
**Anaphylaxis; clinical features and evidence for a mast cell-leukocyte cytokine cascade in humans.**

Brown SGA, Stone SF, et al.

(Brown) Western Australian Institute for Medical Research, Royal Perth Hospital, University of Western Australia, Perth, WA, Australia (Stone, Cotterell) University of Western Australia, Perth, WA, Australia (Fatovich) Royal Perth Hospital, Perth, WA, Australia (Holdgate) Liverpool Hospital, University of New South Wales, Sydney, NSW, Australia (Celenza) Sir Charles Gairdner Hospital, Nedlands, WA, Australia (Coulson) Bunbury Hospital, Bunbury, WA, Australia (Hartnett) Rockingham General Hospital, Rockingham, WA, Australia (Nagree) Fremantle Hospital, Fremantle, WA, Australia (Isbister) Calvary Mater Hospital, University of Newcastle, Newcastle, NSW, Australia

S.G.A. Brown, Western Australian Institute for Medical Research, Royal Perth Hospital, University of Western Australia, Perth, WA, Australia

Background: Anaphylaxis is a serious allergic reaction that can cause death. There have been no large prospective studies to define the clinical features and mediators of severe anaphylaxis in humans. Objectives: To characterize reaction patterns, including delayed deteriorations, and related mediator changes. Methods: Multicenter prospective study of anaphylaxis cases treated in Australian EDs. Structured clinical datasheets were completed during treatment and prior to discharge. Serial blood samples were taken for mast cell tryptase (MCT), histamine, anaphylatoxin (C3a, C4a, C5a), cytokine (Interleukin (IL)-2, IL-6, IL-10, tumour necrosis factor receptor I (TNFRI)) and platelet activating factor acetyl hydrolase (PAF-AH) assays. Logistic regression was used to identify risk factors for severe and delayed reactions and a principal component analysis was used to examine mediator patterns. Results: Of 412 reactions, 315 met a definition for anaphylaxis. Of 97 severe reactions, 45 (46%) were hypotensive, 23 (24%) were hypoxemic, and 29 (30%) were mixed. One patient died. Severe reactions were associated with older age, pre-existing lung disease, and iatrogenic cause. Delayed deteriorations treated with epinephrine occurred in 29 (Table Presented) (7%) and were more common after hypotensive reactions and with coexistent lung disease. Twenty-two of 29 (76%) occurred within 4 hours of initial epinephrine treatment. Of the remaining seven, only two were severe and these occurred after initially severe reactions. All mediators correlated with severity, in particular MCT, histamine, IL-6, IL-10, and TNFRI. These mediators also correlated with the occurrence of delayed deteriorations. Conclusion: We demonstrate the different anaphylaxis reaction types, risk factors, and patterns of mediator release. These explain the findings of previous mortality studies and support current recommendations for observation periods after initial treatment. Multiple inflammatory pathways appear to drive severity, a process that may involve circulating white blood cells. (Figure Presented).

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**Towards a consensus on a hearing preservation classification system.**

Skarzynski H, Van De Heyning P, et al.

(Skarzynski, Skarzynski, Lorens) Institute of Physiology and Pathology of Hearing, Mochnackiego 10, 02-042 Warsaw, Poland (Skarzynski) World Hearing Center, Nadarzyn, Poland (Van De Heyning, De Bodt, Mertens) Antwerp University Hospital, Antwerp, Belgium (Agrawal, Parnes, Zimmermann) London Health Sciences Centre, London, Canada (Arauz) Instituto de ORL, Buenos Aires, Argentina (Atlas) Ear Science Institute Australia, Lions Hearing Clinic, Subiaco, Australia (Baumgartner, Gstoettner) Medizinische Universitat Wien, Universitatsklinik fur Hals-, Nasen- und Ohrenkrankheiten, Vienna, Austria (Caversaccio, Kompis) Universitatsklinik fur HNO, Kopf- und Halschirurgie, Inselspital Bern, Bern, Switzerland (Gavilan, Lassaletta) Hospital la Paz, Madrid, Spain (Godey, Levevre) Centre Hospitalier Universitaire de Rennes, Rennes, France (Green, O'Driscoll) Central Manchester University Hospitals, Manchester Auditory Implant Centre, Manchester, United Kingdom (Hagen, Mlynski) Department of Oto-Rhino-Laryngology, Comprehensive Hearing Center, University of
Conclusion: The comprehensive Hearing Preservation classification system presented in this paper is suitable for use for all cochlear implant users with measurable pre-operative residual hearing. If adopted as a universal reporting standard, as it was designed to be, it should prove highly beneficial by enabling future studies to quickly and easily compare the results of previous studies and meta-analyze their data. Objectives: To develop a comprehensive Hearing Preservation classification system suitable for use for all cochlear implant users with measurable pre-operative residual hearing. Methods: The HEARRING group discussed and reviewed a number of different propositions of a HP classification systems and reviewed critical appraisals to develop a qualitative system in accordance with the prerequisites. Results: The Hearing Preservation Classification System proposed herein fulfills the following necessary criteria: 1) classification is independent from users' initial hearing, 2) it is appropriate for all cochlear implant users with measurable pre-operative residual hearing, 3) it covers the whole range of pure tone average from 0 to 120 dB; 4) it is easy to use and easy to understand.

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Anaphylaxis: Clinical features and evidence for a mast cell-leukocyte cytokine cascade in humans.

Brown SGA, Stone SF, et al.

Background: Prospective human studies of anaphylaxis and its mechanisms have been limited, with few severe cases and/or examining only one or two mediators. Our objective was to define the different clinical patterns of anaphylaxis and the relationships between several mediators and severity.

Method: This was a multicenter prospective study of anaphylaxis cases treated in Australian EDs.
Structured clinical datasheets were completed during treatment and prior to discharge. Serial blood samples were taken for mast cell tryptase (MCT), histamine, anaphylatoxin (C3a, C4a, C5a), cytokine [Interleukin (IL)-2, IL-6, IL-10, tumour necrosis factor receptor I (TNFRI)] and platelet activating factor acetyl hydrolase (PAF-AH) assays. Logistic regression was used to identify risk factors for severe and delayed reactions and a principal component analysis was used to examine mediator patterns.

Results: Of 412 reactions, 315 met a definition for anaphylaxis. Of 97 severe reactions 45 (46%) were hypotensive, 23 (24%) were hypoxemic and 29 (30%) were mixed. One patient died. Severe reactions were associated with older age, pre-existing lung disease and iatrogenic cause. Delayed deteriorations treated with epinephrine occurred in 29 (7%) and were more common after hypotensive reactions and with coexistent lung disease. 22/29 (76%) occurred within 4 h of initial epinephrine treatment. Of the remaining seven, only two were severe and these occurred after initially severe reactions. All mediators correlated with severity, in particular MCT, histamine, IL-6, IL-10 and TNFRI. These mediators also correlated with the occurrence of delayed deteriorations. Conclusion: We demonstrate the different anaphylaxis reaction types, risk factors and patterns of mediator release. These explain the findings of previous mortality studies and support current recommendations for observation periods after initial treatment. Multiple inflammatory pathways appear to drive severity, a process that may involve circulating white blood cells.

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The western dietary pattern is prospectively associated with nonalcoholic fatty liver disease in adolescence.
Oddy WH, Herbison CE, et al.
(Oddy, Herbison, Jacoby, O'Sullivan, Black) Telethon Institute for Child Health Research, Centre for Child Health Research, University of Western Australia, PO Box 855 West, Perth, WA 6872, Australia (Ambrosini) Medical Research Council Human Nutrition Research, Cambridge, United Kingdom (O'Sullivan) School of Exercise and Health Sciences, Edith Cowan University, Joondalup, WA, Australia (Ayonrinde, Olynyk, Beilin, Mori, Adams) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia (Ayonrinde, Olynyk) Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia (Ayonrinde, Olynyk) Curtin Health Innovation Research Institute, Curtin University of Technology, Perth, WA, Australia (Olynyk) Institute for Immunology and Infectious Diseases, Murdoch University, Perth, WA, Australia (Hands) School of Health Sciences, University of Notre Dame, Fremantle, WA, Australia

W.H. Oddy, Telethon Institute for Child Health Research, Centre for Child Health Research, University of Western Australia, PO Box 855 West, Perth, WA 6872, Australia. E-mail: wendyo@ichr.uwa.edu.au

Objectives: Poor dietary habits have been implicated in the development of nonalcoholic fatty liver disease (NAFLD); however, little is known about the role of specific dietary patterns in the development of NAFLD. We examined prospective associations between dietary patterns and NAFLD in a population-based cohort of adolescents. Methods: Participants in the Western Australian Pregnancy Cohort (Raine) Study completed a food frequency questionnaire at 14 years and had liver ultrasound at 17 years (n=995). Healthy and Western dietary patterns were identified using factor analysis and all participants received a z-score for these patterns. Prospective associations between the dietary pattern scores and risk of NAFLD were analyzed using multiple logistic regression. Results: NAFLD was present in 15.2% of adolescents. A higher Western dietary pattern score at 14 years was associated with a greater risk of NAFLD at 17 years (odds ratio (OR) 1.59; 95% confidence interval (CI) 1.17-2.14; P<0.005), although these associations were no longer significant after adjusting for body mass index at 14 years. However, a healthy dietary pattern at 14 years appeared protective against NAFLD at 17 years in centrally obese adolescents (OR 0.63; 95% CI 0.41-0.96; P=0.033), whereas a Western dietary pattern was associated with an increased risk of NAFLD. Conclusions: A Western dietary pattern at 14 years in a general population sample was associated with an increased risk of NAFLD at 17 years, particularly in obese adolescents. In centrally obese adolescents with
NAFLD, a healthy dietary pattern may be protective, whereas a Western dietary pattern may increase the risk. 2013 by the american College of Gastroenterology.
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Anaemia in inflammation-associated colonic tumourigenesis.
Chua A, Ho D, et al.
(Chua, Ho, Klopcic, Trinder) University of Western Australia, Australia (Olynyk) Fremantle Hospital, Australia (Lawrance) Centre for Inflammatory Bowel Diseases, Fremantle Hospital, Australia
A. Chua, University of Western Australia, Australia
Introduction: Inflammatory bowel disease (IBD) is characterised by chronic intestinal inflammation and is associated with an increased risk of colon cancer. Anaemia is a common systemic complication of IBD and is treated with iron supplementation. The aim of this study was to investigate the effects of dietary iron on colonic inflammation and tumourigenesis, anaemia, and the regulation of iron metabolism using a mouse model of inflammation-associated colon cancer. Methods and Materials: Mice were fed either an iron-supplemented (1% carbonyl iron) or control iron (0.02% iron) diet for 4 weeks prior to administration of a single dose of azoxymethane (AOM; 7.4mg/kg wt i.p.) and 1-3 cycles of dextran sodium sulphate (DSS; 2% w/v in drinking water for 7 days followed by 14 days on water) to induce colonic inflammation and tumourigenesis. Colonic inflammation and tumour development were assessed by colonoscopy and histology. Haematology was measured using standard techniques. Gene expression was determined by real-time PCR, plasma IL-6 by ELISA and phosphorylation of Stat3 by immunoblotting. Results: In AOM/DSS-treated mice, colonic inflammation was more severe (p<0.05) and the number and size of colonic tumours were increased with dietary iron loading (p<0.05). Colonic IL-6 gene expression and Stat3 phosphorylation were increased by AOM/DSS treatment and were enhanced by dietary iron (p<0.05). Immunofluorescence demonstrated that both ferritin and IL-6 co-localised with F4/80+ macrophages in the lamina propria of the colonic mucosa in iron-loaded mice suggesting that iron had a direct effect on the IL-6 producing-macrophages. Iron deficiency anaemia was observed in both iron-loaded and control mice following AOM/DSS treatment with decreased haemoglobin levels, MCH and MCV and increased reticulocyte count (p<0.05). These mice also exhibited hypoferraemia (p<0.05) and increased liver iron concentration (p<0.01) indicating the presence of anaemia of inflammation. Dietary iron supplementation, however, did not improve the anaemia. Iron loading increased liver BMP6 gene expression (p<0.05) whilst colonic inflammation had no effect. Liver Hamp1 and Smad7 gene expression was upregulated by dietary iron and downregulated by colonic inflammation despite increased plasma IL-6 levels (p<0.01) and enhanced liver Stat3 phosphorylation (p<0.05). Splenic gene expression of the putative erythroid signalling molecule TWSG1 was elevated with colonic inflammation (p<0.0001) whilst GDF15 was increased only when both inflammation and iron were present (p<0.001). Conclusion: In conclusion, these findings suggest dietary iron promotes colonic inflammation and tumour development via an IL-6/Stat3-mediated pathway. Colonic inflammation was accompanied by the presence of both iron deficiency anaemia and anaemia of inflammation which were not alleviated by dietary iron supplementation. Hepcidin expression was downregulated despite the presence of iron loading and inflammation and this is likely to be due to the presence of anaemia. TWSG1 or transferring saturation may contribute to the erythroid-dependent downregulation of hepcidin.
Publication Types: Conference Abstract
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Changes in gene expression of cholesterol metabolism pathways in mouse models of haemochromatosis.
Introduction: The liver is central to the metabolism of both iron and cholesterol. Cholesterol is synthesised and further metabolised to bile acids in the liver and the liver plays an important role in regulation of iron metabolism. It is also the organ in which excess iron is stored. Clinically, links have been noted between lipid and iron metabolism, with approximately one-third of patients with non-alcoholic fatty liver disease exhibiting altered iron parameters. On a molecular level, we have previously reported that wild-type mice fed iron-deficient, normal or iron-loaded diets exhibited increased hepatic cholesterol and increased hepatic gene expression of enzymes in the cholesterol biosynthesis pathway with increasing hepatic iron burden. In the genetic disorder, haemochromatosis, the liver can become overloaded with iron; however, clinical studies have suggested that lipid metabolism may not be perturbed in haemochromatosis.

Methods and Materials: We investigated hepatic cholesterol metabolism in three mouse models of hereditary haemochromatosis: Hfe-/-, Tfr2Y245X single mutant and Hfe-/- x Tfr2Y245X double mutant animals as well as wild-type controls. Mice were fed normal mouse chow and sacrificed at 10 weeks of age. Hepatic gene expression, total cholesterol and non-haem iron were measured. Liver non-haem iron was similar in Hfe-/- and Tfr2Y245X mice (16.6±0.8 and 17±1 mumolFe/gliver, respectively) and significantly higher in the double mutant animals (22.4±0.7 mumolFe/gliver; P<0.004) than either of the single mutant mice.

Results: Only one group of genes increased significantly with increasing hepatic iron: those involved in cholesterol transport. Gene expression of apolipoproteins A4, C1, C2, C3 and E increased significantly with increasing hepatic iron as did expression of VLDL receptor. In contrast to our findings in wild-type mice, gene expression of cholesterol biosynthetic enzymes did not increase significantly with liver iron burden and there were no differences in hepatic cholesterol between the groups of mutant mice. We also measured expression of genes involved in cholesterol regulation, which similarly, did not increase with increasing hepatic iron. Approximately 50% of cholesterol synthesised in the liver is directed to bile acid synthesis; however, gene expression of bile acid pathway enzymes did not change with respect to hepatic iron burden.

Conclusion: These results suggest that iron-associated cholesterol regulation may be ameliorated by the genetic changes which occur in haemochromatosis.

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Does iron have causal roles in neurodegeneration with brain iron accumulation?-A new view from a mouse model of hemochromatosis.

Heidari M, Johnstone D, et al.
(Heidari, Martin, Milward) University of Newcastle, Australia (Johnstone) University of Sydney, Australia (Graham) Curtin University of Technology, Australia (Olynyk) Fremantle Hospital, Australia (Trinder, Delima, Chua, House) University of Western Australia, Australia

Introduction: It is unclear how the brain is affected in the iron loading disorder hereditary hemochromatosis, which can be caused by mutations in the HFE gene or the transferrin receptor 2 (TFR2) gene. We have investigated brain iron measures and gene transcript levels in a 'double mutant' mouse model of hemochromatosis, the Hfe<sup>-/-</sup>xTfr2<sup>Y245X</sup> mouse, on short-term dietary iron supplementation. Methods and Materials: All mice were male and on an AKR background. Hfe<sup>-/-</sup>xTfr2<sup>Y245X</sup> double mutant mice received a high
iron diet (2% carbonyl iron) for 3 weeks before sacrifice at 12 weeks. Brain iron was assessed by inductively coupled-atomic emission spectroscopy and non-heme iron assay. Ferritin levels were assessed by Western immunoblotting. Iron-supplemented Hfe<sup>-/-</sup>xTfr2<sup>Y245X</sup> double mutant mice had significantly higher levels of brain iron (> 1.7-fold increase, p < 0.025, n > 5/group) and ferritin (2.3-fold increase, p < 0.001, n > 5/group) thanagematched, gender-matched wild-type mice on normal chow. Results: Brain mRNA transcripts were assessed by microarray and real-time reverse transcription-polymerase chain reaction (RT-PCR). Array data were normalized by average and cubic spline methods (Illumina Genome Studio). In total, 760 genes were differentially expressed in the Hfe<sup>-/-</sup>xTfr2<sup>Y245X</sup> brain compared to wild-type brains (p < 0.05, n = 4/group). Analysis for pathway enrichment using the Database for Annotation, Visualization and Integrated Discovery (DAVID v6.7) revealed significant over-representation (Benjamini corrected p = 0.0073) of genes important in the mitogen-activated protein kinase (MAPK) signaling pathway. One gene in the MAPK signaling pathway showing transcript changes was phospholipase A2, group VI (Pla2g6, 1.7-fold decrease, p=0.01). This gene is causatively linked to the severe family of neurogenetic diseases Neurodegeneration with Brain Iron Accumulation (NBIA). Three other NBIA-linked genes also had significantly decreased transcripts: fatty acid 2-hydroxylase (Fa2h, 1.4-fold decrease, p=0.002), ATPase type 13A2 (Atp13a2, 1.1-fold decrease, p=0.04) and chromosome 19 open reading frame 12 (C19orf12, 1.2-fold decrease, p=0.02). This was also validated by real-time RT-PCR. The NBIA genes have rare neurodegenerative disorders with childhood, adolescent or adult onset of severe movement, cognitive or behavioral problems. The term NBIA can be a misnomer as not all patients diagnosed with NBIA based on mutation in an NBIA-associated gene show brain iron accumulation. Also most of the causal genes so far identified have no known relationship with iron, leading some authors to propose that iron is not a direct player in the neuropathology. Conclusion: The finding that brain transcript levels of at least 4 NBIA genes are altered in the hemochromatosis model puts iron back at centre stage as a primary causal factor in NBIA diseases and hints at close relationships between these genes and iron. It also suggests hemochromatosis patients may experience perturbations in brain molecular systems involved in severe neurodegenerative disease. This may contribute to movement impairment and other neurological problems in some patients.

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Iron accumulation in the choroid plexus and other brain barrier components in mouse models of hemochromatosis.

Milward E, Heidari M, et al.
(Milward, Heidari, Acikyol, Moscato) University of Newcastle, Australia (Graham) Curtin University of Technology, Australia (Chua, Delima, House, Trinder) University of Western Australia, Australia (Olynyk) Fremantle Hospital, Australia (Johnstone) University of Sydney, Australia

M. Milward, University of Newcastle, Australia

Introduction: The choroid plexus consists of a layer of epithelial cells that prevents the free exchange of solutes between the blood and cerebrospinal fluid (CSF). It forms part of the barrier structure that has traditionally been considered to protect the brain from damage in disorders such as hereditary hemochromatosis involving excessive iron loading elsewhere in the body. Methods and Materials: We performed Perls' staining enhanced with diaminobenzidine (DAB) on fixed brain tissue from four different mouse models of iron loading and wildtype control mice (all 13 wks of age) to explore the effects of iron overload disorders on iron distribution and accumulation within the brain. The four models were wildtype AKR mice fed a short-term iron-supplemented diet (2% carbonyl iron for 3 weeks), AKR mice with disruption of the Hfe gene (Hfe/-) or transferrin receptor 2 gene (Tfr2Y245X) and AKR mice with simultaneous disruption of each gene (Hfe/-xTfr2Y245X), all on normal chow. All four models have significantly increased hepatic iron concentrations relative to wildtype controls (3-fold to 4-fold increases, p<0.05). However only the Hfe/-xTfr2Y245X model shows increased brain
levels of total iron (by inductively coupled plasma-atomic emission spectroscopy) and non-heme iron (>1.4-fold increase, p<0.025), accompanied by higher levels of ferritin (2.3-fold increase, p=0.0005).

Results: At 3 months of age, Perls' staining was observed in the choroid plexus lining all ventricles in wild-type AKR mice and all models of iron loading. Staining intensity was lowest in wild-type AKR mice, and slightly higher in dietary iron-supplemented mouse. Staining intensity was greater in both single mutant models, with intensity in Tfr2Y245X mice appearing slightly higher than in Hfe-/- mice. The Hfe-/-xTfr2Y245X mice displayed greatest intensity. Staining was sometimes seen in cells lining blood vessels within choroid plexus invaginations however this was typically less intense than in the choroid plexus epithelial cells. At 1 year of age, staining within the choroid plexus of Hfe-/-xTfr2Y245X mice was so intense that cellular structure was obscured. At both times, there was also staining of other cells within the brain, with widespread staining across many regions by 1 year of age.

Conclusion: These observations show that both dietary iron loading and genetic iron loading are accompanied by accumulation of iron within barrier structures lining the brain. This may help protect the brain against damage when body iron levels are high. The choroid plexus transports a range of solutes both into and out of the brain. So the findings may reflect excess iron uptake into the choroid plexus from the blood or CSF, saturation of iron export mechanisms out of the choroid plexus or both. In any event, the staining observed in cells within the brain in younger and older animals suggests that the various brain barriers do not fully protect the brain in iron loading disorders.

Publication Types: Conference Abstract
PMID:71431451

Prevalence and implications of cerebrospinal fluid leukocytosis in papua new guinean children hospitalized with severe malaria.
Laman M, Manning L, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia; Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea.
Abstract. Cerebrospinal fluid (CSF) leukocytosis in severe malaria was assessed in 87 children in Papua New Guinea participating in a detailed longitudinal observational study who had undergone lumbar puncture for further investigation of altered consciousness and/or convulsions. After rigorous exclusion of non-malarial infection, 16 (20.5%) of 78 children with Plasmodium falciparum monoinfection but 0 of 9 with P. vivax/mixed-species malaria had a detectable CSF leukocytosis, which was unrelated to prior, including complex, seizures. There were eight children with a CSF leukocyte density > 10 cells/μL (9.2% of the total sample), half of whom had cerebral malaria (4 of 22, 18.1%). Cerebrospinal fluid leukocytosis is infrequent in severe pediatric malaria, especially in children with P. vivax infections, and it is generally mild. Its presence in a blood slide-positive child should prompt consideration of alternative diagnoses and empiric antibiotic therapy.
PMID:24019433

Endemic (murine) typhus in returned travelers from Asia, a case series: clues to early diagnosis and comparison with dengue.
Raby E, Dyer JR.
Infectious Diseases Service, Fremantle Hospital and Health Service, Fremantle, Western Australia, Australia.
PMID:23358638

Clinical and radiological predictors of outcome for murray valley encephalitis.
A review of the laboratory-confirmed cases of Murray Valley encephalitis (MVE) from Western Australia between 2009 and 2011 was conducted to describe the clinical, laboratory, and radiological features of the disease. The nine encephalitis patients presented with altered mental state and seizures, tremor, weakness, or paralysis. All patients developed a raised C-reactive protein, whereas most developed acute liver injury, neutrophilia, and thrombocytosis. All patients with encephalitis developed cerebral peduncle involvement on early magnetic resonance imaging (MRI). The absence of thalamic MRI hyperintensity during the acute illness, with or without leptomeningeal enhancement, predicted a better neurological outcome, whereas those patients with widespread abnormalities involving the thalamus, midbrain, and cerebral cortex or the cerebellum had devastating neurological outcomes. MRI scans repeated months after acute illness showed destruction of the thalamus and basal ganglia, cortex, or cerebellum. These findings may help clinicians predict the neurological outcome when evaluating patients with MVE. Copyright 2013 by The American Society of Tropical Medicine and Hygiene.

The use of prone CT in the perioperative management of airway obstruction caused by multinodular goitre.

Hunt VJ, English JD.

Fremantle Hospital and Health Service, Fremantle WA, Australia


Alfred Hyperbaric Unit, Alfred Hospital, Melbourne, Victoria; Department of Diving and Hyperbaric Medicine, Prince of Wales Hospital, Sydney, New South Wales; Wesley Centre for Hyperbaric Medicine, Brisbane, Queensland; Department of Diving and Hyperbaric Medicine, Fremantle Hospital, Perth, Western Australia, Australia.

For a large number of ischaemic, infective, inflammatory or traumatic conditions, hyperbaric oxygen therapy is either the only treatment or an adjunct that significantly reduces morbidity and mortality. The primary aim of this review is to identify clinical conditions treated in a paediatric population referred to Australian hyperbaric units. Secondary aims are to describe outcomes of treatment and detail any complications occurring during treatment or during transfer between units. This was a retrospective
A cohort study (January 1998-December 2011) of children treated at four Australian hyperbaric medical units. A total of 112 children underwent 1099 hyperbaric treatments for 14 indications. Ages were not normally distributed with a median age of 14 years (interquartile range 11-16; range 0.25-16 years). Treatments were completed as planned in 81.5% of cases with 25 patients' treatment terminated at the request of physicians, parents or patients. Complications relating to hyperbaric oxygen therapy occurred in 58 treatments (5.3%). Central nervous system oxygen toxicity occurred in 1:366 treatments. Our findings indicate that provision of hyperbaric oxygen therapy to children is feasible in major regional hyperbaric units and is associated with low complication rates. Management of children in an adult hyperbaric facility, however, requires significant cooperation between paediatric, intensive care and hyperbaric consultants, as the need for transfer to another hospital and prolonged transports often impacts on optimal ongoing surgical and intensive care management.

PMID:23362893

The relationship between patient data and pooled clinical management decisions.
Ludbrook G, O’Loughlin E, et al.
Department of Anaesthesia, Royal Adelaide Hospital, Adelaide, South Australia; Department of Anaesthesia and Pain Medicine, Royal Perth Hospital, Perth, Western Australia; and Department of Anaesthesia, Fremantle Hospital, Fremantle, Western Australia, Australia.
A strong relationship between patient data and preoperative clinical decisions could potentially be used to support clinical decisions in preoperative management. The aim of this exploratory study was to determine the relationship between key patient data and pooled clinical opinions on management. In a previous study, panels of anaesthetists compared the quality of computer-assisted patient health assessments with outpatient consultations and made decisions on the need for preoperative tests, no preoperative outpatient assessment, possible postoperative intensive care unit/high dependency unit requirements and aspiration prophylaxis. In the current study, the relationship between patient data and these decisions was examined using binomial logistic regression analysis. Backward stepwise regression was used to identify independent predictors of each decision (at P >0.15), which were then incorporated into a predictive model. The number of factors related to each decision varied: blood picture (four factors), biochemistry (six factors), coagulation studies (three factors), electrocardiography (eight factors), chest X-ray (seven factors), preoperative outpatient assessment (17 factors), intensive care unit requirement (eight factors) and aspiration prophylaxis (one factor). The factor types also varied, but included surgical complexity, age, gender, number of medications or comorbidities, body mass index, hypertension, central nervous system condition, heart disease, sleep apnoea, smoking, persistent pain and stroke. Models based on these relationships usually demonstrated good sensitivity and specificity, with receiver operating characteristics in the following areas under curve: blood picture (0.75), biochemistry (0.86), coagulation studies (0.71), electrocardiography (0.90), chest X-ray (0.85), outpatient assessment (0.85), postoperative intensive care unit requirement (0.88) and aspiration prophylaxis (0.85). These initial results suggest modelling of patient data may have utility supporting clinicians’ preoperative decisions.

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Effectiveness of a patient blood management data system in monitoring blood use in Western Australia.
Mukhtar SA, Leahy MF, et al.
Centre for Population Health Research, Curtin University, Western Australia, Australia.
aqif.mukhtar@curtin.edu.au
The aim of this paper is to describe a linked patient blood management (PBM) data system and to demonstrate its usefulness by presenting the blood usage data obtained. Our existing datasets already collected much of the required information in relation to PBM. However, these datasets were
not linked. A patient identifier was used to link the Patient Administration System with the Laboratory Information System. Data linkage was achieved by linking the Laboratory Information System with the Patient Administration System records where blood transfusion or laboratory result date/time fell between admission and discharge date/time. The two datasets were then consolidated into the PBM data system. Blood usage data obtained from the system showed that between August 2008 and July 2009 there were 59,627 patient completed separations in the pilot hospital. Of the total transfused units, 62% were red blood cells (RBC), followed by fresh frozen plasma (22%), cryoprecipitate (9%) and platelets (8%). Around 50% of RBC transfusions were administered to patients >70 years of age. General medicine represented 21% of RBC usage, followed by haematology (19%), orthopaedics (17%) and general surgery (16%). Patients with 100 g/l pre-transfusion haemoglobin received 9% of RBC transfusions and patients with 71-100 g/l pre-transfusion haemoglobin received 73% of RBC transfusions. The post-transfusion haemoglobin in RBC transfusions exceeded 100 g/l in 33% of patients. Databases were successfully linked to produce a powerful tool to monitor blood utilisation and transfusion practices within a pilot PBM program. This will facilitate effective targeting of PBM strategies and ongoing monitoring of their impact.

Publication Types: Research Support, Non-U.S. Gov't
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Scoring systems for videolaryngoscopes-Reply.
Fremantle, Western Australia.
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Systemic mastocytosis presenting as intraoperative anaphylaxis with atypical features: A report of two cases.
Bridgman DE, Clarke RC, et al.
(Bridgman, Clarke, Sadleir, Stedmon, Platt) Department of Anaesthesia, Sir Charles Gairdner Hospital, Hospital Ave, Nedlands, WA 6009, Australia (Clarke, Sadleir, Platt) Anaesthetic Allergy Referral Centre of Western Australia, Australia (Stedmon) Department of Anaesthesia, Fremantle Hospital, Fremantle, Australia
P.R. Platt, Department of Anaesthesia, Sir Charles Gairdner Hospital, Hospital Ave, Nedlands, WA 6009, Australia. E-mail: peter.platt@uwa.edu.au
Two cases of perioperative cardiovascular collapse are presented that were associated with markedly elevated mast cell tryptase levels shortly after the event, leading to the assumption that an immunoglobin E-mediated, drug-induced anaphylaxis had occurred. However, the clinical picture in both cases was atypical and subsequent skin testing failed to identify a triggering drug. Further blood tests, some weeks later, revealed persistently elevated baseline levels of mast cell tryptase. In both cases bone marrow biopsy and genetic testing confirmed the diagnosis of mastocytosis. We present evidence and speculate that mast cell degranulation was triggered by tourniquet release in the first case and by exposure to peanuts in the second. An atypical presentation of anaphylaxis should alert the anaesthetist to the possibility of previously undiagnosed mastocytosis. 2011 Anaesthesia and Intensive Care.
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(Frawley, Benet, Thistlethwaite, Banham) Alfred Hyperbaric Unit, Alfred Hospital, Department of
Paediatric Anaesthesia and Pain Management, Melbourne, VIC, Australia (Frawley, Benet, Thistlethwaite, Banham) Department of Diving and Hyperbaric Medicine, Prince of Wales Hospital, Sydney, NSW, Australia (Frawley, Benet, Thistlethwaite, Banham) Wesley Centre for Hyperbaric Medicine, Brisbane, QLD, Australia (Frawley, Benet, Thistlethwaite, Banham) Department of Diving and Hyperbaric Medicine, Fremantle Hospital, Perth, WA, Australia

G. Frawley, Alfred Hyperbaric Unit, Alfred Hospital, Department of Paediatric Anaesthesia and Pain Management, Melbourne, VIC, Australia. E-mail: geoff.frawley@rch.org.au

For a large number of ischaemic, infective, inflammatory or traumatic conditions, hyperbaric oxygen therapy is either the only treatment or an adjunct that significantly reduces morbidity and mortality. The primary aim of this review is to identify clinical conditions treated in a paediatric population referred to Australian hyperbaric units. Secondary aims are to describe outcomes of treatment and detail any complications occurring during treatment or during transfer between units. This was a retrospective cohort study (January 1998-December 2011) of children treated at four Australian hyperbaric medical units. A total of 112 children underwent 1099 hyperbaric treatments for 14 indications. Ages were not normally distributed with a median age of 14 years (interquartile range 11-16; range 0.25-16 years). Treatments were completed as planned in 81.5% of cases with 25 patients' treatment terminated at the request of physicians, parents or patients. Complications relating to hyperbaric oxygen therapy occurred in 58 treatments (5.3%). Central nervous system oxygen toxicity occurred in 1:366 treatments. Our findings indicate that provision of hyperbaric oxygen therapy to children is feasible in major regional hyperbaric units and is associated with low complication rates. Management of children in an adult hyperbaric facility, however, requires significant cooperation between paediatric, intensive care and hyperbaric consultants, as the need for transfer to another hospital and prolonged transports often impacts on optimal ongoing surgical and intensive care management. 2011 Anaesthesia and Intensive Care.

Publication Types: Review
PMID:2013161370

The relationship between patient data and pooled clinical management decisions.
Ludbrok GL, O'Loughlin EJ, et al.
(Ludbrok, O'Loughlin, Grant, Corcoran) Department of Anaesthesia, Royal Adelaide Hospital, Eleanor Harrald Building, North Terrace Adelaide, Adelaide, SA 5000, Australia (Ludbrok, O'Loughlin, Grant, Corcoran) Department of Anaesthesia and Pain Medicine, Royal Perth Hospital, Perth, WA, Australia (Ludbrok, O'Loughlin, Grant, Corcoran) Department of Anaesthesia, Fremantle Hospital, Fremantle, WA, Australia (Ludbrok, Grant) Department of Anaesthesia, Discipline of Acute Care Medicine, University of Adelaide, Adelaide, SA, Australia (O'Loughlin, Corcoran) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia

G.L. Ludbrok, Department of Anaesthesia, Royal Adelaide Hospital, Eleanor Harrald Building, North Terrace Adelaide, Adelaide, SA 5000, Australia

A strong relationship between patient data and preoperative clinical decisions could potentially be used to support clinical decisions in preoperative management. The aim of this exploratory study was to determine the relationship between key patient data and pooled clinical opinions on management. In a previous study, panels of anaesthetists compared the quality of computer-assisted patient health assessments with outpatient consultations and made decisions on the need for preoperative tests, no preoperative outpatient assessment, possible postoperative intensive care unit/high dependency unit requirements and aspiration prophylaxis. Backward stepwise regression was used to identify independent predictors of each decision (at P <0.15), which were then incorporated into a predictive model. The number of factors related to each decision varied: Blood picture (four factors), biochemistry (six factors), coagulation studies (three factors), electrocardiography (eight factors), chest X-ray (seven factors), preoperative outpatient assessment (17 factors), intensive care unit requirement (eight factors) and aspiration prophylaxis (one factor). The
factor types also varied, but included surgical complexity, age, gender, number of medications or comorbidities, body mass index, hypertension, central nervous system condition, heart disease, sleep apnoea, smoking, persistent pain and stroke. Models based on these relationships usually demonstrated good sensitivity and specificity, with receiver operating characteristics with the following areas under curve: Blood picture (0.75), biochemistry (0.86), coagulation studies (0.71), electrocardiography (0.90), chest X-ray (0.85), outpatient assessment (0.85), postoperative intensive care unit requirement (0.88) and aspiration prophylaxis (0.85). These initial results suggest modelling of patient data may have utility supporting clinicians’ preoperative decisions. 2011 Anaesthesia and Intensive Care.

PMID:2013161368

A diagnostic conundrum: Heterophilic antibody interference in an adrenocorticotropic hormone immunoassay not detectable using a proprietary heterophile blocking reagent.

Total joint replacement in men: Old age, obesity and in-hospital complications.
(Mnatzaganian, Ryan, Hiller) School of Population Health and Clinical Practice, Discipline of Public Health, The University of Adelaide, Adelaide, SA, Australia (Ryan) Data Management and Analysis Centre, The University of Adelaide, Adelaide, SA, Australia (Norman) School of Surgery, University of Western Australia, Fremantle, WA, Australia (Davidson) Royal Adelaide Hospital, Adelaide, SA, Australia (Hiller) Faculty of Health Sciences, Australian Catholic University, Fitzroy, VIC, Australia G. Mnatzaganian, School of Population Health and Clinical Practice, Discipline of Public Health, The University of Adelaide, SA 5005, Australia. E-mail: george.mnatzaganian@adelaide.edu.au
Background: We assessed risks of incident in-hospital complications and 1-year and 5-year mortality following elective primary total joint replacement (TJR), focusing on obesity. Methods: Longitudinal data from a population-based cohort of 819 men who had had TJR were integrated with validated hospital morbidity data and mortality records. Complications recorded in the index admission were classified as major or minor by 13 independent orthopaedic surgeons. Results: Of 819 men (mean age 76.3 (SD 4.5) years), 331 patients (40.4%) had an in-hospital complication from whom 155 (18.9%) had at least one major complication that was classified as potentially life threatening. Obesity and age were independently associated with increased risk of major complications. Compared with patients without complications, those with major complications experienced significantly greater mortality in 1 year (5.8% versus 1.2%, P = 0.001) and 5 years (16.8% versus 8.0%, P = 0.002) following TJR. In Cox regressions, age, Charlson Co-morbidity index and major complications were independently associated with 1-year mortality. Age and Charlson Co-morbidity index were also associated with 5-year mortality. Similarly, risk of dying within 5 years of TJR was higher among patients with class II obesity compared with patients with normal weight. The most frequently reported complications were those in the cardio-respiratory and general systems. Complications in the cardio-respiratory system significantly increased hazard of 1- and 5-year mortality. Conclusion: The elderly and the obese are more likely to develop adverse outcomes following a primary TJR. Our findings may assist clinicians in better selecting elderly patients for surgery, and informing them about their individual level of risk.
2012 Royal Australasian College of Surgeons.
PMID:22963511

Does a bipolar hemiprosthesis offer advantages for elderly patients with neck of femur fracture? A clinical trial with 261 patients.
Previous studies comparing unipolar and bipolar hemiarthroplasty for treatment of displaced intracapsular femoral neck fractures in elderly patients have often lacked methodological power and yielded conflicting clinical results. The objective of this study was to compare the clinical outcomes from each implant in a randomized cohort of elderly patients with intracapsular fracture of the femoral neck treated with a cemented hemiprosthesis. Methods: This study is a clinical trial of 261 patients (82.0+/−7.9 years) who were randomly assigned to one of the two treatment groups: group 1 (n=133) received a cemented bipolar implant and group 2 (n=128) received a unipolar head with the same stem. At 12 months post-surgery, pain and functional abilities were quantified by blinded assessors using the Oxford and Harris Hip Scores, Verbal Numerical Rating Score and Six-Minute Walk. The Mann-Whitney U-test and t-test for independent samples were used to compare results between the groups (P<0.05). Results: There were no significant differences in any clinical scores between the groups. Results from the Six-Minute Walk indicated no difference in functional walking ability or endurance (P=0.446) between the groups. Self-selected pain ratings also did not differ between groups (P=0.236). Patients receiving the unipolar prosthesis had significantly reduced abduction (P=0.0001) and internal rotation (P=0.047) in the operated hip compared to the non-operated hip. Conclusion: These short-term results suggest that unipolar implants share many of the advantages of the bipolar prosthesis but can be manufactured at substantially lower cost. These implants may be appropriate for the less-active elderly patient, particularly when used with bone cement. 2013 The Authors ANZ Journal of Surgery 2013 Royal Australasian College of Surgeons. PMID:23320780

Re: Safe introduction of a new surgical technique: Remote telementoring for posterior retroperitoneoscopie adrenalectomy.
(Louie-Johnsun) Department of Urology, Gosford Hospital, Gosford, NSW, Australia (Liodakis)
Department of Urology, Austin Hospital, Melbourne, VIC, Australia (Sofield) Department of Urology, Fremantle Hospital, WA, Australia
M. Louie-Johnsun, Department of Urology, Gosford Hospital, Gosford, NSW, Australia
Publication Types: Letter
PMID:23465214

Understanding the effects of tobacco smoke on the pathogenesis of aortic aneurysm.
Norman PE, Curci JA.
From the School of Surgery, University of Western Australia, Fremantle, Australia (P.E.N.); and Department of Surgery, Section of Vascular Surgery, Washington University School of Medicine, Saint Louis, MO (J.A.C.).
Aneurysmal arterial disease is a vascular degenerative condition that is distinct from atherosclerotic and other occlusive arterial diseases. There is regionalization of the predisposition to aneurysm formation within the vascular tree, and the pathological process varies with location. Infrarenal abdominal aortic aneurysm (AAA) is the most common manifestation of aneurysmal disease, and smoking is the dominant risk factor. Smoking is a much greater risk factor for AAA than for
atherosclerosis. In addition to playing a role in the pathogenesis of AAA, smoking also increases the rate of expansion and risk of rupture of established AAA. The mechanistic relationship between AAA and smoking is being established by the use of enhanced animal models that are dependent on smoke or smoke components. The mechanisms seem to involve durable alterations in vascular smooth muscle cell and inflammatory cell function. This review examines the clinical, epidemiological, and mechanistic evidence implicating smoking as a cause of aneurysms, focusing on AAA.

PMID:23685557

**Everolimus limits aortic aneurysm in the apolipoprotein e-deficient mouse by downregulating C-C chemokine receptor 2 positive monocytes.**
Moran CS, Jose RJ, et al.
(Moran, Jose, Moxon, Rush, Golledge) Vascular Biology Unit, Queensland Research Centre for Peripheral Vascular Disease, James Cook University, Townsville, QLD, Australia (Roomberg, Korner) Comparative Genomics Centre, School of Pharmacy and Molecular Sciences, James Cook University, Townsville, QLD, Australia (Norman) School of Surgery, University of Western Australia, Fremantle Hospital, Fremantle, WA, Australia (Rush) School of Veterinary and Biomedical Sciences, James Cook University, Townsville, QLD, Australia (Korner) Cellular Immunology, Menzies Research Institute, University of Tasmania, Hobart, TAS, Australia

**OBJECTIVE:** We aimed to determine the effect of mechanistic target of rapamycin inhibitor everolimus on abdominal aortic aneurysm within the angiotensin II (A2)-infused apolipoprotein E-deficient mouse model. **APPROACH AND RESULTS:** Abdominal aortic aneurysm was induced via subcutaneous infusion of A2. Flow cytometry demonstrated increased circulating and aortic C-C chemokine receptor 2 (CCR2) monocytes during A2 infusion. The number of CCR2 monocytes present within the aorta was positively correlated with suprarenal aortic diameter. Simultaneous infusion of everolimus via a second subcutaneous osmotic micropump inhibited A2-induced aortic dilatation. Using flow cytometry and Western blot analysis, decreased aortic dilatation was associated with reduced development of CCR2 bone marrow monocytes, fewer numbers of circulating CCR2 monocytes, and lower aortic CCR2 concentration. In vitro, everolimus inhibited A2-stimulated production of interferon (IFN)-α and IFN-induced CCR2 expression in apolipoprotein E-deficient mouse bone marrow monocytes. Further, everolimus diminished IFN/lipopolysaccharide-stimulated M1 polarization in apolipoprotein E-deficient mouse bone marrow monocyte-differentiated macrophages. **CONCLUSIONS:** Systemic administration of everolimus limits aortic aneurysm in the A2-infused apolipoprotein E-deficient mouse model via suppressed development of bone marrow CCR2 monocytes and reduced egress of these cells into the circulation. 2013 American Heart Association, Inc.

PMID:2013187967

**Australian consumer perceptions of peer support.**
Henderson AR, Kemp V.
School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, Australia.

**INTRODUCTION:** Peer support in mental health service delivery is a relatively new development in Western Australia, occurring only in the last decade. Consequently, what is known about peer support in mental health has been largely drawn from the overseas literature. The purpose of the present study was to identify how consumers of mental health services in Western Australia viewed the impact that peer support workers had on their life.

**METHODS:** The nominal group technique was the method used to collect and analyze the data from nine participants living in the community who were supported by a peer support worker; the role of the
peer support worker was to encourage healthy lifestyle behaviors.

RESULTS: The results indicate that the main influences of a peer worker for consumers were motivation, increased social interaction, living a healthier lifestyle, positive mental attitude and building confidence.

DISCUSSION: It was concluded that participants viewed the support they received as a positive experience, which contributed to building confidence and enabled participants to make lifestyle changes. However, the results need to be viewed with caution, not only because of the small sample size, but also because the peer workers and the participants were all male. Results may well be different where the role and gender of the support worker and consumer are different. Copyright 2012 Wiley Publishing Asia Pty Ltd.

