning assessment (sIFA) and lean body mass (LBM) were assessed. Safety assessments included recording of adverse events (AEs) and serious AEs. Results: 251 patients (mean[SD] age: 68.1[8.2] years; 162[64.5%] men; mean time since sIBM diagnosis: 4.6[3.53] years) were randomized and treated. Participants on placebo and 1 mg/kg bimagrumab had a mean 6MWD decrease from baseline to Week 52 of 8.96 and 10.27 m, respectively, vs. an increase of 9.63 m for 3 mg/kg and 8.63 m for 10 mg/kg bimagrumab. Differences between treatment vs. placebo did not reach statistical significance (p>0.1). No consistent differences in quadriceps QMT were observed vs. placebo. However, at Week 52, there was less deterioration (mean treatment difference: 5.10; 0-100 scale) in the patient-reported outcome (PRO) instrument, sIFA, in 10 mg/kg bimagrumab vs. placebo (p=0.03), resulting in a clinically relevant and statistically significant increase in responders in this group (55% vs. 30%; p=0.0115). Bimagrumab showed a dose-dependent increase in LBM vs. placebo (mean treatment ratios: 3 and 10 mg/kg vs. placebo: 1.033 and 1.058, respectively). At Week 52, the difference was statistically significant for the 3 and 10 mg/kg doses (p<0.0001). The most frequently reported AEs in the bimagrumab groups were diarrhea and muscle spasm. About one-third patients in all groups reported serious AEs, except for bimagrumab 3 mg/kg (17.5%). Conclusion: Bimagrumab was well-tolerated, increased LBM and showed a potential benefit in PRO, but did not reach the primary endpoint of improving 6MWD or showed an improvement in muscle strength.

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New opportunities, new frontiers: Case files from the first 12 months of Western Australia’s only obstetric unit with on site interventional radiology.

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Background: The role of interventional radiology (IR) in the management of acute obstetric haemorrhage has not been well explored in Western Australia, due to the separation of tertiary obstetrics from hospitals with IR capacity. Fiona Stanley Hospital opened in February 2015 and houses the state’s first same-site obstetric and IR facilities. We report on the first five cases managed collaboratively between obstetric and radiology services in our unit. Cases: Five cases of major obstetric haemorrhage have been managed with the use of IR techniques in our unit. A combination of uterine artery and internal iliac artery embolisation has been used to treat two cases of antenatally diagnosed placenta accreta, two cases of massive obstetric haemorrhage due to uterine atony, and a case of massive haemorrhage due to a broad ligament haematoma. Three of the five cases were transferred in from other hospitals in WA. All five cases required emergency, or short-notice, mobilisation of specialist anaesthetic, radiology, obstetric and neonatal teams. There were no cases of severe neonatal or maternal morbidity and no patient required a hysterectomy following an embolisation procedure. Discussion: Fiona Stanley Hospital has the capacity and expertise to safely manage obstetric cases which may benefit from emergency embolisation. This is the first time this service has been easily accessible for obstetric patients in WA. It is expected that the utilisation of this service will expand further in the future.
Introduction: Maternal near-miss (MNM) identification is a growing means of assessing both the quality of care and burden of morbidity in the obstetric population within Australia and internationally. Despite this, limited research into the validity and suitability of published identification criteria has been performed within an urban Australian hospital setting. The aim of this study was to retrospectively assess obstetric ICU admissions using published MNM identification criteria at Rockingham General Hospital (RGH), in order to determine the factors leading to MNM identification and differences between the various criteria. Methods: A data collection tool comprising of six published MNM identification criteria was employed against three years of ICU admissions (94) under the obstetric service at RGH. Fleiss' Kappa, average pairwise Cohen's Kappa and Krippendorf's Alpha were used to assess the level of agreement between the six criteria. To determine individual factors driving identification, a principle component function analysis was performed. Results: 11.6% to 44.6% of cases were identified as MNM, depending upon the criteria. All criteria exhibited poor levels of agreement between one another with only a small number of variables contributing the majority of variance in classification. Discussion: Currently published MNM identification criteria are poorly suited to the studied patient cohort, exhibiting poor inter-criteria reliability with only a small number of variables driving classification as MNM.

Introduction: The dynamic nature of operating teams creates many challenges including effective planning and communication. The purpose of the present study is to examine the utility of multidisciplinary team briefings on staff engagement, patient safety, and theatre efficiency. Team briefings are 5-min discussions involving all theatre staff and is executed prior to the list commencing. The purpose is to share information, build trust and ownership, as well as proactively plan for challenges. Methods: The first study leveraged structured observations (N = 134) and multi-source survey data to examine the impact on staff engagement and patient safety (N = 118). The second study examined the potential impact on theatre efficiency using theatre management system and self-report data (N = 85). Results: Independent samples t-test results demonstrated teams that briefed reported significantly higher team and job satisfaction than teams that did not brief. Furthermore, the quality of surgeon communication with OT staff was negatively correlated with near misses (r = -0.23, p > 0.05), and team non-technical skills was the single strongest predictor of minor complications (r = -0.37, p < 0.01). Support was also found for the impact of briefings on total list time (r = -0.23, p = 0.05) and overall patient care time (r = -0.33, p = 0.003). Discussion: We will briefly discuss potential mechanisms through which the benefits are observed and provide insights into the implementation of briefings within the surgical context. Additional resources available from www.transformativeworkdesign.com.

Introduction: Obstetric anal sphincter injuries are a significant cause of morbidity in obstetrics, with an incidence of 11% to 20% in the published literature. The aim of this study was to determine the incidence of Obstetric anal sphincter injuries in the obstetric population at the study hospital. Methods: A retrospective study of all obstetric operative deliveries (N = 12,178) between 2015 and 2016. Surgery was defined as an accepted obstetric anal sphincter injury (AI) if complications were present during the delivery, or had surgery within 72 hours postpartum. Results: 503 (4.1%) women experienced an AI during their delivery. Discussion: The incidence of Obstetric anal sphincter injuries in this study was significantly higher than other studies. This may be due to the study hospital's focus on perineal management, and the use of a standardized definition of AI.
Introduction: Obstetric Anal Sphincter Injuries (OASIS) are a disruption of the anal sphincter after vaginal delivery. Complications from OASIS can significantly impact a woman's quality of life. Assessment of OASIS in a new obstetric centre is pertinent to ensure adherence to guidelines and optimal patient care. The objective of this study was to identify rates, risk factors, intraoperative management and follow up for OASIS in the Obstetric Unit at Fiona Stanley Hospital (FSH) in Western Australia. Methods: Two retrospective audit of the online birth register were performed, December 2014 to March 2015 and July 2015 to November 2015. Patients were stratified according to parity, type of tear, antenatal and intrapartum risk factors, intraoperative management, immediate post-operative management and follow-up reviews. RANZCOG rates and guidelines were used as the national benchmark. Results: The rate of OASIS was <3%. Nulliparous patients had higher rates than multiparous patients. 3A tears were most common. Risk factors most associated with OASIS were nulliparity, prolonged second stage and instrumental deliveries. Intraoperative and post-operative management was almost 100% in all patients. Outpatient physiotherapy followup was >90% while gynaecology follow-up was 65%. Discussion: At Fiona Stanley Hospital, the rate of OASIS in nulliparous patients was at national standard but higher for multiparous patients. The excellent in-hospital management of OASIS is indicative of vigilance, availability of resource, and compliance to local protocol. Adequate follow-up remains a challenge for any new obstetric service.


The impact of the cook cervical ripening balloon on the induction of labour process at Fiona Stanley Hospital.

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Introduction: The Cook Cervical Ripening Balloon for labour induction was introduced at Fiona Stanley Hospital in October 2015 in place of the Foley catheter. Methods: The initial audit of 18 patients was conducted in January 2016 to establish the safety and effectiveness of this new intervention. We considered the indications for induction, how the device was being used and the outcomes for those who received the ripening balloon compared to the overall FSH obstetric population. Results: The initial audit suggested that the Cook Balloon was a safe and acceptable intervention. Vaginal delivery rates were encouraging, especially given that high risk patients were being induced by this method. However, there was variation in how the device was being used and many patients that would have been suitable for the balloon were being induced by other methods. Therefore, the consultant body met to standardise the insertion technique and the duration of treatment. A training session on insertion was organised for midwifery and medical staff. Staff was encouraged to counsel and assess antenatal patients so that inductions were by the most appropriate method. The admission time for induction was reviewed with the aim of reducing the admission to delivery interval and improving patient flow. A FSH specific information leaflet was to be developed for patients. A reaudit is planned for autumn 2016. Discussion: The catheter appears to be an acceptable induction of labour method. Staff training, standardised practice and antenatal counselling should be beneficial to patients and the maternity unit.

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Taurocholate induces proliferation and biliary differentiation of liver progenitor cells resulting in hepatic stellate cell chemotaxis: Insights into the pathogenesis of pediatric CF liver disease.

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Cystic fibrosis liver disease (CFLD) causes progressive biliary cirrhosis in children with CF, yet its cause(s) and early
pathogenesis is incompletely understood. We hypothesized that a bile acid-induced Ductular Reaction (DR) is associated with early fibrosis development. We evaluated the DR by CK7 immunohistochemistry in liver biopsies from 60 children with CFLD, staged for fibrosis, and compared these with biopsies from children with non-CFLD neonatal cholestasis (n=8) and normal liver (n=4). We have previously reported that the bile acid, taurocholate is elevated in children with CFLD and we hypothesised that a bile acid-induced Ductular Reaction (DR) was associated with early fibrosis development. Here we report that biliary levels of taurocholate in CFLD children positively correlated with the DR. We examined the possible mechanisms of DR induction from taurocholate by treating liver progenitor cells (LPCs) with taurocholate to assess the impact on three key events in the evolution of the DR: LPC proliferation, biliary differentiation of LPCs and hepatic stellate cell (HSC) chemotaxis. Treatment of LPCs with taurocholate initiated a significant (p<0.001) increase in cell proliferation over two days. Furthermore, LPCs treated with taurocholate showed time-dependent enhanced expression of genes associated with cholangiocyte differentiation (CK19, p<0.0001; Connexin-43, p<0.0001), while the hepatocyte differentiation marker HNF4a was suppressed (p=0.0376). Taurocholate induced LPC expression of chemokines including MCP-1, MIP1alpha, and RANTES. Conditioned medium from taurocholate-treated LPCs induced HSC chemotaxis, which was then significantly inhibited by anti-MIP1a neutralizing antibody (p<0.01). This study demonstrates that taurocholate promotes LPC proliferation, biliary differentiation and development of the DR, with subsequent induction of chemokines, which recruit HSCs therefore may drive fibrogenesis. Taken together, these observations support the hypothesis that elevated biliary taurocholate plays a role in mediating the DR and fibrogenesis associated with CFLD.

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-3 fatty acid ethyl esters diminish postprandial lipemia in familial hypercholesterolemia.

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Context: Impaired postprandial chylomicron metabolism induces hypertriglyceridemia and may increase the risk of atherosclerotic cardiovascular disease. Omega-3 fatty acid ethyl ester (-3 FAEE) supplementation decreases plasma triglycerides. However, its effect on postprandial chylomicron metabolism in familial hypercholesterolemia (FH) has not yet been investigated. Objective: We aimed to examine the effect of -3 FAEE supplementation on postprandial responses in plasma triglycerides, very-low-density lipoprotein (VLDL) apolipoprotein B (apoB)-100, and apoB-48 in FH patients receiving standard cholesterol-lowering treatment. Design, Setting, and Patients: We carried out an 8-week open-label, randomized, crossover intervention trial to test the effect of oral supplementation with 4 g/d -3 FAEE (46% eicosapentaenoic acid and 38% docosahexaenoic acid) on postprandial triglyceride, VLDL-apoB-100, and apoB-48 responses in FH patients after ingestion of an oral fat load. Outcomes Measures: Plasma total and incremental triglyceride, VLDL-apoB-100, and apoB-48 responses in FH patients after ingestion of an oral fat load. Outcomes Measures: Plasma total and incremental triglyceride, VLDL-apoB-100, and apoB-48 0-10 hour area under the curve (AUC). Results: -3 FAEE supplementation significantly (P <.05 in all) reduced concentrations of fasting plasma triglyceride (-20%), apoB (-8%), VLDL-apoB-100 (-26%), and apoB-48 (-36%); as well as systolic blood pressure (-6%) and diastolic blood pressure (-6%). Postprandial triglyceride and VLDL-apoB-100 total AUCs (-19% and -26%, respectively; P < .01) and incremental AUCs (-18% and -35%, respectively; P < .05), as well as postprandial apoB-48 total AUC (-30%; P < .02) were significantly reduced by -3 FAEE supplementation. Conclusion: Supplementation with -3 FAEEs improves postprandial lipemia in FH patients receiving standard care; this may have implications for further reducing atherosclerotic cardiovascular disease in this high-risk patient group. Copyright © 2016 by the Endocrine Society.

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Detection of hereditary haemochromatosis using haematology parameters.

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Introduction: Elevated serum transferrin saturation and ferritin levels are the commonest screening abnormalities for detecting C282Y homozygous hereditary haemochromatosis (HH). Previous studies suggest that subjects with HH exhibit different peripheral blood erythrocyte parameters compared to non-HH subjects. The aim of this study was to evaluate haemoglobin concentration (Hb), mean cell volume (MCV), mean cell haemoglobin (MCH), and mean cell Hb concentration (MCHC) as screening tests for asymptomatic HH. Methods: Peripheral blood Hb, MCV, MCH and MCHC values were obtained from consecutive asymptomatic subjects with HH (42 male and 30 female) attending a large community-based clinic. Values were obtained prior to and immediately following phlebotomy treatment. Healthy plasma donors from the Australian Red Cross Blood Service (220 male and 216 female) served as a control group. Comparisons between groups were performed using parametric t tests. Receiver-operator curve (ROC) analysis was performed to determine the optimal sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for each parameter. Results: The mean ages for male and female HH subjects at diagnosis (45 y and 45 y, respectively) were similar to those of control male (42 y) and female (40 y) subjects. Serum ferritin levels at diagnosis for male HH (1182 +/- 250 mug/L) and female HH subjects (479 +/- 64 mug/L) were significantly higher than control values (male 164 +/- 19 mug/L, female 108 +/- 19 mug/L, p<0.01)). Prior to treatment, and compared with controls, male and female HH subjects had significantly higher Hb values (male HH 155 +/- 2, female HH 138 +/- 2, male control 147 +/- 1, female control 128 +/- 1 g/L, p<0.0001), MCV values (male HH 92.7 +/- 0.6, female HH 95.4 +/- 0.7, male control 88.7 +/- 0.3, female control 89.6 +/- 0.3 fL, p<0.0001), MCH (male HH 32.1 +/- 0.3, female HH 32.1 +/- 0.3 pg, p<0.0001) and MCHC (male HH 346 +/- 2, female HH 337 +/- 2, male control 338 +/- 1, female control 332 +/- 1 g/L, p<0.01). Following treatment of HH subjects (end of treatment male ferritin 59 +/- 8 mug/L, female ferritin 70 +/- 8 mug/L), MCV, MCH and MCHC values all declined significantly compared with pre-treatment values but were still all significantly elevated compared with control values. Areas under the curve from ROC analysis were as follows - Hb (male 0.71, female 0.77), MCV (male 0.77, female 0.77), MCH (male 0.81, female 0.82), MCHC (male 0.67, female 0.67). For both genders MCH>31 pg had sensitivity (male 78%, female 83%), specificity (male and female 76%), PPV (male 76%, female 77%), NPV (male 77%, female 81%). Conclusions: Asymptomatic male and female HH subjects have significantly higher Hb, MCV, MCH and MCHC values compared with control subjects. These differences persist following treatment. A MCH value greater than 31 pg should prompt further assessment for HH.

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Percutaneous transhepatic biliary drainage-a single centre experience over 10 years.

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Background: Percutaneous transhepatic biliary drainage (PTBD) is an established palliative treatment for obstructive jaundice after unsuccessful endoscopic biliary drainage. The published success and survival rate post PTBD varied significantly in different studies. Aims: To review a single Australian institution experience with PTBD performed between 2005 and 2015 with emphasis on (1) indications, (2) level of biliary obstruction and approach of PTBD (3)
number of procedures and the number of stents required (4) survival post-procedure and factors affecting survival.

Subjects and Methods: Three-hundred one procedures were performed in 251 patients over 10 years. One-hundred six females and 145 males, with a mean age 66.37 (range 7-94 years), had a median hospital stay 12 days (IQR 7, 21). Statistical analysis was performed using related sample Friedman's two-way analysis of variance, Pearson chi-squared and log-rank test. The study has been approved by the institutional human research ethics committee. Results: Technical success rate was 98.8%. One-hundred one (40.2%) patients underwent successful biliary drainage in a single stage procedure whereas 97 (38.6%) and 32 (12.7%) patients required two and three stage procedures, respectively. One-hundred twelve patients required a single stent whereas 44 and 28 patients required two and three stents, respectively. In addition, uncovered wallstent (n = 163, 64.9%) was the most commonly utilised stent for PTBD. Malignant biliary obstruction (MBO) was the most common indication for PTBD (n = 189, 75.3%) followed by benign conditions (n = 62, 24.7%). MBO was due to cholangiocarcinoma (n = 64), pancreatic adenocarcinoma (n = 50) and metastasis (n = 37). Percutaneous puncture of right lobe ducts was the most frequently used approach (n = 133). Obstruction in the hilar region was the most common finding (n = 101) followed by distal common bile duct obstruction (n = 61). Brushing of lesions was performed in 75 cases, and it confirmed malignancy in 52 cases. The median bilirubin level before procedure was 193 mumol/L (IQR 87, 340). The median bilirubin post procedure at day 3, 7 and 30 was 108.5 mumol/L (IQR 42, 217), 70.5 mumol/L (IQR 27, 155) and 23 mumol/L (IQR 13, 42), respectively. Biochemical success (fall in bilirubin >30%) was achieved at day 3, 7 and 30 in 57.7%, 74.4% and 86.9% of cases, respectively. Survival at 3 months, 6 months, 12 months and 36 months was 70.6%, 48.2%, 32.1% and 15.5%, respectively. The robust predictors of survival were indication for biliary drainage and bilirubin level post procedure. Survival analysis demonstrated that patients with benign conditions had a significantly better survival at 6 months (p = 0.018) and 1 year (p = 0.001). Furthermore, survival was inversely related to bilirubin quartiles at 6 months (p = 0.02) and 1-year (p = 0.006) post procedure. Conclusion: PTBD has high technical and biochemical success. The robust predictors of survival are the indications for PTBD and fall in bilirubin at 6 months and 1 year.

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Results of vedolizumab use in the ‘real world’.
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Background and Aims: Vedolizumab was approved for the treatment of moderate to severe Crohn’s disease (CD) and ulcerative colitis (UC) on the PBS on 1 August 2015. The published data from the registration studies of this medication have been impressive for UC and to a lesser extent, for CD. The aim of this study was to evaluate the efficacy and safety of vedolizumab in the treatment of moderate to severe CD and UC in the ‘real world’ setting. Methods: This was a retrospective chart analysis of 21 patients that completed at least 3 induction doses of vedolizumab (300 mg) at two tertiary hospitals. Patients were at least 18 years of age and satisfied the PBS criteria for the treatment of moderate to severe CD and UC with vedolizumab. Only patients with complete data were included. Efficacy was defined by a response (CDAI drop of 100 points for CD and a 30% or a 3 point drop in partial mayo score for UC), or remission (CDAI<150 for CD or partial Mayo score <2 with no individual score >1 for UC). Results: Twenty-one patients met the inclusion criteria. Ten (48%) were males. The mean age in years was 41. Nine patients (43%) had CD, and the rest had UC. The mean duration of disease was 8 years. The mean duration of treatment with vedolizumab for both conditions overall was 26 weeks. Ten patients had failed 1 anti-TNFa agent, while another 7 had failed 2 agents. Twelve of 21 (57%) patients were not on an immunomodulator at the time of vedolizumab commencement due to intolerance or previous inefficacy. Overall, at the time of follow up, as of 5 May 2016, 18 patients (85%) had achieved a response (89% for CD, 83% for UC), and 15 (71%) had achieved remission (78% for CD, 67% for UC). Neurological symptoms were the most commonly reported adverse event, including headaches (n = 2), memory loss and mild confusion in 1 patient. The latter patient also had severe prolonged nasopharyngitis. No hospitalisations or deaths occurred during the follow up period. No patients had required surgery at the time of follow up. Conclusions: The efficacy of vedolizumab in ‘real world’ practice appears to be superior to published data, and no major safety concerns have been observed.
Taurocholate induces proliferation and biliary differentiation of progenitor cells and stellate cell chemotaxis: Insights into the pathophysiology of CF liver disease.

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Cystic fibrosis liver disease (CFLD) causes progressive biliary cirrhosis in children with CF, yet its cause(s) and early pathogenesis are incompletely understood. We have previously reported that the bile acid taurocholate is elevated in children with CFLD, and we hypothesized that a bile acid-induced ductular reaction (DR) was associated with early fibrosis development. Here we report that the DR is significantly increased in children with CFLD and that biliary levels of taurocholate positively correlated with the DR. We examined possible mechanisms of DR induction by treating liver progenitor cells (LPCs) with taurocholate to assess the impact on three key events in the evolution of the DR: LPC proliferation, biliary differentiation of LPCs, and hepatic stellate cell (HSC) chemotaxis. Treatment of LPCs with taurocholate initiated a significant (P<0.001) increase in cell proliferation over 2 days. Furthermore, LPCs treated with taurocholate showed time-dependent enhanced expression of genes associated with cholangiocyte differentiation (CK19, P<0.0001; Connexin-43, P<0.0001), while the hepatocyte differentiation marker HNF4alpha was suppressed (P = 0.0376). Taurocholate induced LPC expression of chemokines including MCP-1, MIP1alpha, and RANTES (regulated on activation, normal T-cell expressed and secreted). Conditioned medium from taurocholatetreated LPCs induced HSC chemotaxis, which was then significantly inhibited by anti-MIP1alpha neutralizing antibody (P<0.01). This study demonstrates that taurocholate promotes LPC proliferation, biliary differentiation and development of the DR, with subsequent induction of chemokines, which recruit HSCs therefore may drive fibrogenesis. Taken together, these observations support the hypothesis that elevated biliary taurocholate plays a role in mediating the DR and fibrogenesis associated with CFLD.

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Association between arthritis phenotypes and HFE genotypes in the HealthIron study.

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Background: Arthropathy affects up to 80% of type 1 haemochromatosis patients. It is a progressive debilitating disease that increases the risk of joint replacements. The relationship between the development of arthritis and the different type of HFE mutations is not clearly defined although some studies have suggested the increased risk of developing arthritis with HFE mutations. Hand arthropathy is one of the hallmark features of HH, particularly the second and third metacarpophalangeal joints. Identifying the different type of joints involved will aid the diagnosis of
arthritides secondary to hereditary haemochromatosis (HH). Objectives: The aim of the study was to investigate the association between different HFE genotypes and arthritis outcomes and to identify the most commonly affected hand joints in HH. Methods: A random sample of 1438 genotyped (wild type; C282Y homozygotes, C282Y heterozygous, C282Y compound heterozygotes, H63D homozygotes, and H63D heterozygous) participants from the Melbourne Collaborative Cohort Study were invited to participate in the HealthIron study that examines the disease burden of HH. The participants underwent a physical examination, completed questionnaires and provided a blood sample. The clinicians were blinded to the genotype and examined the metacarpophalangeal (MCP) joints of both hands for features of arthropathy. The presence of one or more features, including bony spurs, effusions and tenderness, were recorded for each digit of both hands (including MCP joints) as binary data. Statistical analysis was performed using logistic regression models, adjusting for gender and menopause status, to examine the association between different HFE genotypes and the presence of any features in either hand. Results: The presence of bony spurs, effusion or tenderness in either hand was increased in the 2nd and 3rd MCP joints of C282Y homozygotes, with an odds ratio of 1.4 (95% CI 0.8-2.4) and 1.3 (95% CI 0.8-2.3), respectively; in compound heterozygotes (C282Y/H63D) with odds ratio 1.5 (95% CI 0.9-2.5) and 1.5 (95% CI 0.9-2.4), respectively; and in H63D heterozygotes with odds ratio 1.4 (95% CI 0.8-2.4) and 1.3 (95% CI 0.8-2.3), respectively, when compared with the wild type. Arthropathy features in 1st MCP joint are also increased in C282Y homozygotes with odds ratio 1.3 (95% CI 0.7-2.3) when compared with the wild type and in the 5th MCP joint of H63D heterozygotes with odds ratio 1.34 (95% CI 0.4-4.6). Although these odds are increased, they did not reach statistical significance. Conclusions: Abnormalities were consistently seen in the 2nd and 3rd MCP joints in HH. A new trend towards observing abnormalities in the 1st MCP joint in C282Y homozygotes may be increased in this study. Also, the H63D mutation may play an important part in developing arthropathy in HH.