The potential role of homocysteine mediated DNA methylation and associated epigenetic changes in abdominal aortic aneurysm formation.
(Krishna, Golledge) The Vascular Biology Unit, Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, James Cook Drive, Douglas, Townsville, QLD 4811, Australia (Dear) Department of Medicine, Monash University, Australia (Craig) Early Life Epigenetics, Murdoch Children Research Institute and Department of Paediatrics, University of Melbourne, Royal Children's Hospital, Melbourne, Australia (Norman) School of Surgery, University of Western Australia, Fremantle, WA, Australia

J. Golledge, The Vascular Biology Unit, Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, James Cook Drive, Douglas, Townsville, QLD 4811, Australia. E-mail: jonathan.golledge@jcu.edu.au

Previous studies have suggested that homocysteine (Hcy) has wide-ranging biological effects, including accelerating atherosclerosis, impairing post injury endothelial repair and function, deregulating lipid metabolism and inducing thrombosis. However, the biochemical basis by which hyperhomocysteinemia (HHcy) contributes to cardiovascular diseases (CVDs) remains largely unknown. Several case-control studies have reported an association between HHcy and the presence of abdominal aortic aneurysms (AAA) and there are supportive data from animal models. Genotypic data concerning the association between variants of genes involved in the methionine cycle and AAA are conflicting probably due to problems such as reverse causality and confounding. The multifactorial nature of AAA suggests the involvement of additional epigenetic factors in disease formation. Elevated Hcy levels have been previously linked to altered DNA methylation levels in various diseases. Folate or vitamin B12 based methods of lowering Hcy have had disappointingly limited effects in reducing CVD events. One possible reason for the limited efficacy of such therapy is that they have failed to reverse epigenetic changes induced by HHcy. It is possible that individuals with HHcy have an "Hcy memory effect" due to epigenetic alterations which continue to promote progression of cardiovascular complications even after Hcy levels are lowered. It is possible that deleterious effect of prior, extended exposure to elevated Hcy concentrations have long-lasting effects on target organs and genes, hence underestimating the benefit of Hcy lowering therapies in CVD patients. Therapies targeting the epigenetic machinery as well as lowering circulating Hcy concentrations may have a more efficacious effect in reducing the incidence of cardiovascular complications. 2013 Elsevier Ireland Ltd.

Primary localized cutaneous nodular amyloidosis successfully treated with cyclophosphamide.
Tong PL, Walker WA, et al.
(Tong) Sir Charles Gairdner Hospital, University of Western Australia, Perth, Australia (Walker)
Primary localized cutaneous nodular amyloidosis (PLCNA) is a rare subtype of localized cutaneous amyloidosis and can be associated with various connective tissue disorders. It can be difficult to treat and past therapies include surgical excision, dermabrasion, electrodessication and curettage, cryotherapy and laser therapy. We present a case of a middle-aged woman with PLCNA associated with CREST (calcinosis, Raynaud phenomenon, oesophageal motility disorders, sclerodactyly and telangiectasia) syndrome and Sjogren's syndrome responding to cyclophosphamide with no new amyloid deposits and resolution of skin ulceration after many years of resistance to drug therapy. It is important to monitor these patients for progression into systemic amyloidosis.

PMID:2013088547

E-ageing: Development and evaluation of a flexible online geriatric medicine educational resource for diverse learners.
Beer, Christopher: christopher.beer@uwa.edu.au
Beer, Christopher: WA Centre for Health and Ageing, University of Western Australia, Crawley, WAU, Australia, christopher.beer@uwa.edu.au
Watson, Natasha: WA Centre for Health and Ageing, University of Western Australia, Crawley, WAU, Australia Massarotto, Alicia: Fremantle Hospital, Fremantle, WAU, Australia Caputo, Lisa: School of Medicine and Pharmacology, University of Western Australia, Crawley, WAU, Australia Flicker, Leon: WA Centre for Health and Ageing, University of Western Australia, Crawley, WAU, Australia Beer, Christopher: WA Centre for Health and Ageing, University of Western Australia, Crawley, WAU, Australia
Aims: To determine preferred content and format for online education modules in aged care among inter-professional learners; to develop resources that meet user preferences. Methods: Stakeholders were interviewed. A survey was administered to all health/medical students and teachers at The University of Western Australia. An iterative process was used to develop modules, and user feedback was collated. Results: The educational needs of each discipline related primarily to foundation level knowledge in major aged care topics. Stakeholders sought modules incorporating communication skills, cultural and social issues and the importance of a multidisciplinary approach to aged care. Students from all disciplines sought online materials that are interactive, engaging, case-based and locally relevant. Online modules were developed. Evaluation of the modules by users has been strongly positive. Conclusion: There was consensus regarding the major curricular areas that online resources should encompass. The e-ageing modules developed in this project have been evaluated positively by users. (PsycINFO Database Record (c) 2014 APA, all rights reserved) (journal abstract).
Publication Types: Empirical Study; Quantitative Study
PMID:2013-45458-008

Re: Fasting blood glucose predicts response to extended-release metformin in gestational
Basu A.
Publication Types: Letter
PMID:24289065

Barriers to the 4-h rule: What causes delays for gynaecology patients in the emergency department?
Pakmehr S, Petersen RW, et al.
(Pakmehr, Petersen, Quinlivan) Department of Obstetrics and Gynaecology, Joondalup Health Campus, Joondalup, WA 6027, Australia (Pakmehr, Petersen) Edith Cowan University, Perth, WA, Australia (Quinlivan) University of Notre Dame, Fremantle, WA, Australia (Quinlivan) Women's and Children's Health Research Institute, University of Adelaide, Adelaide, SA, Australia
J.A. Quinlivan, Department of Obstetrics and Gynaecology, Joondalup Health Campus, Joondalup, WA 6027, Australia. E-mail: quinlivanj@ramsayhealth.com.au
Objectives To explore factors that led to noncompliance with the 4-h rule for gynaecology patients in a general emergency department. Methods A cross-sectional cohort study was performed at a general emergency department. The files of all female patients aged from birth to 100 years presenting from 1 January 2009 to 31 December 2010 were screened. Those patient's files where a coded gynaecological diagnosis was made were reviewed. A time flow analysis was then undertaken of 580 consecutive files to evaluate barriers to admission or discharge of patients within the 4-h period. A further 300 files were audited to determine whether suboptimal management by emergency department staff contributed towards delays. Results There were 134 438 presentations to the emergency department, of which 2968 were gynaecology presentations (2.2%). The overall compliance with the 4-h rule was 66%. Patients with acute triage status, who were pregnant or who were eventually admitted, were more likely to be managed in compliance with the 4-h rule. The main barriers to compliance were incomplete examinations by emergency department staff; waiting for ultrasound examinations and blood test results; delays waiting for specialty review; and delays caused by initial review by surgical teams. Conclusion Specific barriers to compliance with the 4-h rule can be identified in gynaecology patients. Strategies specific to overcome these barriers can be developed to improve compliance.
PMID:2013115599

Experience from a GP cultural competence training workshop-Australia's first.
(Johri, John, Isaac) University of Western Australia, Perth, Australia (Johri) Armadale Health Service, Mental Health, Perth, Australia (Yeak, Moore) South Metropolitan Health Service, Mental Health Strategy and Leadership Unit, Perth, Australia (John) Bentley Health Service, Mental Health, Perth, Australia (Isaac) Fremantle Health service, Mental Health, Perth, Australia
N. Johri, University of Western Australia, Perth, Australia
Background: General practitioners (GPs) form the cornerstone for delivery of mental health services for the majority of the population. It is only a small proportion of persons needing mental health care who receive inputs exclusively from the specialised mental health sector. There is worldwide evidence that GPs need capacity building to help them diagnose and manage common mental disorders and effectively provide mental health-related services. Australia is culturally a very diverse country. One in four Australians is born overseas. If those with a parent born overseas or those who speak a language other than English at home is included, the proportion is about 50%. Improving the health-care provision for patients from a culturally and linguistically diverse (CALD) background is recognised and the Federal as well as State governments are committed to this. Objectives: 1. Develop the course
content and a feasible methodology for training workshops for GPs to deal with patients from a CALD background. 2. Evaluate such a workshop through a pre/post training assessment of trainees.

Methods: Culture competency training workshop for GPs working with CALD populations was conducted and evaluated. Findings and conclusion: Cultural competency training for GPs offers numerous challenges and opportunities. The need of such training for all GPs working with CALD populations in the current Australian mental health services context will be highlighted. The need for longer-term evaluation of such training and continued support for trained GPs is recognised.


Antinuclear antibody test.
MBBS, FRACP, FRCPA, is a Consultant Immunologist, Fremantle Hospital and Princess Margaret Hospital for Children, Western Australia.
The antinuclear antibody (ANA) test is widely used as a serological marker of autoimmune disease. Antinuclear antibodies are immunoglobulins or antibodies that bind to one or more antigens expressed within the nucleus of human cells. Used selectively, the ANA test can be a useful laboratory tool to help confirm or exclude the diagnosis of systemic rheumatic disease. However, the relatively high prevalence of ANAs in other inflammatory conditions, as well as healthy individuals, can make a positive result difficult to interpret.

Antinuclear antibody test.

Perceptions of barriers to discussing and testing for sexually transmitted infections in a convenience sample of general practice patients.
Baker JR, Arnold-Reed DE, et al.
School of Medicine, University of Notre Dame Australia, Fremantle, WA, Australia.
We aimed to identify patient perceptions of barriers to discussing sexually transmitted infections (STIs) at the primary care level. An anonymous questionnaire was available to patients (16-70 years) in the waiting room of four metropolitan Perth general practices. Results are based on 370 participant views (9.5% of the potential target population). Patients felt comfortable discussing STIs with their general practitioner (GP) and their level of comfort would be enhanced if they knew their GP had a special interest or qualification in sexual health. Willingness to discuss issues increased or remained unchanged if the GP took time to explain it to them or was a good listener. Patients were willing to discuss STIs if they were a new patient and irrespective of the GP’s gender and age. Fewer patients were willing to discuss STIs if they knew the GP socially. Patients who had sex with a new partner were willing to request a STI test from their GP. Patients were not embarrassed if discussion was initiated in a consultation unrelated to sexual health and did not mind discussing the topic in the presence of a partner or parent, though this depended on circumstances. Waiting room STI test advertising did not affect patient comfort level. Patients would involve their GP when seeking information about STIs. Patients have fewer barriers to discussing sexual health matters than perceived by GPs.

Team effort to provide more convenient care.
Fordham A.
Fremantle Hospital and Health Service, Western Australia.


Drivers for change: Western Australia Patient Blood Management Program (WA PBMP), World Health Assembly (WHA) and Advisory Committee on Blood Safety and Availability (ACBSA).

Farmer SL, Towler SC, et al. (Farmer, Towler, Leahy, Hofmann) Patient Blood Management Program Team, Office of the Chief Medical Officer, Western Australia Department of Health, Perth, WA, Australia (Farmer, Hofmann) School of Surgery, Faculty of Medicine Dentistry and Health Sciences, University of Western Australia, Perth, WA, Australia (Farmer, Towler, Hofmann) Centre for Population Health Research, Curtin Health Innovation Research Institute, Curtin University, Perth, WA, Australia (Towler) Intensive Care Unit, Royal Perth Hospital, Perth, WA, Australia (Towler) Edith Cowan University, Perth, WA, Australia (Leahy) Schools of Medicine and Pharmacology, Pathology and Laboratory Medicine, University of Western Australia, Perth, WA, Australia (Leahy) Haematology Department and Patient Blood Management Program, Fremantle Hospital, Fremantle, WA, Australia

S.L. Farmer, PO Box 232, Glen Forrest, WA 6071, Australia. E-mail: sfarm@ozemail.com.au

Patient blood management is now high on national and international health-system agendas. Serious supply challenges as a result of changing population dynamics, escalating cost of blood, ongoing safety challenges and questions about transfusion efficacy and outcomes are necessitating change in transfusion practice. Numerous initiatives are underway to bring about change, including the institution of comprehensive patient blood management programmes. In 2008, the Western Australia Department of Health initiated a 5-year project to implement a comprehensive health-system-wide Patient Blood Management Program with the aim of improving patient outcomes while reducing costs. Clinically, the Program was structured on the three pillars of patient blood management, namely (1) optimising the patient’s own red cell mass, (2) minimising blood loss and (3) harnessing and optimising the patient-specific anaemia reserve. It employs multiple strategies to bring about a cultural change from a blood-product focus to a patient focus. This Program was undertaken in a State that already had one of the lowest red blood cell issuance rates per 1000 population in the developed world (30.47 red blood cell units per 1000 population). The Program identified reasons and drivers for practice change. From financial years 2008-09 to 2011-12, issuance has progressively decreased in Western Australia to 27.54 units per 1000. During the same years, despite increasing activity, total issuance of red blood cells to the entire State decreased from 70,103 units to 65,742. Nationally and internationally, other initiatives are underway to bring about change and implement patient blood management. The World Health Assembly in May 2010 adopted resolution WHA63.12 endorsing patient blood management and its three-pillar application. The United States Advisory Committee on Blood Safety and Availability met in 2011 to consider the implications of this resolution and its implementation. 2012 Elsevier Ltd. All rights reserved.

Publication Types: Review
PMID:2013242264
The mechanistic, diagnostic and prognostic utility of biomarkers in severe malaria.
Manning L, Davis TM.
School of Medicine & Pharmacology, Fremantle Hospital & Health Service, The University of Western Australia, 35 Stirling Highway, Crawley, WA 6009, Australia.
Malaria remains an important global cause of severe illness and mortality. This literature review summarizes available data on how biomarkers might be applied to diagnose, prognosticate and provide mechanistic insights in patients with severe malaria. Of the large number of candidate biomarkers, only PfHRP2 has consistently demonstrated clinical utility and, when incorporated into rapid antigen detection tests, has shown diagnostic sensitivity above 95%, which is at least as good as light microscopy. As a quantitative test, PfHRP2 also shows some promise in differentiating severe malarial from non-malarial disease in areas where asymptomatic carriage of malaria parasites is common, and possibly as a tool to estimate sequestered parasite burden and subsequent mortality. Biomarkers such as pLDH and panmalarial antigen have lower sensitivity for non-falciparum malaria in rapid antigen detection tests. There is an urgent need to discover and validate better biomarkers for incorporation into rapid antigen detection tests in countries where Plasmodium vivax is a common cause of severe disease. A large number of host-derived acute-phase reactants, markers of endothelial dysfunction and immune mediators have been proposed as biomarkers. Although they have provided mechanistic insights into the immunopathology of severe malaria, their roles as clinical tools remain uncertain.
PMID:23734797

A comparison of patient and tumour characteristics in two UK bladder cancer cohorts separated by 20 years.
Bryan RT, Zeegers MP, et al.
(Bryan, James) School of Cancer Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom (Zeegers, Van Roekel, Cheng) Department of Public Health, Epidemiology and Biostatistics, School of Population Sciences, University of Birmingham, Birmingham, United Kingdom (Zeegers) Department of Genetics and Cell Biology, Maastricht University Medical Centre, Maastricht, Netherlands (Bird, Collins, Howman) Cancer Research UK Clinical Trials Unit, School of Cancer Sciences, Birmingham, United Kingdom (Grant) Birmingham Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom (Dunn, Iqbal) Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, Coventry, United Kingdom (Bathers, Khan) Primary Care Clinical Sciences, University of Birmingham, Birmingham, United Kingdom (Deshmukh, James) Department of Histopathology, University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital, Birmingham, United Kingdom (Wallace) Surgery (Fremantle Hospital), University of Western Australia (M509), Crawley WA, Australia
R.T. Bryan, School of Cancer Sciences, University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom. E-mail: r.t.bryan@bham.ac.uk
Objectives To compare patient and tumour characteristics at presentation from two large bladder cancer cohorts, with recruitment separated by 15-20 years To identify significant differences in the West Midlands’ urothelial cancer of the bladder (UCB) population during this period. Patients and Methods Data were collected prospectively from 1478 patients newly diagnosed with UCB in the West Midlands from January 1991 to June 1992 (Cohort 1), and from 1168 patients newly diagnosed with UBC within the same region from December 2005 to April 2011 (Cohort 2). Gender, age, smoking history, and tumour grade, stage, type, multiplicity and size at presentation were compared using a Pearson chi-square test or Cochran-Armitage trend test, as appropriate. Result Cohort 2 had a higher proportion of male patients (P = 0.021), elderly patients (P < 0.001), grade 3 tumours (P < 0.001), Ta/T1 tumours (P = 0.008), multiple tumours (P < 0.001), and tumours of <=2 cm in diameter (P < 0.001). Conclusions There were significant differences between the cohorts. These differences are potentially explained by an ageing population, changes in grading practices, improved awareness of
important symptoms, improved cystoscopic technology, and reductions in treatment delays. Regional cohorts remain important for identifying changes in tumour and patient characteristics that may influence disease management in the UK and beyond. 2013 BJU International.

PMID:2013414668


Retrograde ureteric stent insertion in the management of infected obstructed kidneys.
(Flukes, Mcmillan, Hayne, Kuan, Rukin) Department of Urological Surgery, Fremantle Hospital, Fremantle, Australia (Hayne) School of Surgery, University of Western Australia, Fremantle, Australia (Rukin) Department of Urological Surgery, New Cross Hospital, Wolverhampton, United Kingdom
S. Flukes, Department of Urological Surgery, Fremantle Hospital, Fremantle, Australia

Introduction and Objectives: A n infected, obstructed kidney is a urological emergency. Acute management is prompt decompression of the collecting system. Classical teaching suggests that retrograde instrumentation of the infected system is more hazardous than percutaneous nephrostomy, but clinical evidence does not support this view. We present our experience with retrograde ureteric stent insertion as our primary treatment modality. Methods : We performed a prospective analysis of all infected obstructed cases presenting to Fremantle Hospital over a ten-month period from February 2012 to November 2012. Inclusion criteria include clinical evidence of infection (based on systemic inflammatory response syndrome criteria) or positive microbiological cultures as well as radiological evidence of obstructing calculi. Results : Twenty nine patients with an infected obstructed kidney secondary to calculi were included in the analysis. Patients’ mean age was 57 years old (19-88 years) and 14 of 29 were male. The majority of patients were Caucasian, n = 24 (83%). Positive microbiological cultures were found in 22 patients (75%). Seven patients (24%) required an ICU admission, for inotropic support (100%), ventilatory support (60%) and renal replacement therapy (40%). Four of these patients (57%) went to ICU pre-intervention for both inotropic and ventilatory support. Ninety-seven percent of patients had a successful retrograde stent insertion, with one patient requiring a nephrostomy secondary to failed stent placement. Median length of stay was 5 days (1-21 days). The most common infective organism was Escherichia coli, n = 11 (38%). Conclusions: Our series shows favorable results using a retrograde approach, with 97% successful stent placement. Early pre- and post-operative urine and blood cultures are recommended to aid positive microbiological cultures and guide antibiotic therapy. Retrograde stent insertion is a suitable first line treatment option for the infected obstructed kidney.

Publication Types: Conference Abstract
PMID:71037590


Open partial nephrectomy: An ideal modular based training operation?
(Kugathasan, Lok, Lewis, Hayne, John Rukin, Wallace) Department of Urological Surgery, Fremantle Hospital, Wolverhampton, United Kingdom (Hayne) School of Surgery, University of Western Australia, Wolverhampton, United Kingdom (John Rukin) Department of Urological Surgery, New Cross Hospital, Wolverhampton, United Kingdom
G. Kugathasan, Department of Urological Surgery, Fremantle Hospital, Wolverhampton, United Kingdom

Introduction + Objectives : W ith the advent of laparoscopic surgery, trainee ‘ s experience of open renal surgery is becoming limited. Renal access and mobilisation, as well as hilum control are becoming diminishing skills. Our trainees are taught open partial nephrectomy in a modular structure including incision, vessel and ureteric localisation, kidney mobilisation, tumour excision and kidney reconstruction. We performed a retrospective review of our trainee performed procedures to determine if this is an appropriate training operation. Methods : W e report a retrospective review of cases
performed over a 3-year period, 2010 to 2012. Our trainees performed components of the operation as modular steps assisted by a senior, experienced consultant. We collected data on indications, operative time, cold ischaemic time, renal function, resection margin status, tumour reoccurrence and complications. Results: 39 patients, with a median age of 56 years and 2.5:1 male to female ratio, underwent an open partial nephrectomy. Five patients had an absolute indication, 3 relative and 31 elective indications for nephron sparing surgery. Median operative time was 153 minutes (Range 85-243 mins). The mean tumour size was 28 mm (10-47 mm), with a median cold ischaemic time of 31 mins (12-43 mins). Histology revealed 31 renal cell carcinomas and 8 benign tumours (20%). There were no positive tumour margins and our mean tumour margin clearance was 2.3 mm (0.1-7 mm). There was no radiological evidence of reoccurrence at median follow up of 11 months. Mean increase in postoperatively creatinine at last clinical review was 8 umol/L. Median length of stay was 4 days (Range 3-14 days). One patient had a significant postoperative bleed (2.5%), requiring super-selective arterial vessel embolisation. There was no urinary leak. Conclusion: We advocate that open partial nephrectomy is an excellent training operation, particularly with respect to the principles of open renal surgery. Our data supports the notion that trainee’s can be taught this operation by adopting a supervised, modular based approach with excellent outcomes as compared to the contemporary literature.

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Logan C, Hawks C, et al.
(Logan, Hawks, Hayne) Fremantle Hospital, Urology Department, Fremantle, WA, Australia (Logan, Hayne) University of Western Australia, School of Surgery, WA, Australia (Cohen) Uropath Pty Ltd, Perth, WA, Australia (Hawks, Cohen, Hayne) Western Australian Urologic Research Organisation, Perth, WA, Australia (Cohen) University of Western Australia, School of Pathology, Laboratory Medicine, WA, Australia

C. Logan, Fremantle Hospital, Urology Department, Fremantle, WA, Australia
Introduction and Objectives: We have previously presented data from Uropath Pty Ltd (UP), a specialist uropathology service, that showed rural men had higher rates of cancer diagnosis, higher grade tumours and underwent fewer radical prostatectomies. (Ooi et al.) We aimed to identify if these findings were replicated with those of our public tertiary hospital pathology department. Methods: * Between 2000 and 2011, 948 cases of prostate cancer were diagnosed at Fremantle PathWest (FP), Fremantle Hospital, Western Australia. * We determined the tumour stage (pT) and Gleason score (GS) for the first 500 cases of which the total number of prostate biopsies with histopathology reports was 286 * Remoteness area (RA) was determined by postcode on pathology reports and classified according to the Australian Bureau of Statistics classification: (RA 1-2 urban, RA 3-5 rural) * Cases by RA were; RA 1-2 (n = 261), RA 3-5 (n = 25) * Comparison of urban-rural difference of prostate cancer was made including RA classification and Gleason score (GS) * Comparison was made between FP and UP data based on RA and GS and compared using a chi-square test Results: * No difference in GS based on RA for FP was identified (p > 0.05) * The difference in proportions for GS were similar for both urban and rural cohorts in both groups: FP - GS 6, 40% (RA1-2) and 56% (RA3-5) respectively, compared to UP - 30% (RA1-2) and 27% (RA3-5) respectively. A chi-square test was performed (p < 0.001) * There were very large differences in proportions of GS 6 vs. 7 vs. 8-10 between UP and FP Conclusions: No differences in GS based on RA for the FP group were identified though this study was underpowered. Proportions of each GS were strikingly different between the two laboratories. This may represent a difference in assignment of Gleason score by the reporting pathologists as opposed to a true difference in Gleason score. This is of concern and may result in inappropriate treatment decisions. (Table Presented).

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Has there been stage progression in bladder cancer in Western Australia? A report on the WA Cancer Registry Data from 1982-2011.
Logan C, Hawks C, et al.
(Logan, Marr, Wallace, Hayne) University of Western Australia, School of Surgery, Perth, Australia
(Logan, Hawks, Wallace, Hayne) Fremantle Hospital, Urology Department, Fremantle, Australia
(Hawks, Hayne) Western Australian Urologic Research Organisation, Perth, Australia
C. Logan, University of Western Australia, School of Surgery, Perth, Australia
Introduction and Objectives: Bladder cancer (BC) is the only major cancer with deteriorating outcomes in Australia. Australian BC 5 year survival has worsened for both males (69% to 62%) and females (65% to 55%) between 1982-1986 and 2000-2004. Possible explanations have included age at diagnosis, coding changes and stage progression. We examined the Western Australian Cancer Registry (WACR) data and re-coded individual histopathology reports to determine whether coding errors and/or stage progression have contributed to this worsening survival. State based cancer registries record T1-T4 disease as invasive BC. CIS and Ta disease are recorded but not published in cancer statistics. Methods: * A random sample of 300 patients was selected from the WACR data between 1982 and 2011. * Three time periods were selected that spanned the AIHW Report that included the BC survival data; 1982-1986, 2000-2004 and 2007-2011. * 100 cases from each time period, including 50 classified as invasive and 50 classified as in situ cancers, were randomly selected. * WACR data was extracted including the linked histopathology reports. * A clinical nurse with training in the pathologic staging of BC, recoded each case based on the histopathology report. * For the periods 1982-86, 2000-04, 2007-11 degree No invasive cancers were miscoded as in-situ cancers degree 53% (95CI 39.4-66.3%) vs 25% (95CI 14.9-38.8%) vs 10% (95CI 4.4-21.8%) in-situ cancers were incorrectly coded as invasive (Ta/T1) (p < 0.001) degree 27% (95CI 16.2-40.2%) vs 33% (95CI 21.7-47.5%) vs 45% (95CI 31.9-58.7%) stage T2 or higher were identified (p < 0.05) Conclusion: CIS &Ta disease were frequently miscoded as invasive disease. Th is occurred most notably during the periods 1982-1986 and less so subsequently. If similar coding errors have occurred nationally this would contribute to the worsening survival as reported by AIHW. An increasing proportion of T2 or greater disease is demonstrated between the periods 1982-1986 and 2007-2011. These data suggest that both coding errors and higher stage disease have contributed to the worsening survival seen in BC. Eff orts to improve BC outcomes are urgently required. Increased awareness of BC symptoms (haematuria) and better access to diagnostic services may reduce presentation at late stage. (Figure Presented).
Publication Types: Conference Abstract
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Health economic analysis of the one stop haematuria clinic at Fremantle Hospital.
Logan C, Li I, et al.
(Logan, Hayne) University of Western Australia, School of Surgery, WA, Australia (Logan, Hawks, Lee, Hayne) Fremantle Hospital, Urology Department Fremantle, WA, Australia (Hawks, Hayne) Western Australian Urologic Research Organisation, Perth, WA, Australia (Li, Johnson) University of Western Australia, School of Population Health, Perth, WA, Australia
C. Logan, University of Western Australia, School of Surgery, WA, Australia
Introduction and Objectives: We have previously reported on the clinical outcomes of the first 500 patients (May 2008-February 2011) from the One Stop Haematuria Clinic (OSHC) at Fremantle Hospital. Th is is a rapid access/diagnostic clinic for investigation of haematuria. Th is is a report of a preliminary economic analysis that has been conducted comparing the OSHC and conventional public hospital outpatient clinic (OPC) model of care. Methods: Description of OSHC and OPC Models of Care at Fremantle Hospital. Direct personnel salary savings (1,000) patients to date seen by the OSHC = $73, 000 The above savings of $73 per patient reflect only direct personnel costs (UC/NP/RN). It does not reflect additional $ savings such as: * Infrastructure and staffing costs
involved in two additional outpatient appointments with the OPC model * Additional Patient Assisted Transport Scheme (PATS) costs for rural patients with the OPC model due to additional outpatient appointments Other savings that are difficult to quantify using the OSHC model include: * Continuity of patient care (same UC at initial consult and cystoscopy) * Time savings to patients with reduced number of appointments * Decreased time to diagnosis and subsequent treatment Complete data analysis will be included in the final presentation. Conclusions : A s reported previously, the OSHC model of care is an efficient and effective method in the prompt assessment of haematuria, the rapid diagnosis of urologic pathology and subsequent streamlining of further treatment in a public tertiary hospital setting. The economic analysis has also demonstrated that there are substantial cost savings by using the OSHC in comparison to the standard OPC model of care.

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**Web-based learning: The future in undergraduate surgical teaching.**

Logan C, Lok AH, et al. (Logan, Brown, Hayne) University of Western Australia, School of Surgery, WA, Australia (Logan, Lok, Hayne) Fremantle Hospital, Urology Department Fremantle, WA, Australia (Ooi) Sir Charles Gairdner Hospital, Nedlands, WA, Australia (Leece, Davine, Jonas-Dwyer) University of Western Australia, Faculty of Medicine, Dentistry and Health Sciences Education Centre, WA, Australia (Hayne) Western Australian Urologic Research Organisation, Perth, WA, Australia

**C. Logan, University of Western Australia, School of Surgery, WA, Australia**

**Introduction and Objectives: W** *e have developed, assessed and introduced eight interactive web-based learning modules for fourth year medical students at the University of Western Australia (UWA) delivering core topics in urological and general surgery. Each module is presented in an engaging and interactive fashion utilising web-based software. The interactive format of the modules maximises the learning gain for students emphasising the core knowledge and skills of surgical curricula. The ultimate aim of the project was to better prepare medical students for surgical attachments and for their future career in medicine where they will commonly encounter urological and general surgical problems. Methods : * Fourth year medical students were approached to take part in a study to test their level of surgical knowledge and the effectiveness of the web-based learning modules. * Qualitative feedback on the content, design and construction of the modules was sought from urologists, general surgeons, other surgical consultants, junior medical staff, nursing staff and medical students. * 4 Urological surgery (US) and 4 General surgery (GS) modules were developed * A pilot study of the 4 US modules was performed * An electronically marked MCQ quiz testing key messages before and after the modules and a feedback score after completion were collected * Ethical approval from the University of Western Australia (UWA) Human Research Ethics Committee was obtained * The MCQ type pre-test was completed online and subsequently access to the learning modules was permitted. A further post-test was then requested at the end of the learning module and pre and post-test scores were recorded Results : L earning modules were assessed independently. * US cohort, 62 out of 218 UWA 4th year medical students completed the pre-test. Mean pre-test score (n = 62) was 22/40 (55%) with post-test scores (n = 10) improving to 32/40 (82%). * GS cohort, 94 out of a possible 220 UWA 4th year medical students completed the pre-test. Mean pre-test score (n = 94) was 21/28 (75%) and post-test score (n = 51) improving to 26/28 (93%). C onclusions : C ompletion of the learning modules improved the test mean score. Improvements in post-test score were 18% (GS) and 27% (US) respectively. Mean US module pre-test scores suggest the modules are pitched at an appropriate level. The GS modules may be targeted below the appropriate level given the high pre-test scores. Due to the variability in student schedules and clinical demands, providing surgical learning modules online, supports and enhances student flexibility in learning core surgical knowledge. Results from this study are encouraging and suggest that online learning modules are a useful tool and can be modified to enhance the learning experience for the students during their surgical terms. The learning modules have now been incorporated into the UWA surgical curriculum.
Is laparoscopic pyeloplasty a suitable procedure for urological trainees?


Introduction and Objectives: Laparoscopic pyeloplasty is considered the gold standard treatment for ureteropelvic junction [UPJ] obstruction, with success rates around 85-98%. In the public system our urological trainees, under the supervision of a consultant, have primarily performed this technically challenging procedure. We report our outcomes [trainee series] and further compare the functional [renographic] results with a personal series from the supervising consultant performed in the private sector [consultant series].

Methods: This retrospective audit was performed over a 4-year period, 2007-2011. Data was collected from electronic records and patient notes. The primary outcome measure was improvement on MAG3 renography post operatively. Secondary outcomes included operative time, length of stay, improvement in post operative split function, post procedure complications and re-do procedures.

Results: The trainee series consisted of 36 cases. Mean patient age was 45 years [19-78 years old], with the majority female [31 patients, 65%]. Median theatre time was 2 hours and 58 mins, with a median length of stay of 4 days [3-15 days]. Average split function improvement was less than 5%. Post-op complications include urine leaks [5%] and UTI [8%]. Post-operative resolution of obstruction on MAG3 was seen in 25 [70%] cases. Of those who failed 64% had a second procedure with the rest managed conservatively. Ten out of 12 [85%] in the consultant series showed resolution of obstruction on MAG3 and 1 [8%] required a re-do pyeloplasty.

Conclusion: Our trainee-supervised series shows inferior outcomes to those in the reported literature. Less renographic resolution of obstruction was seen than in the consultant series. Trainees should be at an advanced stage in all aspects of laparoscopic surgery, including laparoscopic suturing, before performing this procedure.

Management of penile cancer in Western Australia: Descriptive epidemiology, patterns of care and survival over the last 15 years.


Introduction and Objectives: Primary malignant penile cancer is uncommon, with an incidence of <1:100,000 in developed countries. Western Australian Urologists combined treat approximately 10 cases per annum, however the exact number has not been published. This retrospective study provides the first state-based descriptive data set for penile cancer in Australia and describes the epidemiology, stage distribution, patterns of care and mortality of patients with penile cancer in WA prior to 2011. Methods: The Western Australian Cancer Registry (WACR) was utilized to identify all patients diagnosed with penile cancer (ICD-10 code C60) between 1st January 1992 and 31st December 2007. Histopathology reports were examined on-site at the WACR and each patient staged using the 2009 TNM classification of penile cancer. Linked data on patient demographics, hospital admission and mortality were included and corroborated by hospital chart review. Epidemiology and
pathological stage distribution were determined and overall survival and 5-year cancer specific survival calculated by stage for all cases. Results: There were 147 men between the age of 21 and 95 diagnosed with penile cancer in WA. The median age at diagnosis was 63. The number of cases per year ranged from 4 to 14, with an overall incidence of 0.9 cases per 100,000 men. 42 men (29%) were rural patients. The rural incidence was 1.6 cases per 100,000 men. The overall stage distribution was: pTis (36%), pTa (2%), pT1a (32%), pT1b (8%), pT2 (16%), pT3 (5%), pT4 (1%). Sixteen men had lymph node metastases; N1 (2), N2 (6), N3 (8). Twenty-six hospitals and 57 surgeons performed 163 curative-intent procedures. The caseload was divided 63% in the public and 37% in the private sector. For T1a disease organ-preserving surgical technique was only used in 67% of cases. 28% of cases received a partial amputation and 5% a total amputation. All T2 and T3 disease were treated by partial or total amputation. The 5-year cancer specific survival (CSS) for all invasive cancer cases was 81%. For rural patients however this was only 67%. By stage, 5-year CSS was: Ta 100%, T1a 97%, T1b 100%, T2 53%, T3 40%, T4 0%. For patients with nodal metastases, 5-year CSS was only 38%. Conclusions and Discussion: Penile cancer incidence in WA is comparable to Europe and the Americas. Too many surgeons and hospitals are treating the small number of cases. Though survival for T1 disease is excellent there is evidence of significant overtreatment, with only 67% of patients receiving organ-preserving surgery. There is a marked over-representation of rural patients and a poorer 5-year CSS is demonstrated in this group. A centralised penile cancer service has now been adopted in WA.

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A randomised controlled trial comparing use of lignocaine periprostatic nerve block alone and in combination with diclofenac suppository for patients undergoing transrectal ultrasound (TRUS) guided biopsy of prostate.

Ooi WL, Hawks C, et al.
(Ooi, Hayne) School of Surgery, University of Western, Australia (Hawks, Hayne) Department of Urology, Fremantle Hospital, WA, Australia (Hawks, Hayne) West Australian Urologic Research Organisation, Australia

W.L. Ooi, School of Surgery, University of Western, Australia

Introduction and Objectives: Transrectal ultrasound (TRUS)-guided prostate biopsy is the gold standard for diagnosing prostate cancer and can be safely performed under local anaesthetic (LA). Though generally well tolerated patients may still report pain during LA prostate biopsy. Our study compared combination diclofenac suppository and lignocaine peri-prostatic nerve block (PPNB) vs lignocaine PPNB alone for TRUS-guided prostate biopsy. Pain experienced during and after the biopsy and the safety of both regimes were assessed in this placebo controlled single-blind randomised controlled trial. Patients and Methods: * Ninety six patients under-going TRUS-biopsy were randomised into 1) lignocaine periprostactic nerve block and placebo suppository or 2) lignocaine periprosthetic nerve block and 100 mg diclofenac suppository. * Pain scores were recorded using the Numerical Rating Scale for pain (0-10) at the following periods: 1. Introduction of probe 2. During biopsy 3. 1 hour post-biopsy 4. Later that evening 5. 1 day after biopsy * Patients were asked if a repeat TRUS-guided prostate biopsy was required, would they choose for it to be performed under local or general anaesthesia/sedation. Conclusion: * A small difference in pain scores was demonstrated one hour post biopsy in the combination group though this is of doubtful clinical significance. * Using additional diclofenac suppository with PPNB is not recommended to decrease pain or improve tolerability of TRUS-guided prostate biopsy. * PPNB TRUS biopsy is extremely well tolerated. Over 80% of patients would elect for subsequent LA biopsy if required. (Table Presented).

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Impact of the introduction of drug eluting stents on clinical outcomes in patients undergoing percutaneous and surgical coronary artery revascularisation procedures in Western Australia. Sanfilippo FM, Rankin JM, et al.

Background: Increasing rates of percutaneous coronary intervention (PCI) and decreasing rates of coronary artery bypass graft (CABG) surgery followed the introduction of drug eluting stents in Western Australia in 2002. We assessed the impact of these changes on one-year outcomes for the total population of patients undergoing coronary artery revascularisation procedures (CARP) in Western Australia between 2000-2004.

Methods: Clinical and linked administrative data (inpatient admissions and death) were merged for all patients who had their first CARP with stent or CABG in Western Australia between 2000-2004. The clinical data were collected from all hospitals in Western Australia where CARP procedures are performed. We calculated the unadjusted (Kaplan-Meier) and adjusted (Cox) risks for one-year death (all-cause), death (all-cause) or admission for myocardial infarction (MI), target vessel revascularisation (TVR) and the composite outcome of death/MI/TVR (major adverse cardiac events, MACE).

Results: Over the study period, there were 14,118 index CARPs. The use of drug eluting stents increased from 0% to 95.8% of PCI procedures, and PCI procedures increased from 61.1% to 74.4% of all CARPs. There were no temporal changes in adjusted one-year mortality or death/MI. Overall, adjusted one-year MACE fell from 11.3% in 2000 to 8.5% in 2004 (p<0.0001) due to a significant reduction in TVR in the PCI group.

Conclusion: The introduction of drug eluting stents and resulting changes in coronary revascularisation strategies were not associated with changes in the one-year risk of major clinical endpoints (death or death/MI), but were associated with a significant reduction in the risk of MACE, driven entirely by a reduction in TVR after PCI. This real world study supports the effectiveness of drug eluting stents in reducing repeat procedures in the total CARP population without increasing the risk of death or MI.


Background: The use of drug eluting stents increased from 0% to 95.8% of PCI procedures, and PCI procedures increased from 61.1% to 74.4% of all CARPs. There were no temporal changes in adjusted one-year mortality or death/MI. Overall, adjusted one-year MACE fell from 11.3% in 2000 to 8.5% in 2004 (p<0.0001) due to a significant reduction in TVR in the PCI group.
Background: As demand for Emergency Department (ED) services continues to exceed increases explained by population growth, strategies to reduce ED presentations are being explored. The concept of ambulance paramedics providing an alternative model of care to the current default 'see and transport to ED' has intuitive appeal and has been implemented in several locations around the world. The premise is that for certain non-critically ill patients, the Extended Care Paramedic (ECP) can either 'see and treat' or 'see and refer' to another primary or community care practitioner, rather than transport to hospital. However, there has been little rigorous investigation of which types of patients can be safely identified and managed in the community, or the impact of ECPs on ED attendance.

Methods/Design: St John Ambulance Western Australia paramedics will indicate on the electronic patient care record (e-PCR) of patients attended in the Perth metropolitan area if they consider them to be suitable to be managed in the community. 'Follow-up' will examine these patients using ED data to determine the patient's disposition from the ED. A clinical panel will then develop a protocol to identify those patients who can be safely managed in the community. Paramedics will then assess patients against the derived ECP protocols and identify those deemed suitable to 'see and treat' or 'see and refer'. The ED disposition (and other clinical outcomes) of these 'ECP protocol identified' patients will enable us to assess whether it would have been appropriate to manage these patients in the community. A systems modelling approach will be used to assess the likely impact on ED crowding.

Discussion: To date the efficacy, cost-effectiveness and safety of alternative community-based models of emergency care have not been rigorously investigated. This study will inform the development of ECP protocols through the identification of types of patient presentation that can be considered both safe and appropriate for paramedics to manage in the community.

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Does self reflection and insight correlate with academic performance in medical students?
Carr SE, Johnson PH.
School of Medicine and Pharmacology Fremantle Hospital Unit, Faculty of Medicine Dentistry and Health Science, University of Western Australia, PO Box 480, Fremantle WA 6959, Australia. paula.johnson@uwa.edu.au.

BACKGROUND: Medical students in academic difficulty are often described as lacking insight. The Self Reflection and Insight Scale (SRIS) is a tool for measuring insight which has been validated in medical students. We investigated whether self reflection and insight scores correlate with academic performance in Year 4 medical students from a six year undergraduate medical degree, and whether self reflection and insight changes after one year of clinical training.

METHODS: Self reflection and insight scores were measured in 162 students at the start of Year 4 at the University of Western Australia. Performance in end of year written and clinical exams was monitored and correlated with SRIS. Seventy of the students were surveyed again at the start of Year 5 to see if scores changed or were stable after one year of full time clinical training.

RESULTS: We found no correlation between self reflection or insight and academic performance in written and clinical exams. There was a significant increase in recognition of the need for self
reflection in Year 5 compared with Year 4.
CONCLUSIONS: While no correlation was found between this measure of self reflection and insight with academic performance, there was an increase in students’ recognition of the need for reflection after one year of clinical studies. This study is a valuable first step towards a potentially exciting research domain and warrants further longitudinal evaluation with larger cohorts of students using additional measures of achievement.
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A comprehensive investigation of variants in genes encoding adiponectin (ADIPOQ) and its receptors (ADIPOR1/R2), and their association with serum adiponectin, type 2 diabetes, insulin resistance and the metabolic syndrome.
School of Medicine and Pharmacology, Fremantle Hospital Unit, The University of Western Australia, Nedlands, Western Australia, Australia.
BACKGROUND: Low levels of serum adiponectin have been linked to central obesity, insulin resistance, metabolic syndrome, and type 2 diabetes. Variants in ADIPOQ, the gene encoding adiponectin, have been shown to influence serum adiponectin concentration, and along with variants in the adiponectin receptors (ADIPOR1 and ADIPOR2) have been implicated in metabolic syndrome and type 2 diabetes. This study aimed to comprehensively investigate the association of common variants in ADIPOQ, ADIPOR1 and ADIPOR2 with serum adiponectin and insulin resistance syndromes in a large cohort of European-Australian individuals.
METHODS: Sixty-four tagging single nucleotide polymorphisms in ADIPOQ, ADIPOR1 and ADIPOR2 were genotyped in two general population cohorts consisting of 2,355 subjects, and one cohort of 967 subjects with type 2 diabetes. The association of tagSNPs with outcomes were evaluated using linear or logistic modelling. Meta-analysis of the three cohorts was performed by random-effects modelling.
RESULTS: Meta-analysis revealed nine genotyped tagSNPs in ADIPOQ significantly associated with serum adiponectin across all cohorts after adjustment for age, gender and BMI, including rs10937273, rs12637534, rs1648707, rs16861209, rs822395, rs17366568, rs3774261, rs6444175 and rs17373414. The results of haplotype-based analyses were also consistent. Overall, the variants in the ADIPOQ gene explained <5% of the variance in serum adiponectin concentration. None of the ADIPOR1/R2 tagSNPs were associated with serum adiponectin. There was no association between any of the genetic variants and insulin resistance or metabolic syndrome. A multi-SNP genotypic risk score for ADIPOQ alleles revealed an association with 3 independent SNPs, rs12637534, rs16861209, rs17366568 and type 2 diabetes after adjusting for adiponectin levels (OR=0.86, 95% CI=(0.75, 0.99), P=0.0134).
CONCLUSIONS: Genetic variation in ADIPOQ, but not its receptors, was associated with altered serum adiponectin. However, genetic variation in ADIPOQ and its receptors does not appear to contribute to the risk of insulin resistance or metabolic syndrome but did for type 2 diabetes in a European-Australian population.
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A diagnostic dilemma of central skull base osteomyelitis mimicking neoplasia in a diabetic patient.
Ganhewa AD, Kuthubutheen J.
(Ganhewa) Royal Perth Hospital, Perth, Australia (Kuthubutheen) Department of ENT, Fremantle Hospital, Perth, WA, Australia
A.D. Ganhewa, Royal Perth Hospital, Perth, Australia. E-mail: dasun_ganhewa@hotmail.com
We present a case which illustrates the diagnostic difficulty in distinguishing between osteomyelitis of
the central skull base and base of skull tumours. A woman in her early forties presented with seizures and multiple cranial nerve palsies. She also had a background of chronic otalgia and poorly controlled diabetes mellitus. The clinical diagnosis of skull base osteomyelitis (SBO) was made, but both MRI and bone scans were unable to distinguish this from a skull base malignancy on imaging criteria. Eventually biopsies were required to exclude the diagnosis of malignancy and the patient was treated for central SBO. Copyright 2013 BMJ Publishing Group. All rights reserved.

Presacral tumours: a rare case of a dermoid cyst in a paediatric patient.

Jones M, Khosa J.
Department of General Surgery, Fremantle Hospital, Perth, Western Australia, Australia.

Presacral tumours are considered very rare tumours with their incidence being around 1:40 000. Presacral dermoid tumours, part of the family of presacral tumours, usually present in the female adult population. They are benign tumours arising from all the three germ cell layers. Presentation in a paediatric population, defined as an individual under the age of 18 years, is extremely rare. A 15-year-old girl presented with abdominal pain present for 5 years diagnosed as a somatisation disorder. Upon further investigation with abdominal CT and MRI a diagnosis of a presacral mass was made. A laparoscopic-assisted transabdominal excision of the mass was performed and histopathology confirmed the radiological suspicion of a presacral dermoid cyst. As there are no reports of a presacral dermoid cysts being excised and reported in the paediatric surgical literature, we hope to highlight this pathology as a potential cause of abdominal pain in the paediatric population.

Non-lethal? Penetrating chest injury due to beanbag bullet.

Thakur S, Teloken PE, et al.
Department of Cardiothoracic Surgery, Fremantle Hospital, Fremantle, Western Australia, Australia.
docsanjaythakur@hotmail.com

We report a case of serious lung injury from beanbag bullet. A 46-year-old gentleman, shot with beanbag bullets was brought to the emergency department. Upon arrival he was in obvious respiratory distress and complained of severe pain in the right chest. A 3.0x3.5 cm entry wound on the right parasternal area was identified. Chest x-ray revealed a right haemopneumothorax, parenchymal changes at the right lung base and a radiopaque foreign body. A right-sided intercostal chest tube was inserted, draining air and 750 ml of blood. After stabilisation patient underwent a right thoracotomy. A beanbag bullet was found in the oblique fissure of the right lung, with extensive haematoma of the middle lobe. The bullet and skin fragments overlying the lung and along the bullet track were extracted. The pleural cavity was washed with normal saline and haemostasis was confirmed. The patient had an uneventful postoperative recovery.

Cross vascular risk for first and recurrent hospitalised atherothrombosis determined retrospectively from linked data.

Briffa TG, Nedkoff LJ, et al.
(Briffa, Nedkoff, Knuiman, Hickling, Bremner, Sanfilippo) School of Population Health, University of Western Australia, Crawley, WA, Australia (Hankey) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia (Hankey) Department of Neurology, Sir Charles Gairdner Hospital, Perth, WA, Australia (Norman) School of Surgery, University of Western Australia,
Fremantle, WA, Australia (Hung) Sir Charles Gairdner Hospital Unit, School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia (Thompson) Department of Cardiovascular Medicine, Sir Charles Gairdner Hospital Unit, Perth, WA, Australia
T.G. Briffa, School of Population Health, University of Western Australia, Crawley, WA, Australia. E-mail: tom.briffa@uwa.edu.au

Objectives: To determine the sex-specific and age-specific risk ratios for the first-ever and recurrent hospitalisation for cerebrovascular, coronary and peripheral arterial disease in persons with other vascular history versus without other vascular history in Western Australia from 2005 to 2007. Design: Cross-sectional linkage study. Setting: Hospitalised population in a representative Australian State. Participants: All persons aged 34-85 years between 1 January 2005 and 31 December 2007 were hospitalised with a principal diagnosis of atherothrombosis. Data sources: Person-linked file of statutory-collected administrative morbidity and mortality records. Main outcome measures: Sex-specific and age-specific risk ratios for the first-ever and recurrent hospitalisations for symptomatic atherothrombosis of the brain, coronary and periphery using a 15-year look-back period lead to the determining of prior events. Results: Over 3 years, 40 877 (66% men; 55% firstever) were hospitalised for atherothrombosis. For each arterial territory, age-specific recurrent rates were higher than the corresponding first-ever rates, with the biggest difference seen in the youngest age groups. For all types of first-ever atherothrombosis, the rates were higher in those with other vascular history and the risk ratios declined with an advancing age (trend: all p<0.0001) and remained significantly >1 even for 75-84 years old. However, for recurrent events, the rates were marginally higher in those with other vascular history and no risk ratio age trend was apparent with several not significantly >1 (trend: all p>0.13). Conclusions: This study of hospitalised atherothrombosis suggests first-events predominate and that the risk of further events in the same or other arterial territory is very high for all ages and both sexes, accentuating the necessity for an early and sustained active prevention.

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The 2012 ABC orthopaedic fellowship in North America: May 24 to July 2.
University of Western Australia, Department of orthopaedics and trauma, Fremantle Hospital, Alma street, Western Australia 6160, Australia.
In May 2012, in airports across the globe, seven orthopaedic surgeons bravely said goodbye to their loved ones, and slowly turned towards their respective aircraft. Filled with expectation and mild trepidation they stepped into the unknown... the ABC fellowship of 2012.
PMID: 23632687

The surgical anatomy of the piriformis tendon, with particular reference to total hip replacement: A cadaver study.
Roche JJW, Jones CDS, et al.
(Roche) Forth Valley Royal Hospital, Stirling Road, Larbet FK5 4WR, United Kingdom (Jones) Lecturer University of Adelaide, School of Medical Sciences, Adelaide, SA 5005, Australia (Khan) University of Western Australia, 35 Stirling Highway, Crawley, WA 6009, Australia (Roche, Jones, Khan, Yates) Fremantle Hospital, Alma Street, Fremantle, WA 6160, Australia
J.J.W. Roche, Fremantle Hospital, Alma Street, Fremantle, WA 6160, Australia. E-mail: j.roche@doctors.org.uk
The piriformis muscle is an important landmark in the surgical anatomy of the hip, particularly the posterior approach for total hip replacement (THR). Standard orthopaedic teaching dictates that the tendon must be cut in to allow adequate access to the superior part of the acetabulum and the femoral medullary canal. However, in our experience a routine THR can be performed through a posterior approach without sacrificing this tendon. We dissected the proximal femora of 15 cadavers in order to
clarify the morphological anatomy of the piriformis tendon. We confirmed that the tendon attaches on the crest of the greater trochanter, in a position superior to the trochanteric fossa, away from the entry point for broaching the intramedullary canal during THR. The tendon attachment site encompassed the summit and medial aspect of the greater trochanter as well as a variable attachment to the fibrous capsule of the hip joint. In addition we dissected seven cadavers resecting all posterior attachments except the piriformis muscle and tendon in order to study their relations to the hip joint, as the joint was flexed. At flexion of 90\textdegree the piriformis muscle lay directly posterior to the hip joint. The piriform fossa is a term used by orthopaedic surgeons to refer to the trochanteric fossa and normally has no relation to the attachment site of the piriformis tendon. In hip flexion the piriformis lies directly behind the hip joint and might reasonably be considered to contribute to the stability of the joint. We conclude that the anatomy of the piriformis muscle is often inaccurately described in the current surgical literature and terms are used and interchanged inappropriately. 2013 The British Editorial Society of Bone & Joint Surgery.

PMID:2013416345


A double-blinded randomized evaluation of alfentanil and morphine vs fentanyl: Analgesia and sleep trial (DREAMFAST).

Lee A, O’Loughlin E, et al.

BackgroundPatients using fentanyl patient-controlled analgesia (PCA), the standard first-line choice in our hospitals, commonly complain of postoperative sleep disruption due to pain. The aim of this study was to determine whether the PCA combination of alfentanil and morphine, which provides longer analgesia without compromising onset speed, would improve postoperative pain-related sleep interference.

MethodsTwo hundred and twelve adults undergoing major surgery where PCA was the planned principal postoperative analgesic modality were randomized to either the combination of alfentanil and morphine (Group AM) or fentanyl (Group F). The primary outcome was pain-related awakenings during the second postoperative night as measured by the study questionnaire, based on the St Mary’s Hospital Sleep Questionnaire. Analgesic efficacy, other sleep measures, and opioid-related side-effects were also assessed.

ResultsThere was no difference in pain-related sleep disturbance between the groups, with 41% of Group AM and 53% of Group F waking due to pain (P=0.10). Group AM had better rest and dynamic analgesia in the first 24 h with fewer requiring rescue ketamine infusion during the 2 day study period (2 vs 14%, P=0.001). Those in Group AM experienced less nausea and vomiting in the second 24 h (18 vs 35%, P=0.028) but more pruritus (40 vs 23%, P=0.013). ConclusionsDespite better early postoperative analgesia, pain-related sleep interference was not improved by the PCA combination of alfentanil and morphine. Australian New Zealand Clinical Trials RegistryRef: ACTRN12608000118303. 2012 The Author [2012]. Published by Oxford University Press on behalf of the British Journal of Anaesthesia. All rights reserved.

PMID:2013054231


The effect of different treatment modalities on the calcification potential and cross-linking stability of bovine pericardium.

Van Den Heever JJ, Neethling WML, et al.

(Van Den Heever, Smit) Department of Cardiothoracic Surgery, School of Medicine, University of the
Porcine heart valves and bovine pericardium exhibit suitable properties for use as substitutes in cardiothoracic surgery, but must meet several requirements to be safe and efficient. Treatment with glutaraldehyde (GA) renders some of these requirements, but calcification and degradation post-implant remain a problem. This study aimed to identify additional biochemical treatments that will minimize calcification potential without compromising the physical properties of pericardium.

Pericardium treated with GA calcified severely after 8 weeks in the subcutaneous rat model, compared to tissue treated with higher concentrations of glycosaminoglycans (GAG) and commercial Glycar patches. GA, lower concentrations GAG and Glycar pericardium had high denaturation temperatures due to enhanced cross-linking. Tensile strength of GA tissue was significantly lower than GAG-treated or Glycar tissues, due to lower water content with resultant lower flexibility and suppleness.

Pericardium treated with 0.01 M GAG gave acceptable denaturation temperatures, tensile strength and reduced calcification potential. All tissue treatments evoked comparable host immune responses, and no significant difference in resistance to enzymatic degradation. Ineffective stabilization and fixation of cross-links following GAG treatment, as well as limited penetration into the pericardium, resulted in GAG leaching out into the surrounding host tissue or storage medium, and prohibits safe clinical use of such tissue. 2012 Springer Science+Business Media B.V.


Prognostic significance of silent myocardial infarction in newly diagnosed type 2 diabetes mellitus: United Kingdom prospective diabetes study (UKPDS) 79.

Davis TME, Coleman RL, et al.

Background-: We aimed to determine the prevalence of silent myocardial infarction (SMI) in people with newly diagnosed type 2 diabetes mellitus and its relationships to future myocardial infarction (MI) and all-cause mortality. Methods and Results-: We examined data from the 5102 patients in the 30-year UK Prospective Diabetes Study (UKPDS) and used Cox proportional hazards regression to examine outcomes by SMI status. Of 1967 patients with complete baseline data, 326 (16.6%) had ECG evidence of SMI (Minnesota codes 1.1 or 1.2) at enrollment. Those with SMI were more likely to be older, female, sedentary, and nonsmokers compared with those without SMI. Their mean blood pressure was greater despite more intensive antihypertensive treatment; they were more likely to be taking aspirin and lipid-lowering therapy; and they had a greater prevalence of microangiopathy. Fully adjusted hazard ratios for those with versus those without SMI in multivariate models that included UKPDS Risk Engine variables were 1.58 (95% confidence interval, 1.22-2.05) for fatal MI and 1.31 (95% confidence interval, 1.10-1.56) for all-cause mortality. Hazard ratios for first fatal or nonfatal MI and for first nonfatal MI were nonsignificant. The net reclassification index showed no improvement when SMI was added to these models, and the integrated discrimination index showed that SMI marginally improved the prediction of fatal MI and all-cause mortality. Conclusions-: About 1 in 6 UKPDS patients with newly diagnosed type 2 diabetes mellitus had evidence of SMI, which was independently associated with an increased risk of fatal MI and all-cause mortality. However, identification of SMI does not add substantively to current UKPDS Risk Engine predictive variables.
PMID:2013143624

To describe a case of tolosa hunt syndrome presenting as optic neuritis.
Rayside M, Wertheim M.
Publication Types: Conference Abstract

Lower plasma testosterone or dihydrotestosterone, but not estradiol, is associated with symptoms of intermittent claudication in older men.
Yeap BB, Alfonso H, et al.
School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia; Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle, WA, Australia.
OBJECTIVE: In men, testosterone (T) levels decline with age, and lower T predicts all-cause and cardiovascular mortality. However, the associations of T and its metabolites, dihydrotestosterone (DHT) and estradiol (E2), with symptomatic peripheral arterial disease remain unclear. We assessed associations of T, DHT and E2 with lower limb intermittent claudication in older men.
DESIGN: Cross-sectional study.
PARTICIPANTS: Community-dwelling men aged 70-89 years resident in Perth, Western Australia.
MEASUREMENTS: Intermittent claudication was ascertained by the Edinburgh Claudication Questionnaire. Early morning, plasma T, DHT and E2 were assayed using liquid chromatography-tandem mass spectrometry.
RESULTS: There were 268 men with intermittent claudication and 2435 without claudication or any leg pain. Men with nonspecific leg pain (n = 986) were excluded. After adjusting for age, smoking, BMI, waist/hip ratio, hypertension, dyslipidaemia, diabetes, creatinine and prevalent cardiovascular disease (CVD), higher T was associated with reduced risk of having claudication (per 1 SD increase, odds ratio [OR] = 0.80, 95% confidence interval [CI] = 0.69-0.94, P = 0.006; quartiles, Q4/Q1, OR = 0.54, 95% CI = 0.36-0.81). Higher DHT was associated with reduced risk of having claudication (per 1 SD increase, OR = 0.86, 95% CI = 0.73-1.00, P = 0.048; Q4/Q1, OR = 0.64, 95% CI = 0.43-0.95). E2 was not associated with claudication (per 1 SD increase, OR = 0.96, 95% CI = 0.83-1.11, P = 0.565; Q4/Q1, OR = 0.88, 95% CI = 0.60-1.29).
CONCLUSIONS: Lower T or DHT levels, but not E2, are associated with symptoms of intermittent claudication in older men. Reduced exposure to androgens may represent a causal factor or biomarker for symptomatic peripheral arterial disease. Further studies are needed to examine underlying mechanisms and evaluate therapeutic options in ageing men. 2013 John Wiley & Sons Ltd.
Publication Types: Research Support, Non-U.S. Gov't
PMID:23509861

Associations of insulin-like growth factor-I and its binding proteins and testosterone with frailty in older men.
Yeap BB, Paul Chubb SA, et al.
School of Medicine and Pharmacology, University of Western Australia, Perth; Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle.
OBJECTIVE: Ageing is associated with frailty and decreased anabolic hormones, insulin-like growth factor-I (IGF-I) and testosterone. We hypothesized that components of the IGF-I system, in conjunction with testosterone, modulate frailty risk in the elderly. We examined associations between IGF-I, its binding proteins IGFBP1 and IGFBP3 and testosterone with frailty in men.
DESIGN: Observational study of 3,447 community-dwelling men aged 70-89 years assessed in 2001-04, with 1,654 reassessed in 2008-09.

METHODS: Baseline total IGF-I, IGFBP1, IGFBP3 and testosterone were assayed. Frailty was assessed using the FRAIL scale, comprising 5 domains: fatigue; difficulty climbing stairs; difficulty walking >100m; >5 illnesses; weight loss >5%. Men with >=3 domains were considered frail.

RESULTS: At baseline, 527 men (15.3%) were frail. Frail men had lower IGFBP3 (3,630ng/ml vs not frail: 3,800ng/ml, P<0.001) and comparable IGFBP1 (23.5 vs 21.5ng/ml, P=0.09). In multivariate analyses, higher IGFBP1 was associated with increased prevalence of frailty (highest vs lowest quartile Q4:Q1, adjusted odds ratio [OR]=1.39, 95% CI=1.03-1.88). New-onset frailty arose in 260 (17.5%) of 1,484 men. Lower baseline IGF-I predicted new-onset frailty (Q1:Q4 OR=1.48, 95% CI=1.00-2.20) as did higher IGFBP1 (Q4:Q1 OR=1.59, 95% CI=1.01-2.50). Men with both IGF-I and free testosterone in Q1 had greater odds of prevalent frailty (OR=2.13, 95% CI=1.54-2.95).

CONCLUSIONS: Older men with higher IGFBP1 level, or both lower IGF-I and testosterone, are more likely to be frail, while those with lower IGF-I and higher IGFBP1 are more likely to become frail. Components of the IGF-I system may be biomarkers or independent predictors of frailty.


Neuropathic pain components are common in patients with painful cervical radiculopathy, but not in patients with nonspecific neck-arm pain.

Tampin B, Slater H, et al.

*School of Physiotherapy, Curtin Health Innovation Research Institute, Curtin University Departments of +Physiotherapy ++Neurosurgery, Sir Charles Gairdner Hospital, Perth Pain Medicine Unit, Fremantle Hospital and Health Service, Fremantle, WA, Australia.

OBJECTIVES: The aim of this study was to investigate, using quantitative sensory testing (QST) parameters and the painDETECT (PD-Q) screening questionnaire, the presence of neuropathic pain (NeP) in patients with unilateral painful cervical radiculopathy (CxRAD) and in patients with unilateral nonspecific neck-arm pain associated with heightened nerve mechanosensitivity (NSNAP).

METHODS: All patients completed the PD-Q before QST. QST was performed bilaterally in the maximal pain area and the affected dermatome in 23 patients with painful C6 or C7 radiculopathy and in 8 patients with NSNAP following a C6/7 dermatomal pain distribution.

RESULTS: Patients with CxRAD demonstrated a significant loss of sensory function in mechanical (P<0.021) and vibration sense (P<0.003) on the symptomatic side compared with the asymptomatic side in both tested body regions and in the dermatome reduced cold detection (P=0.021) and pressure pain sensitivity (P=0.005), findings consistent with nerve root damage. These sensory alterations in the maximal pain area/symptomatic side are confirmative for the presence of NeP. In contrast to these QST data, only 30% of patients with CxRAD demonstrated a NeP component according to the PD-Q score. In patients with NSNAP, a significant side-to-side difference was demonstrated for warm detection threshold in the dermatome (P=0.030). The PD-Q score indicated that NeP components were unlikely in this group.

DISCUSSION: QST data suggest that NeP is likely to be observed in patients with painful CxRAD, but not in patients with NSNAP.

PMID:23364214


Association between depression and hospital outcomes among older men.


(Matthew Prina, Brayne) Department of Public Health and Primary Care (Prina, Brayne), Cambridge Institute of Public Health, Cambridge University, Cambridge, United Kingdom (Matthew Prina, Hankey, Flicker, Almeida) Western Australia Centre for Health and Ageing, Centre for Medical Research,
Background: Studies that have investigated the relation between depression and the type, nature, extent and outcome of general hospital admissions have been limited by their retrospective designs and focus on specific clinical populations. We explored this relation prospectively in a large, community-based sample of older men. Methods: A cohort of 5411 men aged 69 years and older enrolled in the Health in Men Study was assessed at baseline for depressive symptoms, defined as a score of 7 or higher on the 15-item Geriatric Depression Scale. Participants were followed for 2 years for occurrence and number of hospital admissions, type of hospital admission, length of hospital stay and inpatient death as recorded in the Western Australian Data Linkage System. Results: Of 339 men with depressive symptoms, 152 (44.8%) had at least 1 emergency hospital admission, compared with 1164 of 5072 (22.9%) nondepressed men (p < 0.001). In multivariate analyses, the presence of depressive symptoms was a significant independent predictor of hospital admission (hazard ratio 1.67, 95% confidence interval [CI] 1.38-2.01), number of hospital admissions (incidence rate ratio [IRR] 1.22, 95% CI 1.07-1.39) and total length of hospital stay (IRR 1.65, 95% CI 1.36-2.01). Interpretation: Participants with depressive symptoms were at higher risk of hospital admission for nonpsychiatric conditions and were more likely to have longer hospital stays and worse hospital outcomes, compared with nondepressed participants. These results highlight the potential to target this high-risk group to reduce the burden of health care costs in an aging population. 2013 Canadian Medical Association or its licensors.

PMID:2013087524


Standards of practice in the field of hearing implants.

(Van de Heyning, Kleine Punte) Department of Otorhinolaryngology, Antwerp University Hospital, Antwerp, Belgium (Adunka, Buchman, Dillon, Pillsbury) The University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, United States (Arauz) Instituto de ORL, Buenos Aires, Argentina (Atlas, Eikelboom) Ear Science Institute Australia, Nedlands, Australia (Baumgartner, Gstoettner) Vienna General Hospital, University Clinic of Ear Nose and Throat Diseases, Vienna, Austria (Brill, Hagen, Mlynski) Ear, Nose and Throat Clinic and Polyclinic, Wurzburg University, Wurzburg, Germany (Bruce, Green, O'Driscol) Manchester Auditory Implant, Central Manchester University Hospitals, Manchester, United Kingdom (Caversaccio, Kompis, Senn) Bern University Hospital, University Clinic for Ear Nose Throat, Head and Neck Surgery, Bern, Switzerland (Eskilsson, Karltopor) Karolinska University Hospital, Stockholm, Sweden (Gavilan, Lassaletta) Hospital La Paz, Madrid, Spain (Godey) University Hospital of Rennes, Rennes, France (Han, Li) Capital University of Medical Sciences, Beijing, China (Iwasaki, Usami) Shinshu University School of Medicine, Matsumoto, Japan (Kameswaran, Rajeswaran) Madras Ear Nose Throat Research Foundation, Chennai, India (Kuthubuthen, Rajan) Fremantle Hospital and Health Service, Fremantle, Australia (Kuzovkov, Sugarova, Yanov) St Petersburg Ear Nose Throat and Speech Research Institute, St Petersurg, Russian Federation (Lorens, Skarzynski, Skarzynski) Institute of Physiology and Pathology of Hearing, Nadarzyn, Poland (Manikoth, Pulibalathingal) Ear Nose Throat Super Speciality Institute and

**Intensive care unit mobility practices in Australia and New Zealand: A point prevalence study.**
(Berney, Denehy) Department of Physiotherapy, School of Health Sciences, University of Melbourne, Melbourne, VIC, Australia (Berney) Austin Health, Melbourne, VIC, Australia (Harrold) Curtin University, Perth, WA, Australia (Harrold, Webb) Royal Perth Hospital, Perth, WA, Australia (Webb) University of Western Australia, School of Medicine and Pharmacology, Perth, WA, Australia (Seppelt) Intensive Care Medicine, Nepean Hospital, Sydney, NSW, Australia (Seppelt) Sydney West Area Health Service, Sydney, NSW, Australia (Seppelt) The George Institute for Global Health, Sydney, NSW, Australia (Patman) School of Physiotherapy, University of Notre Dame, Perth, WA, Australia (Patman) Fremantle Hospital and Health Service, Perth, WA, Australia (Thomas) Royal Brisbane and Women's Hospital, Brisbane, QLD, Australia
L. Denehy, Department of Physiotherapy, School of Health Sciences, University of Melbourne, Melbourne, VIC, Australia. E-mail: l.denehy@unimelb.edu.au

Objectives: To develop a comprehensive set of items describing physiotherapy mobilisation practices for critically ill patients, and to document current practices in intensive care units in Australia and New Zealand, focusing on patients having > 48 hours of mechanical ventilation. Design: Prospective, observational, multicentre, single-day, point prevalence study. Participants and setting: All patients in 38 Australian and New Zealand ICUs at 10 am on one of three designated days in 2009 and 2010. Main outcome measures: Demographic data, admission diagnosis and mobilisation practices that had occurred in the previous 24 hours. Results: 514 patients were enrolled, with 498 complete datasets. Mean age was 59.2 years (SD, 16.7 years) and 45% were mechanically ventilated. Mobilisation activities were classified into five categories that were not mutually exclusive: 140 patients (28%) completed an in-bed exercise regimen, 93 (19%) sat over the side of the bed, 182 (37%) sat out of bed, 124 (25%) stood and 89 (18%) walked. Predefined adverse events occurred on 24 occasions (5%). No patient requiring mechanical ventilation sat out of bed or walked. On the study day, 391 patients had been in ICU for > 48 hours. There were 384 complete datasets available for analysis and, of these, 332 patients (86%) were not walked. Of those not walked, 76 (23%) were in the ICU for > 7 days. Conclusion: Patient mobilisation was shown to be low in a single-day point prevalence study. Future observational studies are required to confirm the results.
PMID:24289506


**Iron and hepatic carcinogenesis.**
Tirnitz-Parker JE, Glanfield A, et al.
School of Biomedical Sciences, Curtin University, Curtin Health Innovation Research Institute, Perth, School of Medicine and Pharmacology, The University of Western Australia, Fremantle Australia.
Iron is an essential co-factor for life; however, a physiologically optimal balance is critical. Too much or too little iron can have detrimental effects on human health. In this article, we explore the relationships
between iron and hepatocellular carcinoma (HCC). Iron can act as a modulating co-factor in a range of chronic liver diseases and can accelerate the development of liver injury, fibrosis, cirrhosis, and ultimately HCC. Iron can, however, also act as a sole factor in the causation of liver cirrhosis and HCC in individuals with hereditary hemochromatosis (HH). We overview the regulation of normal iron metabolism and the role of iron in wound healing and associated cell types as well as in pathophysiology that predispose to HCC. We review how these injury processes are inextricably linked, providing a mechanistic basis for understanding how iron and hepatic injury potentially result in HCC.

PMID:23879586

**Non-HFE iron overload: Is phlebotomy the answer?**
Hazeldine S, Trinder D, et al. (Hazeldine, Olynyk) Department of Gastroenterology, Fremantle Hospital, PO Box 480, Fremantle, WA 6959, Australia (Trinder, Olynyk) School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, WA, Australia (Trinder) Western Australian Institute for Medical Research, Fremantle Hospital, Fremantle, WA, Australia (Olynyk) Curtin Health Innovation Research Institute, Curtin University, Bentley, WA, Australia (Olynyk) Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, WA, Australia J.K. Olynyk, Department of Gastroenterology, Fremantle Hospital, PO Box 480, Fremantle, WA 6959, Australia. E-mail: john.olynyk@health.wa.gov.au
Iron is an essential factor for life, however a physiologically optimal balance is critical. In this article we explore the role of iron as a co-factor in a range of chronic liver diseases and how it may contribute to the development of liver injury, fibrosis, cirrhosis and ultimately hepatocellular carcinoma. Whilst iron depletion therapy through phlebotomy is the most effective method of reducing iron stores, it is unclear whether this offers utility in the therapy of liver diseases in which iron is not the primary insult resulting in tissue injury. Here we examine the emerging evidence in the field of non-HFE hereditary haemochromatosis conditions associated with iron overload - is phlebotomy the answer? 2012 Springer Science+Business Media New York.
PMID:2013294432

**The impact of social cognition training on recovery from psychosis.**
Henderson AR.
Community, Culture & Mental Health Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, Western Australia, Australia.
PURPOSE OF REVIEW: Social cognition training is an emerging intervention, which aims to ameliorate impairment in social interaction and improve functional outcomes in persons with a psychosis. This article reviews the research conducted on the impact of this intervention published in English language journals over the past 2 years.
RECENT FINDINGS: Social cognition training comprises three types of programs; targeted, broad-based, and comprehensive - targeted programs being the most effective. Programs largely focus on the domains of facial affect, or emotion recognition (FAR), Theory of Mind (ToM), and attributional bias. There is some evidence that ToM is amenable to change, but not FAR and attributional bias. SUMMARY: Interventions designed to ameliorate impairment in social functioning largely involve a skills training laboratory model underpinned by social learning theory. The evidence for the effectiveness of current social cognition training strategies to improve functional outcome for persons with psychosis in general and schizophrenia in particular remains equivocal. Clearly, further work is required beyond the laboratory training model and future research may well benefit from the inclusion of longitudinal naturalistic studies.
PMID:23867660
Nephropathy in Australian Aboriginal and Anglo-Celt patients with type 2 diabetes: The Fremantle Diabetes study phase II.

Davis TME, Hunt K, et al.
(Davis, Hunt, McAullay, Davis) Fremantle, Australia, Perth, Australia
T.M.E. Davis

Nephropathy frequently complicates type 2 diabetes in Aboriginal patients but there has been no detailed comparison of its prevalence and predictors between racial groups in a multi-cultural Australian setting. We studied 105 Aboriginal type 2 patients (mean+SD age 54.2+11.9 years, 34.3% males) and 827 Anglo-Celts (ACs; aged 67.5+10.6 years, 51.4% males) from the community-based Fremantle Diabetes Study Phase II. All had valid data including serum creatinine (from which estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease (CKD) Epidemiology Collaboration equation) and urinary albumin:creatinine. The percentage of Aboriginal patients with an eGFR <60 ml/min/1.73m2 (26.9%) was similar to that in the AC group (32.2%; P=0.31), but the Aboriginal patients were more likely to have albuminuria (normo-/micro-/macro-37.6/36.6/25.8 % vs 60.2/34.5/5.4 %, respectively, P<0.001). Based on the Kidney Disease Improving Global Outcomes prognostic CKD categories, 19.6% of Aboriginal patients were at very high risk (eGFR 30-59 and at least microalbuminuria, eGFR <30, or renal replacement) vs 10.0% of ACs (P<0.001). In a logistic regression model adjusting for potential confounders including age and diabetes duration, Aboriginality was associated with an odds ratio of 6.72 (95% CI 2.86-15.78) for very high risk of CKD (P<0.001). In individual logistic regression models in the two groups, a very high risk of CKD was independently and positively associated with retinopathy and systolic blood pressure in the Aboriginal group (P<0.012), and with age, diabetes duration and serum HDL-cholesterol (inversely) in the AC group (P<0.001). Intermittent claudication was a significant associate in both (P<0.003). The substantially increased risk of CKD in type 2 indigenous Australians may reflect an increased susceptibility to microvascular complications in general and to the effects of systolic hypertension in the case of nephropathy.

Publication Types: Conference Abstract
PMID:71287010

Use and hypoglycemic consequences of basal insulin in community-based type 2 diabetes: The Fremantle diabetes study phase II.

Davis WA, Bruce DG, et al.
(Davis, Bruce, Davis) Fremantle, Australia
W.A. Davis, Fremantle, Australia

There have been few studies of the use and effects of basal insulin in well-characterized community-based type 2 patients. We used baseline data collected between 2008 and 2011 as part of the observational prospective Fremantle Diabetes Study (FDS) Phase II to determine i) the prevalence of basal insulin use and ii) the frequency of associated self-reported hypoglycemia in a real-world setting. Standardized questionnaires included details of diabetes treatment, any hypoglycemia in the past year and severe hypoglycemic episodes requiring second-party assistance. Of 1,551 type 2 FDS patients, 149 (9.6%) were on basal insulin. They were of mean+SD age 64.6+11.2 years, 56% were male, and they had a median [inter-quartile range] diabetes duration 15.0 [10.4-19.8] years and HbA1c 7.8 [6.8-8.9]%. Of these, 83% were on glargine and 14% isophane, both government-subsidised for this indication, and 3% detemir, with or without additional pre-meal shortacting insulin and/or oral agents. Over half (51%) reported hypoglycemia during the previous year with 11% experiencing a severe event. In the 91 (61.1%) on basal insulin alone, those on glargine (n=78) experienced 5+16 non-severe and 0.2+0.7 severe events/year compared with 4+9 and 0.0+0.0 events/year, respectively, in those on isophane/detemir (n=13; P>0.80 by Poisson log-linear generalized linear modeling). The 58 (38.9%) using basal plus pre-meal shortacting insulin experienced 6+17 non-severe and 0.2+0.6 severe events/year vs 4+15 and 0.2+0.6 events/year, respectively, in those on basal insulin alone.
One in 10 community-based Australians with type 2 diabetes are treated with basal insulin, mostly glargine, with just over a third using additional pre-meal short-acting insulin. Consistent with available data, hypoglycemia was relatively frequent in these patients including severe episodes in patients on basal insulin alone.


Associations between postural hypotension and neuropathy in type 2 diabetes: The Fremantle Diabetes study phase II.

Davis TME, Knapp A, et al.

(Davis, Knapp, Davis) School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia

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

Background and aims: Due to its association with mortality, it has been recommended that autonomic function be assessed at diagnosis of type 2 diabetes and then annually. The equipment and protocols for such testing are not widely available. A simple surrogate of autonomic dysfunction is orthostatic hypotension (OH) which may also be more frequent in patients with peripheral sensory neuropathy. The aim of this study was, therefore, to evaluate the relationship between OH and neuropathic complications of type 2 diabetes. Materials and methods: We studied 417 unselected type 2 patients from the Fremantle Diabetes Study Phase II who underwent assessment of autonomic neuropathy between 2009 and 2012 using i) the ANS 2000 (DE Hokanson Inc, US) which measures R-R variation with deep breathing (Mean Circular Resultant and expiration/inspiration (E/I) ratio), during and after the Valsalva manoeuvre (maximal heart rate during the manoeuvre/the lowest heart rate after the manoeuvre), and on standing (the 30:15 Stand test or R-R interval at beat 30/R-R interval at beat 15), and ii) EZscan (Impeto Medical, France) which generates autonomic risk and kidney scores based on sudomotor function. OH was defined as a fall of >20 mm Hg systolic or >10 mm Hg diastolic blood pressure on standing. Peripheral sensory neuropathy was defined using the clinical portion of the Michigan Neuropathy Screening Instrument. Multiple logistic regression (forward conditional stepwise variable selection with >0.10 for removal) was used to determine independent associates of OH. Results: The mean±SD age of the patients was 65.8±10.9 years, 54.2% were male, their median [inter-quartile range] diabetes duration was 10.0 [4.1-17.2] years, and 109/414 (26.3%) had OH (3 could not stand). The characteristics of those with and without OH are summarised in the Table. In logistic regression, OH was independently associated with supine systolic blood pressure (OR (95%C): 1.28 (1.12-1.46), P<0.001 for a 10 mm Hg increase), diabetes duration (1.21 (1.04-1.40), P=0.012 for a 5-year increase), Loge(30:15 Stand) (0.35 (0.16-0.75), P=0.007), and the EZscan autonomic risk score (0.97 (0.95-0.99), P=0.011. There was no significant bivariate correlation between the latter two measures (r=-0.002, P=0.96). Conclusion: In our community-based patients, OH was independently associated with longer diabetes duration and a higher supine systolic blood pressure, but not peripheral sensory neuropathy. Both the 30:15 Stand test (a lower score indicates abnormal cardiovascular parasympathetic function) and the EZScan autonomic risk score (a lower score correlates with sympathetic sudomotor dysfunction) were also independent associates of OH. These data suggest that i) OH is a manifestation of complex dysfunction of parasympathetic and sympathetic systems, and ii) EZscan, a quick and simple procedure, can contribute to prediction of cardiovascular autonomic dysfunction independently of conventional heart rate-based tests. (Table Presented).

Davis WA, Hamilton EJ, et al.
(Davis, Hamilton, Zakaria, Davis) School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia

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

Background and aims: Most studies that have examined the relationship between diabetes and hip fractures have utilized administrative databases and/or have had limited/incomplete data including recognized hip fracture risk factors. The aim of this study was to determine the incidence and predictors of hip fracture in well-characterized community-based patients with type 2 diabetes.

Materials and methods: We studied a cohort of 1,296 type 2 diabetic participants (mean+SD age 64.0+11.3 years, 49% male, median diabetes duration 4.0 years) in the longitudinal observational Fremantle Diabetes Study Phase I (FDS1) together with 5,159 age-, gender- and postcode-code-matched non-diabetic residents. All deaths and hospitalisations in the state of Western Australia (WA) are recorded in the WA Data Linkage System which was used to provide outcomes from 1982 until end-December 2010. The main outcome measure was incident hospitalization for/with hip fracture between FDS1 study entry in 1993-6 and end-2010. In the diabetic cohort only, mobility was assessed by self-administered questionnaire and peripheral sensory neuropathy was defined using the clinical portion of the Michigan Neuropathy Screening Instrument. Cox proportional hazards modelling was used to identify independent predictors of first hospitalization for/with hip fracture during follow-up.

Results: During 12.0+5.4 years of follow-up, 86 (6.6%) patients were hospitalized on 135 separate occasions for a fractured hip (8.7/1,000 patient-years). This compared with 285 matched non-diabetic residents fracturing their hip on 471 occasions during 13.3+5.0 years' follow-up (6.8/1,000 patient-years). The incidence of hip fracture amongst those with type 2 diabetes was thus 28% higher than in matched non-diabetic residents (incident rate ratio (IRR) (95% CI): 1.28 (1.05-1.55), P=0.011).

Amongst the diabetic patients, older age, female sex, lower BMI, peripheral sensory neuropathy (hazard ratio [95% CI]: 2.10 [1.31-3.36]), and any reduction in mobility (1.98 [1.18-3.32]) were independently associated with risk of first hospitalization for/with hip fracture (P<0.010). Conclusion: The risk of hip fracture is moderately increased among community-dwelling type 2 diabetic patients compared with matched non-diabetic residents. Peripheral sensory neuropathy and reduced mobility both double the risk of hip fracture in patients with type 2 diabetes. Further research is required to determine if hip fractures can be prevented in diabetic patients, especially older females, through interventions aimed at optimal detection and management of mobility and peripheral neuropathy.

Publication Types: Conference Abstract

PMID:71439737

A validated bowel-preparation tolerability questionnaire and assessment of three commonly used bowel-cleansing agents.

Lawrance IC, Willert RP, et al.
Centre for Inflammatory Bowel Diseases, Fremantle Hospital, Fremantle, WA, Australia, ian.lawrance@uwa.edu.au.

BACKGROUND AND STUDY AIMS: Bowel-cleansing studies are frequently underpowered, poorly designed, and with subjective assessments. Consensus on tolerability of the bowel-cleansing agents is thus lacking. This study developed and validated a bowel-preparation tolerability questionnaire and used it to assess the tolerability of three bowel-cleansing agents, sodium phosphate (NaP), polyethylene glycol (PEG), and sodium picosulphate (Pico), in a prospective randomized single-blinded trial of ambulatory patients.

PATIENTS AND METHODS: The bowel-preparation tolerability questionnaire was validated in 125 consecutive patients and then bowel-preparation agent tolerability was assessed in 634 patients in a prospective randomized single-blinded trial.
RESULTS: The questionnaire's internal consistency was satisfactory with good to excellent "test-retest" reliability for aggregate tolerability and visual analogue scores. Validity assessment confirmed it as reliable and accurate. Of 634 patients, 97.8% took >75% of the allocated preparation and 98.9% completed the questionnaire. Overall, Pico was better tolerated than PEG (p<0.001) and NaP (p<0.001). NaP was better tolerated than PEG (p<0.001). Regardless of the bowel-preparation agent used, males tolerated them better than females (p=0.009) as did patients having their procedure in the AM. Older patients, however, tolerated all preparations better than younger patients (p=0.006).

CONCLUSIONS: This study used the first validated bowel-preparation tolerability questionnaire and identified that age, sex, and procedure time all impacted tolerability. Overall, Pico was best tolerated, but PEG's tolerability in patients >=60 years was equal to that of Pico and NaP, suggesting that PEG can be recommended for older patients to avoid the electrolyte disturbances associated with the osmotic preparations.

PMID:23095990


Comparison of venous glucose to finger-prick glucose in patients with diabetes under hyperbaric hyperoxic conditions: a pilot study.

Mclroy D, Banham ND.
Hyperbaric medicine registrar, Hyperbaric Medicine Unit, Fremantle Hospital, at the time of the study. 154 B Samson Street, White Gum Valley, WA 6162, Australia, Phone: +61-(0)407-445-602, E-mail: davidmclroy75@hotmail.com.

Medical Director, Hyperbaric Medicine Unit, Fremantle Hospital, Fremantle, WA, Australia.

INTRODUCTION: Blood glucose is commonly measured in diabetic patients undergoing hyperbaric oxygen treatment (HBOT) from a 'finger-prick' capillary sample. Although this method is an accurate reflection of venous glucose under normal conditions it has not been validated under hyperbaric, hyperoxic conditions.

METHODS: Four patients with diabetes mellitus undergoing HBOT had venous blood samples drawn simultaneously with routine capillary samples before, during and immediately after three of four HBOT sessions. The Bland-Altman method of assessing agreement between these two measures was used separately for the three time periods.

RESULTS: The relationship between venous and finger-prick glucose at room air was altered significantly by HBOT. The bias (finger-prick minus venous measurements) was significantly less than zero during the HBOT session but not immediately after completion of the session. Owing to the small sample size, the limits of agreement straddled zero at all time points, although the lower limit was close to zero during treatment (finger measurement appeared to be higher than venous measurement on room air and lower than venous undergoing HBOT).

CONCLUSION: Finger-prick capillary sampling may not be an accurate reflection of venous glucose during HBOT.

PMID:24510329


Livedoid vasculopathy successfully treated with hyperbaric oxygen.

Banham ND.

Hyperbaric Medicine Unit, Fremantle Hospital, P O Box 480, Fremantle WA 6160, Australia. N.Banham@health.wa.gov.au

Livedoid vasculopathy is a painful, ulcerating condition of the lower legs, ankles and feet with the typical histological feature of hyalinising vascular change of dermal blood vessels with minimal inflammation. Therapeutic interventions have been diverse and varyingly successful. We report a biopsy-proven case in a 27-year-old male, which responded rapidly and completely to hyperbaric oxygen therapy. A few such cases have been reported previously, but only in dermatological journals, not in the hyperbaric medicine literature.
Outcomes in older patients requiring comprehensive allied health care prior to discharge from the emergency department.


(Arendts, Fitzhardinge, Pronk) Centre for Clinical Research in Emergency Medicine, Western Australian Institute for Medical Research, Perth, WA, Australia (Arendts, Fitzhardinge, Pronk) School of Primary, Aboriginal and Rural Health Care, University of Western Australia, Perth, WA, Australia (Hutton) South Metropolitan Health Service, Western Australian Department of Health, Fremantle, WA, Australia

G. Arendts, CCREM, Level 5 MRF Building, Rear 50 Murray Street, Perth, WA 6000, Australia. E-mail: glenn.arendts@uwa.edu.au

Objectives: There is increasing focus on use of multidisciplinary services within the ED to facilitate discharge of older patients that might otherwise require hospitalisation. The risks associated with this are not well established. We aimed to determine whether older patients requiring allied health-facilitated discharge from the ED were at increased risk of hospital readmission and death after discharge.

Methods: A prospective comparative study with matched controls. Patients aged 65 years and over presenting to the ED underwent risk screening. Those with a positive screen formed the intervention group and received comprehensive allied health input from a care coordination team (CCT) prior to discharge. We prospectively enrolled 1098 patients to the intervention group and matched these 1:1 with controls deemed low risk on risk screening. The primary outcome measure was ED re-attendance within 28 days. Patients were followed up for a minimum of 1 year for other outcomes.

Results: At 28 days, there was a 3% absolute difference in the re-attendance rate to ED (17.9% cases, 14.8% controls, P = 0.05) and no mortality difference (1.4% cases, 1.3% controls, P = 0.85). At 1 year, cases had a higher incidence of unplanned hospitalisation (43.4% vs 29.5%, P < 0.001) but not death (10.7% vs 10.2%, P = 0.66). Conclusions: Facilitated discharge of selected older adults by a CCT is relatively safe in the short term. Such patients have an increased likelihood of hospitalisation in the year after discharge. The 1 year mortality rate even in a 'low-risk' discharged population is 10%. 2013 The Authors EMA 2013 Australasian College for Emergency Medicine and Australasian Society for Emergency Medicine.

Pulmonary decompression illness.

Gibbs CR, Blake DF, et al.

(Gibbs, Blake) Emergency Department, The Townsville Hospital, Townsville, QLD, Australia (Smart) Department of Diving and Hyperbaric Medicine, Royal Hobart Hospital, Hobart, Tasmania, Australia (Banham) Department of Diving and Hyperbaric Medicine, Fremantle Hospital, Fremantle, WA, Australia

C.R. Gibbs, Emergency Department, The Townsville Hospital, Townsville, QLD, Australia

Determining the true burden of general practice patients in the emergency department: Getting closer.