The diagnostic consequence of routine repeat gastroscopy after upper gastrointestinal ulcer diagnosis.
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Background: The practice of routine repeating gastroscopy after 6 weeks to confirm healing of gastric ulcers, exclude cancer and diagnose Helicobacter pylori infection is commonplace, though the evidence supporting this is weak. Aims: To determine the diagnostic consequence and effect of the timing of routine repeating gastroscopy within a few weeks of an endoscopic gastroduodenal ulcer diagnosis. Methods: The endoscopy database of a tertiary hospital was examined to identify individuals with an ulcer diagnosis in the keywords over a 2-year period. We documented the patient characteristics, size and Forrest criteria description of the most severe ulcer described, the timing of repeat gastroscopy and the findings and recommendations from repeat gastroscopy. Results: We identified 210 patients (57% male) as having an upper gastrointestinal ulcer diagnosis during the 2-year study period. Median age was 73 (IQR 61-82) years. Patients with oesophageal ulcers (n = 26) were excluded, leaving 184 patients. The largest ulcers were reported in the gastric antrum (33%), duodenal bulb (30.4%), proximal stomach (16.3%), pylorus (12%) and other/not recorded (8.3%). The most common indications for gastroscopy were melaena (41.4%), haematemesis (11.1%), haematemesis with melaena (12.8%), unspecified bleeding (14.4%) and abnormal imaging (2.2%). The majority of ulcers (54.6%) had high risk Forrest classification Ia-IIb lesions but only 28.5% of ulcers were larger than 10mm diameter. During the initial gastroscopy, biopsies were taken in 75 (41%), diagnosing cancer in 5/75 (6.7%), while endoscopic haemostatic therapy was applied in 48.4% of cases. H. pylori was tested for in 70% and was positive in 35%. Follow up gastroscopy was performed in 82 (45%), 38% under 6 weeks, and revealing cancer in 1 patient (0.5%) who had a >20mm diameter ulcer that was not biopsied during the first gastroscopy. Two patients with a histologic cancer diagnosed during initial gastroscopy underwent repeat gastroscopy but with no further biopsies. High-risk ulcers were seen in 3.3% of cases during repeat gastroscopy. In each of these, a high-risk ulcer had been identified during the initial gastroscopy and the repeat gastroscopy performed within 1-4 weeks afterwards.
Endoscopic therapy was applied in 5.4% during the repeat gastroscopy. There were no high-risk ulcer features when gastroscopy was performed >6 weeks after the initial ulcer diagnosis. Age >60 years was the only independent
predictor of malignancy (odds ratio 3.27, 95% CI 1.61-6.65, P = 0.001). Gender, ulcer size and location did not predict cancer. Conclusions: Ulcers were most common in the gastric antrum and duodenal bulb and the majority had high-risk features, though few were large. Biopsies, when taken during the initial gastroscopy, are able to diagnose cancer. Repeating the gastroscopy earlier than 6 weeks, except to assess re-bleeding or safety of restarting anticoagulation or antiplatelet treatment, does not appear to provide a diagnostic or therapeutic consequence. Vigilance for malignant gastroduodenal ulcers in patients aged >60 years is important.

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**Discrete effects of obesity and NAFLD on iron metabolism and haematology parameters.**
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Background: Obesity and non-alcoholic fatty liver disease (NAFLD) are burgeoning clinical and public health problems affecting children through to adults, particularly in industrialized countries. Whilst risk of NAFLD is most commonly related to an overweight or obese phenotype, the mechanisms underpinning its development and progressive impact are still not well-understood. Obesity is a known risk factor for both iron deficiency and dysregulated iron metabolism. It is unknown whether the effects of NAFLD on iron metabolism are simply reflective of obesity or discrete in nature. Methods: A community-based cohort of 17-year-olds (N = 963) had ultrasound assessment for fatty liver, and after excluding excessive alcohol intake, the presence or absence of NAFLD was confirmed. In this study of the relative impact of obesity and NAFLD on iron metabolism and haematological parameters in these adolescents, we have focussed on differentiating the effects of NAFLD not attributable to general adiposity (as measured by age- and sex-adjusted BMI z-scores) or other metabolic dysfunction. Linear regression has been utilized to investigate associations with serum iron and red blood cell indices including haemoglobin (Hb) and mean corpuscular volume (MCV). Results: NAFLD was diagnosed in 57/501 (11.3%) males and 89/462 (19.3%) females and was associated with higher BMI measures (% NAFLD in the lean: 53/727 = 7.3%, overweight 33/145 = 22.8%, obese 60/91 = 65.9%; p<0.0001). Serum ferritin correlated positively with BMI z-scores (p = 0.0008) and after adjustment for BMI and sex there was little difference between measures of NAFLD and non-NAFLD individuals (p = 0.8). Conversely, the impact of NAFLD on serum iron was more pronounced than that of general adiposity (Fig. 1), with average levels of those affected 8.4% lower than those without NAFLD (p = 0.02). Similarly, lower levels of both Hb and MCV were observed in NAFLD subjects (Hb: -0.21 g/L, p = 0.02; MCV: -1.02 fL, p = 0.003; sex and BMI adjusted). Notably, the observed impact of NAFLD on measures of serum iron, Hb and MCV became more apparent with increasing BMI, and the findings remained consistent when the strong negative associations of C-reactive protein and leptin were additionally considered in the modelling. Moreover, the effects were not altered by parameters of the metabolic syndrome. Conclusions: In this study of adolescents transitioning into adulthood, NAFLD independently increased the risk of functional iron deficiency and impaired haemoglobinisation. Further research is required to determine if this could potentially contribute to symptoms of iron deficiency in NAFLD subjects and impact on the ability to lose weight. (Figure Presented).

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*Sofosbuvir/velpatasvir with ribavirin is effective retreatment for patients who failed NSSA regimens.*
Galhenage S, Gane EJ, et al.
Introduction: The phase 2 studies of sofosbuvir (SOF) in combination with the pangenotypic HCV NS5A inhibitor velpatasvir (VEL), with or without ribavirin (RBV) and the pangenotypic HCV protease inhibitor GS-9857, assessed dose (25 mg or 100 mg VEL), treatment duration (4-12 weeks), and the need for RBV use. The SVR rates across all treatment groups ranged from 58% to 100%. This current study evaluated the safety and efficacy of the once-daily fixed-dose combination tablet of sofosbuvir/velpatasvir (SOF/VEL) + RBV for 24 weeks in patients from these phase 2 studies who experienced virologic failure. Methods: This was a single arm, open-label study of HCV-infected subjects who failed treatment in the phase 2 studies (GS-US-342-0102, GS-US-342-0109, and GS-US-337-1122). Patients received SOF/VEL (400 mg/100 mg daily) in combination with weight based RBV (1,000 or 1,200 mg daily) for 24 weeks. The primary endpoint was sustained virologic response 12 weeks after treatment (SVR12). Secondary endpoints included safety, tolerability, resistance, and additional efficacy outcomes. Results: A total of 69 subjects were enrolled and treated with SOF/VEL + RBV for 24 weeks. Overall 77% were male, 88% were White, 33% had IL28B CC genotype, and 26% had compensated cirrhosis. The genotype (GT) distribution was 54% GT1, 20% GT2, and 26% GT3. Overall, 43% had NS5A resistance-associated variants at baseline. Of the 65 patients included in this interim analysis, 91% achieved an SVR12. One patient discontinued treatment due to irritability. The most common AEs were fatigue (32%), nausea (22%), and headache (17%). Conclusion: Among patients who failed initial treatment with SOF/VEL +/-RBV for 8-12 weeks, retreatment with a longer duration of SOF/VEL + RBV for 24 weeks is effective, safe, and well tolerated. SOF/VEL + RBV may be a retreatment strategy for patients who have failed NS5A inhibitor-based HCV treatment. DOI:http://dx.doi.org/10.1111/jgh.13519

Radio-guided occult lesion localisation using Iodine-125 seeds (ROLLIS) randomised controlled trial: Impact on patient satisfaction.

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Objectives/Introduction: Radioguided occult lesion localisation using iodine-125 seed (ROLLIS) is an emerging alternative to standard hookwire localisation (HWL). We present patient satisfaction survey results from an ongoing randomised controlled trial (RCT) comparing ROLLIS and HWL. Methods and materials: In the institutional ethics board approved RCT, participants with biopsy proven breast cancer were randomised and underwent either ROLLIS insertion or HWL prior to excision at three major Western Australian tertiary health institutions. Patient satisfaction surveys were administered consisting of questions pertaining to additional stress and discomfort caused by the localisation procedure. Participants provided a score for the questions on a Likert scale from 1 to 7. In all cases, higher scores reflected greater stress and discomfort. Clinical parameters were also obtained. Statistical analysis of localisation technique against the scores of the questionnaire was performed. Results: Satisfaction responses from 217 participants were obtained, with 108 participants randomised to HWL and 109 randomised to ROLLIS. Participants who underwent ROLLIS were less likely to report greater stress (OR 0.53, p = 0.014) and discomfort (OR 0.54, p = 0.016) than if they underwent HWL. Conclusion: These findings indicate that pre-operative localisation with ROLLIS induces less stress and discomfort in breast cancer patients undergoing breast conserving surgery when compared to conventional HWL.

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Enhancement of cervical and thoracic vertebrae as a diagnostic pitfall for metastatic infiltration.

Carraro V, Nascimento DO, et al.

Learning objectives: Considering the prevalence of this finding, we aim to provide a careful approach in order to avoid misinterpretation of enhancing bony lesions, even in the oncological patient, in the setting of SVC obstruction.

Background: SVC obstruction is due to malignancy in the majority of cases, but is also a recognised complication of trauma and fibrosing mediastinitis owing to granulomatous infection, autoimmune disease or drugs. With the development of SVC obstruction, blood is diverted via venous collaterals. Four classic collateral pathways involving the azygos and hemiazygos, internal mammary and lateral thoracic, superficial thoracoabdominal and vertebral venous plexuses have been described and proven by venography(1). The presence of contrast in the venous circulation may lead to enhancement of the vertebral venous plexuses, causing an increase in vertebral density, which can be mistaken for bony metastases. Imaging findings or procedure details: Opacification of intravertebral veins and capillary spaces, manifested by a patchy increase in vertebral density. Conclusion: Patients with superior vena cava (SVC) obstruction demonstrating retrograde filling of the vertebral venous collateral systems, causing enhancement of the thoracic vertebrae, may be mistaken for metastatic infiltration. Awareness of this phenomenon is important as failure to recognise it could result in a false-positive diagnosis of bony metastatic disease.

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Pictorial review of incidental adnexal masses.

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Learning Objectives: Incidental adnexal masses are an increasingly common finding, often posing a management dilemma for radiologists. We discuss imaging features of common incidental adnexal masses seen on ultrasound in asymptomatic women. We discuss appropriate management recommendations for benign and potentially significant lesions. Background: There is a broad differential of adnexal masses which extends from functional to neoplastic lesions, lesions within and external to the ovary. Two recent papers and the IOTA criteria1 outline salient imaging features grouping lesions into benign/probably benign, indeterminate however probably benign and cysts with characteristics worrisome for malignancy. This enables better identification of a management pathway2, 3. Many non-neoplastic cysts have characteristic features which do not require further imaging4. Recommendations are based on patient demographics such as is the patient pre-menopausal, early menopausal and late menopausal2. Trans-abdominal ultrasound may progress to trans-vaginal ultrasound with increasing use of MRI for further evaluation of complex lesions. We also assess the appearances of the normal ovary in a premenopausal female. Imaging Findings OR Procedure Details: Features to assess include whether the ovary is seen separate to the lesion may suggest a diagnosis which includes para-ovarian/ para-tubal pathology or a benign peritoneal inclusion cyst which often does not require further follow up. The size and nature of the cyst should be assessed to determine whether it is functional, simple or complex. Features of complex cysts include vascularity, papillary projections, septa or solid components being present1. Size of the adnexal mass correlated with menopausal status is a key determinant for follow up. For example, simple cysts in a premenopausal female <5 cm do not require follow up however unless the simple cyst is <1 cm in a postmenopausal female, annual ultrasound is the minimal follow up recommended 2. Imaging features of benign/probably benign, indeterminate and adnexal masses worrisome for malignancy will also be discussed. Conclusion: Appropriate management of incidental adnexal masses in asymptomatic women is salient in determining necessity for further work up. Work up includes gynecological review +/- additional imaging. Targeted
evaluation also assists to alleviating patient anxiety from over-investigation of likely benign lesions.