Publication Types: Editorial


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PMID:2013093224

PMID:24308612
Serial multiple biomarkers in the assessment of suspected acute coronary syndrome: Multiple infarct markers in chest pain (MIMIC) study.
Macdonald SPJ, Nagree Y, et al.
(Macdonald, Fatovich, Brown) Centre for Clinical Research in Emergency Medicine, Royal Perth Hospital, Perth, WA, Australia (Macdonald, Fatovich, Phillips, Brown) Western Australian Institute for Medical Research, Perth, WA, Australia (Macdonald, Nagree, Fatovich, Phillips, Brown) University of Western Australia, Perth, WA, Australia (Nagree) Emergency Medicine, Fremantle Hospital, Fremantle, WA, Australia (Macdonald) Emergency Department, Armadale Health Service, PO Box 460, Armadale WA 6992, Australia
S.P.J. Macdonald, Emergency Department, Armadale Health Service, PO Box 460, Armadale WA 6992, Australia. E-mail: stephen.macdonald@health.wa.gov.au
Objective To evaluate the accuracy of a 2-h serial multiple biomarker (SMB) protocol for exclusion of myocardial infarction (MI) in the Emergency Department. Methods A prospective, multicentre, observational study enrolled patients undergoing evaluation for possible MI. Blood samples at presentation and 2 h later were analysed for myoglobin, creatinine kinase-MB, troponin-I and B-natriuretic peptide. Thrombolysis in Myocardial Infarction (TIMI) score and National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand (NHF/CSANZ) guideline for acute coronary syndrome were used to determine clinical risk. Primary outcome was MI diagnosed at index presentation. Secondary outcome was composite of all-cause mortality, MI and previously unplanned coronary revascularisation within 30 days. Results 1758 patients were recruited. 168 (11%) of 1501 with data sufficient for analysis had MI, and 223 (14%) of 1620 had a secondary outcome. SMB sensitivity and specificity were 0.90 (95% CI 0.84 to 0.94) and 0.41 (95% CI 0.39 to 0.44) for MI. For 30-day outcome, SMB sensitivity and specificity were 0.84 (95% CI 0.78 to 0.88) and 0.41 (95% CI 0.39 to 0.44), compared with standard 8-12 h troponin sensitivity and specificity of 0.79 (95% CI 0.73 to 0.84) and 0.96 (95% CI 0.95 to 0.97). Combined with risk scores, SMB had sensitivity and specificity for MI of 0.99 (95% CI 0.96 to 1.00) and 0.11 (95% CI 0.09 to 0.12) for TIMI score 0, compared with 0.98 (95% CI 0.94 to 0.99) and 0.31 (95% CI 0.29 to 0.34) for NHF/CSANZ low/intermediate risk groups. Conclusions SMB alone is not sufficiently sensitive to exclude MI. Combined with risk scoring, SMB appears to identify patients at lower risk. This requires prospective validation. Copyright 2013 BMJ Publishing Group Ltd and the College of Emergency Medicine.

Higher free thyroxine levels are associated with all-cause mortality in euthyroid older men: The Health in Men Study.
Yeap BB, Alfonso H, et al.
(Yeap, Hankey, Flicker, Chubb) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia (Yeap) Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle, WA, Australia (Alfonso, Flicker) Western Australian Centre for Health and Ageing, Centre for Medical Research, University of Western Australia, Perth, WA, Australia (Golledge) Vascular Biology Unit, School of Medicine and Dentistry, James Cook University, Townsville, QLD, Australia (Norman) School of Surgery, University of Western Australia, Perth, WA, Australia (Chubb) PathWest Laboratory Medicine, Fremantle and Royal Perth Hospitals, Perth, WA, Australia B.B. Yeap, School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia. E-mail: byeap@cyllene.uwa.edu.au
Objective: Thyroid dysfunction predicts poorer health outcomes, but the relationship between thyroid hormone levels within the reference range and mortality in older adults remains unclear. In this study, we examined the associations between the concentrations of free thyroxine (FT4) and TSH and all-cause mortality in older men without thyroid disease. Subjects and methods: We performed a longitudinal study in community-dwelling men aged 70-89 years. Men with thyroid disease or taking thyroid-related medications were excluded. Baseline FT4 and TSH levels were assayed. Incident
deaths were ascertained using data linkage. Results: There were 3885 men without thyroid disease followed for (mean ± SD) 6.4 ± 1.5 years, during which time 837 had died (21.5%). Men who had died had higher baseline FT4 levels (16.2 ± 2.3 vs 15.8 ± 2.1 pmol/l, P < 0.001), but comparable TSH levels (2.4 ± 1.5 vs 2.3 ± 1.5 mIU/l, P = 0.25). After accounting for age, smoking, physical factors and medical comorbidities, higher circulating FT4 levels predicted all-cause mortality (quartile Q4 vs quartiles Q1-Q3: FT4 levels > 17.32 vs ≤ 17.32 pmol/l: adjusted hazard ratio (HR) = 1.19, 95% CI 1.02-1.39, P = 0.025). TSH levels did not predict mortality. After excluding men with subclinical hyperthyroidism or hypothyroidism, there were 3442 men and 737 who had died (21.4%). In these men, higher FT4 levels remained independently associated with all-cause mortality (quartile Q4 vs quartiles Q1-Q3: adjusted HR = 2.19, 95% CI 1.02-1.41, P = 0.032). Conclusions: Higher FT4 levels are associated with all-cause mortality in euthyroid older men, independently of conventional risk factors and medical comorbidities. Additional research is needed to determine whether or not this relationship is causal and to clarify the utility of thyroid function testing to stratify mortality risk in ageing men. 2013 European Society of Endocrinology.

PMID: 20136170


Designing a new scale to measure anxiety symptoms in Parkinson's disease: Item selection based on canonical correlation analysis.


Background and purpose: The lack of appropriate measures has hindered the research on anxiety syndromes in Parkinson's disease (PD). The objective of the present cross-sectional, international study was to identify shared elements and grouping of components from anxiety scales as a basis for designing a new scale for use in PD. Methods: For this purpose, 342 consecutive PD patients were assessed by means of the Mini International Neuropsychiatric Inventory (depression and anxiety sections), the Clinical Global Impression of severity of the anxiety symptoms, the Hamilton Anxiety Rating Scale (HARS), the Neuropsychiatric Inventory (section E), the Beck Anxiety Inventory (BAI) and the Anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A). Results: As the HADS-A showed a weak correlation with the HARS and BAI, it was not considered for more analyses. HARS and BAI exploratory factor analysis identified nine factors (62% of the variance), with only two of them combining items from both scales. Therefore, a canonical correlation model (a method to identify relations between components of two groups of variables) was built and it showed four factors grouping items from both scales: the first factor corresponded to 'generalized anxiety'; the second factor included muscular, sensory and autonomic 'non-specific somatic symptoms'; the third factor was dominated by 'respiratory symptoms'; and the fourth factor included 'cardiovascular symptoms'. Conclusions: BAI is heavily focused on panic symptoms, whilst HARS is more focused towards
generalized anxiety symptoms. The new scale should include additional components in order to assess both episodic and persistent anxiety as well as items for evaluation of avoidance behaviour.

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PMID:2013440617

Low back pain-related beliefs and likely practice behaviours among final-year cross-discipline health students.
Briggs AM, Slater H, et al.
(Briggs) Department of Health, Government of Western Australia, Perth, Australia (Slater, Smith, Chua) Curtin Health Innovation Research Institute, Curtin University, Perth, Australia (Slater, Smith) School of Physiotherapy, Curtin University, Perth, Australia (Slater) Pain Medicine Unit, Fremantle Hospital, Australia (Parkin-Smith) School of Chiropractic and Sports Science, Murdoch University, Perth, Australia (Watkins) School of Medicine and Pharmacology, University of Western Australia, Perth, Australia
A.M. Briggs, Department of Health, Government of Western Australia, Perth, Australia. E-mail: andrew.briggs@health.wa.gov.au
Background: Evidence points to clinicians' beliefs and practice behaviours related to low back pain (LBP), which are discordant with contemporary evidence. While interventions to align beliefs and behaviours with evidence among clinicians have demonstrated effectiveness, a more sustainable and cost-effective approach to positively developing workforce capacity in this area may be to target the emerging workforce. The aim of this study was to investigate beliefs and clinical recommendations for LBP, and their alignment to evidence, in Australian university allied health and medical students.
Methods: Final-year students in chiropractic, medicine, occupational therapy, pharmacy and physiotherapy disciplines in three Western Australian universities responded to a survey.
Demographic data, LBP-related beliefs data [modified Health Care Providers Pain and Impact Relationship Scale (HC-PAIRS) and the Back Pain Beliefs Questionnaire (BBQ)] and activity, rest and work clinical recommendations for an acute LBP clinical vignette were collected. Results: Six hundred two students completed the survey (response rate 74.6%). Cross-discipline differences in beliefs and clinical recommendations were observed (p > 0.001). Physiotherapy and chiropractic students reported significantly more helpful beliefs compared with the other disciplines, while pharmacy students reported the least helpful beliefs. A greater proportion of chiropractic and physiotherapy students reported guidelineconsistent recommendations compared with other disciplines. HC-PAIRS and BBQ scores were strongly associated with clinical recommendations, independent to the discipline of study and prior experience of LBP. Conclusions: Aligning cross-discipline university curricula with current evidence may provide an opportunity to facilitate translation of this evidence into practice with a focus on a consistent, cross-discipline approach to LBP management. 2012 European Federation of International Association.
PMID:2013410976

Self-reported sensory descriptors are associated with quantitative sensory testing parameters in patients with cervical radiculopathy, but not in patients with fibromyalgia.
Tampin B, Briffa NK, et al.
(Tampin, Briffa, Slater) Curtin Health Innovation Research Institute, School of Physiotherapy, Curtin University, Perth, WA, Australia (Tampin) Department of Physiotherapy, Sir Charles Gairdner Hospital, Perth, WA, Australia (Tampin) Department of Neurosurgery, Sir Charles Gairdner Hospital, Perth, WA, Australia (Slater) Fremantle Hospital and Health Service, Pain Medicine Unit, Fremantle, WA, Australia
B. Tampin, Curtin Health Innovation Research Institute, School of Physiotherapy, Curtin University, Perth, WA, Australia. E-mail: bvdh@iinet.net.au
Background: The painDETECT questionnaire (PD-Q) has been used as a tool to characterize sensory abnormalities in patients with persistent pain. This study investigated whether the self-reported sensory descriptors of patients with painful cervical radiculopathy (CxRAD) and patients with fibromyalgia (FM), as characterized by responses to verbal sensory descriptors from PD-Q (sensitivity to light touch, cold, heat, slight pressure, feeling of numbness in the main area of pain), were associated with the corresponding sensory parameters as demonstrated by quantitative sensory testing (QST). Methods: Twenty-three patients with CxRAD (eight women, 46.3 ± 9.6 years) and 22 patients with FM (20 women, 46.1 ± 11.5 years) completed the PD-Q. Standardized QST of dynamic mechanical allodynia, cold and heat pain thresholds, pressure pain thresholds, mechanical and vibration detection thresholds, was recorded from the maximal pain area. Comparative QST data from 31 age-matched healthy controls (HCs; 15 women) were obtained. Results: Patients with CxRAD demonstrated a match between their self-reported descriptors and QST parameters for all sensory parameters except for sensitivity to light touch, and these matches were statistically significant compared with HC data (p ≤ 0.006). The FM group demonstrated discrepancies between the PD-Q and QST sensory phenotypes for all sensory descriptors, indicating that the self-reported sensory descriptors did not consistently match the QST parameters (p = ≤ 0.017). Conclusion: Clinicians and researchers should be cautious about relying on PD-Q as a stand-alone screening tool to determine sensory abnormalities in patients with FM. 2012 European Federation of International Association. PMID:2013410959


Is hypovitaminosis D associated with abdominal aortic aneurysm, and is there a dose-response relationship?
Wong YYE, Flicker L, et al.
(Wong, Flicker) Western Australian Centre for Health and Ageing, Centre for Medical Research, Western Australian Institute for Medical Research, Perth, Australia (Wong, Flicker, Yeap, McCaul) School of Medicine and Pharmacology, University of Western Australia, Perth, Australia (Wong, Flicker) Department of Geriatric Medicine, Royal Perth Hospital, Perth, Australia (Yeap) Department of Endocrinology and Diabetes, Fremantle Hospital, Perth, Australia (Hankey) Department of Neurology, Royal Perth Hospital, Perth, Australia (Norman) School of Surgery, University of Western Australia, Perth, Australia
Y.Y.E. Wong, Western Australian Centre for Health and Ageing, Centre for Medical Research, Western Australian Institute for Medical Research, Perth, Australia. E-mail: ewong@meddent.uwa.edu.au

Objective This study aims to investigate the association between plasma 25-hydroxyvitamin D (25(OH)D) concentrations with the presence of abdominal aortic aneurysm (AAA) and aortic diameter. Design An observational study of 4233 community-dwelling men aged 70-88 years, who participated in a randomised controlled trial of screening for AAA. Methods Infrarenal aortic diameter measured by ultrasound and 25(OH)D by immunoassay. Results A total of 311 men (7.4%) with AAA (defined as aortic diameter ≥30 mm) comprised the study. Multivariable models were adjusted for age, smoking, cardiovascular disease, hypertension, diabetes, dyslipidaemia, body mass index and serum creatinine concentration. Amongst men with the lowest 25(OH)D quartile of values compared with the highest quartile, the adjusted odds ratio of having an AAA increased in a graded fashion from 1.23 (95% confidence interval (CI) 0.87-1.73) for AAA ≥30 mm to 5.42 (95% CI 1.85-15.88) for AAA ≥40 mm. Similarly, there was a dose-response relationship between 25(OH)D concentrations and the size of the AAA: every 10-nmol l<sup>-1</sup> decrease in 25(OH)D levels was associated with 0.49 mm (95% CI 0.11-0.87) increase in mean aortic diameter. Conclusions Low vitamin D status is associated with the presence of larger AAA in older men, and there is a graded inverse relationship between 25(OH)D concentrations and AAA diameter. Further research is needed to clarify the mechanisms underlying these associations. 2013 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved. PMID:2013325746
Hormones and health outcomes in aging men.

Yeap BB.

School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia; Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle, Western Australia, Australia. Electronic address: byeap@cyllene.uwa.edu.au.

Increasing age is a predictor of ill-health and mortality related to cardiovascular disease and to frailty, a syndrome characterized by deterioration of multiple organ systems leading to loss of physiological reserve, diminished capacity to cope with stressors, and increased risk of disability and death. As men grow older, their levels of testosterone decline while the prevalence of ill-health increases. Observational studies have linked lower testosterone levels with cardiovascular disease and mortality in middle-aged and older men. More recently, lower testosterone has been shown to predict reduced sexual activity and frailty in aging men. Additional studies are needed to determine whether lower testosterone is a biomarker or a potentially treatable risk factor for poorer health outcomes in older men. During aging, the response of the pituitary-thyroid axis alters to manifest higher thyrotropin levels. The presences of subclinical hypo- and hyper-thyroidism predict adverse cardiovascular outcomes. Newer results indicate that in euthyroid older men, differences in free thyroxine levels within the normal range predict specific health outcomes including frailty. Clarification of the roles of endogenous testosterone and thyroxine in the genesis of ill-health during male aging offers the prospect of future intervention to preserve health and well-being in this growing population. Copyright 2012 Elsevier Inc. All rights reserved.

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The impact of phlebotomy in non-alcoholic fatty liver disease: Interim results of a randomized controlled trial.


(Adams) Medicine and Pharmacology, University of Western Australia, Nedlands, WA, Australia (Adams, Ching) Gastroenterology and Hepatology, Sir Charles Gairdner Hospital, Perth, WA, Australia (House, St. Pierre) School of Physics, University of Western Australia, Nedlands, WA, Australia (Crawford) School of Medicine, University of Queensland, Brisbane, QLD, Australia (Stuart) Gastroenterology, Princess Alexandra Hospital, Brisbane, QLD, Australia (Webb) Hematology, Fremantle Hospital, Perth, WA, Australia (Kava, Olynyk) Gastroenterology, Fremantle Hospital, Perth, WA, Australia

L. Adams, Medicine and Pharmacology, University of Western Australia, Nedlands, WA, Australia

Iron is implicated in the pathogenesis of liver injury and insulin resistance. Consequently iron removal by phlebotomy has been proposed as a treatment strategy for patients with non-alcoholic fatty liver disease (NAFLD). We wished to examine the impact of iron reduction by phlebotomy on liver injury, hepatic steatosis and insulin resistance in patients with NAFLD by performing a prospective 6-month randomized controlled trial. Interim results of the initial 53 completed subjects are presented. Methods: Subjects with imaging confirmed NAFLD by performing a prospective 6-month randomized controlled trial. Interim results of the initial 53 completed subjects are presented. Methods: Subjects with imaging confirmed NAFLD were randomly allocated to phlebotomy plus lifestyle advice or lifestyle advice only. Phlebotomy was performed every 2-3 weeks as tolerated, aiming for a ferritin<100. Subjects were assessed at baseline and end of study for liver injury (aminotransaminases, Hepascore) and hepatic steatosis and iron content using magnetic resonance imaging. Insulin resistance was assessed using HOMA (fasting glucose and insulin) and the insulin sensitivity index (ISI) based upon the frequently sampled oral glucose tolerance test. Results: 63 of a planned 66 subjects have been screened and randomized with 53 subjects completed. The mean (±SD) age was 52 (+/-11) years with 33 (62%) being male. The baseline median (IQR) serum ferritin was 392 (201-685) mcgm/l, transferrin saturation 29% (23-35%), liver iron concentration 1.0 (0.6-1.5) mg/gm and hepatic fat index 0.17 (0.10-0.30). Phlebotomy (n=26) and control (n=27) groups had similar anthropometric, biochemical and metabolic parameters apart from serum cholesterol, which was significantly higher in the controls [232 (35)mg/dl vs. 186 (35) mg/dl, p<0.001]. Subjects in the
phlebotomy group underwent a median of 6 (IQR 3-8) venesections which were tolerated well without complications. Subjects in the phlebotomy group had a significantly greater reduction in serum ferritin over the study period compared to controls (284 (114-510) mcgm/l vs. 64 (25-156) mcgm/l, p=0.002). After 6 months, there was no difference in liver aminotransaminases, Hepascore values, hepatic steatosis, hepatic iron concentration, HOMA or ISI (p>0.2 for all). No significant differences between groups were noted at end of study after stratification by baseline serum ferritin, number of venesections, hepatic iron concentration or hepatic steatosis content. Conclusions: Interim results do not support a role of phlebotomy to improve liver enzymes, hepatic fat or insulin resistance in subjects with NAFLD.

Publication Types: Conference Abstract
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**Efficacy and safety of an interferon-free regimen of MK-5172+ribavirin for 12 Weeks or 24 weeks in treatment naive, non-cirrhotic subjects with HCV GT1 infection: The C-SPIRIT study.**

Gane EJ, Ari ZB, et al. (Gane) New Zealand Liver Transplant Unit, Auckland City Hospital, Auckland, New Zealand (Ari) Liver Disease Center, Sheba Medical Center, Ramat Gan, Israel (Mollison) Fremantle Hepatitis Services, Fremantle Hospital, Fremantle, WA, Australia (Zuckerman) Liver Unit, Carmel Medical Center, Haifa, Israel (Bruck) Department of Gastroenterology and Liver Diseases, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel (Baruch) Liver Unit, Rambam Healthcare Campus, Haifa, Israel (Wahl) Merck Research Laboratories, Kenilworth, NJ, United States (Bhanja, Hwang, Zhao, Robertson) Merck Research Laboratories, Upper Gwynedd, PA, United States

**Purpose:** MK-5172 is a potent, pan-genotypic, second generation hepatitis C virus (HCV) NS3/4A protease inhibitor with a high genetic barrier to resistance. Several interferon-free regimens of direct-acting antiviral agents (DAAs) have been reported to achieve high rates of SVR. Efficacy appears to depend on potency, viral genotype (GT), and patient characteristics. This study evaluates the interferon-free, single DAA regimen of MK-5172 + ribavirin (RBV) in patients with HCV GT 1 infection who express the IL28B CC genotype. Methods: Treatment- naive, non-cirrhotic, IL28B CC genotype patients with HCV GT1 infection were randomized to receive 12 or 24 weeks of MK-5172 100 mg QD + weight-based RBV BID. Patients in the 12-week arm with detectable HCV RNA at treatment week (TW) 4 had their treatment duration extended to 24 weeks. Weekly assessments were performed during treatment. Follow-up visits occurred 4, 12, and 24 weeks after end of treatment. HCV-RNA samples were assessed using COBAS Taq- Man v2.0. Futility was defined as HCV-RNA >=25 IU/mL at TW4. Results: 26 patients (17 male / 9 female) were enrolled. One patient discontinued on day 1 because his wife was pregnant. Of the remaining patients, 12 had HCV GT1a infection and 13 had GT1b. Mean baseline HCV-RNA was approximately 9.0 x 106 IU/mL. All but two patients had achieved HCV-RNA of TND by TW6. As of May 28, 2013, 15 subjects had completed TW12. One patient had confirmed viral breakthrough at TW6 and stopped treatment. All remaining patients maintained viral suppression during treatment. The most frequently reported adverse events (>10%) were headache (6, 23%), asthenia (6, 23%), anemia (3, 12%), dyspepsia (3, 12%), nausea (3, 12%), and insomnia (3, 12%). There were no SAEs or treatment discontinuations. ALT was elevated at baseline in 16 patients (range, 34-252), but normalized on treatment in all patients. Nine patients had transient, mild (grade 1-2) elevations in total bilirubin on treatment (range, 1.12- 2.45). Conclusion: Patients with HCV GT1a or GT1b infection receiving MK-5172 + RBV achieved rapid and sustained HCV RNA suppression. One patient had viral breakthrough at TW6. SVR12 and resistance data will be presented. These results support further evaluation of IFN-free regimens with MK-5172. (Table Presented).

Publication Types: Conference Abstract
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**Association between liver-specific gene polymorphisms and their expression levels with nonalcoholic fatty liver disease.**

Adams LA, White SW, et al.

(Adams, Ayonrinde, Mori, Beilin) School of Medicine and Pharmacology, University of Western Australia (UWA), Perth, Australia (Adams) Department of Gastroenterology and Hepatology, Sir Charles Gairdner Hospital, Perth, Australia (Adams, Pennell) Telethon Institute of Child Health Research, Perth, Australia (White, Marsh, Maganga, Pennell) School of Women's and Infant Health, UWA, Perth, Australia (Lye, Connor, Palmer) Samuel Lunenfeld Research Institute, Toronto, Canada (Ayonrinde, Olynyk) Fremantle Hospital, Fremantle, Australia (Ayonrinde, Olynyk) Curtin Health Innovation Research Institute, Bentley, Australia (Olynyk) Western Australian Institute of Medical Research, Perth, Australia (Palmer) Genetic Epidemiology and Biostatistics Platform, Ontario Institute for Cancer Research, Toronto, Canada (Hamdorf) School of Surgery and Pathology, UWA, Perth, Australia

L.A. Adams, School of Medicine and Pharmacology, University of Western Australia, Sir Charles Gairdner Hospital, 4th floor, G Block, Verdun St, Nedlands WA 6009, Australia. E-mail: leon.adams@uwa.edu.au

Genetic factors account for a significant proportion of the phenotypic variance of nonalcoholic fatty liver disease.

**Hepatology. 2013; 58(4): 1306-1314.**

**Importance of cardiometabolic risk factors in the association between nonalcoholic fatty liver disease and arterial stiffness in adolescents.**

Huang RC, Beilin LJ, et al.

(Huang, Beilin, Ayonrinde, Mori, Olynyk, Burrows) School of Medicine and Pharmacology, University of Western Australia (UWA), Nedlands, Australia (Huang) School of Paediatrics and Child Health, UWA, Nedlands, Australia (Ayonrinde, Olynyk) Department of Gastroenterology, Fremantle Hospital, Fremantle, Australia (Ayonrinde, Olynyk) Curtin Health Innovation Research Institute, Curtin University, Bentley, Australia (Olynyk) Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, Australia (Hands) University of Notre Dame, Fremantle, Australia (Adams) Department of Gastroenterology and Hepatology, Sir Charles Gairdner Hospital, Nedlands, Australia

R.-C. Huang, Medical Research Building, Level 4 Rear 50 Murray Street, GPO Box X2213, Perth, WA 6847, Australia. E-mail: rae-chi.huang@uwa.edu.au

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide and is regarded as the hepatic manifestation of the metabolic syndrome. In adults, NAFLD is a determinant of arterial stiffness and cardiovascular risk, independent of the metabolic syndrome. Our aim was to ascertain if NAFLD is associated with arterial stiffness, independent of cardiometabolic factors in a population-based cohort of adolescents. The 17-year-olds (n = 964) from an Australian birth cohort had measures of anthropometry, blood pressure, fasting insulin, glucose, lipids, and NAFLD by ultrasound. Two-step cluster analysis identified youth at high metabolic risk. Measures of arterial stiffness (pulse wave velocity [PWV] and augmentation index corrected for heart rate [AI@75]) were obtained using applanation tonometry. The overall prevalence of NAFLD was 13.3%. The "high risk" metabolic cluster at age 17 years included 16% males and 19% females. Compared to "low risk," the "high risk" cluster participants had greater waist circumference, triglycerides, insulin, systolic blood pressure, and lower high-density lipoprotein (HDL) cholesterol (all P < 0.0001). Those who had NAFLD but were not in the "high risk" metabolic cluster did not have increased PWV or AI@75. However, males and females who had NAFLD in the presence of the metabolic cluster had greater PWV (b = 0.20, 95% confidence interval [CI] 0.01 to 0.38, P = 0.037). Males who had NAFLD in the presence of the metabolic cluster had greater AI@75 (b = 6.3, 95% CI 1.9 to 10.7, P = 0.005). Conclusion: NAFLD is only associated with increased arterial stiffness in the presence of the "high risk" metabolic cluster. This suggests that arterial stiffness related to the presence of NAFLD is predicated on the presence of an adverse metabolic profile in adolescents. 2013 by the American Association for the Study of Liver Diseases. PMID:2013622345
liver disease (NAFLD); however, very few predisposing genes have been identified. We aimed to (1) identify novel genetic associations with NAFLD by performing a genome-wide association study (GWAS), and (2) examine the biological expression of the strongest genetic associations in a separate cohort. We performed GWAS of a population-based cohort (Raine Study) of 928 adolescents assessed for NAFLD by ultrasound at age 17. Expression of genes with single nucleotide polymorphisms (SNPs) that were associated with NAFLD at a significance level of \( P < 10^{-5} \) was examined in adults with NAFLD and controls by quantifying hepatic messenger RNA (mRNA) expression and serum levels of protein. After adjustment for sex and degree of adiposity, SNPs in two genes expressed in liver were associated with NAFLD adolescents: group-specific component (GC) (odds ratio \([OR]\), 2.54; \( P = 1.20 \times 10^{-6} \)) and lymphocyte cytosolic protein-1 (LCP1) (OR, 3.29; \( P = 2.96 \times 10^{-6} \)). SNPs in two genes expressed in neurons were also associated with NAFLD: lipid phosphate phosphatase-related protein type 4 (LPPR4) (OR, 2.30; \( P = 4.82 \times 10^{-6} \)) and solute carrier family 38 member 8 (SLC38A8) (OR, 3.14; \( P = 1.86 \times 10^{-6} \)). Hepatic GC mRNA was significantly reduced (by 83%) and LCP1 mRNA was increased (by 300%) in liver biopsy samples from patients with NAFLD compared to controls (\( P < 0.05 \)). Mean serum levels of GC protein were significantly lower in patients with NAFLD than controls (250 +/- 90 versus 298 +/- 90, respectively; \( P = 0.004 \)); GC protein levels decreased with increasing severity of hepatic steatosis (\( P < 0.01 \)). Conclusion: The association between GC and LCP1 SNPs and NAFLD as well as altered biological expression implicate these genes in the pathogenesis of NAFLD. 2012 American Association for the Study of Liver Diseases.

PMID:2013083922


Improved sustained virological response with pegylated interferon alpha-2b compared with alpha-2a, (and ribavirin) in chronic hepatitis C genotypes 2 and 3.
(Mollison, Miczkova) Hepatitis Services, Fremantle Hospital, Fremantle, WA, Australia (Cheng)
Gastroenterology, Royal Perth Hospital, Perth, VIC, Australia (Manning) School of Medicine and Pharmacology, UWA, Fremantle, WA, Australia
L. Mollison, Hepatitis Services, Fremantle Hospital, Fremantle, WA, Australia
Purpose: The optimal formulation of pegylated interferon a (PEGIFa) as part of combination therapy with ribavirin (RBV) is uncertain for patients infected with hepatitis C genotypes 2 and 3. Methods: A multivariate analysis of prospectively collected treatment data from two tertiary centres on 351 treatment naive HCV genotype 2 or 3 patients who received PEG-IFa2a or b plus ribavirin. Results: Univariate analyses demonstrate that PEG-IFa-2b based regimens achieved a higher sustained virological response (SVR) than PEG-IFa-2a (77.9% versus 62.0%, \( P = 0.0012 \)). On multivariate analyses PEG-IFa-2b appeared superior to PEG-IFa-2a with an odds ratio (OR) and 95% confidence interval (\([CI]95\)) for SVR of 2.19 (\([CI]95\) 1.35-3.52, \( P = 0.0005 \)). Genotype was a significant predictor of outcome in the multivariate model with 80% of genotype 2 but only 67.7% of genotype 3 subjects achieving SVR (OR 2.66 [\([CI]95\) 1.35- 5.92]). Increasing age was negatively associated with SVR (OR 0.97 [\([CI]95\) 0.94-0.99]). Some of the differences in SVR are explained by higher relapse rates with PEG-IFa-2a (\( P = 0.009 \)). Conclusions: PEG-IFa-2b and RBV achieves higher SVR rates than PEG-IFa-2a and RBV in genotype 2 and 3 chronic HCV infection. There is less relapse with PEG-IFa-2b. Genotype 2 infections are considerably easier to cure. SVR is higher in younger patients. These findings should influence choice of PEG-IFa in the era of direct acting anti-viral drugs in therapy of genotypes 2 and 3.
Publication Types: Conference Abstract
PMID:71308568

Periprosthetic fractures around polished collarless cemented stems: The effect of stem design
on fracture pattern.
Erhardt JB, Khoo PP, et al.
(Erhardt) Department of Orthopaedic Surgery, Kantonsspital St. Gallen, St. Gallen, Switzerland
(Erhardt, Khoo, Stoffel, Yates) Fremantle Orthopaedic Unit, University of Western Australia, Australia
(Stoffel) Orthopaedic Unit, Kantonsspital Chur, Chur, Switzerland
J. B. Erhardt, Kantonsspital St.Gallen, Rorschacherstrasse 95, CH 9007 St.Gallen, Switzerland. E-mail: johannes.erhardt@kssg.ch

Background: Predictable patterns of periprosthetic fracture have been observed around polished double tapered stems. Finite element studies have suggested that triple-tapered stems cause less cement strain in torsion compared to double-tapered stems. Hence, we hypothesised that the in vitro behaviour of implanted double- and triple-tapered polished stems, like the CPT (Zimmer, Warsaw, USA) or C-Stem (DePuy, Leeds, UK) when subjected to pathological torsional loads may cause different patterns of periprosthetic fractures. Methods: Ten double-tapered stems (CPT) and ten triple-tapered stems (C-Stem) were cemented into synthetic femur bones. A constant axial compression load of 100 N and a torsional pre-load of 0.1 N.m were applied using a biaxial testing machine. The distal femur was then loaded in external rotation at 45 degrees until failure. Results: Seven of the 10 CPT stems fractured at the level of the stem body while fracturing the cement mantle at the same level. In three of ten of the CPT stems and all ten C-Stems, the synthetic bone fractured at the tip of the prosthesis while the cement mantle remained intact. This was significant for the resulting fracture pattern (P = 0.001). There was no significant difference between the groups for either torque (P = 0.13) or angle at failure (P = 0.49). Interpretation: This biomechanical study indicates that the CPT and C-Stem create a different fracture pattern under the same loading condition. The C-Stem (a triple tapered stem) may produce lower strain in torsion to the cement mantle of a cemented THA. However, fractures that do occur may be more difficult to treat than those produced around a stem like the CPT subjected to comparable loading. 2013 Wichtig Editore.
PMID:2013688907

Transnational validation of the Australian algorithm for virtual crossmatch allocation in kidney paired donation.
Bohmig GA, Fidler S, et al.
(Bohmig) Division of Nephrology and Dialysis, Medical University Vienna, Vienna, Austria (Fidler, Christiansen) Department of Immunology, PathWest, Royal Perth Hospital, Perth, WA, Australia (Fidler, Christiansen) School of Pathology and Laboratory Medicine, University of Western Australia, Perth, WA, Australia (Fischer) Department for Blood Group Serology, Medical University Vienna, Vienna, Austria (Ferrari) Department of Nephrology, Fremantle Hospital, Perth, WA, Australia (Ferrari) School of Medicine and Pharmacology, University of Western Australia, Australia
P. Ferrari, Department of Nephrology, Fremantle Hospital, Perth, WA 6160, Australia. E-mail: paolo.ferrari@health.wa.gov.au

An independent pool of 16 incompatible live donor-recipient pairs registered at the Vienna transplant unit was applied to test whether virtual crossmatch allocation used in the Australian kidney paired donation (KPD) program reliably predicts negative crossmatches. High resolution HLA data were entered into the computer-matching algorithm and allocation was performed excluding any DSA. >. 2000MFI. CDC and flow crossmatch data of recipients against any of the donors were available for 112 crossmatch combinations. The computer program identified 19 possible pairings in 2-way or 3-way chains in multiple combinations. The top ranked combination included one 3-way and two 2-way ABO-compatible chains. Where crossmatches were available all recipients were CDC crossmatch negative with the computer-matched donor. Excluding allocation of KPD donors in the presence of DSA. >. 2000MFI had a negative predictive of 99.9% for CDC and 96.4% for flow crossmatch. In the 12 pairings with >=1 DSA against crossmatched donors there was a negative CDC and flow crossmatch. These results show excellent correlation between matching using virtual crossmatch and actual crossmatch results. Using the 2000MFI cut-off the number of potentially unacceptable CDC and
flow crossmatch positive pairings identified by virtual crossmatching is low, but some potential
crossmatch negative pairings are missed
PMID:2013247220

**Addressing alcohol addiction: Lessons from a hospital based audit.**
Chand P, Naveen CK, et al.
(Chand, Naveen, Murthy) Department of Psychiatry, Centre for Addiction Medicine, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore 560 029, India (Isaac) Fremantle Hospital, The University of Western Australia (M704), 35 Stirling Highway, CRAWLEY WA 6009, Australia
P. Chand, Department of Psychiatry, Centre for Addiction Medicine, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore 560 029, India. E-mail: prabhat.chand@yahoo.com
Publication Types: Letter
PMID:2013203344

**Evaluation of bioactive compounds produced by Nocardia levis MK-VL_113 & Streptomyces tendae TK-VL_333 for cytotoxic activity.**
Chand P, Naveen CK, et al.
(Chand, Naveen, Murthy) Department of Psychiatry, Centre for Addiction Medicine, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore 560 029, India (Isaac) Fremantle Hospital, The University of Western Australia (M704), 35 Stirling Highway, CRAWLEY WA 6009, Australia
P. Chand, Department of Psychiatry, Centre for Addiction Medicine, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bangalore 560 029, India. E-mail: prabhat.chand@yahoo.com
Publication Types: Letter
PMID:2013203343

**Genetic susceptibility in IBD: Overlap between ulcerative Colitis and Crohn's disease.**
Doecke JD, Simms LA, et al.
(Doecke) Australian E-Health Research Centre, QLD, Australia (Doecke) CSIRO Preventative Health Flagship, Macquarie University, Parkville, VIC, Australia (Doecke) Department of Mathematics and Information Sciences, CSIRO, Australia (Simms, Huang, Hanigan, Krishnaprasad, Radford-Smith) Queensland Institute of Medical Research, Department of Inflammatory Bowel Diseases, Brisbane, Australia (Zhao, Montgomery) Queensland Institute of Medical Research, Department of Molecular Epidemiology, Brisbane, Australia (Radford-Smith) Department of Gastroenterology, Royal Brisbane and Women's Hospital, Brisbane, Australia (Krishnaprasad, Andrews) Department of Gastroenterology and Hepatology, Royal Adelaide Hospital and School of Medicine, University of Adelaide, Adelaide, Australia (Roberts) Department of Biochemistry, University of Otago, Dunedin, New Zealand (Mahy) Department of Gastroenterology, Townsville Hospital, Townsville, Australia (Bampton) Department of Gastroenterology and Hepatology, Flinders Medical Centre, Adelaide, Australia (Lewindon) Department of Gastroenterology, Royal Children's Hospital, Herston, Brisbane, Australia (Lewindon, Florin, Radford-Smith) Department of Medicine, University of Queensland, Australia (Florin) Mater Health Services, Brisbane, Australia (Lawrance) School of Medicine and Pharmacology, University of Western Australia, Perth, Australia (Lawrance) Centre for Inflammatory Bowel Diseases, Fremantle Hospital, Fremantle, Australia (Gearry) Dept of Gastroenterology, and Dept of Medicine, University of Otago, Christchurch Hospital, Christchurch, New Zealand
G.L. Radford-Smith, Queensland Institute of Medical Research, Department of Inflammatory Bowel
Background: The etiology of ulcerative colitis (UC) and Crohn's disease (CD) involves both genetic and environmental components. Multiple UC and CD susceptibility genes have been identified through genome-wide association studies and subsequent meta-analyses. These studies have also highlighted the presence of genes common to both diseases, and shared with several other autoimmune disorders. The aim of this study was to identify single nucleotide polymorphisms (SNPs) recently identified by the International IBD Genetics Consortium (IIBDGC) demonstrating that highly significant associations with CD could also confer genetic susceptibility to UC. Methods: Statistical modeling was performed on 29 CD-associated SNPs. The study comprised of 1652 UC cases from the Australia and New Zealand IBD Consortium and 2363 Australian population-based controls. Results: After adjustment for multiple comparisons, only one SNP, rs3024505, was significantly associated with UC (P < 0.001). Independent chi-square analyses identified odds ratios of 2.22 (1.48-3.37) for the rare homozygous genotype, and 1.20 (1.06-1.35) for the minor allele. Five other SNPs demonstrated moderate to weak associations with UC. Conclusions: Of the 29 SNPs conferring high genetic susceptibility to CD, 28 were not associated with UC, thus indicating that for this SNP set there is a low level of overlap between the two major forms of IBD. Only one SNP, rs3024505 (Chr 1q32.1, upstream of IL10), was associated with susceptibility to UC. The identification of this SNP replicates a finding from Franke et al (2008), where the rs3024505 SNP was strongly associated with UC across multiple European populations. Copyright 2013 Crohn's & Colitis Foundation of America, Inc.


Oral tacrolimus for the treatment of refractory inflammatory bowel disease in the biologic era.
Thin LW, Murray K, et al.
Centre for Inflammatory Bowel Diseases, Fremantle Hospital, Fremantle, Australia.
lenathin@gmail.com

BACKGROUND: Patients with inflammatory bowel disease who are refractory to standard therapies frequently require surgery. The long-term efficacy of tacrolimus in patients who fail standard immunosuppressive and antitumor necrosis factor alpha therapy is unknown.

METHODS: Thirty-five patients (11 Crohn's disease and 24 ulcerative colitis) with medication-resistant disease were treated with oral tacrolimus and reviewed retrospectively. Patients were commenced on tacrolimus 0.1 mg/kg/day, with a trough level targeted between 8 and 12 ng/mL. Clinical response or remission at 30 days, 90 days, and 1 year was assessed. The overall risk of requiring surgery and predictive factors were also assessed.

RESULTS: All patients had failed a thiopurine, 5 (14%) had also failed methotrexate, while 90% had a primary or secondary nonresponse, or an incomplete response, to an antitumor necrosis factor alpha agent. The proportions that achieved a clinical response at 30 days, 90 days, and 1 year was 65.7%, 60%, and 31.4%, respectively, whereas the corresponding proportions in remission were 40%, 37.1%, and 22.9%. The cumulative risk of requiring surgery was 40.4% at 1 year and 59.3% at 2 years with a median time to surgery of 22 months (range, 0.5-84 months). Patients who were steroid refractory, or dependent, before starting tacrolimus were more likely to have surgery (P = 0.006), whereas patients who were able to achieve or maintain a clinical response with tacrolimus by 90 days were less likely (P = 0.004).

CONCLUSIONS: Tacrolimus is able to induce a clinical response in a third and remission in a fifth of medically refractory patients with inflammatory bowel disease at 1 year. A 90-day therapeutic trial is worthwhile in difficult to treat patients.


The impact of bacterial and viral co-infection in severe influenza.
Webb SAR, Ginn AN, et al. (Blyth, Kok, Dwyer, Ginn, Iredell) Centre for Infectious Diseases and Microbiology Laboratory Services, Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital, Sydney, NSW, Australia (Blyth) School of Paediatrics and Child Health, University of Western Australia, Princess Margaret Hospital, Perth, WA, Australia (Blyth) Department of Paediatric and Adolescent Medicine, Princess Margaret Hospital, Perth, WA, Australia (Webb) Intensive Care Unit, Royal Perth Hospital, Perth, WA, Australia (Webb) School of Medicine and Pharmacology, School of Population Health, University of Western Australia, Perth, WA, Australia (Kok, Dwyer, Ginn, Seppelt, Iredell) Sydney Medical School, University of Sydney, Sydney, NSW, Australia (van Hal, Foo) Department of Microbiology and Infectious Diseases, Sydney South West Pathology Service - Liverpool, South Western Sydney Local Health Network, Sydney, NSW, Australia (van Hal) Antibiotic Resistance and Mobile Elements Group, Microbiology and Infectious Diseases Unit, School of Medicine, University of Western Sydney, Sydney NSW, Australia (Foo) Infection Management and Control Service (IMACS), Wollongong Hospital, Wollongong, NSW, Australia (Kesson) Infectious Diseases and Microbiology Service, Children's Hospital Westmead, Sydney, NSW, Australia (Kesson) Discipline of Paediatrics and Child Health, University of Sydney, Sydney, NSW, Australia (Seppelt) Department of Intensive Care Medicine, Nepean Hospital, Sydney, NSW, Australia (Bennett, Ong, Nand, Reece, Sara) Bankstown Hospital, Sydney, Australia (Bishop) Campbelltown Hospital, Sydney, Australia (Festa M., Li, Kesson A.) Children's Hospital Westmead, Sydney, Australia (Blythe D., Palermo A.) Fremantle Hospital, Fremantle, Australia (Parr M., Micallef S., van Hal S.J.) Liverpool Hospital, Liverpool, United Kingdom (Hoiling L., Seppelt I., Weisbrodt L., Branley J.) Nepean Hospital, Penrith, Australia (Shehabi Y., Campbell M., Stockdale V., Rawlinson W.D., Outhred A.) Prince of Wales Hospital, Randwick, Australia (Erickson S.) Princess Margaret Hospital for Children, Perth, Australia (Chamberlain J., Gould A., McEntaggart G., Webb S., Flexman J.) Royal Perth Hospital, Perth, Australia (Inskip D., Lamb D., Myburgh J., Sidoli R.) St. George Hospital, Sydney, Australia (Numa A., Williams G., Young J.) Sydney Children's Hospital, Sydney, Australia (Boyd R., Nayyar V., Skelly C., Stachowski E., Blyth C.C., Dwyer D.E., Foo H., Iredell J.R., Kok J., McPhie K., Patterson J.) Westmead Hospital, Sydney, Australia (Sterba M., Johnson B.) Wollongong Hospital, Australia C.C. Blyth, Faculty of Medicine, Dentistry and Health Sciences, School of Paediatrics and Child Health, University of Western Australia, Princess Margaret Hospital, Level 4, Administration Building, Roberts Road, M561, Subiaco, WA 6008, Australia. E-mail: christopher.blyth@uwa.edu.au

Background Many questions remain concerning the burden, risk factors and impact of bacterial and viral co-infection in patients with pandemic influenza admitted to the intensive care unit (ICU).

Objectives To examine the burden, risk factors and impact of bacterial and viral co-infection in Australian patients with severe influenza. Patients/Methods A cohort study conducted in 14 ICUs was performed. Patients with proven influenza A during the 2009 influenza season were eligible for inclusion. Demographics, risk factors, clinical data, microbiological data, complications and outcomes were collected. Polymerase chain reaction for additional bacterial and viral respiratory pathogens was performed on stored respiratory samples. Results Co-infection was identified in 233-269% of patients with severe influenza A infection: viral co-infection, 32-34% and bacterial co-infection, 205-247%. Staphylococcus aureus was the most frequent bacterial co-infection followed by Streptococcus pneumoniae and Haemophilus influenzae. Patients with co-infection were younger [mean difference in age=846years (95% CI: 018-1674years)], less likely to have significant co-morbidities (320% versus 662%, P=0004) and less frequently obese [mean difference in body mass index=686 (95% CI: 177-1196)] compared to those without co-infection. Conclusions Bacterial or viral co-infection complicated one in four patients admitted to ICU with severe influenza A infection. Despite the co-infected patients being younger and with fewer co-morbidities, no significant difference in outcomes was observed. It is likely that co-infection contributed to a need for ICU admission in those without other risk factors for severe influenza disease. Empiric antibiotics with staphylococcal activity should be strongly considered in all patients with severe influenza A infection. 2012 Blackwell Publishing Ltd.