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Painless visible haematuria: An algorithmic approach to diagnosis.
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Learning Objectives: Any single episode of visible haematuria (VH) is significant and may be a sign of serious underlying disease, including malignancy.1 Prompt diagnosis is essential and appropriate imaging strategies, based on risk stratification, are discussed. Background: The prevalence of all urologic malignancies among patients who present with VH is 22.0-24.2%.2-4 Symptoms overlap with benign disorders, therefore diagnosis is often delayed and can lead to a worsened prognosis. A literature search of MEDLINE through PubMed was conducted in September 2015 for evidence regarding imaging in VH. The following diagnostic imaging algorithm for painless VH (pVH) takes into consideration the pre-test probabilities for UCC and has been proposed by combining best evidence with expert consensus. Imaging Findings: Ultrasound (US) 1 Has a higher sensitivity (96% versus 25%) and negative predictive value (98% versus 91%) than IVU in detecting abnormalities of the upper urinary tract (UUT).5-7 2 Useful in radiation-sensitive populations (children, pregnancy and child-bearing age women). However, when compared with CT, US has an overall lower sensitivity in detecting urinary tract abnormalities.6 Computed tomographic urography (CTU): Has a sensitivity of 88-100% and specificity of 93-100% for UCC detection 8 but is associated with a relatively high dose of ionising radiation.5-9 Magnetic resonance urography (MRU): Is emerging as an alternative method for imaging the urinary tract and is useful especially in imaging obstructive uropathy. Its sensitivity in detecting urothelial lesions remains under investigation but is believed to be lower than CTU.5, 10 Static-fluid MRU is useful for patients with renal impairment. Demonstrates promising results for diagnosing bladder tumours (T2WI+DWI) and UUT cancers (T1 + T2WI+DWI), with good sensitivities and excellent inter-observer agreement.11, 12 Cystoscopy: Remains the reference standard for detection of lower urinary tract (bladder) urothelial tumours 9,13 and should be performed following initial non-invasive imaging on all patients with pVH and risk factors for malignancy, regardless of age.13 Conclusion: In low risk patients (<40 years of age) with pVH and risk factors for malignancy, regardless of age.13 CTU is still the method of choice for the evaluation of the urinary bladder and should not be replaced by any excretory imaging technique.8.

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The diagnostic imaging dilemmas of suspected pulmonary embolism in pregnancy: What is the current evidence?
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Learning Objectives: To address the diagnostic dilemmas of imaging of pregnant patients with suspected pulmonary embolism. Background: Pulmonary embolism (PE) accounts for up to 20% of pregnancy-related deaths.1 Decision to image is confounded with concerns regarding ionising radiation (IR) exposure to fetus and mother. However, the risks of a missed PE diagnosis or inappropriate anticoagulation often outweigh this concern.2 A search of PubMed database from January 2000-January 2016 identified relevant original articles, systematic reviews and clinical guidelines which were critically appraised. The resultant evidence-based imaging pathway was endorsed by ‘Diagnostic Imaging Pathways’ expert editorial panel members to gain consensus, in consultation with the editor.

Imaging Findings: Chest radiography should be performed to exclude other causes of symptoms and triaging patients to either CT pulmonary angiography (CTPA) or lung scintigraphy (VQ) if further thoracic imaging is required.3, 4 D-dimer levels are often elevated in pregnancy, but a normal Ddimer with low clinical suspicion has a high negative predictive value (NPV).5-7 A positive D-dimer and/or leg symptoms warrant lower limb compression ultrasonography (CUS). A proximal deep vein thrombosis justifies anticoagulation treatment and renders thoracic imaging unnecessary. However, only 10% of patients with PE have an abnormal ultrasound, therefore if CUS is negative the diagnosis should be pursued with pulmonary vascular imaging.6 The choice of VQ or CTPA is complex and lacks consensus; both have equivalent NPV.3 The reported non-diagnostic rates for CTPA and VQ in pregnancy are variable but comparable.2, 3, 8 However, for patients with a normal CXR, the rate of non-diagnostic CTPA was five-fold higher compared to VQ.9 Therefore, if the CXR is normal, VQ is preferred and conversely CTPA is if the CXR is abnormal. 2, 4, 6, 9, 10 The choice should also be based on radiation exposure, the likelihood of alternate diagnoses, availability of resources, and the presence of contra-indications to iodinated contrast media. Maternal IR dose is considerably larger with CTPA resulting in an increased risk of breast cancer.11 Fetal dose does not vary significantly between VQ and CTPA, particularly in second and third trimesters, and is acceptable with either modality. Neither test should be withheld in pregnant women with clinical suspicion of PE.12 Conclusion: The choice of imaging in pregnant patients with suspected PE is complex and multifactorial. Protocols for imaging should be aimed at minimizing IR to mother and fetus. The risk of missing the diagnosis of PE is greater than the radiation risk.

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Assessing the accuracy of ultrasound for axillary nodal status.
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Background: Ultrasound-guided biopsy of breast lesions is accompanied by axillary ultrasound at the time of the procedure. Based on sonographic and clinical findings, a decision on axillary sampling is made by the radiologist.1,2,3 The results of axillary sampling are ancillary to the primary breast lesion histology in determining patients’ management with sentinel lymph node biopsy or axillary nodal clearance. Various studies have demonstrated a wide range of sensitivities and specificities for axillary ultrasound in assessing axillary nodal involvement 1,4-6. Consequently, the recommended role for axillary ultrasound remains unclear. Purpose: To determine the role of axillary ultrasound in guiding management of breast lesions which have been referred for core biopsy. Primary objective: To conduct an audit on the accuracy of axillary ultrasound in detecting axillary lymph node metastases in patients who are under the care of the breast surgeons at two tertiary hospitals. Secondary objective: To determine the association between false positive results and sonographic features of cortical thickness, cortical irregularity, and loss of fatty hilum. The relationship between pathological disease burden and false negative results will also be examined. Methods and materials: Retrospective data collection was performed from 1st April 2012 to 30th September 2015. A search of the theatre list view was performed for patients who had undergone axillary sentinel lymph node biopsy or axillary clearance at the centers between 1st April 2012 and 30th September 2015. Data was gathered through IMPAX and iSOFT Clinical Manager on axillary nodal involvement at ultrasound, whether nodal sampling was undertaken, and final histopathology results. Results: Ultrasound was found to have a sensitivity of 0.41 and specificity of 0.91. The PPV was 0.816 and the NPV was 0.625. The false positive rate is 0.0854 and false negative rate is 0.592. The diagnostic ultrasound images were reviewed for the seven false positive results. All seven demonstrated cortical irregularity, and none showed loss of the normal fatty hilum. In five out of the seven cases, the
maximal cortical thickness was 3 mm or greater. Out of forty-five false negative results, three only had isolated
tumour cells, eight had micrometastases, sixteen had macrometastases of up to 10 mm without extracapsular spread,
and fourteen had macrometastases with extracapsular spread. Four results were only classified as "nodal metastases".
Exclusion of micrometastases and isolated tumour cells increases the sensitivity of ultrasound to 47.7% and specificity
to 92.5%. Conclusion: Ultrasound has low sensitivity and high specificity for determining axillary nodal involvement.

Spectrum of imaging findings of breast lesions on CT: A pictorial review.
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Learning Objectives: 1 To illustrate the spectrum of breast lesions on CT 2 To describe CT features predictive of
malignancy 3 To discuss further management of CT detected breast lesions Background: Incidental lesions in the
breast are commonly detected, in the range of 0.05% to 1.3% of chest CT’s1. It is important for general radiologists to
be aware of the spectrum of CT appearances to be able to detect these lesions and effect appropriate management.
Most breast incidentalomas are reportedly benign and therefore knowledge of benign and malignant features on CT
is valuable for stratification of high risk cases. Features predictive of malignancy described in literature include
irregular shape, rim enhancement1, irregular margins2, and higher density3. Imaging Findings OR Procedure Details:
Benign breast lesions most commonly encountered are fibroadenomata. They have been described as circumscribed,
round or oval masses that may demonstrate coarse pop-corn like calcifications4. Other benign lesions include
post-operative scarring, haematoma/seroma and abscess, for which a past medical history would be valuable.
Fibrocystic change in the breast can present as asymmetric soft tissue attenuation on CT. The most common
malignant breast lesion is invasive ductal carcinoma (IDC), which on CT is a dense, speculated mass with marked early
or peripheral enhancement. 4 There may be adjacent pleomorphic calcifications. Invasive lobular carcinoma is less
common, accounting for 10 to 15% of invasive breast cancers. It does not commonly present as a mass due to the
infiltrating nature of its growth, causing little disruption of architecture and may therefore present as asymmetric soft
tissue density with or without a mass on CT. Conclusion: CT is a common investigation and therefore incidental
findings in the breast are potentially frequently encountered by all general radiologists. Although some CT features
may be helpful in predicting malignant from benign breast lesions, CT is not the best modality for assessment of
breast lesions. Further management generally involves clinical breast examination and ultrasonography. For women
above the age of 35, mammography is also indicated and MRI and biopsies may be required. Any suspicion should
result in a low threshold for referral for further investigation, preferably to a dedicated breast centre.

Strategies for medical management of pediatric eosinophilic esophagitis: A systematic review of randomized,
controlled trials.
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Background: Eosinophilic esophagitis (EoE) is associated with significant morbidity in children. Strategies for
optimizing outcomes of EoE are hence essential. Objective: To conduct a systematic review (SR) of strategies for
medical management of EoE in children. Methods: We conducted a SR of randomized, controlled trials (RCT) of
medical interventions in children with EoE, using the Cochrane methodology. Databases, including PubMed, EMBASE,
CINAHL, Cochrane Central Library and Google Scholar, were searched up to mid-March 2016. Primary outcomes were
histological and symptomatic remission. Secondary outcomes were improvement in histological and endoscopic
parameters and adverse effects. Results: A total of 6 RCTs (n=497) with low-to-unclear risk of bias were included. The studied interventions included topical oral steroids, swallowed enteral steroids and anti-IL-5 agents. Pooling of data from all trials was not possible due to significant heterogeneity in interventions. A meta-analysis of data (n=141) from three RCTs (oral viscous budesonide: 2, fluticasone: 1) showed significant histological remission in the intervention vs. control group participants [RR: 10.32 (3.04, 35.03), p=0.0002]. Compared with anti-IL-5 agents, the studies assessing steroids reported high rates of clinical remission. Clinical remission did not correlate with histological improvement in all studies. Except for systemic corticosteroids, there were no significant adverse effects related to other interventions. Conclusion: Limited, low-quality evidence exists on the effects of various interventions in children with EoE. Treatment with swallowed steroids showed beneficial effects in EoE. Large, well-designed RCTs are essential to confirm these findings.

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Higher concentrations of serum iron and transferrin saturation but not serum ferritin are associated with cancer outcomes.

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BACKGROUND: Although the carcinogenic potential of iron has been shown, evidence from observational studies that have linked serum iron variables and cancer outcomes has been inconsistent.

OBJECTIVE: We investigated whether higher iron concentrations increased risk of cancer outcomes.

DESIGN: A prospective examination of iron biomarkers as independent risk factors for cancer was assessed in 1597 men and 1795 women aged 25-79 y who participated in the 1994/1995 Busselton Health Survey and had relevant data, no history of cancer before the survey, and serum ferritin concentrations >20 mug/L. Follow-up for incident cancers and death from cancer was available to 2010. Proportional hazards regression modeling was performed to investigate if iron status predicted cancer incidence and mortality.

RESULTS: After adjustments for age, smoking, drinking, anthropometric and biochemical variables, or menopausal status (breast cancer), higher serum iron concentrations and transferrin saturation were associated with increased risks of incident nonskin cancer [HR for iron: 1.83 (95% CI: 1.21, 2.76; P < 0.01); HR for transferrin saturation: 1.68 (95% CI: 1.18, 2.38; P < 0.01)] including breast cancer [HR for iron: 2.45 (95% CI:1.12, 5.34; P < 0.05); HR for transferrin saturation: 1.90 (95% CI:1.02, 3.56; P < 0.05)] in women. Transferrin saturation was also associated with a greater risk of cancer death (HR: 2.48; 95% CI: 1.28, 4.82; P < 0.01). In men, higher iron concentrations were associated with reduced risks of incident nonskin cancer (HR: 0.65; 95% CI: 0.42, 0.99; P < 0.05) including colorectal cancer (HR: 0.34; 95% CI: 0.12, 0.95; P < 0.05). There was no association between serum iron and colorectal cancer risk in women. Serum ferritin was not associated with cancer risk or cancer death.

CONCLUSIONS: Higher transferrin saturation or serum iron concentrations were associated with increased nonskin cancer risk and increased risk of cancer death. Conversely, in men, higher serum iron concentrations were associated with decreased risk of nonskin cancer. The molecular basis for the observed differences in the association between serum iron and nonskin cancer risk is unclear.

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The Impact of Left Ventricular Mass on Diastolic Blood Pressure Targets for Patients With Coronary Artery Disease.

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BACKGROUND: Defining the optimal diastolic blood pressure (DBP) for patients with hypertension and coronary artery disease (CAD) is an ongoing challenge in part because of the concern that low DBP may have adverse cardiac effects (the J curve hypothesis).

METHODS: Left ventricular mass (LV mass) was measured on the echocardiogram of individuals (N = 92) with CAD who had coronary blood flow (CBF) in the left anterior descending (LAD) artery estimated from artery diameter and DBP distal to coronary stenosis.

RESULTS: CBF approached 0 in a small but defined proportion of persons at DBP of 70mm Hg. CBF was significantly lower in persons with higher LV mass (above the median of 83g/m(2)) when DBP was >75mm Hg. Higher electrocardiogram QRS voltage (sum of S V1 and R in V6), in the absence of LV hypertrophy (LVH), identified persons with significantly lower CBF at DBP > 80mm Hg. In multivariate analysis, LV mass was a significant CBF determinant after adjusting for DBP and CAD severity. LV mass has a major impact on CBF when DBP is >70mm Hg, while DBP is the primary determinant of CBF when DBP is <70mm Hg. Multivariate analysis confirmed a significant interaction between LV mass and DBP.

CONCLUSIONS: DBP < 70mm Hg is associated with a progressively greater proportion in whom CBF in the LAD approaches 0. For DBP > 70mm Hg, persons with higher LV mass, even in the absence of LVH, have lower CBF, suggesting LV mass is an important consideration when DBP is reduced in patients with CAD.

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Cytomegalovirus reactivation in the critically ill septic intensive care patient: pathogen or passenger?

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The Lower Limb Functional Index - A reliable and valid functional outcome assessment in burns.

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Lower limb injuries account for up to 40% of all burns in Western Australia and affect physical function. Lower limb specific functional assessments are available to monitor recovery, yet no scale has been assessed for use in burns. The Lower Limb Functional Index (LLFI) which is validated in musculoskeletal patients was investigated for applicability in burn. Reliability was assessed using Cronbach’s alpha, principal components analysis and Rasch analysis. Validity was assessed using Spearman’s correlation coefficient with quality of life assessments (BSHS-B & SF-36) and physical assessments (TUG & ankle ROM). Regression analysis was performed with burn severity measures, time of recovery and location of the burn. The LLFI-10 was applied 1368 times on 739 patients at regular time points. It was internally consistent (alpha>0.8) and unidimensional. Associations were demonstrated with the BSHS-B and SF-36 (rho=-0.56 to -0.72, p<0.001), TUG (rho=0.41, p<0.001) and ankle ROM (rho=-0.31 to -0.35, p<0.001). The LLFI-10 also showed associations (p<0.001) with time since injury (rho=-0.29), age (rho=0.12) and TBSA (rho=0.12). The LLFI-10 is a reliable and valid tool to assess function in lower limb burns. This study supports the use of the LLFI-10 as part of a battery of assessment for lower limb burn recovery.


Prevalence and prognosis of a low serum testosterone in men with type 2 diabetes: the Fremantle Diabetes Study Phase II.

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BACKGROUND: Because published studies have usually involved imprecise assays and selected patients with limited additional data and follow-up, the consequences of a low serum testosterone in diabetes are unclear. This study assessed the prevalence, associates and prognosis of a low testosterone in community-dwelling men with type 2 diabetes.

DESIGN: Longitudinal observational study.

PATIENTS: 788 men (mean +/- SD age: 65.8 +/- 11.3 years) followed for 4.0 +/- 1.1 years.
MEASUREMENTS: Serum testosterone, SHBG, erectile dysfunction (ED; Sexual Health Inventory for Men score <22), anaemia (haemoglobin <130 g/l), all-cause mortality.

RESULTS: The mean ± SD total serum testosterone by liquid chromatography/mass spectrometry was 13.1 ± 5.9 nmol/l (30.6% <10 nmol/l). Most men with a total testosterone <10 nmol/l (67.0%) had a normal/low serum LH. Serum testosterone was independently associated with anaemia (P < 0.001), but not ED (P = 0.80), in logistic regression models. The optimal cut-point (Youden Index) for anaemia was 9.8 nmol/l (sensitivity 53.6%, specificity 75.4%). During the follow-up, 102 men (12.9%) died. There was a U-shaped relationship between total serum testosterone quintiles and death (P = 0.003, log rank test). The middle quintile (>11.1 to <13.7 nmol/l) had the lowest risk and there was a 78% increased risk for highest (>16.9 nmol/l) vs lowest (<8.6 nmol/l) quintile in Cox proportional hazards modelling (P = 0.036). Free serum testosterone and SHBG quintiles were not associated with death.

CONCLUSIONS: These data provide some support for the general conventional serum testosterone <10 nmol/l cut-point in identifying an increased risk of anaemia and the subsequent death in men with type 2 diabetes, but indicate that high-normal levels are also an adverse prognostic indicator.

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Optical coherence tomography angiography for longitudinal monitoring of vascular changes in human cutaneous burns.

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Assessment of vasculature is an important aspect of monitoring healing of cutaneous burn injuries. Recent advances in optical coherence tomography (OCT) have enabled it to be used to perform high-resolution imaging of the cutaneous vasculature in vivo, with the potential to provide a superior alternative to the conventional assessment of scoring skin color. The goal of this study is to investigate the feasibility of OCT angiography for longitudinal monitoring of vasculature and identification of vascular features in human cutaneous burns. We integrate several OCT imaging protocols and image-processing techniques into a systematic method for longitudinal monitoring and automatic quantification. The demonstration of this method on a partial-thickness burn shows the accurate co-location of longitudinal scans; characteristic vascular features in different healing phases; and eventual decrease of the elevated vasculature area density and vessel diameter to normal levels. Such a method holds promise for longitudinal monitoring of vasculature in burn injuries as well as in other cutaneous vascular pathologies and responses to treatment.

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Vitamin T overdose?: examining the phenomenon of widespread use of the broad spectrum antimicrobial piperacillin/tazobactam.

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Recovery and borderline personality disorder: A description of the innovative Open Borders program.


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Although Recovery-oriented approaches to delivering mental health services are now promoted in health services across the globe, there is an ongoing need to adapt these approaches to meet the unique needs of consumers with a diagnosis of borderline personality disorder. The lived experience of borderline personality disorder includes emotional dysregulation, intense and unstable relationships, self-harming behaviours, fear of abandonment, and a limited capacity to cope with stress. These experiences present a range of challenges for those who deliver Recovery-oriented services and advocate the principles of empowerment and self-determination. This paper describes a novel crisis intervention program, “Open Borders,” which has been established to meet the unique needs of people with a borderline personality disorder diagnosis. Open Borders is a Recovery-oriented model that is run at a public, state-wide residential facility for mental health consumers in Western Australia, and offers alternative pathways to achieving mental health Recovery, including self-referral and short-term admission to a residential facility. The aims of the program are to break the cycle of hospital admission, reduce rates of self-harm, and support the complex Recovery journey of consumers with a diagnosis of borderline personality disorder. Open Borders provides an exemplar for other health service organisations seeking to establish Recovery-oriented crisis intervention alternatives.

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Genomic insights into the emergence and spread of international clones of healthcare-, community- and livestock-associated meticillin-resistant Staphylococcus aureus: Blurring of the traditional definitions.

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The evolution of meticillin-resistant Staphylococcus aureus (MRSA) from meticillin-susceptible S. aureus has been a result of the accumulation of genetic elements under selection pressure from antibiotics. The traditional classification of MRSA into healthcare-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA) is no longer relevant as there is significant overlap of identical clones between these groups, with an increasing recognition of human infection caused by livestock-associated MRSA (LA-MRSA). Genomic studies have enabled us to model the epidemiology of MRSA along these lines. In this review, we discuss the clinical relevance of genomic studies, particularly whole-genome sequencing, in the investigation of outbreaks. We also discuss the blurring of each of the three epidemiological groups (HA-MRSA, CA-MRSA and LA-MRSA), demonstrating the limited relevance of this classification.

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Development and evaluation of a secondary reference panel for BCR-ABL1 quantification on the International Scale.

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Molecular monitoring of chronic myeloid leukemia patients using robust BCR-ABL1 tests standardized to the International Scale (IS) is key to proper disease management, especially when treatment cessation is considered. Most laboratories currently use a time-consuming sample exchange process with reference laboratories for IS calibration. A World Health Organization (WHO) BCR-ABL1 reference panel was developed (MR(1)-MR(4)), but access to the material is limited. In this study, we describe the development of the first cell-based secondary reference panel that is traceable to and faithfully replicates the WHO panel, with an additional MR(4.5) level. The secondary panel was calibrated to IS using digital PCR with ABL1, BCR and GUSB as reference genes and evaluated by 44 laboratories worldwide. Interestingly, we found that >40% of BCR-ABL1 assays showed signs of inadequate optimization such as poor linearity and suboptimal PCR efficiency. Nonetheless, when optimized sample inputs were used, >60% demonstrated satisfactory IS accuracy, precision and/or MR(4.5) sensitivity, and 58% obtained IS conversion factors from the secondary reference concordant with their current values. Correlation analysis indicated no significant alterations in %BCR-ABL1 results caused by different assay configurations. More assays achieved good precision and/or sensitivity than IS accuracy, indicating the need for better IS calibration mechanisms.

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Identification of factors influencing patient satisfaction with orthopaedic outpatient clinic consultation: A qualitative study.
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BACKGROUND: In recent years, new models of health service delivery in orthopaedic outpatient clinics, including physiotherapists working in orthopaedic triage roles, have become increasingly common. Evaluation of patient satisfaction with orthopaedic clinic services is dependent on an understanding of factors influencing patient satisfaction in this clinical context.

OBJECTIVES: The objective of this study was to identify the factors influencing patient satisfaction with orthopaedic outpatient clinic services.

STUDY DESIGN: A cross-sectional, qualitative design including focus groups and interviews.

METHODS: Interviews and focus group sessions were undertaken with 36 participants representing patients, health professionals and clinical support staff in an orthopaedic outpatient clinic. Interviews and focus groups provided a rich narrative which was subjected to a process of thematic analysis.

RESULTS: The analysis identified seven themes influencing patient satisfaction with orthopaedic clinic assessment. These themes were clinic waiting time, clinical contact time, trust, empathy, communication, expectation and relatedness.

CONCLUSIONS: Understanding factors influencing patient satisfaction is important to inform organisational and
clinical processes that aim to foster high levels of patient satisfaction. Clinician awareness of the interpersonal issues
which dominate stakeholders’ perspectives of patient satisfaction may improve the patient experience and potentially
foster patient behaviours toward a therapeutic advantage. An understanding of these factors in the context of
orthopaedic clinics is also important in the development of questionnaires designed to evaluate patient satisfaction
with health service delivery.


**Laxative Related Primary Hyperphosphatemic Tumoral Calcinosis Identified by Bone Scintigraphy.**
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We describe a case of a 40-year-old female patient presenting with tumor calcinosis where hypertrophic pulmonary
osteoarthropathy (HPOA) was suspected given her extensive history of malignancy. Plain X-rays did not show reveal
the typical periarticular calcification but did show appearances consistent with HPOA. Bone scintigraphy with
(99m)Tc-methylene diphosphonate (MDP) is a sensitive investigation in the detection of hypertrophic
osteoarthropathy but did not show findings characteristics of HPOA like bilateral symmetrical increased uptake of the
radiopharmaceutical along the cortical margins of the long bones. The final diagnosis of tumor calcinosis was only
made after low dose computerized tomography chest showed a moderated sized amorphous calcified cluster in the
apical segment of the right upper lobe consistent. In conclusion, bone scintigraphy continues to be a useful
investigation for both common and rare conditions like tumor calcinosis. The unusual three phase bone scan finding of
diffuse activity throughout both lung fields, which turned out to to be tumoral calcinosis is highlighted in this case.