PMID:2013100540
A prospective analysis of the functional and radiological outcomes of minimally invasive plating in proximal humerus fractures.

Acklin YP, Stoffel K, et al.
(Acklin, Sommer) Kantonsspital Graubunden, Loestr. 170, CH-7000 Chur, Switzerland (Stoffel)
Orthopaedic Surgery, Fremantle Hospital, University of Western Australia, 35 Stirling Highway, Crawley, WA 6009, Australia
Y.P. Acklin, Kantonsspital Graubunden, Loestr. 170, CH-7000 Chur, Switzerland. E-mail: yvespascal.acklin@ksgr.ch

Background: Locking-plate osteosynthesis is a well-established treatment option for proximal humerus fractures. The standard approach is delta-pectoral, but few data using the minimally invasive antero-lateral delta-split approach exist. The aim of the study was to prospectively evaluate shoulder function and radiological outcome after a minimally invasive antero-lateral delta-split approach. Materials and methods: From December 2007 to October 2010, 124 patients with proximal humerus fractures were treated with locking-plate osteosynthesis using a minimally invasive antero-lateral delta-split approach. Complete prospective clinical and radiographic data were available for 97 patients for a minimum 1-year follow-up period. Results: After a follow-up period of 18 +/- 6 months, the patients achieved a mean absolute Constant score of the injured shoulder of 75 +/- 11, equalling 91% of the contralateral shoulder Constant score (p < 0.01). Implant-related complications (e.g., screw perforation) were observed in seven patients (7.2%), and avascular necrosis occurred in eight patients (8.2%). Damage to the ventral branch of the axillary nerve was recorded in four cases (4%) without any clinical consequences. The mean delay between trauma and surgery was 0.5 days. The procedures were performed by a total of 16 surgeons who required an average of 73 +/- 27 min of OR time and 108 +/- 121 s of fluoroscopy time. Conclusions: Minimally invasive osteosynthesis using angle-stable implants for proximal humerus fractures demonstrated good functional results. Compared to the literature, this minimally invasive procedure resulted in a shorter operation time and may have reduced the avascular necrosis rate. Level of evidence: Level IIb, monocentric prospective cohort study. 2012 Elsevier Ltd. PMID:2013179589


Culture-positive pleural infection diagnosed in western Australian intensive care units (ICU).

Fysh E, Yogendran A, et al.
(Fysh, Roberts, Baker) Sir Charles Gairdner Hospital, Intensive Care, Perth, Australia (Fysh, Yogendran, Lee, Rosenstengel) Pleural Diseases Unit, Sir Charles Gairdner Hospital, Perth, Australia (Kay) PathWest, Perth, Australia (Palermo) Fremantle Hospital, Intensive Care, Fremantle, Australia
E. Fysh, Sir Charles Gairdner Hospital, Intensive Care, Perth, Australia

Introduction. The incidence of pleural infection is rising and mortality rates remain high, especially in hospital-acquired cases (1). Few studies exist of pleural infection in mixed (surgical and medical) intensive care units (ICU). One single-centre, medical ICU study did suggest a different microbiology and even higher mortality-up to 40 % in this setting compared to 15 to 20 % for pleural infection overall (2). However, the incidence microbiology and outcomes of pleural infections diagnosed while patients are in the ICU remain unclear. This is a significant hindrance to the advancement of patient care. OBJECTIVES. To interrogate a large, multicentre database of culture-positive pleural fluid specimens and determine 1) the incidence, 2) microbiology, 3) need for surgery and 4) the mortality associated with culture-positive pleural infection diagnosed in two tertiary ICU's in Perth, Western Australia.

METHODS. All pleural fluid microbiology specimens from Western Australian public hospitals are processed by PathWest laboratories. The PathWest database was interrogated to find all patients with positive pleural fluid culture between 1st Jan 2006 and 31st Dec 2011. All patients located in the Sir Charles Gairdner and Fremantle Hospital ICU's when the specimens were taken were studied further. Clinical data regarding the four objectives were collected from the case records and analysed. Follow up was until discharge from hospital or death. RESULTS. Incidence: 9,116 patients were admitted to the two mixed medical/surgical ICU's over 6 years. 45 (0.5 %) patients had culture positive pleural fluid
specimens whilst in intensive care. 40 of these had sufficient clinical data available to confirm clinical
evidence of pleural infection. Mean (sd) APACHE II score of infection cohort was 21.7 (+: 6.7). 12 (30 
%) infections were parapneumonic, 13 (32.5 %) postsurgical, 5 (12.5 %) traumatic and 10 (25 %) from
non-pulmonary sepsis. Microbiology: 31 patients (77.5 %) grew gram positive organisms (19
Staphylococcus sp) 3 (7.5 %) gram negative, 2 (5 %) yeast, 1 (2.5 %) mycobacterium and 3 (2.5 %)
had mixed organisms. Surgery: 7 (17.5 %) patients underwent surgical decortication. Mortality: 13
medically managed patients (32.5 %) died vs. 0 surgically treated patients (p = 0.07, Fischer Exact
test). CONCLUSIONS. 1) One in two hundred patients in intensive care suffered from culturepositive
pleural infection. 2) Fewer than one third of pleural infections were parapneumonic. 3) Mortality
remains unacceptably high.
Publication Types: Conference Abstract
PMID:71446294

Evaluation of a tissue-engineered bovine pericardial patch in paediatric patients with
congenital cardiac anomalies: initial experience with the ADAPT-treated CardioCel(R) patch.
Fremantle Heart Institute, Fremantle Hospital, School of Surgery, University of Western Australia,
Fremantle, Western Australia.
OBJECTIVES: This study evaluated the safety, efficacy and clinical performance of the tissue-
engineered ADAPT bovine pericardial patch (ABPP) in paediatric patients with a range of congenital
cardiac anomalies.
METHODS: In this single-centre, prospective, non-randomized clinical study, paediatric patients
underwent surgery for insertion of the ABPP. Primary efficacy measures included early (<30 day)
morbidity; incidence of device-related complications; haemodynamic performance derived from
echocardiography assessment at 6- and 12-month follow-up and magnetic resonance imaging findings
in 10 randomly selected patients at 12 months. Secondary measures included device-handling
characteristics; shape and sizing characteristics and perioperative implant complications. The Aristotle
complexity scoring system was used to score the complexity level of all surgical procedures. Patients
completing the 12-month study were eligible to enter a long-term evaluation study.
RESULTS: Between April 2008 and September 2009, the ABPP was used in 30 paediatric patients. In
the 30-day postoperative period, no graft-related morbidity was observed. In total, there were 5 deaths
(2 in the 30-day postoperative period and 3 within the first 6 postoperative months). All deaths were
deemed due to comorbid non-graft-related events. Echocardiography assessment at 6 and 12 months
revealed intact anatomical and haemodynamically stable repairs without any visible calcification of the
patch. Magnetic resonance imaging assessment in 10 patients at 12 months revealed no signs of
calcification. Fisher’s exact test demonstrated that patients undergoing more complex, higher risk
surgical repairs (Aristotle complexity score >8) were significantly more likely to die (P = 0.0055, 58%
survival compared with 100% survival for less complex surgical repairs). In 19 patients,
echocardiographic data were available at 18-36 months with no evidence of device calcification,
infection, thromboembolic events or device failure.
CONCLUSIONS: This study demonstrates the safety and efficacy of this engineered bovine
pericardial patch as a cardiovascular substitute for surgical repair of both simple and more complex
congenital cardiac defects.
PMID:23832918

Derivation of a nomogram to estimate probability of revisit in at-risk older adults discharged
from the emergency department.
(Arendts) Centre for Clinical Research in Emergency Medicine (CCREM), Western Australian Institute
Estimation of the risk of revisit to the emergency department (ED) soon after discharge in the older population may assist discharge planning and targeting of post discharge intervention in high risk patients. In this study we sought to derive a risk prediction calculator for this purpose. In a prospective observational study in two tertiary ED, we conducted a comprehensive assessment of people aged 65 and over, and followed them for a minimum of 28 days post discharge. Cox proportional hazard models relating any unplanned ED revisit in the follow up period to observed risk factors were used to compute a probability nomogram. From 1,439 patients, 189 (13.1%) had at least one unplanned revisit within 28 days. Revisit probability was weighted towards chronic and difficult to modify risk factors such as depression, malignancy and cognitive impairment. We conclude that the risk of revisit post discharge is calculable using a probability nomogram. However, revisit is largely related to immutable factors reflecting chronic illness burden, and does not necessarily reflect poor ED care during the initial index presentation. 2013 SIMI.

PMID:23462889

Muscle disorders: The latest investigations.
Ghaoui R, Clarke N, et al.
(Ghaoui) Department of Neurology, Royal North Shore Hospital, University of Sydney, Sydney, NSW, Australia (Clarke) INMR, Sydney Medical School, Children's Hospital at Westmead and Discipline of Paediatrics and Child Health, University of Sydney, Sydney, NSW, Australia (Hollingworth) Department of Immunology, Pathwest, Sir Charles Gairdner Hospital, University of Western Australia, Perth, WA, Australia (Needham) Australian Neuromuscular Research Institute, Fremantle Hospital, Perth, WA, Australia
R. Ghaoui, Royal North Shore Hospital, St Leonards, Sydney, NSW 2065, Australia. E-mail: roula.ghaoui@health.nsw.gov.au
Patients with muscle disorders can present a diagnostic challenge to physicians because of the different ways they can present and the large number of different underlying causes. Recognition of the 'myopathic phenotype' coupled with investigations usually including electrodiagnostic and histological investigations have been essential for diagnosing the underlying cause of a myopathy. Despite these standard investigations, some patients can remain undiagnosed. New tests including more specific antibody tests for immune-mediated myopathies and the introduction of next-generation sequencing promise to revolutionise diagnostic approaches for immune and inherited myopathies, but clinical expertise remains essential to choose the most appropriate tests and interpret the results. The aim of this review is to provide an overview of the different presentations to the neuromuscular clinic and the latest investigations that can be helpful in the diagnosis of muscle disorders. 2013 The Authors Internal Medicine Journal 2013 Royal Australasian College of Physicians.
PMID:2013561288

Characteristics and prognosis of Asian patients with type 2 diabetes from a multi-racial Australian community: the Fremantle Diabetes Study.
Tan ED, Davis WA, et al.
School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia,
Background: Asian migrants represent an expanding proportion of the Australian population and are from a region with an increasing diabetes burden. There are few data detailing the characteristics and outcome of type 2 diabetes in Asian Australians.

Aims: To determine whether the phenotype and prognosis of Asians with type 2 diabetes differ from those in Anglo-Celt (AC) patients from the same Australian community.

Methods: We studied 44 Asian and 796 AC patients from the Fremantle Diabetes Study. Each had a detailed assessment between 1993 and 1996, and was invited to annual reviews for >=5 years. Data linkage provided additional endpoints to end-2010. Cox proportional hazards modelling was used to determine predictors of cardiovascular disease (CVD) death and all-cause mortality.

Results: The prevalence of type 2 diabetes in Asians and the general population in Fremantle was similar (1.5% vs 1.6%; P = 0.60). The Asian patients were younger, less obese and less likely to be hypertensive than the AC subjects, but they had a higher retinopathy prevalence (27.3% vs 13.5%; P = 0.023). During up to 18 years of follow up, 12 Asians and 428 AC patients died, 2 (16.7%) vs 205 (47.9%) from CVD (P = 0.040). Asian ethnicity was independently protective against CVD death (hazard ratio 0.13 (95% confidence interval: 0.02-0.96); P = 0.046) but not all-cause mortality (hazard ratio 0.58 (95% confidence interval: 0.31-1.10); P = 0.10).

Conclusions: The phenotype of type 2 diabetes in a relatively small group of well-characterised Asian Australians differed from that in AC patients from the same urban community. Their favourable cardiovascular prognosis may reflect a healthy migrant effect.

PMID: 23869413

Adolescent fatty liver disease.

Ayonrinde O.
(Ayonrinde) Fremantle Hospital, Fremantle, WA, Australia

O. Ayonrinde, Fremantle Hospital, Fremantle, WA, Australia

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disorder in Australia. Though predominantly diagnosed in adults, NAFLD and its metabolic risk factors are increasingly described during childhood and adolescence. NAFLD in adolescence has similar metabolic risk associations to NAFLD in adults and may herald increased risk of adult metabolic disorders, including type 2 diabetes mellitus, atherosclerotic cardiovascular disease and cirrhosis. Insights into NAFLD pathogenesis and opportunities to influence the hepatic and metabolic destinies of individuals with NAFLD may be possible by identifying children at risk of NAFLD. This presentation describes the evolution and metabolic significance of NAFLD in Western Australian adolescents. Amongst 1170 adolescents, aged 17 years, in the longitudinal Western Australian Pregnancy Cohort (Raine) Study there was a 15.2% prevalence of NAFLD diagnosed by liver ultrasound. NAFLD was more common in females. Gender-defined anthropometric, serum biochemistry, dietary and parental factors during childhood or in adolescence were associated with a diagnosis of NAFLD at age 17 years. Adolescents with NAFLD had a more adverse metabolic phenotype, with greater adiposity, insulin resistance, dyslipidaemia, raised liver enzymes and adipocytokine abnormalities compared with those without NAFLD. Parental pre-pregnancy BMI, infant nutrition and child or adolescent adiposity from age 3 to 17 years were associated with the diagnosis of NAFLD at age 17 years. Conclusion: NAFLD in adolescents is common, has similarities to NAFLD in adults and has identifiable early in life risk associations.

Publication Types: Conference Abstract
PMID: 71166744

Mannose binding lectin (MBL) deficiency is a heritable risk factor for multiple serious infections (SI) in rheumatoid arthritis.
Aim: Infection is the leading cause of death in rheumatoid arthritis (RA). Increasing age and the use of corticosteroids (CS) are known risk factors (RF) for serious infection (SI). MBL, a glycosylated protein is a component of the innate immune system, which has diverse functions including opsonisation and complement-mediated killing of various micro-organisms. The aim of this study was to determine whether severe MBL deficiency is a RF for multiple SIs in RA or in ankylosing spondylitis (AS) or psoriatic arthritis (PsA).

Methods: From 01/01/2007 to 30/01/2013, patients with RA (n = 202), AS (n = 38) and PsA (n = 42) derived from the clinics of a single Rheumatologist were enrolled in a clinical database. Serum MBL concentrations were determined mostly at the commencement of synthetic or biologic DMARD therapy. Results: Multiple SIs were observed in 7 RA patients (3.5%), 6 of whom had MBL concentrations <=56 ng / mL and all of whom had MBL concentrations <=400 ng / mL (OR = 35.8, 95% CI 4.1-308.6, P = 0.0011). Multiple SIs were observed in 3 AS patients (7.9%), none of whom had MBL concentrations <=56 ng / mL and in 1 PsA patient (2.4%), who did not have an MBL concentration <= 56 ng / mL. Conclusions: MBL deficiency is a RF for multiple SI in RA, but not AS or PsA. In RA, the risk for one SI in MBL deficiency (OR = 4.2) is comparable to that of maintenance therapy with CS at doses >= 5 mg per day (OR = 4.9). However the risk for multiple SIs in homozygous MBL deficiency is much greater still (OR = 35.8). Risk profiling may minimise the morbidity and mortality associated with SI in RA. The development of SI risk calculators incorporating serum MBL measurements may enable clinicians to make safer therapeutic decisions.

Publication Types: Conference Abstract
PMID:71048172

Mannose binding lectin (MBL) deficiency is more frequent in rheumatoid arthritis with coexistent diffuse bronchiectasis than in rheumatoid arthritis alone or diffuse bronchiectasis alone.

(Makin) Royal Perth Hospital, WA, Australia (Kendall, Carroll) Fremantle Hospital, WA, Australia (Bulsara) University of Notre Dame, WA, Australia

Aim: There is a well-recognized association between rheumatoid arthritis (RA) and diffuse bronchiectasis (dBr), the basis of which is unknown. Mannose binding lectin (MBL) is a component of the innate immune system. MBL deficiency has been associated with increased susceptibility to infection. The aim of this study was to determine whether MBL deficiency occurs more frequently in persons who have RA and co-existent dBr. Methods: An audit of serum MBL concentrations was carried out over a 4-year period in 3 groups of patients viz: rheumatoid arthritis and diffuse bronchiectasis (RA + dBr, n = 19), rheumatoid arthritis alone (RA, n = 127) and diffuse bronchiectasis alone (dBr, n = 33) Results: Significantly lower serum MBL concentrations were observed in the RA + dBr group compared to the dBr alone group (901.4 +/- 260.9 ng/ml vs. 1568.7 +/- 196.7 ng/ml; p = 0.040) or the RA alone group (901.4 +/- 260.9 ng/ml vs. 1537.5 +/- 195.8 ng/ml; p = 0.023). There was a significant difference in the proportion of patients who were MBL deficient in the three groups (Fisher's exact test, p = 0.025). Patients with RA + dBr had a four fold increase in risk for MBL deficiency compared to patients with RA alone (OR = 4.01; 95% CI 1.33-12.12, p = 0.014) after controlling for age and gender. Male patients were significantly less likely to be MBL deficient (p = 0.016). Conclusions: Statistically significantly lower concentrations of MBL were observed in patients with RA + dBr compared to RA alone and dBr alone. This finding raises the possibility that MBL deficiency may predispose to dBr in patients with RA.

Publication Types: Conference Abstract
At least 90% of all HIV in Australia is transmitted sexually. Most people who are HIV positive remain sexually active. STI rates are increasing in Australia. Intercurrent STIs both increase risk of transmission and acquisition of HIV. It is important to discuss sexual risk with HIV positive people. Screening is crucial as many infections are asymptomatic. Acquisition of STIs can lead to an increase in viral load and it is important to recognise and treat STIs appropriately within the setting of HIV. There are also important Public Health issues to consider with regard to transmission. Case based examples will be discussed to illustrate these topics.

Publication Types: Conference Abstract

PMID:71166752

Description of Case: Idiopathic giant oesophageal ulcers are mostly described in patients with acquired immunodeficiency syndrome from HIV infection. Cases in immunosuppressed patients from organ transplantation are rarely reported. A 25 year old man with end-stage kidney disease from reflux nephropathy underwent a deceased-donor kidney transplantation in November 2011. It was a cytomegalovirus (CMV) positive donor to CMV naive recipient. Immunosuppression consisted of Tacrolimus, Mycophenolate Mofetil and Prednisolone, along with Valganciclovir as CMV prophylaxis. He presented with severe odynophagia five months posttransplantation. Initial gastroscopy revealed a large 3 cm mideosophageal ulcer. Serum CMV polymerase chain reaction (PCR) was negative, as was immunoperoxidase staining for CMV in the ulcer biopsy. Odynophagia and dysphagia worsened despite high dose proton-pump inhibitor and Helicobacter pylori eradication therapy, with serial gastroscopies showing a progressive enlarging circumferential oesophageal ulcer. Multiple biopsies failed to demonstrate any CMV cytopathic changes, with persistent negative immunoperoxidase staining. A transient rise in CMV viral load which peaked at 1630 copies per millilitre was noted seven months posttransplantation and correlated with cessation of Valganciclovir. A three week course of intravenous Ganciclovir made no improvement to symptoms or endoscopic appearance, despite an undetectable serum CMV PCR. Parenteral nutrition support was initiated three months after onset of symptoms. A diagnosis of idiopathic giant oesophageal ulcer was made. Intravenous corticosteroid, hydrocortisone 200 mg per day, was associated with rapid clinical improvement, and repeat gastroscopy eight days later showed significant healing of the ulcer. A follow-up gastroscopy four weeks later confirmed complete healing complicated by stricture formation, necessitating endoscopic dilatation. Issues of Interest in the Case 1. Idiopathic giant oesophageal ulcer is not exclusive to the HIV population but is also observed in patients with solid organ transplantation. 2. Diagnosis of giant oesophageal ulcer requires exclusion of other causes, particularly CMV-related gastrointestinal complications. 3. Pathogenesis of idiopathic giant oesophageal ulcer is poorly understood, but immunosuppression appears to be a predisposing factor. 4. In line with evidence suggested in the literature, giant oesophageal ulcer is a steroid responsive condition. 5. Early diagnosis and treatment of idiopathic giant oesophageal ulcer may prevent fibrotic complications of this rare condition.

Publication Types: Conference Abstract

PMID:71166864
A comparative study of hearing aids and round window application of the vibrant sound bridge (VSB) for patients with mixed or conductive hearing loss.
Marino R, Linton N, et al.
Marino, Roberta: roberta@specialisthearing.com.au
Marino, Roberta, PO Box 862, Inglewood, WAU, Australia, 6932, roberta@specialisthearing.com.au
Marino, Roberta: Ear Science Institute Australia, Subiaco, WAU, Australia Linton, Nicola: Ear Science Institute Australia, Subiaco, WAU, Australia Eikelboom, Robert H.: Ear Science Institute Australia, Subiaco, WAU, Australia Statham, Elle: Ear Science Institute Australia, Subiaco, WAU, Australia Rajan, Gunesh P.: Head and Neck Surgery Unit, School of Surgery, University of Western Australia, Fremantle, WAU, Australia

Objective: This study was undertaken to determine the efficacy of the round window (RW) application of the vibrant soundbridge (VSB) in patients with mixed or conductive hearing loss. Design: Speech in quiet and in noise were compared to preoperative data attained with conventional hearing aids so that each subject served as his or her own control in a single test protocol. Study sample: Eighteen adults implanted monaurally with the VSB in the poorer hearing ear. Experience with the VSB ranged from nine to 25 months. Results: Sixteen of the 18 subjects were successful VSB users, wearing their device all waking hours. There was no significant deterioration in the averaged bone conduction results preoperatively versus post-operatively (p > 0.05). Speech recognition in quiet results were not significantly different to performance attained whilst wearing hearing aids (p > 0.05). Speech recognition in noise performance was substantially improved with use of the VSB in most test conditions. Conclusions: For the majority of the subjects, the VSB was an effective method of hearing restoration for their mixed and conductive hearing loss . (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Publication Types: Empirical Study; Quantitative Study
PMID:2013-11155-001

Smoking is associated with lower age, higher grade, higher stage, and larger size of malignant bladder tumors at diagnosis.
Van Roekel EH, Cheng KK, et al.
(Van Roekel, Cheng, Billingham, Zeegers) Department of Public Health, Epidemiology and Biostatistics, School of Health and Population Sciences, University of Birmingham, Birmingham B15 2TT, United Kingdom (Van Roekel) Department of Epidemiology, GROW - School for Oncology and Developmental Biology, Maastricht University, Maastricht, Netherlands (James, Billingham, Murray, Bryan) School of Cancer Sciences, University of Birmingham, Birmingham, United Kingdom (Wallace) School of Surgery, University of Western Australia, Fremantle, Australia (Zeegers) Department of Complex Genetics, Cluster of Genetics and Cell Biology, NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center+, Maastricht, Netherlands

K.K. Cheng, Department of Public Health, Epidemiology and Biostatistics, School of Health and Population Sciences, University of Birmingham, Birmingham B15 2TT, United Kingdom. E-mail: k.k.cheng@bham.ac.uk
Smoking is a strong risk factor of bladder cancer (BC), but it is currently unclear whether smoking is also associated with severity of BC at diagnosis. We performed a large hospital-based case-comparison study, examining the relation between smoking and clinical characteristics of BC at diagnosis. A total of 1,544 cases from participating hospitals in the West Midlands were recruited between 19 December 2005 and 21 April 2011. Eligible cases were adult BC patients without a previous history of this disease. At time of diagnosis, semi-structured face-to-face interviews were conducted by trained research nurses to collect smoking information. Clinical characteristics were obtained from medical records. Linear mixed models were performed to calculate predicted means in clinical outcomes for a variety of smoking behaviors. A p < 0.05 was considered statistically significant. After adjustment for age and gender, current smokers were on average 4.0 years younger at
diagnosis (95% CI: -5.9 to -2.0), had larger tumors (mean difference: 0.48 cm, 95% CI: 0.04-0.91), a higher T stage (mean difference: 0.25, 95% CI: 0.08-0.41), and a borderline significantly higher grade than never smokers (mean difference: 0.15, 95% CI: 0.00-0.30). Our results suggest that smoking could be associated with a more malignant phenotype of BC at diagnosis. More research is needed on the relation between smoking and prognosis, but our results could strengthen the message about the potential risks of smoking to these patients. Copyright 2013 UICC. PMID:2013310923

Increased serum angiopoietin-2 is associated with abdominal aortic aneurysm prevalence and cardiovascular mortality in older men.
(Golledge, Clancy) Department of Surgery, School of Medicine and Dentistry, James Cook University Townsville, Townsville, QLD 4811, Australia (Yeap, Hankey) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia (Yeap) Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle, WA, Australia (Norman) School of Surgery, University of Western Australia, Perth, Australia

J. Golledge, Department of Surgery, School of Medicine and Dentistry, James Cook University Townsville, Townsville, QLD 4811, Australia. E-mail: jonathan.golledge@jcu.edu.au

Background: Angiopoietin-2 (Angpt2) has been implicated in the mediation and regulation of angiogenesis and inflammation which are believed to be critical mechanisms in the pathogenesis of both abdominal aortic aneurysm (AAA) and cardiovascular events. The aim of this study was to assess whether serum Angpt2 was associated with the prevalence of AAA and the occurrence of cardiovascular mortality in older men. Methods: A cohort of 997 elderly men was recruited in 1996-99. Aortic ultrasound identified an AAA in 308 (31%). In 2001-04, blood was collected and serum Angpt2 later measured by immunoassay. The association of Angpt2 with AAA was assessed using multiple regression analysis. All men were followed by means of the Western Australia Data Linkage System until July 31st 2009. The association of Angpt2 with cardiovascular mortality was assessed using Cox proportional hazard analysis. Results: Median serum Angpt2 was significantly higher (3.16 ng/ml, inter-quartile range 2.51-4.54) in men with AAA compared with men without AAA (2.70 ng/ml, inter-quartile range 2.03-3.72; p < 0.001). After adjusting for cardiovascular risk factors, men with serum Angpt2 in the highest quartile (> 3.95 ng/ml) had a 2.57-fold (95% CI 1.66-3.97, p < 0.001) increased odds of AAA and a 4.12-fold (95% CI 1.90-8.94, p < 0.001) increased relative risk of cardiovascular mortality compared to men with serum Angpt2 in the lowest quartile (< 2.13 ng/ml). Conclusions: Serum Angpt2 is elevated in men with AAA and associated with an increased risk of cardiovascular mortality in older men. 2012 Elsevier Ireland Ltd. PMID:2013505464

Downward trend in the prevalence of hospitalisation for atherothrombotic disease.
Briffa TG, Nedkoff L, et al.
(Briffa) M431, School of Population Health, University of Western Australia, 35 Stirling Hwy, Crawley WA 6009, Australia (Nedkoff, Knuiman, Geelhoed, Hickling, Sanfilippo, Bremner, Hobbs) University of Western Australia, Perth, Australia (Norman) Fremantle Hospital and University of Western Australia, Perth, Australia (Hung, Thompson) Sir Charles Gairdner Hospital, University of Western Australia, Perth, Australia (Hankey) Royal Perth Hospital and University of Western Australia, Perth, Australia T.G. Briffa, M431, School of Population Health, University of Western Australia, 35 Stirling Hwy, Crawley WA 6009, Australia. E-mail: Tom.Briffa@uwa.edu.au

Background: The prevalence of hospitalised atherothrombotic disease affecting the coronary, cerebrovascular and peripheral vasculature is expected to increase due to improving survival, ageing and changing risk factor profiles. This study determined sex, age-standardised and age-specific (35-
54, 55-69, 70-84 years) prevalence of atherothrombotic disease and its association with diabetes and chronic kidney disease in Western Australian residents from 2000 to 2007. Methods: In a cross-sectional and longitudinal study, person-linked hospitalisations for atherothrombotic disease were obtained using records from 1985. From 2000 to 2007, total and vasculature-specific prevalence of atherothrombotic disease (as a principal diagnosis) was calculated using a 15-year lead-in to determine prior disease and comorbidity. Results: In 2007, 45,916 (8.6%) men and 22,782 (4.3%) women in Western Australia had established atherothrombotic disease and about 25% had diabetes, 10% had chronic kidney disease, and 5% had both. From 2000 to 2007 the estimated average annual change in age-standardised atherothrombotic disease prevalence was - 0.6%/year (95% CI - 0.8, -0.4) in men and - 0.7%/year (95% CI - 1.0, -0.4) in women. Similar modest declines were seen in age-standardised prevalence of monovascular and polyvascular atherothrombotic disease. The proportion of cases with diabetes increased by about 5%/year, the proportion having chronic kidney disease increased slowly in women (1.5%/year) and was stable in men, and the proportion with both comorbidities increased at about 9%/year. Conclusion: The age-standardised prevalence of atherothrombotic disease requiring hospitalisation has been in marginal decline in Western Australia this decade, despite the proportion of affected persons with diabetes and/or chronic kidney disease steadily rising. 2011 Elsevier Ireland Ltd.

PMID:2013177047


Too little, too late: Mental health nursing education in Western Australia, 1958-1994.

Henderson AR, Martyr P.

Community Culture and Mental Health Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle Clinical Research Centre, Gascoyne House, Graylands Hospital, Mount Claremont, Western Australia, Australia.

Mental health nursing education in Australia has undergone a significant transition in the last 50 years, influenced by national inquiries, national decisions, and international trends in nursing education. But mental health nursing education had also accumulated decades of history in each state, including sometimes unequal relations with general nursing. Complex inter- and intra-professional relationships at state level influenced this educational transition in each state, and Western Australia provides an example of this influence. Using a range of published and unpublished sources, including oral histories, this paper describes the revision of the mental health nursing curriculum in Western Australia from 1958, responses to the call for transition to the tertiary sector between 1976 and 1984, and the final transition of mental health nursing education to university level in Western Australia in 1994. Mental health nursing's educational standards improved only gradually in Western Australia from 1958 onwards, compared with professional advances in general nursing in the same period. Factors which may have held back these improvements include mental health nursing's professional conservatism, which was outpaced by general nursing's growing radicalization at the national level. A lack of professional confidence and cohesion left mental health nursing unable to respond effectively to rapid external changes in the 1960s and 1970s, and vulnerable to absorption and dominance by general nursing education programs. 2012 North Metropolitan Area Health Service, Mental Health. International Journal of Mental Health Nursing 2012 Australian College of Mental Health Nurses Inc. PMID:22809369


Association of fish consumption and omega 3 supplementation with quality of life, disability and disease activity in an international cohort of people with multiple sclerosis.

Jelinek GA, Hadgkiss EJ, et al.

(Jelinek, Hadgkiss, Weiland, Marck, Van Der Meer) Emergency Practice Innovation Centre, St Vincents Hospital, Daly Wing, Fitzroy, VIC 3045, Australia (Jelinek) Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC, Australia (Weiland) Department of
The role of fish consumption and omega 3 supplementation in multiple sclerosis (MS) is controversial, although there is some evidence to support a beneficial effect. We surveyed a large cohort of people with MS recruited via Web 2.0 platforms, requesting information on type of MS, relapse rates, disability, health-related quality of life, frequency of fish consumption and omega 3 supplementation, including type and dose, using validated tools where possible. We aimed to determine whether there was an association between fish consumption and omega 3 supplementation and quality of life, disability and disease activity for people with MS. Univariate and multivariate analyses were undertaken. Of 2469 respondents, 1493 (60.5%) had relapsing-remitting MS. Those consuming fish more frequently and those taking omega 3 supplements had significantly better quality of life, in all domains, and less disability. For fish consumption, there was a clear dose-response relationship for these associations. There were also trends towards lower relapse rates and reduced disease activity; flaxseed oil supplementation was associated with over 60% lower relapse rate over the previous 12 months. Further dietary studies and randomised controlled trials of omega 3 supplementation for people with MS are required, preferably using flaxseed oil. Copyright 2013 Informa Healthcare USA, Inc.


Determinants and costs of community nursing in patients with type 2 diabetes from a community-based observational study: The Fremantle Diabetes Study.


School of Medicine & Pharmacology, University of Western Australia, Australia
Curtin University, Western Australia, Australia

Background: Despite widespread use, there is little information on the extent and impact of community nursing to patients with type 2 diabetes. Objective: To determine the incidence, predictors and costs of community nursing provision to patients with type 2 diabetes in a large community-based representative study of diabetes in an urban Australian setting. Design: Prospective observational study utilising data linkage. Setting: Postcode defined region in Fremantle, Australia. Participants: All patients with type 2 diabetes enrolled in the Fremantle Diabetes Study between 1993 and 1996 Methods: Eligible patients were followed from July 1997, when home nursing data first became available, to death or census in November 2007. Home nursing data from the major community nursing service provider were linked with data from the Fremantle Diabetes Study. Cox and zero-inflated negative binomial (ZINB) regression modelling was used to identify predictors of incident home visits and visit frequency, respectively. Direct costs were estimated from the service provider's unit costs. Results: During a mean ± SD 8.6 ± 2.9 years of follow-up, 27.8% of 825 patients (aged 65.2 ± 10.3 years at study entry; 51.2% male) received 21,878 home nursing visits (median frequency 31 [interquartile range 9-85] visits, range 1-1446 visits). In Cox and ZINB models, predictors of home nursing included older age, physical disability measures and macrovascular and microvascular complications. Insulin use was an important predictor of the frequency of visits whilst ethnic and economic factors predicted lower frequency. The estimated cost of home nursing, extrapolated nationally, adds 5% to the total Australian direct health care costs of diabetes. Conclusions: Home nursing is frequently utilized in the management of type 2 diabetes with considerable individual variation in the use of this service. Given the associated costs, further research into how home nursing can best be employed is indicated.

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Effect of exercise modality and intensity on postexercise interleukin-6 and hepcidin levels.

Sim M, Dawson B, et al.
(Sim, Dawson, Landers, Peeling) School of Sport Science, Exercise and Health, University of Western Australia, Crawley, WA, Australia (Swinkels, Tjalsma) Laboratory of Genetic, Endocrine and Metabolic Diseases, Radboud University Medical Centre, Nijmegen, Netherlands (Trinder) School of Medicine and Pharmacology, University of Western Australia, Fremantle, WA, Australia
M. Sim, School of Sport Science, Exercise and Health, University of Western Australia, Crawley, WA, Australia

The effect of exercise modality and intensity on Interleukin-6 (IL-6), iron status, and hepcidin levels was investigated. Ten trained male triathletes performed 4 exercise trials including low-intensity continuous running (L-R), low-intensity continuous cycling (L-C), high-intensity interval running (H-R), and high-intensity interval cycling (H-C). Both L-R and L-C consisted of 40 min continuous exercise performed at 65% of peak running velocity (vVO2peak) and cycling power output (pVO2peak), while H-R and H-C consisted of 8x3-min intervals performed at 85% vVO2peak and pVO2peak. Venous blood samples were drawn pre-, post-, and 3 hr postexercise. Significant increases in postexercise IL-6 were seen within each trial (p < .05) and were significantly greater in H-R than L-R (p < .05). Hepcidin levels were significantly elevated at 3 hr postexercise within each trial (p < .05). Serum iron levels were significantly elevated (p < .05) immediately postexercise in all trials except L-C. These results suggest that, regardless of exercise mode or intensity, postexercise increases in IL-6 may be expected, likely influencing a subsequent elevation in hepcidin. Regardless, the lack of change in postexercise serum iron levels in L-C may indicate that reduced hemolysis occurs during weight-supported, low-intensity activity.

The West Australian intravenous minocycline and tPA stroke study (WAIMATSS): Progress update.
Blacker DJ, Prentice D, et al.
(Blacker, Hankey) Department of Neurology, Sir Charles Gairdner Hospital, Perth, WA, Australia
(Blacker) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia
(Prentice, Hankey, Kohler, Kho, Claxton) Stroke Unit, Royal Perth Hospital, Perth, WA, Australia
(Bynevelt) Department of Radiology, Sir Charles Gairdner Hospital, Perth, WA, Australia (Bates, Kho) Comprehensive Stroke Unit, Swan District Hospital, Midland, WA, Australia (Alvaro, Kelly) Neurology Department, Fremantle Hospital, Fremantle, WA, Australia
D.J. Blacker, Department of Neurology, Sir Charles Gairdner Hospital, Perth, WA, Australia

Background: Haemorrhagic transformation (HT) is a feared complication of thrombolytic therapy for acute stroke. At the SSA meeting in 2012, we presented the details of the WAIMATSS protocol. We now present an update on recruitment, including some illustrative cases. Aims: To test the hypothesis that patients treated with IV minocycline and tPA have fewer intracranial haemorrhages than those treated with tPA alone. Methods: Patients treated with IV tPA up to 4.5 hours will be randomised to IV minocycline 200 mg BID for five doses commencing less than 6 hours after symptom onset versus standard post tPA care. An protocol amendment approved by ethics in October 2012, now allows for an assent process to be utilised, in addition to informed consent. The primary endpoint is “any” ICH identified on CT scan 24 + 8 hours after treatment. CT scans will be examined by neuroradiologists blinded to treatment. Secondary endpoints include; ICH as defined by the ECASS criteria; day one, two and seven NIHSS, and days 30 and 90 modified Rankin and Barthel Index scores. An MRI substudy will compare ICH seen on MRIs performed between days five to seven post treatment. Results: At mid-January 2013, 12 subjects had been enrolled. The only serious adverse event has been an episode of orol-lingual angiooedema in the standard treatment group. Illustrative cases from the main study, and MRI substudy will be shown. Conclusions: WAIMATSS is progressing as planned,
and proving to have a workable protocol, that could be expanded into a phase 3 study.

Publication Types: Conference Abstract
PMID:71565060

(Marsden) School of Health Professions, Plymouth University, United Kingdom (Amesz) Physiotherapy Department, Fremantle Hospital, WA, Australia (Tessari, Ottoboni) Department of Psychology, University of Bologna, Italy
J. Marsden, School of Health Professions, Plymouth University, United Kingdom
Introduction: Laterality recognition is a form of implicit motor imagery where subjects determine the laterality of a pictured hand by subconsciously imagining moving their hand into the position shown in the picture. Motor imagery has been shown to activate the same neural networks as those involved in movement execution. The aim of the study was to assess the incidence of laterality recognition deficits after stroke, their interrelationship with other impairments and their associated lesion location. Method: Thirty-two acute and sub-acute stroke patients were compared to 36 healthy, age-matched controls on assessments of laterality recognition, attention, mental rotation of objects and implicit processing of sidedness. Within the stroke group, the relationship between laterality recognition and functional ability, neglect, hemianopia, structural body description and dyspraxia were explored. Results: Stroke subjects were significantly less accurate (69% vs 80%) and showed delayed reaction times (3.0 secs vs 1.9 secs) when determining the laterality of a pictured hand. Deficits either in accuracy or reaction times were seen in 53% of stroke subjects. Greater inaccuracy of laterality recognition was associated with lower functional ability (R2 = 0.21), slower mental rotation of objects (R2 = 0.20) and dyspraxia (p = 0.03). Lesions involving the motor network, particularly the parietal lobe and frontoparietal network were associated with deficits in laterality recognition. Conclusion: Implicit motor imagery is affected in a significant number of patients after stroke with these deficits related to lesions to the motor networks. Further research is required to determine if treatment programs can improve deficits in laterality recognition and impact functional outcomes after stroke.

Publication Types: Conference Abstract
PMID:71280597

(Kugathasan, Lok, Kuan) Fremantle Hospital, Fremantle, WA, Australia (Rukin) New Cross Hospital, Wolverhampton, United Kingdom (Hayne) University of Western Australia, Perth, WA, Australia
G. Kugathasan, Fremantle Hospital, Fremantle, WA, Australia
Aim: Laparoscopic pyeloplasty is the gold standard treatment for ureteropelvic junction obstruction. Success rates are around 85-98%. In the public system trainees, under consultant supervision perform this procedure. We report our outcomes [trainee series] and compare the functional [renographic] results with a series performed by the supervising consultant in the private sector [consultant series]. Methods: This retrospective audit spanned a 4-year period, 2007-2011. The primary outcome measure was improvement on MAG3 renography. Secondary outcomes included operative time, length of stay, post operative split function and re-do procedures. Results: The trainee series consisted of 36 cases. Average split function improvement was less than 5%. Post-op complications include urine leaks [5%] and UTI [8%]. Post-operative resolution of obstruction on MAG3 was seen in 25 [70%] cases. Of those who failed, 64% underwent a second procedure. Ten out of 12 [85%] patients in the consultant series showed resolution of obstruction on MAG3 and one [8%] required a re-do pyeloplasty. Conclusion: Our trainee-supervised series shows inferior outcomes to those in the reported literature. Less renographic resolution of obstruction was seen than in the
consultant series. Trainees should be at an advanced stage in all aspects of laparoscopic surgery before performing this procedure.

Open partial nephrectomy: An ideal modular based training operation?
Lok A, Lewis VR, et al.
(Lok, Lewis, Kugathasan, Wallace) Fremantle Hospital, Fremantle, WA, Australia (Hayne) University of Western Australia, Perth, WA, Australia (Rukin) New Cross Hospital, Wolverhampton, United Kingdom
A. Lok, Fremantle Hospital, Fremantle, WA, Australia
Aim: With the advent of laparoscopic surgery, trainee's experience of open renal surgery is becoming limited. Supervised by an experienced consultant, our trainees are taught open partial nephrectomy (OPN) in a modular fashion. We review our trainee-performed procedures to determine if this is an appropriate training operation.

Methods: We performed a retrospective review of OPN from 2010-2012, collecting pre and post-operative data. Results: 45 patients, median age of 56 years and M:F ratio of 2.2:1, underwent OPN. Median operative time was 153 minutes (85-243 minutes). Mean tumour size was 28mm (10-70mm), and median cold ischaemic time was 30 minutes (12-43 minutes). Histology revealed 31 renal cell carcinomas and 8 benign tumours (18%). Mean tumour margin clearance was 2.1mm (0-7mm) with no radiological reoccurrence during follow-up. Mean post-operatively creatinine increase was 8umol/L. Median length of stay was 4 days (3-14 days). One patient had a postoperative bleed, requiring super-selective arterial embolisation. We report no urinary leaks. Conclusion: OPN can be successfully taught as a modular based procedure, with comparable outcomes to the contemporary literature. OPN is a particularly good at teaching the principles of open renal surgery. Before becoming a trainer, the supervising urologist must be competent with OPN and potential intraoperative complications.

Changes in body mass in later life and incident dementia.
Power BD, Alfonso H, et al.
(Power) Peel and Rockingham Kwinana Older Adult Mental Health Service, South Metropolitan Area Health Service, 7/5 Goddard Street South, Rockingham, 6168, Australia (Power, Alfonso, Flicker, Almeida) Western Australian Centre for Health and Ageing, Centre for Medical Research, WAIMR, University of Western Australia, Perth, Australia (Power, Alfonso, Almeida) School of Psychiatry and Clinical Neurosciences, University of Western Australia, Perth, Australia (Flicker, Hankey, Yeap) School of Medicine and Pharmacology, University of Western Australia, Perth, Australia (Flicker) Department of Geriatric Medicine, Royal Perth Hospital, Perth, Australia (Hankey) Department of Neurology, Royal Perth Hospital, Perth, Australia (Yeap) Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle, Australia (Almeida) Department of Psychiatry, Royal Perth Hospital, Perth, Australia
B.D. Power, Peel and Rockingham Kwinana Older Adult Mental Health Service, South Metropolitan Area Health Service, 7/5 Goddard Street South, Rockingham, 6168, Australia. E-mail: brian.power@health.wa.gov.au
ABSTRACT Background: There is ongoing debate about whether a decline in body mass represents a true risk factor for dementia, whether it is a phenotypic marker of incipient dementia, or perhaps a marker of another process that increases dementia risk. This study was designed to determine if changes in body mass index (BMI) in later life are associated with hazard of incident dementia over a follow-up period of up to eight years. Methods: Method followed was a prospective cohort study of
4,181 men aged 65-84 years, resident in Perth, Australia. The exposure of interest was change in BMI measured between 1996-1998 and 2001-2004. The outcome was incident dementia, established using the Western Australia Data Linkage System until 2009. We used Cox regression models to establish crude and adjusted hazard of dementia for change in BMI. Results: Compared with men with a stable BMI, those with a decrease in BMI >1 kg/m² had a higher adjusted hazard of dementia (hazard ratio (HR) = 1.89, 95% CI = 1.32-2.70). The cumulative hazard of dementia over follow-up for changes in BMI was greatest for men with a decrease in BMI >1 kg/m²; this trend was apparent for men in all BMI categories (underweight, normal, overweight, obese). A reverse J-shaped association between BMI change and incident dementia was observed, with the lowest dementia rate being for men whose BMI remained stable. Conclusions: Men who maintained a stable body mass had the lowest incidence of dementia. Further studies are needed to clarify causality and assess feasibility of interventional studies to preserve body mass in aging men. International Psychogeriatric Association 2012.