**Single- versus dual-console robotic surgery: dual improves the educational experience for trainees.**

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**Cosmesis and Breast-Related Quality of Life Outcomes After Intraoperative Radiation Therapy for Early Breast
Cancer: A Substudy of the TARGIT-A Trial.**
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PURPOSE: To report the first comprehensive investigation of patient-reported cosmesis and breast-related quality of life (QOL) outcomes comparing patients randomized to risk-adapted single-dose intraoperative radiation therapy (TARGIT-IORT) versus external beam radiation therapy (EBRT) on the TARGIT-A trial.

METHODS AND MATERIALS: Longitudinal cosmesis and QOL data were collected from a subset of TARGIT-A participants who received TARGIT-IORT as a separate procedure (postpathology). Patients completed a cosmetic assessment before radiation therapy and annually thereafter for at least 5 years. Patients also completed the combined European Organization for Research and Treatment of Cancer (EORTC) core questionnaire and Breast-Specific Module in addition to the Body Image after Breast Cancer Questionnaire at baseline and annually thereafter. The combined EORTC questionnaires were also collected 3, 6, and 9 months after wide local excision.

RESULTS: An Excellent-Good cosmetic result was scored more often than a Fair-Poor result for both treatment groups across all time points. The TARGIT-IORT patients reported better breast-related QOL than EBRT patients. Statistically and clinically significant differences were seen at month 6 and year 1, with EBRT patients having moderately worse breast symptoms (a statistically significant difference of more than 10 in a 100-point scale) than TARGIT-IORT patients at these time points.

CONCLUSION: Patients treated with TARGIT-IORT on the TARGIT-A trial have similar self-reported cosmetic outcome but better breast-related QOL outcomes than patients treated with EBRT. This important evidence can facilitate the treatment decision-making process for patients who have early breast cancer suitable for breast-conserving surgery and inform their clinicians.

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Burn injury and long-term nervous system morbidity: a population-based cohort study.

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

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

PARTICIPANTS: Records of 30,997 persons hospitalised for a first burn injury in Western Australia during the period 1980-2012, and 123,399 persons who were age and gender frequency matched with no injury admissions randomly selected from Western Australia’s birth registrations and electoral roll.

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

RESULTS: After adjustment for demographic factors and pre-existing health status, the burn injury cohort had 2.20 times (95% CI 1.86 to 2.61) as many nervous system admissions and 3.25 times the number of days in hospital (95% CI: 2.28 to 4.64) than the uninjured cohort. This increase was found for those who had sustained burns during childhood (<15 years: IRR, 95% CI: 1.97, 1.49 to 2.61) and early to mid-adulthood (15-45 years: IRR, 95% CI: 2.70, 2.06 to 3.55) and older adults (>45 years: IRR, 95% CI: 1.62, 1.33 to 1.97). Significantly elevated first-time postburn admissions were observed for children for 15 years postburn discharge (0-5 years: HR, 95% CI: 1.97, 1.75 to 2.22; 5-15 years: HR, 95% CI: 1.44, 1.28 to 1.63) and for adults 45 years and older at index burn for 5 years postburn only (HR, 95% CI: 1.72, 1.42 to 2.09).

CONCLUSIONS: Burn injury appears to be associated with increased nervous system-related morbidity for many years after burn injury. Further work into the mechanisms and possible treatments to reduce this morbidity are warranted in light of these findings.


Identification of a thalidomide derivative that selectively targets tumorigenic liver progenitor cells and comparing its effects with lenalidomide and sorafenib.

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BACKGROUND & AIMS: The availability of non-tumorigenic and tumorigenic liver progenitor cell (LPC) lines affords a method to screen putative anti-liver cancer agents to identify those that are selectively effective. To prove this principle we tested thalidomide and a range of its derivatives and compared them to lenalidomide and sorafenib, to assess their growth-inhibitory effects.

METHODS: Cell growth, the mitotic and apoptotic index of cell cultures were measured using the Cellavista instrument (SynenTec) using commercially available reagents.

RESULTS: Neither lenalidomide nor thalidomide (100 μM) affected tumorigenic LPCs but killed their non-tumorigenic counterparts. Sorafenib arrested growth in both cell types. All but two derivatives of thalidomide were ineffective; of the two effective derivatives, one (thalidomide C1) specifically affected the tumorigenic cell line (10 μM). Mitotic and apoptotic analyses revealed that thalidomide C1 induced apoptotic cell death and not mitotic arrest.

CONCLUSIONS: This study shows that screens incorporating non-tumorigenic and tumorigenic liver cell lines are a sound approach to identify agents that are effective and selective. A high throughput instrument such as the Cellavista affords robust and reproducible objective measurements with a large number of replicates that are reliable. These experiments show that neither lenalidomide nor thalidomide are potentially useful for anti-liver cancer therapy as they kill non-tumorigenic liver cells and not their tumorigenic counterparts. Sorafenib in contrast, is highly effective, but not selective. One tested thalidomide derivative has potential as an anti-tumor drug since it induced growth arrest; and importantly, it selectively induced apoptotic cell death only in tumorigenic liver progenitor cells.

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MBOAT7 rs641738 increases risk of liver inflammation and transition to fibrosis in chronic hepatitis C.
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Cirrhosis likely shares common pathophysiological pathways despite arising from a variety of liver diseases. A recent GWAS identified rs641738, a polymorphism in the MBOAT7 locus, as being associated with the development of alcoholic cirrhosis. Here we explore the role of this variant on liver inflammation and fibrosis in two cohorts of patients with chronic hepatitis C. In 2,051 patients, rs641738 associated with severe hepatic inflammation and increased risk of fibrosis, as well as faster fibrosis progression. At functional level, rs641738 associated with MBOAT7 transcript and protein levels in liver and blood, and with serum inflammatory, oxidative stress and macrophage activation markers. MBOAT7 was expressed in immune cell subsets, implying a role in hepatic inflammation. We conclude that the MBOAT7 rs641738 polymorphism is a novel risk variant for liver inflammation in hepatitis C, and

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OBJECTIVE: To capture the clinical patterns, timing of key milestones and survival of patients presenting with amyotrophic lateral sclerosis/motor neuron disease (ALS/MND) within Australia.

METHODS: Data were prospectively collected and were timed to normal clinical assessments. An initial registration clinical report form (CRF) and subsequent ongoing assessment CRFs were submitted with a completion CRF at the time of death.

DESIGN: Prospective observational cohort study.

PARTICIPANTS: 1834 patients with a diagnosis of ALS/MND were registered and followed in ALS/MND clinics between 2005 and 2015.

RESULTS: 5 major clinical phenotypes were determined and included ALS bulbar onset, ALS cervical onset and ALS lumbar onset, flail arm and leg and primary lateral sclerosis (PLS). Of the 1834 registered patients, 1677 (90%) could be allocated a clinical phenotype. ALS bulbar onset had a significantly lower length of survival when compared with all other clinical phenotypes (p<0.004). There were delays in the median time to diagnosis of up to 12 months for the ALS phenotypes, 18 months for the flail limb phenotypes and 19 months for PLS. Riluzole treatment was started in 78-85% of cases. The median delays in initiating riluzole therapy, from symptom onset, varied from 10 to 12 months in the ALS phenotypes and 15-18 months in the flail limb phenotypes. Percutaneous endoscopic gastrostomy was implemented in 8-36% of ALS phenotypes and 2-9% of the flail phenotypes. Non-invasive ventilation was started in 16-22% of ALS phenotypes and 21-29% of flail phenotypes.

CONCLUSIONS: The establishment of a cohort registry for ALS/MND is able to determine clinical phenotypes, survival and monitor time to key milestones in disease progression. It is intended to expand the cohort to a more population-based registry using opt-out methodology and facilitate data linkage to other national registries.

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Ten years of lipoprotein apheresis for familial hypercholesterolemia in Malaysia: A creative approach by a cardiologist in a developing country.

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BACKGROUND: Familial hypercholesterolemia (FH) leads to premature coronary artery disease and aortic stenosis, with undertreated severe forms causing death at a young age. Lipoprotein apheresis (LA) is often required for lowering low-density lipoprotein cholesterol levels in severe FH.

OBJECTIVES: The objective of this study was to present the first experiences with LA in Malaysia, between 2004 and 2014.

METHODS: We retrospectively collected data from patient records to assess the effectiveness, adverse effects, patient quality of life, and costs associated with an LA service for genetically confirmed homozygous and heterozygous FH.

RESULTS: We treated 13 women and 2 men aged 6 to 59 years, 10 with homozygous and 5 with heterozygous FH, all on maximally tolerated cholesterol-lowering drug therapy, for a total of 65 patient-years. Acute lowering of low-density lipoprotein cholesterol post apheresis was 56.3 +/- 7.2%, with time-averaged mean lowering of 34.9 +/- 13.9%. No patients experienced any cardiovascular events during the period of receiving LA. Patients receiving LA experienced few side effects and enjoyed reasonable quality of life, but inability to continue treatment was frequent because of cost.

CONCLUSION: LA for severe FH can be delivered effectively in the short term in developing nations, but costs are a major barrier to sustaining this mode of treatment for this high-risk group of patients. New drug therapies for FH, such as the proprotein convertase subtilisin/kexin type 9 inhibitors, microsomal triglyceride transfer protein inhibitors, and apolipoprotein-B100 antisense oligonucleotides may allow improved care for these patients, but costs and long-term safety remain as issues to be addressed.

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Verapamil is less effective than triamcinolone for prevention of keloid scar recurrence after excision in a randomized controlled trial.

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A double-blind randomized controlled trial with a paired split-scar design compared verapamil, an L-type
Ca\(^{2+}\) channel antagonist, and triamcinolone for prevention of keloid recurrence after excision. Ca\(^{2+}\) channel blocking activity of verapamil in keloid cells was explored. One keloid was excised per subject and each wound half randomized to receive intralesional injections of triamcinolone (10 mg/ml) or verapamil (2.5 mg/ml) at monthly intervals (4 doses). Interim analysis was performed after 14 subjects were completed. Survival analysis demonstrated significantly higher keloid recurrence with verapamil compared to triamcinolone 12 months post-surgery (logrank test, \(p = 0.01\)) and higher overall risk of recurrence with verapamil (hazard ratio 8.44, 95% CI 1.62-44.05). The study was terminated early according to the stopping guideline (\(p < 0.05\)). Verapamil is safe but not as effective as triamcinolone in preventing keloid recurrence after excision. Further study is necessary to determine if clinical response to verapamil is linked to modulation of intracellular Ca\(^{2+}\). Copyright © 2016 The Authors.

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**Acute kidney injury in a secondary referral centre: A single-centre, retrospective observational study.**

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Aim: To evaluate the prevalence and presumptive aetiology of acute kidney injury (AKI), appropriate referral to nephrology services and patients’ renal recovery. Background: AKI is common (estimated 7-18%) and is associated with adverse outcomes. Prognosis may be poorer for AKI patients who do not access nephrology services. Methods: The blood results of consecutive patients discharged from the medical units between September to December 2015 (\(n = 1613\)) were analysed for AKI using the creatinine component of the AKI network criteria. The patients who presented with/developed AKI were reviewed to determine presumptive aetiology, whether investigations and referral to nephrology occurred and discharge renal function. Results: AKI was present on admission for 128 patients (8%) and developed as an inpatient in 65 patients (4%). The most common presumptive aetiologies of AKI were sepsis (29%), hypovolemia/hypotension (28%) and multifactorial (28%). Nephrologists managed 53% of patients with AKI and were consulted on management for a further 5%. Inpatient development of AKI occurred in 34 (4.2%) of patients managed by non-nephrologists (Group 1) and 31 (3.8%) patients managed by nephrologists (Group 2). Rates of investigation with ultrasound, urine analysis and vasculitic markers were similar between groups. Creatinine returned to baseline for 14 (18%) and 22 (22%), improved but not to baseline for 36 (47%) and 37 (38%), and deteriorated in 9 (12%) and 17 (18%) of Group 1 and 2, respectively. No patients were commenced on dialysis and 18 patients (10%) died during admission. Conclusions: AKI remains a prevalent presentation and complication of hospital admissions. In this cohort, nephrology input did not create a significant difference in outcomes, although there was no comparison of severity of illness and comorbidities between groups.