Cardiovascular diseases do not influence the mental health outcome of older men with depression over 6 years.
Almeida OP, Alfonso H, et al. (Almeida, Alfonso) School of Psychiatry and Clinical Neurosciences, University of Western Australia, Australia (Almeida, Alfonso, Flicker) Western Australian Centre for Health and Ageing, Centre for Medical Research, University of Western Australia, 35 Stirling Highway, Crawley, Perth, WA 6009, Australia (Almeida) Department of Psychiatry, Royal Perth Hospital, WA, Australia (Yeap, Flicker) School of Medicine and Pharmacology, University of Western Australia, Australia (Yeap) Department of Endocrinology and Diabetes, Fremantle Hospital, WA, Australia (Hankey) Department of Neurology, Royal Perth Hospital, WA, Australia (Hankey, Flicker) Department of Geriatric Medicine, Royal Perth Hospital, WA, Australia

O.P. Almeida, Western Australian Centre for Health and Ageing, Centre for Medical Research, University of Western Australia, 35 Stirling Highway, Crawley, Perth, WA 6009, Australia. E-mail: osvaldo.almeida@uwa.edu.au

Background: The concept of ‘vascular depression’ implies that cardiovascular disease facilitates the onset or persistence of depression in later life, and that the natural course of depression should differ according to whether or not vascular pathology is present. Methods: Population-based cohort of 431 older men were diagnosed with depression (prevalent cases) and followed for up to 6 years. We used the Western Australian Data Linkage System to establish the presence of cardiovascular disease (CVD, documented history of coronary heart disease or stroke) and subsequent persistence or recurrence of depression during follow up (ICD-10 codes). Other measures recorded: age, place of birth, education, social support and disadvantage, smoking history, sensory impairment, medical morbidity burden and use of antidepressants. Results: The age of participants ranged from 69 to 86 years and CVD was present in 212 (49.2%) of them. Depressed men with and without CVD had a similar distribution of demographic, lifestyle, social and clinical factors as men without CVD, but higher medical morbidity. One hundred and twenty six (29.2%) men died and another 43 had a recorded diagnosis of depressive disorder between the baseline assessment and the 31st December 2007. Compared with participants without CVD, the adjusted hazard ratio of recurrent or persistent depression during follow up for participants with CVD was 0.78 (95% confidence interval, 95% CI=0.43-1.42). An additional 30 men were identified with depression during a new clinical assessment in 2008-09. Logistic regression showed that the adjusted odds of depression for men with compared to those without CVD was 0.98 (95% CI=0.61-1.59). Conclusion: Persistence or recurrence of symptoms over 6 years in older men with depression is not influenced by the presence of CVD, which raises doubts about the usefulness and validity of the concept of vascular depression. 2012 Elsevier B.V.

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Anaphylaxis: Clinical patterns, mediator release, and severity.
Centre for Clinical Research in Emergency Medicine, Western Australian Institute for Medical Research, Perth, Australia; University of Western Australia, Crawley, Australia; Royal Perth Hospital, Perth, Australia; Fremantle Hospital, Fremantle, Australia. Electronic address: simon.brown@uwa.edu.au.

BACKGROUND: Prospective human studies of anaphylaxis and its mechanisms have been limited, with few severe cases or examining only 1 or 2 mediators.

OBJECTIVES: We wanted to define the clinical patterns of anaphylaxis and relationships between mediators and severity.

METHODS: Data were collected during treatment and before discharge. Serial blood samples were taken for assays of mast cell tryptase, histamine, anaphylatoxins (C3a, C4a, C5a), cytokines (IL-2, IL-6, IL-10), soluble tumor necrosis factor receptor I, and platelet activating factor acetyl hydrolase. Principal component analysis defined mediator patterns, and logistic regression identified risk factors and mediator patterns associated with reaction severity and delayed reactions.

RESULTS: Of 412 reactions in 402 people, 315 met the definition for anaphylaxis by the National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network. Of 97 severe reactions 45 (46%) were hypotensive, 23 (24%) were hypoxemic, and 29 (30%) were mixed. One patient died. Severe reactions were associated with older age, pre-existing lung disease, and drug causation. Delayed deteriorations treated with epinephrine occurred in 29 of 315 anaphylaxis cases (9.2%) and were more common after hypotensive reactions and with pre-existing lung disease. Twenty-two of the 29 delayed deteriorations (76%) occurred within 4 hours of initial epinephrine treatment. Of the remaining 7 cases, 2 were severe and occurred after initially severe reactions, within 10 hours. All mediators were associated with severity, and 1 group (mast cell tryptase, histamine, IL-6, IL-10, and tumor necrosis factor receptor I) was also associated with delayed deteriorations. Low platelet activating factor acetyl hydrolase activity was associated with severe reactions.

CONCLUSION: The results suggest that multiple inflammatory pathways drive reaction severity and support recommendations for safe observation periods after initial treatment. Copyright 2013 American Academy of Allergy, Asthma & Immunology. Published by Mosby, Inc. All rights reserved.

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The IGSF1 deficiency syndrome: Characteristics of male and female patients.
Joustra SD, Schoenmakers N, et al.
(Joustra, Oostdijk, Wit) Department of Pediatrics, 2300 RC Leiden, Netherlands (Sun, Breuning) Center for Human and Clinical Genetics, 2300 RC Leiden, Netherlands (Joustra, Corssmit, Appelman-Dijkstra, Pereira, Biermasz) Department of Endocrinology and Metabolism, Center for Endocrine Tumors Leiden, 2300 RC Leiden, Netherlands (Schoenmakers, Chatterjee) Leiden University Medical Center, Wellcome Trust-Medical Research Council Institute of Metabolic Science, 2300 RC Leiden, Netherlands (Persani, Bonomi) Metabolic Research Laboratories, Addenbrooke's Hospital, University of Cambridge, Cambridge, United Kingdom (Persani, Campi, Beck-Peccoz) Instituto di Ricovero e Cura a Carattere Scientifico (IRCCS), Istituto Auxologico Italiano, Department of Clinical Sciences and Community Health, Milan, Italy (Campi, Beck-Peccoz) Universita degli Studi di Milano, Milan, Italy (Radetti) Fondazione IRCCS Ca' Granda, Pediatric Unit, Milan, Italy (Zhu, Davis) Bolzano Hospital, School of Medicine and Pharmacology, Italy (Heinen, Van Trotsenburg) Fremantle Hospital Unit, University of Western Australia, Departments of Pediatric Endocrinology, Perth, Australia (Hennekam) Departments of Pediatrics, Netherlands (Varewijck, Janssen) Emma Children's Hospital, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands (Endert) Division of Endocrinology, Laboratory of Endocrinology, Erasmus MC, Rotterdam, Netherlands (Lombardi, Mannens) Department of Clinical Chemistry, Department of Clinical Genetics, Netherlands (Bak, Bernard) Academic Medical Center, University of Amsterdam, Department of Pharmacology and...
Therapeutics, Netherlands (Dattani) McGill University, Developmental Endocrinology Research Group, Montreal, QC, Canada
S.D. Joustra, Department of Endocrinology and Metabolism, Center for Endocrine Tumors Leiden, 2300 RC Leiden, Netherlands. E-mail: S.D.Joustra@lumc.nl

Context: Ig superfamily member1 (IGSF1) deficiency was recently discovered as a novel X-linked cause of central hypothyroidism (CeH) and macro-orchidism. However, clinical and biochemical data regarding growth, puberty, and metabolic outcome, as well as features of female carriers, are scarce.

Objective: Our objective was to investigate clinical and biochemical characteristics associated with IGSF1 deficiency in both sexes.

Methods: All patients (n=42, 24 males) from 10 families examined in the university clinics of Leiden, Amsterdam, Cambridge, and Milan were included in this case series. Detailed clinical data were collected with an identical protocol, and biochemical measurements were performed in a central laboratory.

Results: Male patients (age 0-87 years, 17 index cases and 7 from family studies) showed CeH (100%), hypoprolactinemia (n = 16, 67%), and transient partial GH deficiency (n = 3, 13%). Pubertal testosterone production was delayed, as were the growth spurt and pubic hair development. However, testicular growth started at a normal age and attained macro-orchid size in all evaluable adults. Body mass index, percent fat, and waist circumference tended to be elevated. The metabolic syndrome was present in 4 of 5 patients over 55 years of age. Heterozygous female carriers (age 32-80 years) showed CeH in 6 of 18 cases (33%), hypoprolactinemia in 2 (11%), and GH deficiency in none. As in men, body mass index, percent fat, and waist circumference were relatively high, and the metabolic syndrome was present in 3 cases.

Conclusion: In male patients, the X-linked IGSF1 deficiency syndrome is characterized by CeH, hypoprolactinemia, delayed puberty, macro-orchidism, and increased body weight. A subset of female carriers also exhibits CeH. 2013 by The Endocrine Society.

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Low vitamin D status is an independent predictor of increased frailty and all-cause mortality in older men: The health in men study.
Wong YYE, McCaul KA, et al.
(Wong, McCaul, Flicker) Western Australian Centre for Health, Ageing, University of Western Australia (M573), Royal Perth Hospital, Level 6, Ainslie House, Perth, WA 6000, Australia (Wong, McCaul, Yeap, Flicker) School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6000, Australia (Yeap) Department of Endocrinology and Diabetes, Fremantle Hospital, Perth, WA 6160, Australia (Hankey) Departments of Neurology, Perth, WA 6000, Australia (Flicker) Departments of Geriatric Medicine, Royal Perth Hospital, Perth, WA 6000, Australia
Y.Y.E. Wong, Western Australian Centre for Health, Ageing, University of Western Australia (M573), Royal Perth Hospital, Level 6, Ainslie House, Perth, WA 6000, Australia. E-mail: ewong@meddent.uwa.edu.au

Context and Objective: Hypovitaminosis D and frailty are common in the older population. We aimed to determine whether 25-hydroxyvitamin D [25(OH)D] concentrations are associated with frailty and mortality. Design: We conducted a prospective cohort study. Setting and Participants: Participants included 4203 older men aged 70-88 years in Perth, Western Australia. Main Outcome Measures: 25(OH)D was measured by immunoassay. Frailty was assessed with the 5-point FRAIL (fatigue, resistance, ambulation, illness, and loss of weight) scale. Mortality was determined from the death registry via the Western Australian Data Linkage System. Results: At baseline, 676 (16.1%) men were frail, as defined by having >=3 deficits (FRAIL scale >=3). In multivariate cross-sectional analysis, low vitamin D status, defined by the lowest quartile of 25(OH)D values (52.9 nmol/L), was associated with increased prevalent frailty (odds ratio, 1.96; 95% confidence interval [CI], 1.52 to 2.52) in comparison to the highest quartile of 25(OH)D values (>81.6 nmol/L). After a mean period of 5.3 years, the adjusted odds ratio of being frail at follow-up for men with low vitamin D and having zero deficit at baseline (FRAIL scale 0) was 1.56 (95% CI, 1.07 to 2.27). Low vitamin D also predicted all-cause mortality over a period of up to 9.2 years (hazard ratio, 1.20; 95% CI, 1.02 to 1.42), independent of
baseline frailty and other covariates. Conclusion: Hypovitaminosis D is associated with prevalent and incident frailty in older men. Hypovitaminosis D also predicts all-cause mortality, independent of frailty. The association between vitamin D and mortality is not solely dependent on the occurrence of frailty. Copyright 2013 by The Endocrine Society.
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**Causality of rhabdomyolysis and combined tetanus, diphtheria and acellular pertussis (Tdap) vaccine administration.**
Department of Nephrology and Transplantation, Fremantle Hospital, Fremantle, Western Australia, Australia.
PMID:23913623

**Crohn's disease and smoking: Is it ever too late to quit?**
Lawrance IC, Murray K, et al.
BACKGROUND: Smoking increases CD risk. The aim was to determine if smoking cessation at, prior to, or following, CD diagnosis affects medication use, disease phenotypic progression and/or surgery.
METHODS: Data on CD patients with disease for >=5yrs were collected retrospectively including the Montreal classification, smoking history, CD-related abdominal surgeries, family history, medication use and disease behaviour at diagnosis and the time when the disease behaviour changed.
RESULTS: 1115 patients were included across six sites (mean follow-up-16.6yrs). More non-smokers were male (p=0.047) with A1 (p<0.0001), L4 (p=0.028) and perianal (p=0.03) disease. Non-smokers more frequently received anti-TNF agents (p=0.049). (p=0.017: OR 2.5 95%CI 1.18-5.16) and those who ceased smoking prior to diagnosis (p=0.045: OR 2.3 95%CI 1.02-5.21) progressed to complicated (B2/B3) disease as compared to those quitting at diagnosis. Patients with uncomplicated terminal ileal disease at diagnosis more frequently developed B2/B3 disease than isolated colonic CD (p<0.0001). B2/B3 disease was more frequent with perianal disease (p<0.0001) and if i.v. steroids (p=0.004) or immunosuppressants (p<0.0001) were used. 49.3% (558/1115) of patients required at least one intestinal surgery. More smokers had a 2nd surgical resection than patients who quit at, or before, the 1st resection and non-smokers (p=0.044: HR=1.39 95%CI 1.01-1.91). Patients smoking >3cigarettes/day had an increased risk of developing B2/B3 disease (p=0.012: OR 3.8 95%CI 1.27-11.17).
CONCLUSION: Progression to B2/B3 disease and surgery is reduced by smoking cessation. All CD patients regardless of when they were diagnosed, or how many surgeries, should be strongly encouraged to cease smoking. Copyright 2013 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved.
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**Implementing guidelines on the prevention of opportunistic infections in inflammatory bowel disease.**
(Walsh) Department of Gastroenterology, St Vincent's Hospital, Sydney, Australia (Weltman) Department of Gastroenterology, Nepean Hospital, Sydney, Australia (Burger, Travis) Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford, United Kingdom (Vivekanandarajah, Connor) Department of Gastroenterology, Liverpool Hospital, Sydney, Australia (Howlett, Radford-Smith) Department of Gastroenterology, Royal Brisbane and Women's Hospital, Brisbane, Australia (Radford-Smith) IBD Group, Queensland Institute of Medical Research, University of Queensland School of
Introduction: Opportunistic infections are a key safety concern in the management of patients with inflammatory bowel disease (IBD). Despite the existence of international guidelines, many gastroenterologists have not adopted routine screening and vaccination. The aim of this study was to modify clinical behaviour by use of a simple screening tool. Methods: A screening and vaccination proforma for hepatitis B, varicella, Influenza, Pneumococcus, human papillomavirus, tuberculosis, hepatitis C and HIV was provided to each participating gastroenterologist. Gastroenterologists were surveyed for awareness of vaccine recommendations and current practice prior to and following the introduction of the proforma. Rates of immunity and the proportion of patients receiving the recommended screening and vaccinations were documented. Results: 30 gastroenterologists at 8 different IBD centres took part in the assessment. A total of 919 patients were included (55% female, 65% Crohn's, 33% ulcerative colitis, 2% indeterminate IBD). Introduction of the proforma increased self-reported gastroenterologist screening from 47% to 97% pre- and post-intervention respectively, p. < 0.001. After the proforma was applied, vaccination against hepatitis B, varicella, Influenza, and Pneumococcus was recommended in 67%, 2.5%, 75% and 69% of the patients respectively. Of these, 42%, 39%, 66% and 49% patients followed the recommendations and were vaccinated. Cervical smears were recommended in 31%, with 62% of these obtaining the recommended cervical smear. Conclusions: Implementation of a screening and vaccination proforma significantly changed gastroenterologist self-reported behaviour. Patient compliance with these recommendations was not optimal and suggests the need for further patient education, in addition to other forms of support.


Smoking and the effect of its cessation on Crohn's disease progression and surgical rates. Lawrance I, Murray K, et al.

Background: Smoking increases the risk of Crohn's disease (CD) and is a prognostic factor under patient control. The aim of this study was to determine if smoking cessation at, prior to, or following, CD diagnosis (Dx) can alter medication use, disease behaviour and need for first or second CD intestinal surgery. Methods: All patients had CD for >5 yrs and data including Montreal classification, smoking history (start/stop date, cigarettes/day), CD-related abdominal surgeries, family history, medication use, disease behaviour at diagnosis (Dx) and follow-up (F/U). Results: 1115 CD patients from 6 centres, with a mean F/U of 16.6yrs, showed that at Dx non-smokers (NS) were more likely to be male (p = 0.047), A1 (p < 0.0001) with L4 (p = 0.028) and perianal (p = 0.03) disease. Disease location (L1, L2 or L3) or behaviour was not different. No differences were seen between smokers' and
NS need at some stage in the disease to use oral or iv steroids, or immunosuppression (IS). NS were more likely to receive an anti-TNF agent (p = 0.049). Logistic regression on B1 disease at Dx showed that terminal ileum (TI) CD was more likely to develop into B2/B3 disease (p = 0.017), as were patients who ceased smoking prior to Dx c/w patients who quit at Dx (p = 0.045). B2/B3 disease was more likely if iv steroids (p = 0.004), IS (p < 0.0001) were required or if there was perianal disease (p < 0.0001). 558 patients required intestinal surgery and modelling with smoking status as a predictor showed that smoking was significant (p = 0.044). Multivariate analysis showed surgery was more common with TI (p < 0.0001) and perianal (p = 0.01) disease, while smoking lost significance. 186 patients underwent a 2nd intestinal resection. A greater proportion of smokers underwent a 2nd surgical resection (401%) than patients who quit at, or before, the 1st surgical resection (29%) and NS (28%) but was not significant. There was a general trend in disease behaviour change and the need for 1st and 2nd surgery with increasing numbers of cigarettes/day smoked. Regression analysis identified cigarettes/day smoked as significantly associated with B2/B3 disease change (0.01). Conclusions: Smoking is a modifiable risk factor. Cessation at Dx reduces the rate of complicated disease as does reducing the number of cigarettes/day smoked. This supports the need for CD patients to be strongly encouraged to cease or at least reduce their smoking.

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5-Aminosalicylate (5-ASA) induced nephrotoxicity in inflammatory bowel disease.
So K, Bewshea C, et al.
(So, Heap, Daneshmend, Ahmad) Royal Devon and Exeter Hospital, Gastroenterology, Exeter, United Kingdom (Bewshea) Royal Devon and Exeter Hospital, IBD Pharmacogenetics Research, Exeter, United Kingdom (Muller) Kent and Canterbury Hospital, Gastroenterology, Canterbury, United Kingdom (Delaney) Kent and Canterbury Hospital, Renal Medicine, Canterbury, United Kingdom (Mulgrew, D'Souza, Kwan, Oram) Royal Devon and Exeter Hospital, Renal Medicine, Exeter, United Kingdom (Irving) Guy's and St Thomas' Hospital, Gastroenterology, London, United Kingdom (Orchard) St Mary's Hospital, Gastroenterology, London, United Kingdom (Hart) St Mark's Hospital, Gastroenterology, London, United Kingdom (Tsianos) University of Ioannina, Gastroenterology, Ioannina, Greece (Annese) Azienda Ospedaliero Universitaria (AOU), Gastroenterology, Careggi, Italy (Silverberg) Mount Sinai Hospital, Gastroenterology, Toronto, Canada (Watermeyer) Groote Schuur Hospital, Gastroenterology, Cape Town, South Africa (Renata) University Hospital Padua, Gastroenterology, Padua, Italy (Radford-Smith) Royal Brisbane and Women's Hospital, Gastroenterology, Brisbane, Australia (Gearry) University of Otago, Gastroenterology, Christchurch, United Kingdom (Russell) Yorkhill Hospital, Gastroenterology, Glasgow, United Kingdom (Wilson) University of Edinburgh, Paediatric Gastroenterology, Edinburgh, United Kingdom (Parkes) Addenbrooke's Hospital, Gastroenterology, Cambridge, United Kingdom (Satsangi, Lees) Western General Hospital, Gastroenterology, Edinburgh, United Kingdom (Weersma) University Medical Center, Gastroenterology, Groningen, Netherlands (Lawrance) Fremantle Hospital, Gastroenterology, Fremantle, Australia (Holden) International Serious Adverse Event Consortium, Chicago, United States

K. So, Royal Devon and Exeter Hospital, Gastroenterology, Exeter, United Kingdom

Background: Nephrotoxicity is a rare idiosyncratic reaction to 5-ASA therapy. The exact pathogenic mechanisms are unknown but it is commonly characterised by progressive interstitial nephritis. This study aims to a) describe the clinical features of this complication b) explore the underlying mechanisms and c) identify clinically useful predictive genetic markers so that these drugs can be avoided, or monitoring intensified, in highrisk patients. Here we report the clinical features. Methods: Patients were recruited from 185 (130 UK) international sites and DNA extracted. Inclusion criteria comprise normal renal function prior to commencing 5-ASA + >=50% rise in creatinine + medical opinion implicating 5-ASA justifies drug withdrawal. An adjudication panel of expert gastroenterologists
and nephrologists assessed causality from detailed case report forms. Patients were assigned "definite" (requires positive rechallenge), "probable", "possible" or "unlikely" cases of 5-ASA nephrotoxicity using the validated Liverpool Adverse Drug Reaction Causality Assessment Tool.

Results: 156 (44.5% Crohn's disease, 71.9% male) patients have been recruited to date. These include 4 definite, 105 probable, 20 possible, 3 unlikely cases and 13 to be adjudicated. One patient with microscopic colitis was excluded. The side effect was seen with all aminosalicylates (mesalazine, balsalazide, olsalazine and sulfasalazine). 5-ASA nephrotoxicity occurred at a median age of 38.2 years (range 7.7-87.7). 78.6% of patients were white British. Two patients had a confirmed family history of 5-ASA-induced renal impairment. 75% of cases were detected by routine blood monitoring. The interval between 5-ASA introduction and first abnormal blood test was 0.2-521.3 months with 22.4% occurring in the first 12 months. The mean peak creatinine recorded was 296.8 micromol/litre (range 112-1726). A renal biopsy was performed in 46.9% cases. 81.1% had a >=20% recovery in peak creatinine on drug withdrawal; of these the mean time to best-recovered renal function was 2 months (range 0.1-252.8) months. Seventeen patients required renal replacement therapy (15 transplantation). Conclusions: This is the largest most detailed study of 5-ASA induced nephrotoxicity. Whilst the incidence is low, the morbidity is high with 12% of patients requiring renal replacement therapy. Early recognition is important as drug withdrawal leads to recovery in only 81.1% of patients. Genome-wide association sequencing (GWAS) will be performed in February 2013.

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Oral tacrolimus for the treatment of refractory inflammatory bowel disease in the biologic era.

Thin L, Murray K, et al.
(Thin) Centre for Inflammatory Bowel diseases, Fremantle Hospital, Fremantle, Australia (Murray) Centre for Applied Statistics, University of Western Australia, Crawly, Australia (Lawrance) Centre for Inflammatory Bowel diseases, Fremantle Hospital, University of Western Australia, Fremantle, Australia
I. Lawrance, Centre for Inflammatory Bowel diseases, Fremantle Hospital, University of Western Australia, Fremantle, Australia

Background: Inflammatory bowel disease patients who are refractory to standard therapies frequently require surgery. The long-term efficacy of tacrolimus in patients who fail standard immunosuppressive and anti-TNF alpha therapy is unknown. Methods: 35 patients (11 CD and 24 UC) with medicationresistant disease were treated with oral tacrolimus and reviewed retrospectively. Patients were commenced on tacrolimus 0.1 mg/kg/day, with a trough level targeted between 8 12 ng/ml. Clinical response or remission, at 30-days, 90-days and 1-year were assessed. The overall risk of requiring surgery and predictive factors were also assessed. Results: All patients had failed a thiopurine, 5 (14%) had also failed methotrexate while 90% had a primary or secondary nonresponse, or an incomplete response, to an anti-TNF alpha agent. The proportion that achieved a clinical response at 30 days, 90 days and 1 year was 65.7%, 60% and 31.4% respectively, while the corresponding proportions in remission were 40%, 37.1% and 22.9%. The cumulative risk of requiring surgery was 40.4% at one year and 59.3% at two years with a median time to surgery of 22 months (range 0.5-84 months). Patients who were steroid refractory, or dependent, prior to starting tacrolimus were more likely to have surgery (P = 0.006), while patients who were able to achieve or maintain a clinical response with tacrolimus by 90-days were less likely (P = 0.004). Conclusions: Tacrolimus is able to induce a clinical response in a third and remission in a fifth of medically refractory IBD patients at one year. A 90 day therapeutic trial is worthwhile in difficult to treat patients.

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Pyoderma gangrenosum of the breast treated with intravenous immunoglobulin.

Sinnya S, Hamza S.
(Sinnya) Princess Alexandra Hospital, 199 Ipswich Road Woolloongabba, QLD 4102, Australia
(Hamza) University of Western Australia, Fremantle Health Services, Alma Street Fremantle, WA 6160, Australia

S. Sinnya, Research Assistant and Honourary, Dermatology Registrar, Unit 25/246 Arthur Street, Newstead, Brisbane, 4006, Australia. E-mail: s.sinnya@uq.edu.au

Background: Pyoderma gangrenosum is a rare neutrophilic dermatosis which leads to necrotic and painful skin ulceration. PG of the breast is extremely rare with 32 documented cases in the current literature. Delay in diagnosis worsens scarring as the ulcers are rapidly expanding, painful and usually slow to heal. Case presentation: We present a case of pyoderma gangrenosum of the breast in a patient with associated rheumatoid arthritis which was initially diagnosed as an infected breast ulcer and later successfully treated with systemic steroids and intravenous immunoglobulin (IVIG).

Conclusion: Even though PG of the breast has been gaining increased recognition over the past two decades, this has been more common in the post-surgical setting. This case highlights the need to consider PG as a differential diagnosis when faced with unusual cases of breast ulceration and the importance of multidisciplinary approach for effective treatment of this condition.

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Management of pancreatic collections with a novel endoscopically placed fully covered self expanding metal stent: The australian experience.

(Chandran, Efthymiou, Vaughan) Department of Gastroenterology Austin Health, Australia (Kaffes)
RPA, NSW, Australia (Kwan) Westmead, NSW, Australia (Chen) Flinders Medical Centre, SA, Australia (Murray) Pindara Private Hospital, QLD, Australia (Williams) St. Vincent's Hospital, NSW, Australia (Welch) Townsville Hospital, QLD, Australia (Chong) Fremantle Hospital, WA, Australia (Gupta) Princess Alexandra, QLD, Australia (Tam) Lyel McEwin, SA, Australia (Devereaux) RBH, QLD, Australia (Nguyen) North Eastern Community Hospital, Australia

S. Chandran, Department of Gastroenterology Austin Health, Australia

Introduction: Since its first description over a decade ago endoscopic ultrasound guided drainage has increasingly become the preferred method in the management of pancreatic fluid collections (PFCs). The aim of our study was to assess the use of a recently developed fully covered metal stents (FCSEMS) for the management of PFCs nationally, including their ease of use compared to plastic stent insertion and its associated complications. Methods: Utilizing the Pyramid database on stent usage nationally we were able to identify practicing endosonographers who had inserted these novel covered metal stent into PFCs. A standardized datasheet capturing patient demographics, aetiology of PFCs, technique utilized for insertion, ease of use compared with plastic stenting and early/late complications was created. End points included their ease of use compared to plastic stent insertion, rates of collection resolution, in addition to peri and post procedural complications. Results: A total of 42 stents were inserted into 39 patients over 14months. Demographics of our cohort were 27 males: 12 females, mean age 50 yrs (range 10 - 82), and aetiology of PFC were predominantly gallstone and alcohol induced pancreatitis (11 and 15 patients respectively). The mean size of PFC was 11 cm (range 6-17 cm) and mean duration of cyst maturation was 16 weeks (range 3-104 weeks). Successful insertion occurred in all cases 42/42 (100%). Early complications included sepsis (2 pts), blocked stent (1 pt), bleeding requiring transfusion (1 pt), and stent migration (1 pt). Late complication was stent in growth precluding stent removal. Resolution of PFC occurred in 24/27 (88.9%) of the stents removed thus far with the remaining three patients requiring surgical intervention. Conclusion: This is the largest audit of a FCSEMS to manage PFCs. Our initial findings suggest that these stents in comparison to the previous standard of pigtail stents are easier to insert, have few complications with the majority experiencing PFC resolution.
Association of IFNL3 polymorphisms with fibrosis progression in viral and non-viral chronic liver disease.


(Eslam, Leung, Douglas, Suppiah, George, Ahlenstiel) Storr Liver Unit, Westmead Millennium Institute and Westmead Hospital, University of Sydney, NSW, Australia (Leung, Suppiah, Stewart, Booth) Institute of Immunology and Allergy Research, Westmead Hospital and Westmead Millennium Institute, University of Sydney, NSW, Australia (Berg) Medizinische Klinik m.S. Hepatologie, Gastroenterologie, Charite, Campus Virchow-Klinikum, Universittsmedizin, Berlin, Germany (Berg) Department of Hepatology, Clinic for Gastroenterology and Rheumatology, University Clinic Leipzig, Leipzig, Germany (Irving) NIHR Biomedical Research Unit, Gastroenterology and the Liver, University of Nottingham, Nottingham, United Kingdom (Mangia) Division of Hepatology, Ospedale Casa Sollievo della Sofferenza, IRCCS, San Giovanni Rotondo, Italy (Sheridan) Institute of Cellular Medicine, Medical School, Newcastle University, Newcastle-upon Tyne, United Kingdom (Abate) Liver Physiopathology Lab, Department of Internal Medicine, University of Turin, Turin, Italy (Weltman) Department of Gastroenterology and Hepatology, Nepean Hospital, Sydney, Australia (Spengler) Department of Internal Medicine I, University of Bonn, Sigmund-Freud- Strasse, Bonn, Germany (Mollison) Fremantle hepatitis services, Sydney, Australia (Cheng) Department of Gastroenterology and Hepatology, Royal Perth Hospital, Australia (Dore) Kirby Institute, University of New South Wales, Sydney, Australia (Dore) St Vincent's Hospital, Sydney, Australia (Powell) Princess Alexandra Hospital, Department of Gastroenterology and Hepatology, Woolloongabba, QLD, Australia (Powell) University of Queensland, School of Medicine, Princess Alexandra Hospital, Woolloongabba, QLD, Australia (Riordan) Gastrointestinal and Liver Unit, Prince of Wales Hospital, University of New South Wales, Sydney, Australia

M. Eslam, Storr Liver Unit, Westmead Millennium Institute and Westmead Hospital, University of Sydney, NSW, Australia

Background and aim: Fibrosis is a common consequence of chronic liver disease irrespective of etiology. Whether IFNL3 polymorphisms influence hepatic inflammation and fibrosis progression remains unclear, particularly for disease etiologies other than chronic hepatitis C (CHC). We examined the impact of IFNL3 polymorphisms on hepatic inflammation and fibrosis in a large cohort of patients with viral (CHC and chronic hepatitis B [CHB]) and non-viral liver diseases. Methods: 2408 patients were included: CHC (N = 1914), CHB (N = 264), and NASH (N = 230). Of these, 1214 patients with CHC had an accurate estimate of the date of infection and a liver biopsy, which enabled assessment of the putative fibrosis progression rate (FPR). A further 106 patients with CHC had paired liver biopsies, a median of 5.01 years apart. All patients were genotyped for IFNL3 polymorphisms rs12979860 and rs8099917. Results: CHC: At baseline biopsy, patients with IFNL3 rs12979860 CC and rs8099917 TT had significantly higher portal inflammation (OR: 1.8, 95% CI: 1.42, 2.28, P = 0.001 and OR: 1.49 [1.18-1.88], P = 0.001) and liver fibrosis (OR: 1.63, [1.29-2.07], P = 0.0001 and OR: 1.31 [1.04-1.65], P = 0.02), respectively. For the FPR analysis, by Cox regression, the adjusted hazards ratio for rs12979860 CC and rs8099917 TT with hepatic fibrosis was 1.5 (1.21-1.86) and 1.43 (1.13-1.80), respectively (P < 0.003 for both). The paired biopsy analysis revealed an increase in the frequency of fibrosis progression in patients with rs8099917 TT compared to non-TT genotypes (53% vs 30%, P = 0.02). For CHB, rs12979860 CC was independently correlated with hepatic inflammation (OR: 4.19, [1.55-11.31], P = 0.005), and fibrosis (2.12, [1.027-4.78], P = 0.04). rs8099917 correlated only with hepatic inflammation (OR: 3.03, [1.09-9.2], P = 0.03). For NASH, rs12979860 CC was independently correlated with moderate/severe portal inflammation (OR: 2.9, [1.21-6.93], P = 0.01). Conclusion: Responder polymorphisms of IFNL3 are associated with increased hepatic inflammation and fibrosis in both viral and non-viral liver disease and may help to identify those at risk for disease progression.
SPARC affects colorectal tumourigenesis by altering tumour microenvironment.

Fu SK, Lloyd FP, et al.
(Fu, Lloyd, Klopcic, Lawrance) Centre for Inflammatory Bowel Diseases, UWA, Fremantle Hospital, Fremantle, WA, Australia (Forrest) Department of Histopathology, Fremantle, WA, Australia
S.K. Fu, Centre for Inflammatory Bowel Diseases, UWA, Fremantle Hospital, Fremantle, WA, Australia

Introduction: Colorectal cancer (CRC) is common but its frequency could be reduced with improved understanding of its pathogenesis. The aim of this study was to determine the potential of secreted protein, acidic and rich in cysteine (SPARC) to impact on the development of colorectal tumours by identifying differences in gene expression levels and inflammatory cell infiltration in a chronic inflammation-induced model of tumourigenesis in SPARC knockout (KO) and wild-type (WT) mice.

Materials and Methods: Colitis-associated tumourigenesis in SPARC knockout (KO) and wild-type (WT) mice was promoted by a single intraperitoneal injection of azoxymethane prior to three cycles of 7 days of dextran sodium sulphate. Tumour size, number and overall tumour burden was assessed endoscopically and histologically. Immunofluorescent (IF) assessment of CD4, CD8a, CD68, F4/80 and Ki67 were performed on tumours. Tumours of similar size were harvested from both models at week 11 and processed for microarray analysis. Whole-genome microarray (Illumina BeadChip, MouseRef 8 v2) compared gene expression in tumours from both genotypes.

Results: All tumours were dysplastic adenomas with high-grade dysplasia and KO animals had more tumours than WT animals (p = 0.005) and no differences were detected in tumour sizes (p = 0.62). IF assessment of the inflammatory cell infiltrates showed significantly fewer CD4-positive, CD8a-positive and CD68-positive cells in KO tumours when compared to WT tumours (all p < 0.0005) but not F4/80 (p = 0.12). KO tumours also had significantly lower numbers of Ki-67+ve cells (p < 0.0005). Microarray analysis identified 6 differentially regulated genes between KO and WT mice (all p < 0.05), 4 were decreased in KO tumours and are involved in the regulation of the immune response (Ifit2, Ido), cell growth and proliferation (Areg, Hoxa7). Two genes were increased in KO tumours with one associating with apoptosis (Erdr1) and one with an unknown function (Hamp2).

Conclusion: The increase in tumour numbers in the absence of SPARC may be a result of reduced immunosurveillance, as suggested by a reduction in CD4-positive and CD8-positive cells (T-helper cells) as well as CD68-positive cells (activated macrophages), in addition to the reduction in gene expression of Ifit2 and Ido (immune regulation). Despite less Ki67-positive cells and lower expression of genes related to cell growth and proliferation (Areg and Hoxa7) together with an increase in a proapoptotic gene (Erdr1) in KO tumours, however, no differences were detected in the tumour sizes between WT and KO animals.

Incidence of latent tuberculosis in an Australian IBD population.

Mill J, Lawrance I.
(Mill, Lawrance) Centre for Inflammatory Bowel Diseases, Fremantle Hospital, WA, Australia
(Lawrance) University Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia

Background: The incidence of tuberculosis (TB) in Australian-born Caucasians is very low at 5.8/100,000, but much higher in both the indigenous population and people born overseas. The use of anti-TNF agents, and even steroids and the thiopurine drugs, are associated with reactivation of TB and thus screening of IBD patients for latent TB prior to treatment is crucial. The aim of this study was to determine the incidence of latent and active TB in the IBD population at a single tertiary referral centre.
hospital. Methods: All subjects were IBD patients of the Centre for Inflammatory Bowel Diseases, Fremantle Hospital. Patient demographics were collected including ethnicity, country of birth, parents' country of birth, smoking history, medication use and the Montreal classification. Each patient was screened for TB at a routine clinic visit by a detailed medical history, physical examination and interferon gamma release assay (Quantiferon gold). Chi-squared test or ANOVA non-parametric t-test were used with significance indicated by p < 0.05. Results: 935 IBD patients were included and 42 (4.5%) patients had a positive Quantiferon gold result suggesting latent TB. No cases of active TB were identified. No significant differences were identified between patients with a positive or negative Quantiferon gold for country of birth, smoking history, medication use or any other demographic factor. A detailed medical history was, however, able to determine TB exposure in many of the Quantiferon gold positive patients. Conclusion: The incidence of latent TB in a Western Australian IBD population is many folds higher than expected. This was not due to the migrant population but rather potentially due to greater mobility of the Australian-born patients than in previous generations. This suggests that universal screening of all IBD patients by detailed exposure history, examination and Quantiferon Gold should be done prior to the commencement of any immnosuppressing medication, and repeated following any potential exposure.

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Early experience on treatment with direct acting antiviral drugs in chronic hepatitis C-interim analysis in Western Australian tertiary centres.

(Rao, Kontorinis, Tarquinio, Kong, Nazareth, Cheng) Departments of Gastroenterology and Hepatology, Royal Perth Hospital, Perth, WA, Australia (Mollison, Galhenage, Totten) Fremantle Hospital, Perth, WA, Australia (Macquillan, Adams, Jeffrey, Vallve) Sir Charles Gairdner Hospital, Perth, WA, Australia

S. Rao, Departments of Gastroenterology and Hepatology, Royal Perth Hospital, Perth, WA, Australia

Background: Direct acting antiviral agents (DAAs) - Telaprevir (TVP) and Boceprevir (BOC) have been approved for the treatment of chronic hepatitis C-genotype 1 patients since April 2013. We report our early experience with DAAs in 3 tertiary hospitals in patients treated through early access and patient familiarization programs. Aims: To evaluate our experience with Telaprevir and Boceprevir with reference to (1) virological response (2) host and viral factors affecting response (3) side effect profile. Methods: A retrospective descriptive analysis of patients treated with DAAs at 3 tertiary hospitals. Data collected from review of medical records included demographics, IL28B genotype, viral response and side effects. Results: To date 86 patients were treated, of whom 72% were males. Mean age was 50 years. 55% were treatment naive. IL28B- homozygous CC genotype (rs12979860) was noted in 30.2% of the patients. In treatment naive patients with IL28B CC genotype (rs12979860), 66.6% treated with Telaprevir and 83% with Boceprevir achieved SVR. Conclusions: Treatment with DAAs was well tolerated with low discontinuation rate. Rash is common with TVP and dysgeusia in BOC group. Although mild anaemia is more common with BOC, Hb < 85 g/L is more common with TVP. Ribavirin dose reduction is common. More patients in BOC than TVP groups received response guided therapy. (Table Presented).

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Direct acting antiviral drugs in chronic hepatitis C and renal toxicity.

(Rao, Kontorinis, Tarquinio, Kong, Nazareth, Cheng) Departments of Gastroenterology and Hepatology, Royal Perth hospital, Perth, WA, Australia (Mollison, Galhenage, Totten) Fremantle
Background: Direct acting antiviral agents (DAAs) - Telaprevir (TVP) and Boceprevir (BOC) have been approved for the treatment of chronic hepatitis C-Genotype 1 patients since April 2013. In the registration trials, renal dysfunction was not observed. Recent preliminary reports suggested that the incidence of renal impairment may be as high as 5%, more common in older patients, and in patients with cirrhosis, diabetes and/or hypertension. We report our early experience with DAAs in 3 tertiary hospitals in patients treated through early access and patient familiarization programs. Aims: To determine the incidence and severity of renal dysfunction in patients treated with DAAs. Methods: Retrospective descriptive analysis of patients treated with DAAs at 3 tertiary centres. Data collected from review of medical records included demographics, viral markers, co-morbid conditions & concurrent medications, biochemical investigations and urinalysis. Results: 86 patients were treated, of whom 72% were males and mean age was 50 years. 34 patients received TVP and 52 BOC. 40.6% of patients had cirrhosis (hepascore >0.90). 47% of patients are currently receiving treatment in the TVP group and 11.5% in the BOC group. 5.8% of patients discontinued treatment in TVP group and 5.7% in BOC group. Only 1 male patient with cirrhosis, aged 75 years, in the Telaprevir cohort developed sustained drop in eGFR of 40% from baseline. He had no significant comorbidities and was not on any concurrent medications. Baseline creatinine was 90 umol/L (normal: 60-110 umol/L) and eGFR >60 ml/min/1.73 m2 (Modification of Diet in Renal Disease formula). Creatinine was noted to rise during week 11 of treatment, peaking at 167 umol/L; eGFR dropped to 35 ml/min/1.73 m2. Urinalysis and renal ultrasonography were normal. Ribavirin dose was reduced from 1200 mg to 800 mg, Peginterferon to 150 mcg from 180 mcg and Telaprevir was continued at 750 mg thrice daily for a further week. An additional patient with cirrhosis, aged 55 years, in the TVP group was noted to have renal impairment during week 12 of treatment with a 40% rise in creatinine and 26% drop in eGFR from baseline. In both patients spontaneous improvement in renal function was noted over the next 2 to 4 weeks following cessation of TVP, with subsequent normalization of creatinine and eGFR to pretreatment levels. In the Boceprevir cohort, 2 patients, aged 65 & 66 years, both with cirrhosis who had normal pre-treatment creatinine and eGFR, were noted to have self-resolving acute kidney injury. One patient developed a 20% rise in creatinine and 15% drop in eGFR from baseline at week 12 of treatment. The other patient developed a 23% rise in creatinine and 10% drop in eGFR from baseline at week 24 of treatment. In both patients renal function spontaneously improved within 1 to 3 weeks. Conclusion: Treatments with DAAs were well tolerated with low discontinuation rate. Renal dysfunction can be associated with triple therapy and may require ribavirin dose reduction. All 4 patients who developed DAA associated nephrotoxicity had cirrhosis. In TVP treated patients, renal impairment occurred during week 11 and week 12 of treatment and resolved after completion of 12 weeks of therapy.


Using a wiki platform to promote guidelines internationally and maintain their currency: Evidence-based guidelines for the nutritional management of adult patients with head and neck cancer.

Brown, T.: teresa_brown@health.qld.gov.au
Brown, T.: Department of Nutrition and Dietetics, Royal Brisbane and Women's Hospital, Level 2 James Mayne Building, Butterfield Street, Herston, QLD, Australia, 4029, teresa_brown@health.qld.gov.au
Brown, T.: Department of Nutrition and Dietetics, Royal Brisbane and Women's Hospital, Brisbane, QLD, Australia Findlay, M.: Department of Nutrition and Dietetics, Royal Prince Alfred Hospital, Sydney, NSW, Australia von Dincklage, J.: Cancer Council Australia, Sydney, NSW, Australia
Background: The present study describes the development of evidence-based practice guidelines for the nutritional management of adult patients with head and neck cancer using a wiki platform to enable wide international stakeholder consultation and maintain currency. Methods: A dietitian steering committee and a multidisciplinary steering committee were established for consultation. Traditional methods of evidence-based guideline development were utilised to perform the literature review, assess the evidence and produce a draft document. This was transferred to a wiki platform for stakeholder consultation and international endorsement processes in Australia, New Zealand and the UK. Data were collected on website traffic utilising Google Analytics. Results: In addition to broad stakeholder consultation through the steering committees, an additional twenty comments were received via the wiki by twelve individuals covering six different professions from three different countries, compared to four comments by e-mail. The guidelines were subsequently endorsed by the dietetic associations of Australia, New Zealand and the UK. During a 4-month period monitoring the use of the guidelines, there were 2303 page views to the landing page from 33 countries. The average number of pages accessed per visit was five and the duration of time spent on the website was approximately 6 min. Conclusions: Using a wiki platform for guideline development and dissemination is a successful method for producing high-quality resources that can undergo wide international stakeholder review and include open public consultation. This can replace conventional methods whereby guidelines can quickly become outdated. (PsycINFO Database Record (c) 2014 APA, all rights reserved) (journal abstract).

Hamstring pain and muscle strains following anterior cruciate ligament reconstruction: a prospective, randomized trial comparing hamstring graft harvest techniques.
Department of Orthopaedics, Fremantle Hospital, Fremantle, Western Australia, Australia.

There is limited information in the literature regarding hamstring pain and muscle strains in patients following anterior cruciate ligament (ACL) reconstruction using hamstring autograft. We sought to investigate whether dividing hamstring tendons distal to the musculotendinous junction rather than forcefully stripping tendons away from the muscle belly during graft harvest resulted in a lower incidence of hamstring pain, muscle strains, and leg flexion strength deficit following commencement of sport-specific training postoperatively. Patients were randomized to either the "Cut" or "Push" groups of hamstring tendon harvesting. All other operative techniques were uniform. A total of 34 (cut = 20, push = 14) patients had a mean follow-up of 30 months, and assessments were conducted by a blinded single practitioner. A customized hamstring strain questionnaire and visual analogue pain score provided information for the study's primary focus: evaluation of postoperative hamstring pain and muscle strains. Leg flexion strength was also measured and a full knee assessment was conducted. The Cincinnati sports activity rating scale (SARS) was used to account for varying degrees of sporting participation and intensity since reconstruction. The "Cut" group's mean visual analogue
score was 10.05 mm, significantly lower than the "Push" group (24.66 mm, p = 0.0398). The Cut group also recorded a significant reduction in the incidence of hamstring strains following ACL reconstruction (5/20 patients 25%) compared with the Push group (7/14 patients 50%, p = 0.045). There was no difference in leg flexion strength between the groups. Of the patients who reported hamstring strains, there was no significant difference in the mean Cincinnati SARS between the groups, nor any difference in overall knee function. The incidence of hamstring pain and muscle strains was significantly reduced in patients receiving the "cut" technique of harvesting hamstring tendons in ACL reconstruction surgery, a difference that was not attributable to a lower level of sporting activity.

Contrast-enhanced magnetic resonance angiography of the peripheral arteries: Technique, tips, pitfalls and problems.
Department of Radiology, Fremantle Hospital and Health Service, Fremantle, Western Australia, Australia.
Contrast-enhanced magnetic resonance angiography is a reliable way to assess peripheral vascular disease. This article reviews the basic physics behind this technique and discusses our institution's experience with regard to the clinical role, recent advances in image acquisition and use of contrast agents. Problems that can affect image quality and interpretation are also highlighted. 2013 The Authors. Journal of Medical Imaging and Radiation Oncology 2013 The Royal Australian and New Zealand College of Radiologists.
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CT features of acute aortic pathology.
Hocking D, Gupta A, et al.
(Hocking, Gupta) Fremantle Hospital, Fremantle, WA, Australia (Ong) Royal Perth Hospital, Perth, WA, Australia
D. Hocking, Fremantle Hospital, Fremantle, WA, Australia
Learning Objectives: Design a poster that succinctly describes the features and pitfalls of acute aortic pathology, which aims to improve the ability and confidence of the trainee in interpreting such findings. Background: Acute aortic pathology is an uncommon condition1,4 that may be encountered by radiology trainees whilst on-call and is recognised by the RANZCR as a "key condition."2 Prompt and accurate diagnosis is critical to the provision of appropriate management as the mortality in the acute setting is high1,3,4. Lack of understanding can generate undue anxiety for the trainee. Imaging Findings: Computed tomographic (CT) studies are selected retrospectively from the Picture Archiving and Communication System (PACS) over a period of 12 months. All cases performed as a thoracic angiogram study are reviewed and those cases which demonstrate teaching points, posed diagnostic difficulty and/or facilitated understanding of the disease process are identified. Imaging findings are categorised into spontaneous, traumatic and iatrogenic conditions. Typical aortic dissection, intramural haematoma, and penetrating atherosclerotic ulcer are presented in the spontaneous category3. Traumatic injuries, including aortic transection and tears of the intima or adventitia, will also be presented4. Iatrogenic injury complicating conventional surgical5 and endovascular intervention6 may also occur, including anastomotic leak or breakdown and dissection, and are discussed separately. Complications such as haematoma, pseudo-aneurysm formation and aortic rupture may occur in any of these categories and are presented in the context of the underlying pathology3,4,5,6. Technical and anatomical artifacts may simulate disease4,6, which are also presented as imaging pitfalls. Conclusion: Acute aortic pathology is an uncommon condition which results in significant mortality if missed. This educational poster aims to alleviate undue anxiety in the trainee radiologist by presenting...
Ossicular fixation—A pictorial review of CT temporal bone findings.
Khangure S, Wood B.
(Khangure, Wood) Fremantle Hospital, Perth, WA, Australia
S. Khangure, Fremantle Hospital, Perth, WA, Australia

Learning Objectives: To discuss the causes of ossicular fixation, illustrate the associated CT temporal bone findings and highlight the diagnostic value of multiplanar reformats. Background: The purpose of the ossicles in the middle ear is to facilitate hearing by conducting vibration of the tympanic membrane to the oval window. Failure of this system can result in conductive hearing loss. Abnormalities of the ossicles that result in conductive hearing loss can be broadly classified into 'fixation' or 'interruption' groups. Imaging Findings: This pictorial review illustrates the CT temporal bone findings seen in association with ossicular fixation. Congenital and acquired conditions are discussed. The diagnostic value of multiplanar reformats, particularly sagittal and coronal oblique planes are highlighted in selected conditions. Conclusion: Many causes of conductive hearing loss due to ossicular fixation can be diagnosed with CT. Multiplanar reformats are helpful for diagnosis of selected conditions.

Should the tip-apex distance (TAD) rule be modified for the proximal femoral nail antirotation (PFNA)? A retrospective study.
Nikoloski AN, Osbrough AL, et al.
(Nikoloski) Fremantle Hospital Orthopaedic Unit, Fremantle Hospital, Level 6, B Block, Alma Street, Fremantle, Western Australia 6160, Australia.
A.N. Nikoloski

Unstable proximal femoral fractures are common and challenging for the orthopaedic surgeon. Often, these are treated with intramedullary nails. The most common mode of failure of any device to treat these fractures is cut-out. The Synthes proximal femoral nail antirotation (PFNA) is unique because it is the only proximal femoral intramedullary nail which employs a helical blade in lieu of a lag screw. The optimal tip-apex distance is 25 mm or less for a dynamic hip screw. The optimal blade tip placement is not known for the PFNA. The aim of this study is to determine if the traditional tip-apex distance rule (<25 mm) applies to the PFNA. A retrospective study of all proximal femoral fractures treated with the PFNA in Western Australian public teaching hospitals between August 2006 and October 2007 was performed. Cases were identified from company and theatre implant use records. Patient demographic data was obtained from hospital records. Fractures were classified according to Arbeitsgemeinschaft fur Osteosynthesefragen/Association for the Study of Internal Fixation. Fracture reduction, distal locking type and blade position within the head (tip-apex distance and Cleveland zone) were recorded from the intraoperative and immediate postoperative radiographs. Postoperative radiographs obtained in the routine treatment of patients were studied for review looking primarily for cut-out. Clinical outcomes were measured with the Oxford hip score. One hundred eighty-eight PFNAS were implanted during the study period, with 178 cases included in this study. Ninety-seven patients could be followed up clinically. There were 18 surgical implant-related failures (19%). The single most common mode of failure was cut-out in six cases (6.2%). Three cut-outs (two medial perforation and one varus collapse) occurred with tip-apex distance (TAD) less than 20 mm. There was no cut-out in cases where the TAD was from 20-30 mm. There were three implant-related failures (nail fracture, missed nail and loose locking screw), four implant-related femoral fractures, two non-unions, two delayed unions and one loss of reduction. The PFNA is a suitable fixation device for the treatment of
unstable proximal femoral fractures. There were still a relatively large number of cut-outs, and the tip-apex distance in the failures showed a bimodal distribution, not like previously demonstrated with dynamic hip screw. We propose that the helical blade behaves differently to a screw, and placement too close to the subchondral bone may lead to penetration through the head.

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Bell L, Hung J, et al.
(Bell, Davis) Department of Endocrinology, Princess Margaret Hospital, Roberts Road, Subiaco, WA 6008, Australia (Hung, Thompson, McQuillan) School of Medicine and Pharmacology, Sir Charles Gairdner Hospital Unit, University of Western Australia, WA, Australia (Knuiman, Divitini, Hunter) School of Population Health, University of Western Australia, WA, Australia (Beilby) School of Pathology and Laboratory Medicine, University of Western Australia, WA, Australia (Mollison) School of Medicine and Pharmacology, Fremantle Hospital Unit, University of Western Australia, WA, Australia (Beilby) Pathwest, QEII Medical Centre, WA, Australia (Hunter) Busselton Population Medical Research Institute, Sir Charles Gairdner Hospital, Perth, WA, Australia
E. Davis, Department of Endocrinology, Princess Margaret Hospital, Roberts Road, Subiaco, WA 6008, Australia. E-mail: elizabeth.davis@health.wa.gov.au

Aim This study aims to analyse the continuous relationship of each cardiometabolic risk factor with body mass index (BMI) and waist circumference percentiles in a population-based sample of children.

Methods A cross-sectional sample of 996 school children aged 6-16.9 years in Busselton, Western Australia, (2005-2007) had anthropometry and fasting blood tests for total cholesterol, high density lipoprotein, low density lipoprotein, triglycerides, glucose, insulin, high-sensitive C-reactive protein, liver function tests and adiponectin. Age- and menarche (for girls)-adjusted means of each risk factor were related to BMI and waist circumference centiles across the full normal-overweight-obese range.

Results The correlations between BMI and waist circumference (boys 0.91 and girls 0.91) and between BMI z-score and waist z-score (boys 0.80 and girls 0.82) were high. An increase in insulin across all centile groups (for BMI and waist circumference) was found in both sexes. An increase was found for diastolic blood pressure and systolic blood pressure z-score, high density lipoprotein, high-sensitive C-reactive protein, alanine transaminase and gamma-glutamyltransferase in only the centile groups >85% for BMI and waist circumference for both sexes. Mixed and sex-discordant results were found for triglycerides, adiponectin and glucose. Conclusion There are important differences in the relationships between increasing BMI/adiposity, and each comorbidity and these relationships can differ between boys and girls. This information has implications for screening and management of adiposity-related cardiometabolic risk factors in children and for public health initiatives to reduce future burden of cardiovascular disease. 2013 Paediatrics and Child Health Division (Royal Australasian College of Physicians).

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Rasch analysis of anxiety scales in Parkinson's disease.
(Forjaz) National School of Public Health, Carlos III Institute of Health, Madrid, Spain (Martinez-Martin) REDISSECC, Spain (Dujardin) Alzheimer Disease Research Unit. CIEN Foundation, Carlos III Institute of Health, Alzheimer Center Reina Sofia Foundation, Madrid, Spain (Marsh) CIBERNED, Spain (Marsh) Neurology and Movement Disorders Unit, Lille University Hospital, Lille, France (Richard) Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, United States (Richard) Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, United States (Starkstein) Department of Neurology, University of Rochester School of Medicine and
Objective: Anxiety is a common non-motor symptom in Parkinson's disease (PD). This study analyzed the measurement properties of three frequently used anxiety scales in PD: the Beck Anxiety Inventory (BAI), the Hamilton Anxiety Rating Scale (HARS), and the Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A). Method: The Rasch model was applied to a multicenter international cohort of 342 patients and assessed the following aspects: fit to the Rasch model, unidimensionality, reliability, response category ordering, item local independence, differential item functioning, and scale targeting. Results: In their original form, the BAI, HARS, and HADS-A, did not fit the Rasch model. A good fit to the Rasch model was only found after significant modifications, including rescoring some items and deleting those failing to fit the model. For the BAI and HADS-A, these adjustments resulted in unidimensionality. The HARS was not unidimensional and separate analyses were performed for its psychic and somatic subscales. Whereas the somatic anxiety subscale fit the Rasch model, this was achieved for the psychic anxiety subscale after modifications. Conclusion: None of the currently used anxiety scales display satisfactory measurement properties for assessing anxiety in PD. The results suggest the need to develop a new disease-specific scale for measuring anxiety in PD. 2013 Elsevier Inc.

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The effects of oral contraception on post-exercise interleukin-6 and hepcidin.

Sim M, Dawson B, et al. (Sim, Dawson, Landers, Peeling) School of Sport Science, Exercise and Health, University of Western Australia, Australia (Swinkels, Tjalsma) Department of Laboratory Medicine, Laboratory of Genetic Endocrine and Metabolic Diseases, Radboud University Medical Centre, Nijmegen, Netherlands (Yeap, Trinder) School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia (Trinder) Western Australian Institute for Medical Research, Nedlands, Australia (Peeling) Western Australian Institute of Sport, Australia

Purpose: Elevations in the master iron regulatory hormone hepcidin have been shown to reduce iron absorption at the gut and iron recycling by the macrophages. Specifically, the inflammatory cytokine interleukin-6 (IL-6) has been demonstrated to be one of the main regulators of hepcidin production (especially after exercise). Previously, hepcidin levels have been reported to peak 3 h post-exercise, possibly altering iron metabolism during this time. Such a response, in combination with poor dietary iron intake and/or menstrual blood loss, may explain the high incidence of iron deficiency amongst female athletes. However, recent animal studies have reported that estradiol supplementation may attenuate hepcidin production. Furthermore, progesterone has also been shown to have an inverse relationship with IL-6. To this end, since both hormones are commonly found in the female oral contraceptive pill (OCP), the effect of exogenous estradiol and progestrogen supplementation on post-exercise IL-6 and hepcidin levels was investigated. Methods: Ten active female current OCP users completed two 40 min treadmill running trials at 75% of their pre-determined peak oxygen uptake velocity (vVO2peak). These trials were randomly performed in two specific phases of an OCP regulated menstrual cycle: (a) Day 2-4, representing a hormone-free withdrawal period (D- 0); (b) Day 12-14, representing the end of the first week of active hormone therapy (D+7). Venous blood samples were drawn pre-, post- and 3 h post-exercise. Results: In both trials, serum IL-6 was significantly elevated (p < 0.05) immediately post-exercise, while serum hepcidin was significantly elevated (p < 0.05) 3 h post-exercise, with no significant differences recorded between trials. Conclusion: These findings suggest that exogenous estradiol and progestrogen supplementation does not attenuate
exercise induced IL-6 or hepcidin production during hormone-deplete (D-0) and hormone-replete phases (D+7) of an OCP regulated menstrual cycle. It appears that any exercise induced increases in IL-6 may override any suppressive effects of estrogen on hepcidin production. As such, future studies looking to investigate similar post-exercise responses may not need to 'control' for different phases of the menstrual cycle, provided participants are current OCP users.

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**Plasma total homocysteine is associated with abdominal aortic aneurysm and aortic diameter in older men.**
Wong YYE, Golledge J, et al.
(Wong, Flicker) Western Australian Centre for Health and Ageing, Centre for Medical Research, Western Australian Institute for Medical Research, Perth, WA, Australia (Wong, Flicker, McCaul, Yeap) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia (Van Bockxmeer) School of Pathology and Laboratory Medicine, University of Western Australia, Perth, WA, Australia (Norman) School of Surgery, University of Western Australia, Perth, WA, Australia (Wong, Flicker) Department of Geriatric Medicine, Royal Perth Hospital, Perth, WA, Australia (Hankey) Department of Neurology, Royal Perth Hospital, Perth, WA, Australia (Van Bockxmeer) Department of Clinical Biochemistry, Royal Perth Hospital, Perth, WA, Australia (Golledge) Vascular Biology Unit, School of Medicine and Dentistry, James Cook University, Townsville, QLD, Australia (Yeap) Department of Endocrinology and Diabetes, Fremantle Hospital, Perth, WA, Australia
Y.Y.E. Wong, PO Box X2213, Perth, WA 6847, Australia. E-mail: ewong@meddent.uwa.edu.au

Objective: This study was conducted to determine whether plasma total homocysteine (tHcy) and the methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism are associated with abdominal aortic aneurysm (AAA) and aortic diameter. Methods: This was a cross-sectional study set in Western Australia of 4248 community-dwelling men aged 70 to 88 years. Infrarenal aortic diameter was measured using ultrasound scan, tHcy was measured by immunoassay, and MTHFR 677T polymorphism was detected by polymerase chain reaction. Results: Adjusted multinomial logistic regression analysis showed the odds of having an AAA (aortic diameter >=30 mm) for men with high tHcy (>=15 mumol/L) compared with those with normal tHcy (<15 mumol/L) was 1.45 (95% confidence interval [CI], 1.10-1.91). Every 5-mumol/L increment in tHcy was associated with 0.15-mm (95% CI, 0.01-0.28 mm) increase in mean aortic diameter. The tHcy concentration was higher in MTHFR TT homozygote individuals than in wild-type CC individuals. There was, however, no apparent association between MTHFR C677T polymorphism with AAA (TT vs CC genotype: odds ratio, 0.97; 95% CI, 0.72-1.31) or aortic diameter (TT vs CC genotype: mean increment of 0.01 mm; 95% CI, -0.63 to 0.65 mm). Conclusions: Elevated tHcy is associated with the presence of AAA in older men. There is also a positive dose-response relationship between tHcy and abdominal aortic diameter. Longitudinal studies and clinical trials of lowering tHcy are required to assess whether these relationships are causal. 2013 by the Society for Vascular Surgery.
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**Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: A systematic review and analysis.**
Fowkes FGR, Rudan D, et al.
(Fowkes, Rudan, Rudan, Williams) Centre for Population Health Sciences, University of Edinburgh, Teviot Place, Edinburgh EH8 9AG, United Kingdom (Rudan) University Hospital Dubrava, Zagreb, Croatia (Aboyans) Department of Cardiology, Dupuytren University Hospital, Limoges, France (Aboyans) INSERM U1094, Tropical Neuro-epidemiology, Limoges, France (Denenberg, Criqui) Department of Family and Preventive Medicine, University of California, San Diego, CA, United States
Background Lower extremity peripheral artery disease is the third leading cause of atherosclerotic cardiovascular morbidity, following coronary artery disease and stroke. This study provides the first comparison of the prevalence of peripheral artery disease between high-income countries (HIC) and low-income or middle-income countries (LMIC), establishes the primary risk factors for peripheral artery disease in these settings, and estimates the number of people living with peripheral artery disease regionally and globally. Methods We did a systematic review of the literature on the prevalence of peripheral artery disease in which we searched for community-based studies since 1997 that defined peripheral artery disease as an ankle brachial index (ABI) lower than or equal to 0.90. We used epidemiological modelling to define age-specific and sex-specific prevalence rates in HIC and in LMIC and combined them with UN population numbers for 2000 and 2010 to estimate the global prevalence of peripheral artery disease. Within a subset of studies, we did meta-analyses of odds ratios (ORs) associated with 15 putative risk factors for peripheral artery disease to estimate their effect size in HIC and LMIC. We then used the risk factors to predict peripheral artery disease numbers in eight WHO regions (three HIC and five LMIC). Findings 34 studies satisfied the inclusion criteria, 22 from HIC and 12 from LMIC, including 112,027 participants, of which 9,347 had peripheral artery disease. Sex-specific prevalence rates increased with age and were broadly similar in HIC and LMIC and in men and women. The prevalence in HIC at age 45-49 years was 5.28% (95% CI 3.38-8.17%) in women and 5.41% (3.41-8.49%) in men, and at age 85-89 years, it was 18.38% (11.16-28.76%) in women and 18.83% (12.03-28.25%) in men. Prevalence in men was lower in LMIC than in HIC (2.89% [2.04-4.07%] at 45-49 years and 14.94% [9.58-22.56%] at 85-89 years). In LMIC, rates were higher in women than in men, especially at younger ages (6.31% [4.86-8.15%] of women aged 45-49 years). Smoking was an important risk factor in both HIC and LMIC, with meta-OR for current smoking of 2.72 (95% CI 2.39-3.09) in HIC and 1.42 (1.25-1.62) in LMIC, followed by diabetes (1.88 [1.66-2.14] vs 1.47 [1.29-1.68]), hypertension (1.55 [1.42-1.71] vs 1.36 [1.24-1.50]), and hypercholesterolaemia (1.19 [1.07-1.33] vs 1.14 [1.03-1.25]). Globally, 202 million people were living with peripheral artery disease in 2010, 69.7% of them in LMIC, including 54.8 million in southeast Asia and 45.9 million in the western Pacific Region. During the preceding decade the number of individuals with peripheral artery disease increased by 28.7% in LMIC and 13.1% in HIC. Interpretation In the 21st century, peripheral artery disease has become a global problem. Governments, nongovernmental organisations, and the private sector in LMIC need to address the social and economic consequences, and assess the best strategies for optimum treatment and prevention of this disease. Publication Types: Review PMID:2013655524


Loss-of-function mutations in the immunoglobulin superfamily member 1 gene (IGSF1) cause a novel, X-linked syndrome of central hypothyroidism and testicular enlargement.
(Schoenmakers, Voshol, Chatterjee) Institute of Metabolic Science, Metabolic Research Laboratories, University of Cambridge, Cambridge, United Kingdom (Sun, Ruivenkamp, Laros, Kriek, Kant, Bosch, Den Dunnen, Breuning) Center for Human and Clinical Genetics, Leiden University Medical Center, Leiden, Netherlands (Oostdijk, Stokvis-Brantsma, Wit) Department of Pediatrics, Leiden University Medical Center, Leiden, Netherlands (Biermasz, Appelman-Dijkstra, Corssmit, Hovens, Pereira) Department of Endocrinology and Metabolic Disorders, Leiden University Medical Center, Leiden, Netherlands (Den Dunnen) Leiden Genome Technology Center, Leiden University Medical Center,
Background Congenital central hypothyroidism occurs either as isolated thyroid-stimulating hormone (TSH) deficiency or in conjunction with other pituitary hormone deficits. Undetected central hypothyroidism is associated with developmental delay in children and adverse cardiometabolic sequelae in adults. Hitherto, mutations in the thyrotropin-releasing hormone receptor gene (TRHR) or the TSHb subunit gene (TSHB) are the only known causes of isolated TSH deficiency. Methods Using whole exome and candidate gene sequencing, we have studied 11 unrelated families with males exhibiting isolated TSH deficiency, testicular enlargement, and variably low serum prolactin levels. Findings We have identified eight distinct mutations and two whole gene deletions disrupting the X-linked immunoglobulin superfamily member 1 gene (IGSF1) in affected males. IGSF1 encodes a pituitary-enriched plasma membrane glycoprotein; disease-associated mutations block trafficking of IGSF1 from the endoplasmic reticulum to the membrane, consistent with loss-of-protein function. Adult male IGSF1 null mice exhibit central hypothyroidism with decreased pituitary TSH content and circulating T3 levels; TSH secretion in response to TRH is blunted and pituitary TRHR mRNA levels are decreased, suggesting that impaired TRH signalling may provide the basis for hypothyroidism. Interpretation Our observations delineate a novel X-linked syndrome in which loss-of-function mutations in IGSF1 cause central hypothyroidism, testicular enlargement, and variable prolactin deficiency, and identify a previously unsuspected role for IGSF1 in hypothalamic-pituitary control of thyroid and testicular function. Variable biochemical penetrance in these families highlights the importance of genetic ascertainment in this syndrome, so that asymptomatic affected individuals can benefit from early initiation of thyroxine treatment.

Time to reconsider steroid injections in the spine?

Davies SJ, Hogg MN, et al.

(Davies, Visser) Fremantle Hospital and Health Service, Perth, WA, Australia (Davies) School of Physiotherapy, Curtin University, Perth, WA, Australia (Hogg) Royal Melbourne Hospital, Melbourne, VIC, Australia (Hogg) Australian Pain Society, Sydney, NSW, Australia

Fremantle Hospital and Health Service, Perth, WA, Australia


Quantifying the proportion of general practice and low-acuity patients in the emergency department.
Nagree Y, Camarda VJ, et al.
(Nagree, Fatovich, Mountain) School of Primary, Aboriginal and Rural Health Care, University of Western Australia, Perth, WA, Australia (Nagree, Camarda, Dey) Fremantle Hospital, Fremantle, WA, Australia (Fatovich) Royal Perth Hospital, Perth, WA, Australia (Cameron) School of Public Health, Monash University, Melbourne, VIC, Australia (Gosbell) Australasian College for Emergency Medicine, Melbourne, VIC, Australia (Mccarthy) Emergency Care Institute, NSW Agency for Clinical Innovation, Sydney, NSW, Australia (Mountain) Sir Charles Gairdner Hospital, Perth, WA, Australia School of Primary, Aboriginal and Rural Health Care, University of Western Australia, Perth, WA, Australia

Objective: To accurately estimate the proportion of patients presenting to the emergency department (ED) who may have been suitable to be seen in general practice. Design: Using data sourced from the Emergency Department Information Systems for the calendar years 2009 to 2011 at three major tertiary hospitals in Perth, Western Australia, we compared four methods for calculating general practice-type patients. These were the validated Sprivulis method, the widely used Australasian College for Emergency Medicine method, a discharge diagnosis method developed by the Tasmanian Department of Human and Health Services, and the Australian Institute of Health and Welfare (AIHW) method. Main outcome measure: General practice-type patient attendances to EDs, estimated using the four methods. Results: All methods except the AIHW method showed that 10%-12% of patients attending tertiary EDs in Perth may have been suitable for general practice. These attendances comprised 3%-5% of total ED length of stay. The AIHW method produced different results (general practice-type patients accounted for about 25% of attendances, comprising 10%-11% of total ED length of stay). General practice-type patient attendances were not evenly distributed across the week, with proportionally more patients presenting during weekday daytime (08:00-17:00) and proportionally fewer overnight (00:00-08:00). This suggests that it is not a lack of general practitioners that drives patients to the ED, as weekday working hours are the time of greatest GP availability. Conclusion: The estimated proportion of general practice-type patients attending the EDs of Perth's major hospitals is 10%-12%, and this accounts for < 5% of the total ED length of stay. The AIHW methodology overestimates the actual proportion of general practice-type patient attendances. PMID:2013387292

Pregabalin: Another option for neuropathic pain.
Visser EJ.
(Visser) Fremantle Hospital, Joondalup Health Campus, St John of God Hospital, Subiaco, WA, Australia (Visser) University of Western Australia, Perth, WA, Australia
E.J. Visser, Fremantle Hospital, Joondalup Health Campus, St John of God Hospital, Subiaco, WA, Australia
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Prevention of cancer in IBD - A balancing act.
Mill J, Lawrance IC.
Centre for Inflammatory Bowel Diseases Fremantle Hospital, WA, USA - ian.lawrance@uwa.edu.au.
two major risk factors for the development of carcinogenesis in inflammatory bowel disease (IBD).
While the natural history of uncontrolled inflammation in the bowel may lead to a higher incidence of colorectal cancer (CRC), surveillance colonoscopy has resulted in earlier detection of dysplasia and cancer, prompting earlier surgical intervention and improved prognosis, while chemoprevention in the form of the anti-inflammatory 5-aminosalicylate acids and immunosuppression could potentially decrease the incidence of CRC. Numerous extra-intestinal cancers such as hepatobiliary and pancreatic malignancies, however, are also noted to be more prevalent in IBD patients particularly with co-existing primary sclerosing cholangitis. Somewhat ironically, however, the medications used to control the inflammation in IBD may also be responsible for the development of other cancers. The increased risk of lymphoma and skin cancers associated with immunosuppressive medication use may potentially be due to loss of immunosurveillance and in the case of lymphoma, the presence of oncogenic viruses (i.e., Epstein-Barr virus). Thus the challenge for both the treating physician and IBD patient is to balance the risk of any potential treatment against patient symptoms and the natural history of uncontrolled inflammation from their disease.

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Molecular Cancer Therapeutics. 2013; 1).
The IMPaCT trial: Individualised Molecular Pancreatic Cancer Therapy. A pilot, randomized, open label Phase II trial assessing first line treatment with gemcitabine or personalized treatment based on tumour molecular signature in patients with metastatic pancreatic cancer. Chantrill L, Johns A, et al. (Chantrill, Johns, Nagrial, Chin, Chou, Pinese, Mead) Kinghorn Cancer Centre, Garvan Institute of Medical Research, Sydney, Australia (Gebski, Sjoquist, Lee, Yip, Miller, Sebastian, Simes) Clinical Trials Centre, University of Sydney, Sydney, Australia (Asghari, Harvey) Bankstown Hospital, Sydney, Australia (Pavlakis) Royal North Shore Hospital, Sydney, Australia (Mukhedkar) Fremantle Hospital, Fremantle, WA, Australia (Grimison) Royal Prince Alfred Hospital, Sydney, Australia (Miller, Pearson, Waddell, Grimmond) Queensland Centre for Medical Genomics, Institute of Molecular Bioscience, Brisbane, Australia (Blankin) Wolfson Wohl Cancer Research Centre, Institute of Cancer Sciences, University of Glasgow, Glasgow, United Kingdom

L. Chantrill, Kinghorn Cancer Centre, Garvan Institute of Medical Research, Sydney, Australia

Background: Less than 5% of patients with metastatic pancreatic cancer survive to 5 years and there have been no major improvements in outcomes over the last 20 years. The use of treatments targeted according to the molecular phenotype of individual tumours may result in improved response and survival compared to standard therapy. Methods: The IMPaCT trial is a multidisciplinary collaboration between the AGITG, NHMRC Clinical Trials Centre, Sydney Catalyst, and the Kinghorn Cancer Centre at Garvan Institute of Medical Research, which houses the Australian Pancreatic Cancer Genome Initiative (APGI). Patients who have available sequence data will be screened for actionable molecular phenotypes and randomized 1:1 to receive standard therapy (gemcitabine) or personalized treatment. Recruitment to the IMPaCT trial is based on the following defined molecular phenotypes: HER2/neu overexpression: personalized treatment with gemcitabine + trastuzumab; BRCA1, BRCA2, and PALB2 mutations: personalized treatment with 5-FU and mitomycin C; Kras wildtype: personalized treatment with gemcitabine + erlotinib. The study will be conducted in two parts: an initial 20 patient pilot trial across 4 Australian sites assessing feasibility, followed by an additional 70 patients to assess progression (90 patients in total). The pilot study is now open and active. Results: The novel trial design involves personalized treatment, where therapies are assigned based on a defined molecular phenotype, in a standard care setting. Stratifying randomization for individual molecular signatures will provide evidence, albeit in small numbers, for confirmation in a larger Phase III trial and broader clinical applicability. Additionally, the study offers the opportunity to explore a number of unique tertiary/correlative objectives, including the planned examination of circulating DNA as a surrogate of survival. Conclusion: The IMPaCT trial exemplifies a strong collaboration between basic scientists, clinicians and clinical trial investigators to illustrate the promises and challenges facing the development and successful testing of personalized therapeutic strategies.
Improved communication with a modified pacing board.
MacDonald E, Emmanuel R.
(MacDonald, Emmanuel) FremantleAustralia
E. MacDonald, FremantleAustralia
Objective: To evaluate the efficacy of using a modified pacing board to facilitate speech fluency in some PD patients. Background: Some Parkinson's disease (PD) patients with dysarthria may experience speech freezing or develop palilalia. A pacing board facilitates speech fluency. Usually it is a paper strip or a wooden board segmented into squares. To initiate speech, clients tap a square. They continue tapping squares as they speak to maintain speech fluency. PD clients using a traditional pacing board were often confused with the lack of clear direction to follow on reaching the final square, defeating the purpose of the pacing board. Methods: A joint speech pathology (SP) and occupational therapy (OT) project was carried out in order to develop the most effective design of a pacing board. Pacing boards of various shapes, sizes and materials were trialled with PD clients attending voice therapy. Observations were made of how effectively they used these in clinic. Four clients selected for the trial were provided with a set of three laminated paper pacing boards in small, medium and large sizes. A survey was developed to find out: - the frequency of the pacing board usage - when and where it was used - its advantages and disadvantages - feedback from partners on the impact on communication. Results: The results of the survey indicated that the majority of clients used the pacing board 4-5 times daily, at home and when attending community groups. 50% of the participants suggested that a strap be added to secure the pacing board on the palm, which correlated with partners' observations. Pacing board size preference was evenly split between the small and medium versions. Conclusions: All participants reported that the pacing board made speech clearer. The survey indicated a preference for a palmshaped medium size pacing board with 4 equidistant indentations, made of plastic. This model was fabricated locally. Currently these plastic pacing boards are loaned to PD clients with dysfluency. An expanded trial of this prototype inexpensive pacing board could benefit greater numbers of those with PD experiencing dysfluency.
Transperineal biopsy of the prostate-is this the future?
Chang DT, Challacombe B, et al.
Transperineal prostate biopsy is re-emerging after decades of being an underused alternative to transrectal biopsy guided by transrectal ultrasonography (TRUS). Factors driving this change include possible improved cancer detection rates, improved sampling of the anteroapical regions of the prostate, a reduced risk of false negative results and a reduced risk of underestimating disease volume and grade. The increasing incidence of antimicrobial resistance and patients with diabetes mellitus who are at high risk of sepsis also favours transperineal biopsy as a sterile alternative to standard TRUS-guided biopsy. Factors limiting its use include increased time, training and financial constraints as well as the need for high-grade anaesthesia. Furthermore, the necessary equipment for transperineal biopsy is not widely available. However, the expansion of transperineal biopsy has been propagated by the increase in multiparametric MRI-guided biopsies, which often use the transperineal approach. Used with MRI imaging, transperineal biopsy has led to improvements in cancer detection rates, more-accurate grading of cancer severity and reduced risk of diagnosing clinically insignificant disease. Targeted biopsy under MRI guidance can reduce the number of cores required, reducing the risk of complications from needle biopsy.
Cerebral sinus venous thrombosis temporally associated with combination tacrolimus/sirolimus immunosuppression.

Graves A, Kulkarni H.
(Graves) Fremantle Hospital, Australia (Kulkarni) Fremantle Hospital Renal Unit, Australia

A. Graves, Fremantle Hospital, Australia

Background: Cerebral sinus venous thrombosis (CSVT) is a rare, but potentially fatal cause of stroke. Established risk factors include inherited and acquired thrombophilic tendencies. The thrombophilic potential of sirolimus can be inferred from excess rates of stent thrombosis with sirolimus drug eluting stents (DES), vessel thrombosis in neoplastic lesions, and occurrence of de novo thrombotic microangiopathies (TMAs) in patients co-administered sirolimus and calcineurin inhibitors (CNIs) or on sirolimus monotherapy. Case Report: We present the case of a 67 year old male, who received a living unrelated renal transplant in August 2007 (3/6 HLA mismatch) for IgA nephropathy. Early post transplant course was complicated by biopsy proven BK virus associated nephropathy (2008) and multiple non-melanoma skin cancers. Tacrolimus was continued due to borderline rejection after its withdrawal in 2009. Myfortic was replaced with azathioprine in Feb 2012 for diarrhoea. Azathioprine was changed to sirolimus in January 2013 due to recurrent skin cancers and cytopathic changes of BK virus on urine analysis. The patient presented with a generalised seizure followed by right hemiparesis secondary to imaging confirmed transverse sinus thrombosis in February 2013, with no prior history of thrombosis. He was treated with levetiracetam and anticoagulation, and sirolimus was replaced by azathioprine. Allograft function did not deteriorate, nor did he demonstrate any significant proteinuria or posttransplant erythrocytosis. The patient achieved a good functional outcome without residual neurological deficits. Conclusion: Sirolimus induced thrombophilia should be considered in transplant patients presenting with CSVT, and use of this agent should be cautioned in patients with pre-existing thrombophilic tendencies.

Renal allograft and bladder malakoplakia in a renal transplant recipient: A clinical dilemma.

(Graves) Fremantle Hospital, Australia (Texler) Fremantle Hospital, Histopathology Unit, Australia (Manning) Fremantle Hospital, Infectious Diseases Unit, Australia (Kulkarni) Fremantle Hospital, Renal Unit, Australia

A. Graves, Fremantle Hospital, Australia

Background: Malakoplakia is an unusual granulomatous inflammatory disorder associated with diminished bactericidal action of leucocytes, often in the context of host immunosuppression. Case Report: We present the case of a 56 year old female cadaveric transplant recipient (surgical date 2010). She was highly sensitised with 96% PRA, moderate DSA (DR8, DR11) and 6/6 mismatch. Borderline vascular rejection was treated with steroids, intravenous immunoglobulin and plasma exchange in the first post-transplant month, with improvement in allograft function to baseline. Maintenance triple immunosuppression included tacrolimus, mycophenolate and steroids. Recurrent urinary tract infections followed from March 2011, with development of a large perinephric collection aspirated in July 2011. This cultured Escherichia coli, treated with intravenous therapy followed by prolonged course of quinolones. Subsequent infections demonstrated progressive resistance to oral therapy. Following this, ultrasound imaging detected a large mass in the graft, and a biopsy diagnosis of renal malakoplakia was made. She was treated with protracted courses of intravenous antibiotics along with mycophenolate discontinuation and dose reduction of tacrolimus and prednisolone. Multiple cystoscopies with biopsy confirmed bladder involvement, with growth of Klebsiella pneumoniae from cultured tissue. Effective control of bacteriuria was achieved with weekly oral fosfomycin (3000 mg) and oral faropenam 150 mg TDS with stable allograft function and reduction in size of the renal lesion. Transplant nephrectomy or withdrawal of immunosuppression was not pursued due to limited options of
renal replacement therapy. Conclusion: Contrary to historical prejudice, renal parenchymal malakoplakia in the transplant recipient may not associate with poor outcomes, if diagnosed and treated aggressively and promptly.

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Management of hyperphosphatemia in haemodialysis patients in an outer metropolitan dialysis unit: the operation phosphate aggressive lowering (OPAL) project.
Light C, Pikoos A, et al.
(Light) Armadale Health Service, Australia (Pikoos) Dietician, Australia (Kulkarni) Armadale Hospital, Fremantle Hospital and Health Services, Australia
C. Light, Armadale Health Service, Australia
Background: Hyperphosphatemia is now a recognised non-traditional risk factor for cardiovascular disease; as a key regulator of vascular calcification it triggers osteochondrogenic differentiation of vascular smooth muscle cells (VSMC), induces VSMC apoptosis, increases Fibroblast Growth Factor 23 levels and decreases Klotho expression. Management of hyperphosphatemia requires robust medication regimen, dietary education and patients’ understanding and committed adherence. Aims: To assess the impact of targeted management in patients with excessively high serum phosphate (>2.00 mmol/L). Methods: A 6-month non-randomised observation study, involving 17 haemodialysis patients with serum phosphate > 2.00 mmol/L. Operation Phosphate Aggressive Lowering (OPAL) task force involved three-pronged approach comprising of Nurse Practitioner, dietician and dialysis nurses. A patients and staff survey was conducted on completion of the project. Results: 13 patients completed the study. Mean (SD) of PO4 mmol/L and PTH pmol/L at entry was 2.38 (0.31) and 79.4 (42.6); at the end of study was 1.67 (0.4) and 58.19 (29.2), 2 patients remained with PO4 > 2.00. Mean (SD) PO4 showed increasing trend [2.38, (0.31)] 3 months post study, reflecting education need for patients and staff. However, patients achieving stringent serum PO4 target (0.6-1.6) improved over time [Entry (nil); 6 months (7); and 9 months (5)] reflecting ongoing improvement in those compliant with intervention. Survey returns were 100% (patients) and 68% (staff). Patients survey demonstrated lack of understanding of hyperphosphatemia, timing of binders but felt beneficial from the project. Nursing survey reflected need for improved understanding of hyperphosphatemia management. Conclusion: An aggressive phosphate lowering task force addressing diet, medication and education delivered promising results in short term. On going sustained multidisciplinary input remains vital to overall hyperphosphatemia management.

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Benefits and costs of an acceptable human leukocyte antigen mismatch program in Australia.
(Nguyen) Sir Charles Gairdner Hospital, Australia (Wong, Craig) Children’s Hospital at Westmead and Centre for Transplant and Renal Research, Australia (Howard) University of Sydney, Australia (Claas) Leiden University Medical Centre, Netherlands (Fidler, D'orsogna, Irish) Royal Perth Hospital, Australia (Chapman) Westmead Hospital, Australia (Ferrari) Fremantle Hospital, Australia
H.D. Nguyen, Sir Charles Gairdner Hospital, Australia
Aims: To determine the benefits and costs of implementing an acceptable mismatch program in Australia. Background: Implementation of an acceptable mismatch program in Europe has improved access to transplantation for highly-sensitised patients on the deceaseddonor waiting list, but the benefits and costs of a similar program in Australia is unclear. Methods: Using a third party perspective, two probabilistic decision analytical models were developed to compare 1) an eplet-defined acceptable mismatch and 2) eplet/Luminex-defined acceptable mismatch program with...
the current deceased-donor allocation model in Australia (n = 10,000, age 18+). The model terminated when all transplant recipients were deceased. Results: Compared with current allocation, an eplet-defined acceptable mismatch model reduces average waiting time for 4 of 28 (14%) highly-sensitised recipients by 34 + 22 months (p = 0.056), with an average gain of 1.32 life-days and $622 savings per patient; whereas an eplet/Luminex-defined acceptable mismatch model reduces the average waiting time for 12 of 23 (52%) highly-sensitised recipients by 37 + 33 months (p = 0.03), with an average 6.00 life-days gained and $2,805 savings per patient. Average increase in waiting time for reallocated recipients in the eplet and eplet/Luminex models were 12 + 9 and 15 + 18 months respectively. Among non-highly-sensitised patients on the waitlist, there was a reduction of 0.09 life-days and $59 excess cost in the eplet-defined acceptable mismatch model and a reduction of 0.60 life-days and $374 excess cost in eplet/Luminex-defined acceptable mismatch model. Conclusions: The integration of an acceptable mismatch program into the deceased-donor kidney allocation reduces waiting-time and provides modest health benefits and cost savings for highly-sensitised patients without incurring significant reduction in overall health benefits and extra costs for non-highly-sensitised candidates on the waitlist.

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KHA-CARI Guideline: Vascular access - Central venous catheters, arteriovenous fistulae and arteriovenous grafts.
(Polkinghorne) Department of Nephrology, Monash Medical Centre, 246 Clayton Road, Melbourne, VIC 3181, Australia (Polkinghorne) Department of Medicine, Monash University, Melbourne, VIC, Australia (Macginley, Owen) Department of Radiology, Austin Health, Melbourne, VIC, Australia (Chin) Department of Renal Medicine, Fremantle Hospital, Fremantle, WA, Australia (Russell) Department of Nephrology, Royal Adelaide Hospital, Adelaide, SA, Australia (Talaulikar) Department of Renal Medicine, Canberra Hospital, Canberra, ACT, Australia (Vale, Lopez-Vargas) Centre for Kidney Research, Children's Hospital at Westmead, Sydney, NSW, Australia

K.R. Polkinghorne, Department of Nephrology, Monash Medical Centre, 246 Clayton Road, Melbourne, VIC 3181, Australia. E-mail: kevan.polkinghorne@monash.edu
PMID:2013680426


Serum gentamicin monitoring is not warranted with use of gentamicin citrate locks for haemodialysis central venous catheter (CVC).
(Ryan, Kulkarni, Ferrari) Fremantle Hospital, Australia
J. Ryan, Fremantle Hospital, Australia
Aim: We analysed the clinical utility of serum gentamicin monitoring with the use of gentamicin-citrate locks (GCL) for central venous catheters (CVC) used for haemodialysis. Background: GCL appear to prevent or reduce the incidence of CVC-associated blood-stream infections. Based on prior studies, ongoing serum gentamicin level monitoring has been advocated to minimise the risk associated with the longterm effect of systemic gentamicin concentrations. The clinical utility of serum gentamicin level monitoring using Gentamicin 10 mg, sodium citrate 31.4 mg in 3 mL sodium chloride 0.9%, which is available as a pre-mixed syringe preparation (Baxter Healthcare) is unclear. Methods: Retrospective cross sectional analysis was performed on haemodialysis patients using GCL for CVC. Serum gentamicin levels on haemodialysis patients using GCL at a single centre between March 2012 and February 2013 were analysed based on the indication for either lock-safety monitoring (CVC lock) or therapeutic drug monitoring (for treatment). Results: CVC for dialysis access was used in 59 patients during the study period, in 303 cases serum samples for gentamicin levels were available. Of these,
16 patients (54 samples) received therapeutic gentamicin for documented systemic infections. Thus, 249 samples in the lock safety monitoring group were analysed. Only 2.6% of samples of GCL monitoring showed gentamicin levels >0.3 mg/L; whilst none of the samples in this group had >2 consecutive samples with levels >0.3 mg/L or levels above >0.5 mg/L. P 0.0). No patients recorded adverse events. Conclusions: Routine monitoring of serum gentamicin levels with gentamicincitrate lock for CVC is expensive and unnecessary.