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**Observational, multicentre, multinational registry of atypical haemolytic uraemic syndrome patients: Review of the baseline characteristics of global and australian cohorts.**

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Aim: To report the characteristics of patients enrolled in the Australian Cohort of the Global aHUS Registry treated with Eculizumab. Background: aHUS is a rare, genetic, life-threatening systemic disease. The Global aHUS Registry, a multi-centre, multi-national, non-interventional registry initiated in April 2012, prospectively collects data on aHUS patients. Eculizumab is a human IgG1k monoclonal antibody directed against C5 preventing formation of the C5-9 membrane attack complex and has been demonstrated to be effective as treatment of this condition. Methods: Patients with a clinical diagnosis of aHUS are eligible for Registry enrolment. Demographics, medical and disease history, laboratory results, treatment, efficacy and safety outcome data are collected at baseline and every 6 months thereafter. Results: As of 29th February 2016, 1054 patients were enrolled in the Global aHUS Registry, including 68 patients in Australia. In the Australian cohort, 34 patients have received Eculizumab. For this group, mean age at diagnosis of aHUS is 34 years (range 0.6-71.4 years), 75% female and 14% had a positive family history. Patients had significant renal dysfunction at commencement of Eculizumab: mean creatinine 162 (range 85-634) mumol/l, 60% of patients required dialysis, and 8 had received a kidney transplant. Eighty percent had received prior plasma exchange. Patients treated with Eculizumab were more likely to have had extra-renal complications than those never treated (cardiovascular symptoms 21% versus 4%, CNS symptoms 36% versus 0%, GIT symptoms 40% versus 0%). The median duration of eculizumab was 0.92 years [range 0-5.8 years]. Of those patients receiving eculizumab, 9 have discontinued treatment. Ongoing follow-up to assess the efficacy of treatment and safety of drug withdrawal is ongoing. Conclusions: Eculizumab use in Australia has increased following the PBS funding of this therapy. Patients who commence drug have a significant burden of extra-renal disease. Analyses of longitudinal data obtained through the aHUS Registry will continue to improve our understanding of aHUS and help optimise management of patients with this rare and life-threatening disease.

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Hospitalisation, treatment delay and the use of imaging in peritoneal dialysis related peritonitis: Outcomes from the prompt study.

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Aim: To determine predictors of hospitalisation and the impact of radiological investigations on treatment delay in the management of peritoneal dialysis-related peritonitis (PDRP). Background: Peritonitis has significant adverse consequences for patients and health providers. Identifying risks for hospitalisation and barriers to effective antibiotic treatment may improve outcomes. Methods: Retrospective review of patients presenting with presumed PDRP in Western Australia between 2012 and 2014. We determined the risks of hospitalisation and the use and value of radiology investigations in the management of patients and the impact on treatment times. Results: In 157 episodes of PDRP, 54% were admitted with an average LOS of 3 days (Q1-Q3 1-6). In a multivariable model, significant predictors of admission were abnormal exit-site (OR 7.7), presentation to a hospital facility (OR 4.1), absence of cloudy bag (OR 5.8), female (OR 3.4) and antibiotic treatment >4 hours after presentation (OR 3.4) but not diabetes or indigenous race. Imaging was performed in 45% of presentations to a tertiary hospital (n = 72). Plain films (91%) were the commonest imaging modality; 82.2% of imaging procedures were either normal or clinically unhelpful. Episodes involving imaging had a median time to antibiotic treatment of 3.1 hours vs 2.8 without imaging (p = 0.22). In episodes with contact to treatment time >4 hours, 65% had imaging performed prior to treatment. Treatment failure occurred in 34.4% of episodes where imaging was performed, versus 23.7% where no imaging was performed (p=0.322). Conclusions: Hospitalisation at presentation with PDRP was more likely in those with significant treatment delay. Half of presentations to a hospital also included an imaging test, most of which had no clinical benefit. Strategies to reduce unnecessary imaging and reduce treatment delays are warranted.

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Modelling compatible pair matching in kidney paired donation.
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Aim: To define allocation metrics that enable compatible pairs (CP) receiving a better-matched kidney in kidney paired donation (KPD) programme, without disadvantage to incompatible pairs (ICP). Background: Participation of CP in KPD could be attractive to CP who have a high degree of HLA-mismatch, if the KPD allocation algorithm provides a better HLA match for the CP recipient. Because KPD programmes were not designed to help CP, it is important to define allocation metrics that enable CP receiving a better-matched kidney, without disadvantage to ICP. Methods: Virtual crossmatch is used for ICP allocation in the Australian KPD programme. The algorithm ignores HLA matching rules and therefore is unlikely to provide better HLA matching to CP. Simulations using 46 ICP and 11 randomly selected CP with 6/6 ABDR mismatch were undertaken. Allocations were preformed adding one CP at a time or all 11 CP at once, without and with exclusion of unacceptable antigens selected to give a virtual cPRA in the range of 70-80% to improve HLA matching in CP recipients. Results: Inclusion of one CP at a time increased matching in ICP by up to 33% and inclusion of all 11 CP at once increased ICP matching by 50%. The difference in the average eplet mismatch (EpMM) with the own donor (78 +/- 19) was significantly lower (57 +/- 15, P<0.02) only when individual CP recipients had unacceptable antigens assigned for exclusion. When the 11 CP were added at once the EpMM with the matched donor was significantly better than with the own donor when they were added without (58 +/- 10, P<0.03) and with (60 +/- 11, P<0.02) exclusion of unacceptable antigens. Only recipients whose EpMM to own donor was >65 significantly reduced the EpMM with the matched donor. Conclusions: CP participation in KPD can increase match rates in ICP and can provide a better immunological profile in CP recipients who have a high EpMM to their own donor when using allocation based on virtual crossmatch. PMID:612312947
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Recurrent anti-glomerular basement membrane antibody disease.
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Background: Anti-Glomerular basement membrane antibody disease (Anti-GBM disease) manifests with Pulmonary Haemorrhage and Rapidly Progressive Glomerulonephritis. It is typically mono-phasic. Case Report: 26-year-old male presented with fevers, cough, haemoptysis and increasing shortness of breath of 5 days duration. He had not noticed any urinary symptoms. He was a current smoker. The past history was significant for the diagnosis of Anti-GBM disease in Feb. 2007 in Victoria when he had presented with haemoptysis and had positive Anti GBM antibody by ELISA (48U/ml; normal<20). He had received Plasma exchange (PEX), corticosteroids and Cyclophosphamide for 6months and had remained well. On current admission, patient was febrile and mildly breathless. BP was normal. Serum creatinine was 62 micromoles/litre. Urinalysis showed 10-100 RBCs x 10^6/litre; urine protein/creatinine ratio was 17mg/mmol. Anti-GBM by fluoro-enzymatic immune assay was negative (2.2u/ml; normal<7). X-ray chest showed diffuse alveolar opacities. With worsening breathlessness whilst on antibiotics, renal biopsy was performed on day 3 which revealed linear staining of GBM with IgG+++ and C3c, with linear kappa and lambda light chains consistent with Anti-GBM disease. There were no crescents or proliferative changes. The patient was started on IV Methyl Prednisolone, PEX and Rituximab. The respiratory symptoms resolved dramatically. Renal function continues to be normal with no proteinuria 4months later. Discussion/Conclusions: It is rare for Anti GBM disease to recur. This patient had predominant respiratory manifestations with normal renal function and negative serum Anti-GBM antibody recurrence. Renal biopsy revealed non-crescentic, non-proliferative GN with linear staining IgG against the GBM thus confirming the diagnosis of Anti-GBM disease and guided the appropriate treatment.
The use of rituximab for glomerulonephritis in Western Australia.
Puttagunta H, Lim K, et al.

Aim: To examine the clinical utility of rituximab (RTX) in glomerulonephritis Background: The management of glomerulonephritis with immunosuppression has limited efficacy and significant toxicity. B-cell depletion with RTX is a potential induction or salvage therapy for glomerulonephritis unresponsive to conventional immunosuppressives.

Methods: We reviewed 54 non-transplant patients who received RTX between January 2014 and December 2015. We extracted data regarding indications, previous therapies, dose and response.

Results: 39/54 patients with complete data acquisition were categorized to Primary Nephrotic Syndrome (PNS, n = 27), Lupus nephritis (n = 6) and Pauci-Immune glomerulonephritis (n = 6). RTX was administered at doses ranging between one dose of 500mg up to 4 weekly doses of 1gram. In PNS, 17/27 (63%) were induced with RTX, 10 with prior clinical remission received maintenance treatment (n = 2) or were reinduced (n = 8) post relapse. Remission rates were 6/6(100%) for membranous, 6/7 for focal sclerosing, 9/10(90%) for Minimal change and 3/4(75%) for mesangioproliferative GN with a median time to remission of 3months (Q1 = 3months, Q3 = 9months). 9/10(90%) of PNS patients achieved remission after failure or relapse with conventional therapies including cyclosporine, cyclophosphamide, tacrolimus, mycophenolate and/or steroids. In patients with Lupus Nephritis, 4 patients with Membranous were unresponsive to treatment and two patients who had Mesangial Proliferative and Diffuse variants respectively underwent remission. Patients with pauci-immune glomerulonephritis showed remission in 2/3 of MPO-ANCA and 2/3 in PR3-ANCA group.

RTX was well tolerated with no significant adverse events nor infection apart from transient infusion related reactions (n = 5/39 %) during the follow up period (median follow up of 16months).

Conclusions: Whilst Rituximab was an effective therapy in Primary Nephrotic Syndrome and Vasculitis, limited efficacy in SLE and variability in dosing warrants additional study.

Effect of fish oil and aspirin on arteriovenous fistula failure in haemodialysis-a randomized controlled trial.

Aim: To determine whether fish oil or aspirin is effective in reducing arteriovenous fistula (AVF) failure. Background: Increasing the use of AVF to improve haemodialysis access outcomes is limited by early thrombosis and maturation failure. Omega-3 polyunsaturated fatty acids (fish oils) have pleiotropic effects upon vascular biology and inflammation, and aspirin impairs platelet aggregation, which may reduce access failure. Methods: In this double-blind, placebo-controlled trial, 567 participants from Australia, Malaysia, New Zealand and the United
Kingdom planning to undergo AVF surgery were randomized to fish oil (4 g/day) or placebo for 12 weeks. Of these, 406 participants were also randomized to aspirin (100 mg/day) or placebo for 12 weeks. The primary outcome was AVF failure at 12 months, a composite of AVF thrombosis and/or abandonment and/or cannulation failure. Results: The proportion of AVF failure in the fish oil and placebo arms was similar (47% versus 47%, relative risk [RR] adjusted for aspirin use 1.03, 95% confidence interval [CI] 0.86-1.23, p = 0.78). Fish oil did not reduce the risk of AVF thrombosis (22% versus 23%, RR 0.98, 95% CI 0.72-1.34, p = 0.90), abandonment (19% versus 22%, RR 0.87, 95% CI 0.62-1.22, p = 0.43) or cannulation failure (40% versus 39%, RR 1.03, 95% CI 0.83-1.26, p = 0.81). There were no significant differences in adverse drug events (9% versus 13%, p = 0.15) including bleeding complications (6% versus 4%, p = 0.26) between the fish oil and placebo arms. The risk of AVF failure did not differ between the aspirin and placebo arms (45% versus 43%, RR 1.05, 95% CI 0.84-1.31, p = 0.68), and adverse events including bleeding were comparable between participants assigned to aspirin or placebo. Conclusions: Neither fish oil nor aspirin was effective in preventing AVF failure.

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Comparison of case mix in tertiary and secondary centre nephrology clinics—does the current activity allotment reflect need?

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Aim: To compare the characteristics of patients currently under active follow up by nephrologists in tertiary and secondary referral settings in metropolitan WA. Background: Allocation of clinicians' time to nephrology outpatients is based on estimates of budgeted activity and anticipated occasions of service. Actual patient numbers, the severity of chronic kidney disease (CKD) or comorbidities are not considered. Methods: Outpatient lists for one tertiary care nephrologist (Centre 1, n = 408) and both nephrologists at a secondary centre (Centre 2, n = 307) were obtained. Clinic letters and blood results were reviewed to determine primary renal diagnosis, age, sex and most recent stage of CKD. Each nephrologist reported their full time equivalent (FTE) allocated to renal clinic; Centre 1 has 0.3 FTE including consultants and junior staff, with a further 0.1 FTE to review letters. Conclusions: In the population studied, secondary centre nephrologists provide outpatient care for an older group with more severe CKD, but fewer dialysis or transplant patients, without junior staff to assist. Neither overall numbers nor patient acuity is currently reflected in allocated FTE. Future workforce modelling could include these more relevant methods of determining demand.

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A randomised controlled trial evaluating everolimus compared to cyclosporine on left ventricular mass index and arterial stiffness after kidney transplantation.

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Aim: The aim of the study is to compare recipients receiving standard dose cyclosporin (CSA) and mycophenolic acid (MPA), changing to everolimus (EVL) or continuing with CSA between 3-4 months post-transplant on left ventricular mass index (LVMI) and arterial stiffness. Background: Conversion from calcineurin-inhibitor (CNI) to mammalian target of rapamycin inhibitors (mTORi) may be cardio-protective with one randomized controlled trial of 30 non-diabetic
kidney transplant recipients showed reduced dose CSA with EVL significantly reduced LVMI after 12 months compared to treatment with CSA and mycophenolate. Methods: We recruited 24 patients in this 18-month randomized, open-label, controlled trial evaluated the effect of CSA withdrawal for EVL at 3-months post-transplant on LVMI (primary outcome), arterial stiffness (aortic augmentation index [AIx] and pulse wave velocity [PWV]) and eGFR (secondary outcomes) compared to CSA and MPA of 24 kidney transplant recipients (with the power to detect a 20% difference in LVMI between groups at 18 months post-transplant with 80% power). No patients were lost to follow-up. Results: The mean donor and recipient age, proportion of live-donors and diabetes were similar between treatment groups. Mean (SD) LVMI was similar at 3 (124 [43] vs 124 [37]gm/m²) and 18 months (124 [36] vs 125 [37]gm/m²) in both EVL and CSA groups (ANOVA P = 0.67). There were no significant differences in mean AIx or PWV between treatment groups at 3 and 18 months or within treatment groups between 3 and 18 months after transplantation. There was a significant improvement in mean (SD) eGFR between 3 and 18 months amongst patients randomized to the EVL group (53 [14] to 64 [13]mL/min/1.73m² < 2</sup>, paired t-test P < 0.01), but not in the CSA group (54 [17] to 53 [18]mL/min/1.73m² < 2</sup>, P = 0.89). Proportion experiencing rejection was similar in both groups and there was no graft loss or death in either group. Conclusion: An immunosuppressive regimen consisting of EVL without CSA may improve allograft function but did not reduce LVMI or arterial stiffness.

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A comparison of arteriovenous fistula failure between malaysian and australian and new zealand participants enrolled in the favoured trial.

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Aim: To describe and compare arteriovenous fistula failure between Australia and New Zealand (ANZ) and Malaysia.

Background: Arteriovenous fistulae (AVF) are the preferred haemodialysis access but limited by early failure in 20-50%. Failure rates in ANZ and Malaysia are unknown. Methods: We assessed 353 participants from ANZ and Malaysia included in the omega-3 fatty acids (Fish oils) and Aspirin in Vascular access OUTcomes in REnal Disease (FAVoured) randomized-controlled trial. AVF failure was defined as a composite of AVF thrombosis and/or abandonment and/or cannulation failure. The composite and each component were compared between participants from ANZ (n = 209) and Malaysia (n = 144) using log binomial regression with adjustment for predictors of AVF failure. Results: The mean age was 55 years, 64% were male and 52% diabetic. At 12 months after AVF creation, 47% of AVF had failed. AVF failure was significantly lower in participants in Malaysia compared to participants in ANZ (54/144 [38%] versus 113/209 [54%], p < 0.01). This remained significant after adjustment (risk ratio [RR] 0.71, 95% confidence interval [CI] 0.53-0.96, p = 0.02). This difference in AVF failure was driven by a lower risk of cannulation failure (42/144 [29%] versus 98/209 [47%], adjusted RR 0.63, 95% CI 0.44-0.91, p < 0.01), while the proportions of AVF thrombosis (25/144 [17%] versus 42/209 [20%), p = 0.91) and abandonment (36/144 [25%] versus 49/209 [23%], p = 0.91) were not different. Conclusions: This analysis confirms the high proportion of AVF failure. However, the risk of AVF failure was significantly lower in Malaysia compared to ANZ and was driven by a lower risk of cannulation failure. Differences in practice patterns, including patient selection, surgical and/or cannulation techniques, likely contributed to the observed differences in outcomes and warrant further investigation.

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Pyroglutamic acidosis: An uncommon condition with common risk factors.
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Background: Accumulation of pyroglutamic acid (5-oxoproline), a by-product of the gamma-glutamyl cycle involved in glutathione synthesis, results in pyroglutamic acidosis (PGA), a high anion gap metabolic acidosis (HAGMA). Although considered rare, with only approximately 50 reported cases, the true incidence is unknown. The commonest known association of therapeutic paracetamol administration, and other risk factors including older age, female gender, liver disease and fluocoxacillin, are all common in hospitalised patients, possibly suggesting significant underreporting. We describe three cases identified in a single hospital over a 10 month period.

Case Report: Case 1. 72-year-old woman with Staphylococcus aureus bacteraemia from an epidural abscess, well treated with decompression and receiving intravenous fluocoxacillin and paracetamol, presented with acute delirium. Secondary causes of delirium were ruled out. Investigations revealed HAGMA (pH 7.28, bicarbonate 8, anion gap 22, lactate 0.7, Cr 60). Elevated urinary 5-oxoproline was detected. Repeat urine analysis following acidosis resolution showed negative 5-oxoproline. Case 2. 74-year-old woman with cirrhosis and Staphylococcus aureus prosthetic joint infection receiving fluocoxacillin and paracetamol developed a persistent HAGMA. Once other causes were ruled out, urine analysis confirmed elevated 5-oxoproline. Case 3. 70-year-old female with alcoholic liver disease with disproportionate HAGMA in the setting of pneumococcal sepsis complicated by acute kidney injury was tested for urine 5-oxoproline which was elevated. In all cases acidosis resolved following paracetamol cessation. Conclusions: Our experience of diagnosing 3 patients over 10 months suggests that PGA is probably more common than thought. Given that paracetamol is a common over the counter medication and other risk factors are highly prevalent in hospitalised patients, physicians need to consider PGA as a differential for unexplained HAGMA.

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Affective disorders, psychosis and dementia in a community sample of older men with and without Parkinson's disease.
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Background Dementia and affective and psychotic symptoms are commonly associated with Parkinson’s disease, but information about their prevalence and incidence in community representative samples remains sparse. Methods We recruited a community-representative sample 38173 older men aged 65-85 years in 1996 and used data linkage to ascertain the presence of PD, affective disorders, psychotic disorders and dementia. Diagnoses followed the International Classification of Disease coding system. Age was recorded in years. Follow up data were available until December 2011. Results The mean age of participants was 72.5 years and 333 men (0.9%) had PD at study entry. Affective and psychotic disorders and dementia were more frequent in men with than without PD (respective odds ratios: 6.3 [95%CI = 4.7, 8.4]; 14.2 [95%CI = 8.4, 24.0] and 18.2 [95%CI = 13.4, 24.6]). Incidence rate ratios of affective and psychotic disorders were higher among men with than without PD, although ratios decreased with increasing
age. The age-adjusted hazard ratio (HR) of an affective episode associated with PD was 5.0 (95%CI = 4.2, 5.9). PD was associated with an age-adjusted HR of 8.6 (95%CI = 6.1, 12.0) for psychotic disorders and 6.1 (95%CI = 5.5, 6.8) for dementia. PD and dementia increased the HR of depressive and psychotic disorders. Conclusions PD increases the risk of affective and psychotic disorders, as well as dementia, among community dwelling older men. The risk of a recorded diagnosis of affective and psychotic disorders decreases with increasing age. Copyright © 2016 Almeida et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

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Higher gastrosophegeal reflux symptoms are associated with better survival: Analysis from the australian IPF registry.
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Background: Gastroesophageal reflux disease (GORD) is common in patients with Idiopathic Pulmonary Fibrosis (IPF) and chronic micro-aspiration may contribute to its pathogenesis. We sought to investigate the impact of GORD on the Australian IPF Registry (AIPFR) cohort. Methods: Data collected for the AIPFR include a questionnaire recording comorbidities, medication use, and symptoms scores (cough severity, and a detailed questionnaire for GORD symptoms). The prevalence of patient-reported GORD, GORD medication use and GORD symptoms was assessed, and the relationship of these parameters evaluated against survival. Results: Of 569 patients enrolled in the AIPFR with complete questionnaires, 230(40.4%) reported a history of GORD diagnosis. 176/230(76.5%) of these patients and 117/339(34.5%) without GORD were receiving GORD treatment. 530/569(93.1%) patients reported at least one GORD symptom. Patients with GORD had higher GORD symptom scores than those without GORD (median 9, 5; p<0.001). GORD symptom scores were higher in patients on GORD treatment than those not receiving treatment (median 8, 5, p<0.001). Higher GORD symptom scores were independently associated with improved survival (HR 0.96, 95%CI 0.92-0.99; p=0.019) after adjustments for age, gender, smoking and disease severity. Specifically, symptoms of heartburn, bloated stomach and acid taste were associated with improved survival. The presence of cough was also highly predictive of increased mortality (HR 4.42, 95%CI 1.07-18.2; p=0.039). GORD treatment had no relationship with survival. Conclusion: GORD and GORD medication use is common in IPF. Increased GORD symptoms were associated with better survival. This suggests that symptomatic GORD is important in the pathobiology of IPF.

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A new stem extractor with specific multigrip pliers for revision hip arthroplasty - A biomechanical investigation.
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Introduction: It was the aim of this biomechanical study to test a new extractor with 2 specific multigrip pliers on
different stem designs and to compare it to a commonly used prefabricated one (UnMod). Methods: The new extractor comprises 2 specific multigrip pliers, 1 neck-pliers and 1 shoulder-pliers. The tests were performed on a tapered and a nontapered neck stem. They were fixed in specific moulds allowing torque adjustability. The first endpoint was maximum grip with the extractors being tested up to 70 hits or failure (pliers off) in maximally fixed stems. The second endpoint was hits/attempts until stem extraction or failure (pliers off > than 5 times) in moderately fixed stems. Results: The best grip on the tapered neck was achieved by the neck-pliers without failure, whereas the others failed consistently (shoulder-pliers: mean 42.9 hits, SD: 3.5/UnMod: 40.1, SD: 5.4; p< 0.01). The shoulder-pliers had the best grip on the nontapered neck withstandng more hits (11.9, SD: 1.9) than the others (neck-pliers: 4.8, SD: 1.7/UnMod: 2.8, SD 1.0; p< 0.01). None of the devices failed to extract the tapered neck (UnMod best: 4, SD: 1.3). The shoulder-pliers were able to extract the nontapered neck in 60% of the tests, whereas the others failed 100%. Conclusions: The new extractor with specific pliers for neck/shoulder grip seems to be a valuable tool for stem extraction in revision hip arthroplasty. Compared to UnMod, the neck-pliers showed better grip on the tapered neck and the shoulder-pliers performed the best on the nontapered neck. Copyright © 2016 Wichtig Publishing. PMID:612543403
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Radiologic and Audiologic Findings in the Temporal Bone of Patients with CHARGE Syndrome.
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BACKGROUND: CHARGE syndrome is a common congenital anomaly. Hearing loss affects 60%-90% of these children. As temporal bone computed tomography (CT) has become more sophisticated, more abnormalities of the middle and inner ear have been found. We present the detailed CT findings for children with CHARGE syndrome and the correlation of the CT findings with audiograms.
METHODS: We performed a retrospective medical records review of 12 patients with CHARGE syndrome, identified between 1990-2011 at Princess Margaret Hospital for Children in Western Australia, who underwent temporal bone CT for evaluation of hearing loss.
RESULTS: We present our findings for the 24 ears in terms of the cochlear, semicircular canal, middle ear, facial nerve, external auditory canal, venous, and jugular anomalies. The internal auditory canal was normal in 83.3% (n=20) of ears. Three (12.5%) ears had enlarged basal turns, and 4 (16.7%) each had hypoplastic and incompletely partitioned apical turns. The majority (n=13, 56.5%) of the vestibules were dysplastic. Up to 70.8% had abnormalities of the semicircular canal. The middle ear cavity was normal in 55% (n=11) of ears; however, up to 80% of the ears had some abnormality of the ossicles, and up to 70% had an abnormality of the facial nerve (7th cranial nerve) segments, especially in the labyrinthine segment. CT findings did not correlate with the audiograms.
CONCLUSION: The management of children with CHARGE syndrome is complex, requiring early evaluation and close attention of the multidisciplinary team. Early identification of hearing deficits is vital for patients' linguistic development.
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