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ANZSN renal supportive care guidelines 2013.
(Brown, Robins, Katz) Departments of Renal Medicine and Medicine, St George Hospital, University of NSW, Sydney, NSW, Australia (Crail) Central and North Adelaide Renal and Transplantation Service, Adelaide, SA, Australia (Masterson) Department of Nephrology, Royal Melbourne Hospital, Melbourne, VIC, Australia (Foote) George Institute for Global Health, Sydney, NSW, Australia (Josland) St George Hospital, Kogarah, NSW, Australia (Brennan) Departments of Renal Medicine and Palliative Medicine, St George Hospital, Kogarah, NSW, Australia (Stallworthy) Department of Renal Medicine, Auckland City Hospital, Auckland, New Zealand (Siva) Fremantle Hospital, Fremantle, WA, Australia (Miller) Palliative Care Service, Department of General Medicine, North Shore, Waitakere Hospitals Waitemata District Health Board, Auckland, New Zealand (Urban) Concord Repatriation Hospital, Concord, NSW, Australia (Sajiv) Alice Springs Hospital, Central Australian Renal Services Northern Territory, Alice Springs, Australia (Glavish) He Kamaka Oranga - Department of Maori Health, Auckland District Health Board, Auckland, New Zealand (May) Tamworth Base Hospital, Tamworth, NSW, Australia (Langham) St Vincent's Hospital, Fitzroy, VIC, Australia (Walker) Department of Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand (Fassett) Royal Brisbane and Women's Hospital, Herston, QLD, Australia (Morton) School of Public Health, University of Sydney, Sydney, NSW, Australia (Stewart) Centre for Health Governance, Law and Ethics, Sydney Law School, University of Sydney, Sydney, Australia (Brennan) Departments of Renal Medicine and Palliative Medicine, St George Hospital, Kogarah, NSW, Australia (Phipps) Orange Base Hospital, Orange, NSW, Australia (Healy) Department of Renal Medicine, Royal Brisbane and Women's Hospital Queensland, Brisbane, Australia (Crail, Berquier) Central and North Adelaide Renal, Transplant Services, Adelaide, SA, Australia
Departments of Renal Medicine and Medicine, St George Hospital, University of NSW, Sydney, NSW, Australia

Publication Types: Review
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Pharmacokinetics and safety of deferasirox in subjects with chronic kidney disease undergoing haemodialysis.
(Maker) School of Veterinary and Life Sciences, Murdoch University, Murdoch, WA 6150, Australia (Maker, Trengove) Metabolomics Australia, Murdoch University, Australia (Trengove) Separation Science and Metabolomics Laboratory, Murdoch University, Australia (Olynyk) Institute for Immunology and Infectious Diseases, Murdoch University, Australia (Siva, Ferrari) Department of Nephrology, Fremantle Hospital and Health Service, Australia (Batty) School of Pharmacy, Curtin University, Australia (Batty, Olynyk) Curtin Health Innovation Research Institute, Curtin University, Australia (Olynyk) Western Australian Institute of Medical Research, Perth, WA, Australia
G.L. Maker, School of Veterinary and Life Sciences, Murdoch University, Murdoch, WA 6150,
Aim Treatment of chronic kidney disease (CKD) includes parenteral iron therapy, and these infusions can lead to iron overload. Secondary iron overload is typically treated with iron chelators, of which deferasirox is one of the most promising. However, it has not been studied in patients with CKD and iron overload. Methods A pilot study was conducted to evaluate the pharmacokinetics and safety of deferasirox in eight haemodialysis-dependent patients, who were receiving intravenous iron for treatment of anaemia of CKD. Deferasirox was administered at two doses (10 mg/kg and 15 mg/kg), either acute (once daily for 2 days) or steady-state (once daily for 2 weeks). Results A dose of 10 mg/kg in either protocol was not sufficient to achieve a plasma concentration in the therapeutic range (acute peak 14.1 and steady-state 22.8 mumol/L), while 15 mg/kg in either protocol maintained plasma concentration well above this range (acute peak 216 and steady-state 171 mumol/L). Plasma concentration observed at 15 mg/kg was well above that expected for this dose (40-50 mumol/L), although no adverse clinical events were observed. Conclusion This study highlights the need to profile drugs such as deferasirox in specific patient groups, such as those with CKD and iron overload. The authors examined the acute and steady-state pharmacokinetics of two-dose protocol of deferasirox in patients undergoing haemodialysis. The study revealed the importance of individual dose profile as the dose response varies in patients with CKD with iron overload.

PMID:2013135480


**Modeling depression in Parkinson disease: disease-specific and nonspecific risk factors.**
Leentjens AF, Moonen AJ, et al.
From the Department of Psychiatry (A.F.G.L., A.J.H.M.), Maastricht University Medical Center, Maastricht; School for Mental Health and Neuroscience (A.F.G.L., A.J.H.M., S.K.), Maastricht University, Maastricht, the Netherlands; Neurology and Movement Disorders Unit (K.D.), Lille University Medical Center, Lille, France; Mental Health Care Line (L.M.), Michael E. DeBakey Veterans Administration Medical Center and Departments of Psychiatry and Neurology, Baylor College of Medicine, Houston, TX; Alzheimer Disease Research Unit and CIBERNED (P.M.-M.), Alzheimer Center Reina Sofia Foundation, Carlos III Institute of Health, Madrid, Spain; Departments of Neurology and Psychiatry (I.H.R.), University of Rochester School of Medicine and Dentistry, Rochester, NY; and School of Psychiatry (S.E.S.), University of Western Australia and Fremantle Hospital, Fremantle, Australia.

OBJECTIVE: To construct a model for depression in Parkinson disease (PD) and to study the relative contribution of PD-specific and nonspecific risk factors to this model.

METHODS: Structural equation modeling of direct and indirect associations of risk factors with the latent depression outcome using a cross-sectional dataset of 342 patients with PD.

RESULTS: A model with acceptable fit was generated that explained 41% of the variance in depression. In the final model, 3 PD-specific variables (increased disease duration, more severe motor symptoms, the use of levodopa) and 6 nonspecific variables (female sex, history of anxiety and/or depression, family history of depression, worse functioning on activities of daily living, and worse cognitive status) were maintained and significantly associated with depression. Nonspecific risk factors had a 3-times-higher influence in the model than PD-specific risk factors.

CONCLUSION: In this cross-sectional study, we showed that nonspecific factors may be more prominent markers of depression than PD-specific factors. Accordingly, research on depression in PD should focus not only on factors associated with or specific for PD, but should also examine a wider scope of factors including general risk factors for depression, not specific for PD.

Publication Types: Research Support, Non-U.S. Gov't
PMID:23946309


**Neuroimaging of first-ever seizure Contribution of MRI if CT is normal.**
The role of neuroimaging in the assessment of a first-ever seizure has not been well-defined, in particular the utility of MRI when CT is normal. The results of neuroimaging (CT brain, MRI brain, or both) in 1,013 adults with first-ever unprovoked seizure were correlated with clinical features and seizure outcome. Epileptogenic lesions were identified in 29%. Of patients with a normal CT who also had MRI, 12% had an epileptogenic lesion on MRI, the strongest independent predictor of which was a focal abnormality on EEG. Patients with an epileptogenic lesion had a higher risk of seizure recurrence, including when this was only evident on MRI. 2013 American Academy of Neurology. PMID:2013728287

Stroke syndromes associated with DWI-negative MRI include ataxic hemiparesis and isolated internuclear ophthalmoplegia.
Watts J, Wood B, et al. (Watts, Wood, Kelly, Alvaro) Fremantle Hospital and Health Service, Fremantle, WA, Australia J. Watts, Fremantle Hospital and Health Service, Fremantle, WA, Australia. E-mail: jwatts@globaldial.com
We present a case series of clinically definite acute stroke with negative diffusion-weighted imaging (DWI). This study retrospectively examined a large population of stroke patients with the aim of identifying which stroke syndromes were more likely to be negative on MRI. Patient records and images were reviewed in order to confirm clinically definite stroke and DWI negativity. A total of 701 patients had MRI during the study period. A total of 16 patients with DWI-negative MRI and clinically definite stroke as diagnosed by experienced stroke consultants were identified. A total of 15 of the 16 cases were classified as either posterior circulation or lacunar strokes, and the most common syndromes were ataxic hemiparesis and isolated internuclear ophthalmoplegia. PMID:2013445869

CT brain findings in a patient with elevated brain cesium levels.
Khangure SR, Williams ES, et al. Department of Radiology, Fremantle Hospital; Perth, Australia - simon.khangure@health.wa.gov.au. We describe the CT findings in the brain of a woman with pathologically proven elevated levels of blood and tissue cesium. The 42-year-old woman had been receiving cesium chloride as a non-mainstream treatment for metastatic breast carcinoma. She presented to hospital following a seizure, and died 48 hours after admission. A brain CT performed on hospital admission showed a diffuse increase in attenuation of brain parenchyma. Autopsy revealed elevated levels of cesium in blood and solid organs including the brain. We hypothesize that the imaging findings are attributable to the abnormally elevated level of brain cesium at the time of the CT scan. To our knowledge, this is the first reported case of this imaging finding. PMID:24355178

Brain transcriptome perturbations in the transferrin receptor 2 mutant mouse support the case for brain changes in iron loading disorders, including effects relating to long-term depression.
Iron abnormalities within the brain are associated with several rare but severe neurodegenerative conditions. There is growing evidence that more common systemic iron loading disorders such as hemochromatosis can also have important effects on the brain. To identify features that are common across different forms of hemochromatosis, we used microarray and real-time reverse transcription polymerase chain reaction (RT-PCR) to assess brain transcriptome profiles of transferrin receptor 2 mutant mice (Tfr2<sup>mut</sup>), a model of a rare type of hereditary hemochromatosis, relative to wildtype control mice. The results were compared with our previous findings in dietary iron-supplemented wildtype mice and Hfe<sup>-/-</sup> mice, a model of a common type of hereditary hemochromatosis. For transcripts showing significant changes relative to controls across all three models, there was perfect (100%) directional concordance (i.e. transcripts were increased in all models or decreased in all models). Comparison of the two models of hereditary hemochromatosis, which showed more pronounced changes than the dietary iron-supplemented mice, revealed numerous common molecular effects. Pathway analyses highlighted changes for genes relating to long-term depression (6.8-fold enrichment, p=5.4x10<sup>-7</sup>) and, to a lesser extent, long-term potentiation (3.7-fold enrichment, p=0.01), with generalized reductions in transcription of key genes from these pathways, which are involved in modulating synaptic strength and efficacy and are essential for memory and learning. The agreement across the models suggests the findings are robust and strengthens previous evidence that iron loading disorders affect the brain. Perturbations of brain phenomena such as long-term depression and long-term potentiation might partly explain neurologic symptoms reported for some hemochromatosis patients. 2013 IBRO.

PMID:2013112566

Peripheral arterial disease increases the risk of subsequent hip fracture in older men: The Health in Men Study.

(Hyde, Flicker) Western Australian Centre for Health and Ageing, Centre for Medical Research, Western Australian Institute for Medical Research, University of Western Australia, Perth WA, Australia (Hyde, Hankey, Flicker) School of Medicine and Pharmacology, University of Western Australia, Perth WA, Australia (Mylankal, Norman) School of Surgery, University of Western Australia, Fremantle Hospital, PO Box 480, Fremantle WA 6959, Australia (Hankey) Department of Neurology, Royal Perth Hospital, Perth WA, Australia

P.E. Norman, School of Surgery, University of Western Australia, Fremantle Hospital, PO Box 480, Fremantle WA 6959, Australia. E-mail: paul.norman@uwa.edu.au

The aim of the present study was to assess whether peripheral arterial disease is associated with an increased risk of hip fracture in a cohort of 12,094 older men. There was no association between
claudication and hip fracture, but there was a significant association with an ankle brachial index (ABI) <0.9. Introduction: It is uncertain whether peripheral arterial disease (PAD) is associated with an increased risk of subsequent hip fracture. The aim of the present study was to assess this in a large cohort of men aged 65 years and over. Methods: Claudication was assessed by means of the Edinburgh Claudication Questionnaire in 12,094 men, and the ABI was measured in 4,321 of these men. Hospitalisations with hip fracture were identified by record linkage. The association between both claudication and an ABI <0.9 and subsequent hip fractures was assessed using survival curves and Cox regression models. Results: Amongst the 12,094 men, the baseline prevalence of claudication according to the ECQ was 5.3 %. Amongst the 4,321 men with ABI results, the prevalence of an ABI <0.9 was 11.7 %. Of the 506 men with an ABI <0.9, 129 (25.5 %) also had claudication. Over a median (range) follow-up of 10.8 (0.3-12.7) years, 343 (2.8 %) of the 12,094 men were admitted to hospital with a hip fracture. There was no association between claudication and subsequent hip fractures (hazard ratio (HR) = 0.95; 95 % confidence interval (CI), 0.60, 1.52). Over a median (range) follow-up of 11.1 (0.06-12.3) years 135 (3.1 %) of the 4,321 men with ABI data were admitted to hospital with hip fractures. There was a significant association between an ABI <0.9 and subsequent hip fracture (HR = 1.69; 95 % CI, 1.08, 2.63). Conclusion: Older men with PAD defined as ABI < 0.9 are at increased risk of hip fracture, whereas the symptom of claudication is not an independent predictor of hip fracture. 2012 International Osteoporosis Foundation and National Osteoporosis Foundation. PMID:2013623836

Tampin B, Briffa NK, et al. (Tampin, Briffa, Slater) School of Physiotherapy and Exercise Science, Curtin Health Innovation Research Institute, Curtin University, GPO Box U1987, Perth, WA 6845, Australia (Tampin) Department of Physiotherapy, Sir Charles Gairdner Hospital, Perth, WA, Australia (Tampin) Department of Neurosurgery, Sir Charles Gairdner Hospital, Perth, WA, Australia (Goucke) Department of Pain Management, Sir Charles Gairdner Hospital, Perth, WA, Australia (Slater) Pain Medicine Unit, Fremantle Hospital and Health Service, Fremantle, WA, Australia B. Tampin, School of Physiotherapy and Exercise Science, Curtin Health Innovation Research Institute, Curtin University, GPO Box U1987, Perth, WA 6845, Australia. E-mail: bvdh@iinet.net.au
The Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain has proposed a grading system for the presence of neuropathic pain (NeP) using the following categories: no NeP, possible, probable, or definite NeP. To further evaluate this system, we investigated patients with neck/upper limb pain with a suspected nerve lesion, to explore: (i) the clinical application of this grading system; (ii) the suitability of 2 NeP questionnaires (Leeds Assessment of Neuropathic Symptoms and Signs pain scale [LANSS] and the painDETECT questionnaire [PD-Q]) in identifying NeP in this patient cohort; and (iii) the level of agreement in identifying NeP between the NeuPSIG classification system and 2 NeP questionnaires. Patients (n = 152; age 52 +/- 12 years; 53% male) completed the PD-Q and LANSS questionnaire and underwent a comprehensive clinical examination. The NeuPSIG grading system proved feasible for application in this patient cohort, although it required considerable time and expertise. Both questionnaires failed to identify a large number of patients with clinically classified definite NeP (LANSS sensitivity 22%, specificity 88%; PD-Q sensitivity 64%, specificity 62%). These lowered sensitivity scores contrast with those from the original PD-Q and LANSS validation studies and may reflect differences in the clinical characteristics of the study populations. The diagnostic accuracy of LANSS and PD-Q the identification of NeP in patients with neck/upper limb pain appears limited. PMID:2013763378
Is chronic pain a disease?
Cohen M, Quintner J, et al.

Objective: The discovery of neuroplastic phenomena such as central sensitization of nociception has challenged pain theory to evolve, to encompass unpredictable and unlikely chronic pain states, and to cope with the emerging complexity of the brain. Recently, the proposition that chronic pain is a disease in its own right has gained currency, based upon functional and structural changes in the brain constituting a distinctive pathology. Proponents have expanded the theory to identify "eudynia" ("good" pain) and "maldynia" ("bad" pain). Methods: A critical examination of the proposition that chronic pain is a disease was conducted within the framework of evolution of pain medicine theory. Results: Three dominant theories were identified: specificity theory (the "hard-wired" nervous system); neuroplasticity theory (the "soft-wired" nervous system); and pain-as-a-disease. The progression from specificity theory to neuroplasticity theory was based upon empirical evidence and conceptual clarity. The latter theory confronts the uncertainty and the unpredictability of pain, and offers explanations for conditions where ongoing noxious input is not discernible. However, not only does pain-as-a-disease elevate the neurophysiological mechanisms underlying the experience of chronic pain to the status of a disease, but also it conceives of pain as a "thing" that is itself capable of producing an effect. This reasoning is found to be faulty on two grounds: the confusion of pain as a symptom, a cause, and a pathology; and the fallacy that can arise when an interpretation is claimed to be a truth. Conclusions: The proposition that chronic pain is a disease cannot be supported on clinical and pathological grounds, as well as in terms of ways of knowing. The promulgation of "good" and "bad" pain has the potential to obstruct necessary dialogue for advancing the science and treatment of pain. We suggest a way forward to resolve this impasse. 2013 American Academy of Pain Medicine.

Deep Resequencing of GWAS Loci Identifies Rare Variants in CARD9, IL23R and RNF186 That Are Associated with Ulcerative Colitis.

Objective: The discovery of neuroplastic phenomena such as central sensitization of nociception has challenged pain theory to evolve, to encompass unpredictable and unlikely chronic pain states, and to cope with the emerging complexity of the brain. Recently, the proposition that chronic pain is a disease in its own right has gained currency, based upon functional and structural changes in the brain constituting a distinctive pathology. Proponents have expanded the theory to identify "eudynia" ("good" pain) and "maldynia" ("bad" pain). Methods: A critical examination of the proposition that chronic pain is a disease was conducted within the framework of evolution of pain medicine theory. Results: Three dominant theories were identified: specificity theory (the "hard-wired" nervous system); neuroplasticity theory (the "soft-wired" nervous system); and pain-as-a-disease. The progression from specificity theory to neuroplasticity theory was based upon empirical evidence and conceptual clarity. The latter theory confronts the uncertainty and the unpredictability of pain, and offers explanations for conditions where ongoing noxious input is not discernible. However, not only does pain-as-a-disease elevate the neurophysiological mechanisms underlying the experience of chronic pain to the status of a disease, but also it conceives of pain as a "thing" that is itself capable of producing an effect. This reasoning is found to be faulty on two grounds: the confusion of pain as a symptom, a cause, and a pathology; and the fallacy that can arise when an interpretation is claimed to be a truth. Conclusions: The proposition that chronic pain is a disease cannot be supported on clinical and pathological grounds, as well as in terms of ways of knowing. The promulgation of "good" and "bad" pain has the potential to obstruct necessary dialogue for advancing the science and treatment of pain. We suggest a way forward to resolve this impasse. 2013 American Academy of Pain Medicine.
Genome-wide association studies and follow-up meta-analyses in Crohn's disease (CD) and ulcerative colitis (UC) have recently identified 163 disease-associated loci that meet genome-wide significance for these two inflammatory bowel diseases (IBD). These discoveries have already had a tremendous impact on our understanding of the genetic architecture of these diseases and have directed functional studies that have revealed some of the biological functions that are important to IBD (e.g. autophagy). Nonetheless, these loci can only explain a small proportion of disease variance (~14% in CD and 7.5% in UC), suggesting that not only are additional loci to be found but that the known loci may contain high effect rare risk variants that have gone undetected by GWAS. To test this, we have used a targeted sequencing approach in 200 UC cases and 150 healthy controls (HC), all of French Canadian descent, to study 55 genes in regions associated with UC. We performed follow-up genotyping of 42 rare non-synonymous variants in independent case-control cohorts (totaling 14,435 UC cases and 20,204 HC). Our results confirmed significant association to rare non-synonymous coding variants in both IL23R and CARD9, previously identified from sequencing of CD loci, as well as
identified a novel association in RNF186. With the exception of CARD9 (OR = 0.39), the rare non-
synonymous variants identified were of moderate effect (OR = 1.49 for RNF186 and OR = 0.79 for
IL23R). RNF186 encodes a protein with a RING domain having predicted E3 ubiquitin-protein ligase
activity and two transmembrane domains. Importantly, the disease-coding variant is located in the
ubiquitin ligase domain. Finally, our results suggest that rare variants in genes identified by genome-
wide association in UC are unlikely to contribute significantly to the overall variance for the disease.
Rather, these are expected to help focus functional studies of the corresponding disease loci. 2013
Beaudoin et al.
PMID:2013610254

The Effect of Dosing Regimens on the Antimalarial Efficacy of Dihydroartemisinin-Piperaquine:
A Pooled Analysis of Individual Patient Data.
Achan J, Adam I, et al.
(Achan) Uganda Malaria Surveillance Project, Kampala, Uganda (Adam) University of Khartoum,
Khartoum, Sudan (Arinaitwe) Infectious Diseases Research Collaboration, Kampala, Uganda (Ashley)
Shoklo Malaria Research Unit, Mae Sot, Thailand (Ashley) Mahidol University, Bangkok, Thailand
(Awab) Mahidol University, Bangkok, Thailand (Awab) Ministry of Public Health, Islamic Republic of
Afghanistan, Kabul, Afghanistan (Ba) Department of Parasitology, University Cheikh Anta Diop, Dakar,
Senegal (Barnes) Division of Clinical Pharmacology, Department of Medicine, University of Cape
Town, Cape Town, South Africa (Bassat) Centro de Investigacao em Saude de Manhica, Manhica,
Mozambique (Bassat) Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Barcelona,
Spain (Borrmann) Kenya Medical Research Institute-Welcome Trust Research Programme, Kilifi,
Kenya (Borrmann) Heidelberg University School of Medicine, Dept. of Infectious Diseases,
Heidelberg, Germany (Bousema) Department of Infection and Immunity, London School of Hygiene
and Tropical Medicine, London, United Kingdom (Bousema) Department of Medical Microbiology,
Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands (Dahal) WorldWide Antimalarial
Resistance Network (WWARN), Oxford, United Kingdom (Dahal) Kenya Medical Research/Centre for
Tropical Medicine, Nuffield Department of Clinical Medicine, Kenya Medical Research, University of
Oxford, Oxford, United Kingdom (D'Alessandro) Institute of Tropical Medicine, Antwerp, Belgium
(D'Alessandro) Medical Research Council Unit, Gambia (Davis) School of Medicine and
Pharmacology, University of Western Australia, Crawley, Australia (Dondorp) Mahidol-Oxford Tropical
Medicine Research Unit, Mahidol University, Bangkok, Thailand (Dondorp) Centre for Tropical
Medicine, Church Hill Hospital, Kenya Medical Research, Oxford, United Kingdom (Dorsey) Department
of Medicine, University of California San Francisco, San Francisco, United States (Drakeley)
Department of Infection and Immunity, London School of Hygiene and Tropical Medicine, Kenya
Medical Research, London, United Kingdom (Fanello) Mahidol-Oxford Research Unit, Mahidol
University, Bangkok, Thailand (Faye) Department of Medical Parasitology, University Cheikh Anta
Diop, Dakar, Senegal (Flegg) WorldWide Antimalarial Resistance Network (WWARN), Oxford, United
Kingdom (Flegg) Kenya Medical Research/ Centre for Tropical Medicine, Nuffield Department of
Clinical Medicine, University of Oxford, Kenya Medical Research, Oxford, United Kingdom (Gaye)
Department of Medical Parasitology, University Cheikh Anta Diop, Dakar, Senegal (Gething) Spatial
Ecology and Epidemiology Group, Department of Zoology, University of Oxford, Kenya Medical
Research, Oxford, United Kingdom (Gonzalez) Centro de Investigacao em Saude de Manhica,
Manhica, Mozambique (Gonzalez) Centre de Recerca en Salut Internacional de Barcelona (CRESIB),
Barcelona, Spain (Guerin) WorldWide Antimalarial Resistance Network (WWARN), Oxford, United
Kingdom (Guerin) Kenya Medical Research/Centre for Tropical Medicine, Nuffield Department of
Clinical Medicine, University of Oxford, Kenya Medical Research, Oxford, United Kingdom (Hay)
Spatial Ecology and Epidemiology Group, Department of Zoology, University of Oxford, Kenya Medical
Research, Oxford, United Kingdom (Hien) Hospital for Tropical Diseases, Ho Chi Minh City,
Vietnam (Hien) Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam (Janssens)
Medecins Sans Frontieres, Phnom Penh, Cambodia (Kamya) Makerere University College of Health
Sciences, Kampala, Uganda (Karema) National Malaria Control Program-TRAC Plus, Ministry of Health, Kigali, Rwanda (Karunajeewa) Medicine Unit, School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia (Kone) Department of Parasitology and Mycology, Abidjan, Cote D'Ivoire (Lell) Institute for Tropical Medicine, University of Tubingen, Tubingen, Germany (Lell) Centre de Recherches Medicales de Lambarene, Lambarene, Gabon (Marsh) Centre for Tropical Medicine, Churchill Hospital, Kenya Medical Research, Oxford, United Kingdom (Marsh) Kenya Medical Research Institute-Wellcome Trust Research Programme, Kilifi, Kenya (Mayxay) Wellcome Trust-Mahosot Hospital-Oxford Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Laos (Mayxay) National University of Laos, Vientiane, Laos (Menendez) Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Barcelona, Spain (Menendez) Centro de Investigacoe en Salude de Manhica(CISM), Manhica, Mozambique (Mens) Royal Tropical Institute, KIT Biomedical Research, Amsterdam, Netherlands (Mens) Centre for Infection and Immunity Amsterdam, (CINEMA), Division of Infectious Diseases, Tropical Medicine and AIDS, Academic Medical Centre, Amsterdam, Netherlands (Meremikwu) Department of Paediatrics, University of Calabar, Calabar, Nigeria (Meremikwu) Institute of Tropical Diseases Research and Prevention, Calabar, Nigeria (Moreira) WorldWide Antimalarial Resistance Network (WWARN), Kenya Medical Research, Oxford, United Kingdom (Moreira) Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Kenya Medical Research, Oxford, United Kingdom (Mueller) Papua New Guinea Institute of Medical Research, Goroka, Papua New Guinea (Mueller) Infection and Immunity Division, Walter and Eliza Hall Institute, Parkville, Australia (Mueller) Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Barcelona, Spain (Nabasumba) Epicentre, Paris, France (Nambozi) Tropical Diseases Research Centre, Ndola, Zambia (Ndiaye) Parasitology and Mycology Laboratory, University Cheikh Anta Diop, Dakar, Senegal (Newton) Wellcome Trust-Mahosot Hospital-Oxford University Tropical Medicine Research Collaboration, Mahosot Hospital, Vientiane, Laos (Newton) Centre for Tropical Medicine, Churchill Hospital, Kenya Medical Research, Oxford, United Kingdom (Nguyen) Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam (Nosten) Shoklo Malaria Research Unit, Mae Sot, Thailand (Nosten) Mahidol University, Bangkok, Thailand (Nosten) Centre for Clinical Tropical Medicine, Churchill Hospital, Kenya Medical Research, Oxford, United Kingdom (Nsanzabana) WorldWide Antimalarial Resistance Network (WWARN), Oxford, United Kingdom (Nsanzabana) Kenya Medical Research/Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Kenya Medical Research, Oxford, United Kingdom (Omar) International Centre for Insect physiology and Ecology (IClPE), Mbita, Kenya (Ouedraogo) Institut de Recherche en Sciences de la Sante, Direction Regionale de l'Ouest, Bobo-Dioulasso, Burkina Faso (Ouedraogo) Centre Muraz, Bobo-Dioulasso, Burkina Faso (Penali) WorldWide Antimalarial Resistance Network (WWARN)-West Africa Regional Centre, Dakar, Senegal (Phyo) Department of Medical Parasitology, University Cheikh Anta Diop, Dakar, Senegal (Price) Shoklo Malaria Research Unit, Tak, Thailand (Price) Menzies School of Health Research and Charles Darwin University, Darwin, Australia (Price) Centre for Tropical Medicine, Churchill Hospital, Kenya Medical Research, Oxford, United Kingdom (Sasithon) Kenya Medical Research/Nsanzabana WorldWide Antimalarial Resistance Network (WWARN), Oxford, United Kingdom (Sasithon) Kenya Medical Research (Thailand) Kilimanjaro Clinical Medical Research Institute, Kilimanjaro Christian Medical Centre, Moshi, Tanzania (Shekalaghe) Ifakara Health Institute, Bagamoyo, Tanzania (Sibley) WorldWide Antimalarial Resistance Network (WWARN), Oxford, United Kingdom (Sibley) Kenya Medical Research/Department of Genome Sciences, University of Washington, Seattle, United States (Smith) WorldWide Antimalarial Resistance Network (WWARN)-Asia Regional Centre, Bangkok, Thailand (Smithuis) Medecins sans Frontieres-Holland, Yangon, Myanmar (Smithuis) Medical Action Myanmar, Yangon, Myanmar (Some) Institut de Recherche en Sciences de la Sante, Bobo-Dioulasso, Burkina Faso (Stepniewska) WorldWide Antimalarial Resistance Network (WWARN), Oxford, United Kingdom (Thailand)
Background: Dihydroartemisinin-piperaquine (DP) is increasingly recommended for antimalarial treatment in many endemic countries; however, concerns have been raised over its potential underdosing in young children. We investigated the influence of different dosing schedules on DP's clinical efficacy. Methods and Findings: A systematic search of the literature was conducted to identify all studies published between 1960 and February 2013, in which patients were enrolled and treated with DP. Principal investigators were approached and invited to share individual patient data with the WorldWide Antimalarial Resistance Network (WWARN). Data were pooled using a standardised methodology. Univariable and multivariable risk factors for parasite recrudescence were identified using a Cox's regression model with shared frailty across the study sites. Twenty-four published and two unpublished studies (n = 7,072 patients) were included in the analysis. After correcting for reinfection by parasite genotyping, Kaplan-Meier survival estimates were 97.7% (95% CI 97.3%-98.1%) at day 42 and 97.2% (95% CI 96.7%-97.7%) at day 63. Overall 28.6% (979/3,429) of children aged 1 to 5 years received a total dose of piperaquine below 48 mg/kg (the lower limit recommended by WHO); this risk was 2.3-2.9-fold greater compared to that in the other age groups and was associated with reduced efficacy at day 63 (94.4% [95% CI 92.6%-96.2%], p<0.001). After adjusting for confounding factors, the mg/kg dose of piperaquine was found to be a significant predictor for recrudescence, the risk increasing by 13% (95% CI 5.0%-21%) for every 5 mg/kg decrease in dose; p = 0.002. In a multivariable model increasing the target minimum total dose of piperaquine in children aged 1 to 5 years old from 48 mg/kg to 59 mg/kg would halve the risk of treatment failure and cure at least 95% of patients; such an increment was not associated with gastrointestinal toxicity in the ten studies in which this could be assessed. Conclusions: DP demonstrates excellent efficacy in a wide range of transmission settings; however, treatment failure is associated with a lower dose of piperaquine, particularly in young children, suggesting potential for further dose optimisation. Please see later in the article for the Editors’ Summary. 2013 Price et al.
Chua AC, Klopcic BR, et al.
School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia, Fremantle, Western Australia, Australia; Western Australian Institute for Medical Research, Perth, Western Australia, Australia.
Chronic intestinal inflammation and high dietary iron are associated with colorectal cancer development. The role of Stat3 activation in iron-induced colonic inflammation and tumorigenesis was investigated in a mouse model of inflammation-associated colorectal cancer. Mice, fed either an iron-supplemented or control diet, were treated with azoxymethane and dextran sodium sulfate (DSS). Intestinal inflammation and tumor development were assessed by endoscopy and histology, gene expression by real-time PCR, Stat3 phosphorylation by immunoblot, cytokines by ELISA and apoptosis by TUNEL assay. Colonic inflammation was more severe in mice fed an iron-supplemented compared with a control diet one week post-DSS treatment, with enhanced colonic IL-6 and IL-11 release and Stat3 phosphorylation. Both IL-6 and ferritin, the iron storage protein, co-localized with macrophages suggesting iron may act directly on IL-6 producing-macrophages. Iron increased DSS-induced colonic epithelial cell proliferation and apoptosis consistent with enhanced mucosal damage. DSS-treated mice developed anemia that was not alleviated by dietary iron supplementation. Six weeks post-DSS treatment, iron-supplemented mice developed more and larger colonic tumors compared with control mice. Intratumoral IL-6 and IL-11 expression increased in DSS-treated mice and IL-6, and possibly IL-11, were enhanced by dietary iron. Gene expression of iron importers, divalent metal transporter 1 and transferrin receptor 1, increased and iron exporter, ferroportin, decreased in colonic tumors suggesting increased iron uptake. Dietary iron and colonic inflammation synergistically activated colonic IL-6/IL-11-Stat3 signaling promoting tumorigenesis. Oral iron therapy may be detrimental in inflammatory bowel disease since it may exacerbate colonic inflammation and increase colorectal cancer risk.
PMID:24223168

Secreted Protein Acidic and Rich in Cysteine (SPARC) Exacerbates Colonic Inflammatory Symptoms in Dextran Sodium Sulphate-Induced Murine Colitis.
Ng YL, Klopcic B, et al.
Centre for Inflammatory Bowel Diseases, School of Medicine and Pharmacology, University of Western Australia, Fremantle, Western Australia, Australia; School of Veterinary and Biomedical Sciences, Murdoch University, Perth, Western Australia, Australia.
BACKGROUND: Secreted Protein Acidic and Rich in Cysteine (SPARC) is expressed during tissue repair and regulates cellular proliferation, migration and cytokine expression. The aim was to determine if SPARC modifies intestinal inflammation.
METHODS: Wild-type (WT) and SPARC-null (KO) mice received 3% dextran sodium sulphate (DSS) for 7 days. Inflammation was assessed endoscopically, clinically and histologically. IL-1beta, IL-4, IL-5, IL-6, IL-10, IL-13, IL-17A, IL-12/IL23p40, TNF-alpha, IFN-, RANTES, MCP-1, MIP-1alpha, MIP-1beta, MIG and TGF-beta1 levels were measured by ELISA and cytometric bead array. Inflammatory cells were characterised by CD68, Ly6G, F4/80 and CD11b immunofluorescence staining and regulatory T cells from spleen and mesenteric lymph nodes were assessed by flow cytometry.
RESULTS: KO mice had less weight loss and diarrhoea with less endoscopic and histological inflammation than WT animals. By day 35, all (n=13) KO animals completely resolved the inflammation compared to 7 of 14 WT mice (p<0.01). Compared to WTs, KO animals at day 7 had less IL1beta (p=0.025) and MIG (p=0.031) with higher TGFbeta1 (p=0.017) expression and a greater percentage of FoxP3+ regulatory T cells in the spleen and draining lymph nodes of KO animals (p<0.01). KO mice also had fewer CD68+ and F4/80+ macrophages, Ly6G+ neutrophils and CD11b+ cells infiltrating the inflamed colon.
CONCLUSIONS: Compared to WT, SPARC KO mice had less inflammation with fewer inflammatory cells and more regulatory T cells. Together, with increased TGF-beta1 levels, this could aid in the more rapid resolution of inflammation and restoration of the intestinal mucosa suggesting that the
The Relationship between Hypomagnesemia, Metformin Therapy and Cardiovascular Disease Complicating Type 2 Diabetes: The Fremantle Diabetes Study.


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

BACKGROUND: Low serum magnesium concentrations have been associated with cardiovascular disease risk and outcomes in some general population studies but there are no equivalent studies in diabetes. Metformin may have cardiovascular benefits beyond blood glucose lowering in type 2 diabetes but its association with hypomagnesemia appears paradoxical. The aim of this study was to examine relationships between metformin therapy, magnesium homoeostasis and cardiovascular disease in well-characterized type 2 patients from the community.

METHODS AND FINDINGS: We studied 940 non-insulin-treated patients (mean +/- SD age 63.4 +/- 11.6 years, 49.0% males) from the longitudinal observational Fremantle Diabetes Study Phase I (FDS1) who were followed for 12.3 +/- 5.3 years. Baseline serum magnesium was measured using stored sera. Multivariate methods were used to determine associates of prevalent and incident coronary heart disease (CHD) and cerebrovascular disease (CVD) as ascertained from self-report and linked morbidity/mortality databases. 19% of patients were hypomagnesemic (serum magnesium <0.70 mmol/L). Patients on metformin, alone or combined with a sulfonylurea, had lower serum magnesium concentrations than those on diet alone (P<0.05). There were no independent associations between serum magnesium or metformin therapy and either CHD or CVD at baseline. Incident CVD, but not CHD, was independently and inversely associated with serum magnesium (hazard ratio (95% CI) 0.28 (0.11-0.74); P=0.010), but metformin therapy was not a significant variable in these models.

CONCLUSIONS: Since hypomagnesemia appears to be an independent risk factor for CVD complicating type 2 diabetes, the value of replacement therapy should be investigated further, especially in patients at high CVD risk.
male sex, prior recent infection-related hospitalization, obesity, albuminuria, retinopathy and Aboriginal ethnicity were baseline variables independently associated with risk of first hospitalization with any infection (P<=0.005). After adjustment for these variables, baseline statin treatment was not significant (hazard ratio (95% CI), 0.70 (0.39-1.25), P=0.22). Statin use at hospitalization for pneumonia among the case-control pairs was similar (23.1% vs. 13.5%, P=0.27).

CONCLUSIONS: The risk of severe infection is increased among type 2 diabetic patients and is not reduced by statin therapy. There are a number of other easily-accessible sociodemographic and clinical variables that could be used to optimize infection-related education, prevention and management in type 2 diabetes.

PMID:23536910


A risk table to assist health practitioners assess and prevent the onset of depression in later life.

Almeida OP, Hankey GJ, et al. (Almeida) School of Psychiatry and oClinical Neurosciences, University of Western Australia, Perth, Australia (Almeida, McCaul, Flicker) WA Centre for Health and Ageing, Centre for Medical Research, University of Western Australia, Perth, Australia (Almeida) Department of Psychiatry, Royal Perth Hospital, Perth, Australia (Hankey, Yeap, Flicker) School of Medicine and Pharmacology, University of Western Australia, Perth, Australia (Hankey) Department of Neurology, Royal Perth Hospital, Perth, Australia (Yeap) Department of Endocrinology, Fremantle Hospital, Fremantle, Australia (Golledge) Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville, Australia (Flicker) Department of Geriatric Medicine, Royal Perth Hospital, Perth, Australia

O.P. Almeida, School of Psychiatry and oClinical Neurosciences (M573), University of Western Australia, 35 Stirling Highway, Crawley, Perth, WA 6009, Australia. E-mail: osvaldo.almeida@uwa.edu.au

Objective: This study aimed to develop a simple risk table of modifiable factors prospectively associated with depression in later life that could be used to guide the assessment, management and introduction of preventive strategies in clinical practice. Methods: This retrospective cohort study included 4636 men aged 65 to 83 years living in the community who denied history of past diagnosis or treatment for depression. They self-reported information about their physical activity, weight and height, smoking history, alcohol consumption and dietary habits, as well as history of hypertension, diabetes, coronary heart disease and stroke. We calculated the body mass index (BMI) in kg/m<sup>2</sup>. Three to 8 years later they were assessed with the Geriatric Depression Scale 15 (GDS-15) and those with a total score of 7 or greater were considered to display clinically significant symptoms of depression. We used binomial exponentiated log-linked general linear models to estimate the risk ratio (RR) and 95% confidence interval (95% CI) of incident depression after adjusting for age, education, marital status and prevalent medical illnesses. We calculated the probability of depression for each individual combination of risk factors and displayed the results in a risk table. Results: Two hundred and twenty-nine men (4.5%) showed evidence of incident depression 5.7 +/- 0.9 (mean. +/- standard deviation) years later. Measured dietary factors showed no association with incident depression. The probability of depression was the highest for older men who were underweight, overweight or obese, physically inactive, risk drinkers and smokers (12.0%, 95% CI = 7.0%, 17.1%), and the lowest for those who had all 4 healthy lifestyle markers: physically active, normal body mass, non-risk drinking and non-smoking (1.6%, 95% CI = 0.6%, 2.5%). The probability
of incident depression fell between these two extremes for different combinations of lifestyle practices. Conclusion: Four modifiable lifestyle factors can be used in combination to produce a risk table that predicts the probability of incident depression over a period of 3 to 8 years. The risk table is simple, informative and can be easily incorporated into clinical practice to guide assessment and risk reduction interventions. 2013.

PMID:2013724001


Intrathecal morphine (ITM) versus femoral nerve block (FNB) for elective primary hip arthroplasty post-operative analgesia.
Jadhav R, Davies A.
(Jadhav, Davies) Anaesthetics, Fremantle hospital Health Service, Fremantle, WA, Australia
R. Jadhav, Anaesthetics, Fremantle hospital Health Service, Fremantle, WA, Australia
Purpose/Objective: Introduction: An ageing population ensures primary hip arthroplasty is commonly performed. Providing good analgesia with minimal side-effects facilitates ambulation and post-operative recovery1,2. This study compares ITM with FNB for post-operative analgesia. Materials and Methods: Fifty-one patients underwent elective primary hip arthroplasty over a 3-month period. Inclusion criteria were those who had 100μg ITM and those who received FNB. Exclusion criteria were chronic pain, and combination of ITM with FNB. Analgesic efficacy was determined by average pain score on VAS and post-operative opioid consumption (morphine equivalent) at 24h and 48h. Average nausea scores, ability to mobilize at 24h and 48h were also recorded. Results: Thirty-one patients met the inclusion criteria. Eleven had ITM and 20 had FNB. Pain scores at 24h were lower with ITM. Sixty-four% scored 0/10 on VAS, 18% 1-3/10, 18% 4-6/10. Ten% patients in FNB group scored 0/10 at 24h, 25% 1-3/10, 60% 4-6/10, 5% 7-10. Average opioid consumption with ITM was 8.6mg and 12.5mg at 24h and 48h respectively, compared with 41.6mg and 17.5mg with FNB. Nausea scores were very similar in both groups. Sixty-four% of patients could mobilize at 24h and all mobilized at 48h with ITM. 45% mobilized at 24h and 80% at 48h with FNB. Conclusions: Primary hip arthroplasty can be adequately managed by a variety of analgesic techniques3. Both ITM and FNB provide good analgesia4, however this study demonstrates reduced pain with ITM, implying superior analgesia1. It may be noted that FNB in addition to ITM is unlikely to add benefit2, but this requires further evaluation.

Publication Types: Conference Abstract
PMID:71366820


Prophylactic ondansetron does not prevent shivering or decrease shivering severity during cesarean delivery under combined spinal epidural anesthesia: a randomized trial.
Browning RM, Fellingham WH, et al.
From the *Department of Anaesthesia and Pain Medicine, Fremantle Hospital; daggerDepartment of Anaesthesia, Princess Margaret Hospital; double daggerDepartment of Anaesthesia, Fremantle Hospital, Western Australia, Australia; section signDepartment of Anaesthesia, Crosshouse Hospital, Ayrshire, Scotland; **School of Medicine and Pharmacology, The University of Western Australia; and daggerdaggerDepartment of Anaesthesia and Pain Medicine, King Edward Memorial Hospital for Women, Perth, Western Australia, Australia.
OBJECTIVES: Cesarean delivery is commonly performed under regional anesthesia, which is often associated with maternal shivering. This can cause distress and interfere with monitoring. The study objective was to evaluate the antishivering efficacy of ondansetron, which reduces the incidence and severity of shivering in nonobstetric patients. We hypothesized that there would be a significant decrease in the incidence and/or severity of shivering in women who are given intravenous ondansetron 8 mg before combined spinal epidural (CSE) anesthesia, when compared with placebo.

METHODS: This was a randomized, double-blinded, parallel-group, placebo-controlled trial of 118
women scheduled for elective cesarean surgery. Women received either intravenous ondansetron 8 mg (n = 58) or saline (n = 60) before CSE anesthesia (intrathecal hyperbaric bupivacaine 0.5% 2.2-2.5 mL plus fentanyl 15 mug). The incidence and severity of shivering, measured on a validated 5-point scale, and other outcomes, such as nausea, pruritus, headache, or satisfaction, were assessed at 3 time points during the surgery and postoperative period. RESULTS: The incidence of shivering at any time point did not differ significantly between groups: ondansetron 41% versus placebo 47% (P = 0.54). The incidence of severe shivering at any time was not significantly different: ondansetron 32% versus placebo 33% (P = 0.79). There were no significant differences between the groups for any secondary outcomes. CONCLUSIONS: Intravenous ondansetron 8 mg before performing CSE anesthesia in women undergoing elective cesarean delivery does not decrease the incidence or severity of shivering.

PMID:23104146

Treating blood pressure to goal by overcoming therapeutic inertia and non-adherence.
[Spanish]
Cumplimiento del objetivo terapeutico en la hipertension mediante la superacion de la inercia y la falta de adhesion al tratamiento.
Ferrari P.
(Ferrari) University of Western Australia, Department of Nephrology, Fremantle Hospital, Perth, WA 6160, Australia
P. Ferrari, University of Western Australia, Department of Nephrology, Fremantle Hospital, Perth, WA 6160, Australia. E-mail: paolo.ferrari@health.wa.gov.au
Hypertension is a common condition and the most frequently managed problem in general practice. High blood pressure (BP) is a leading cause of mortality and disease burden. Globally, it has been difficult to attain optimal hypertension treatment and control rates. Although current practice guidelines recommend treating patients with hypertension to defined BP goals, the approach is not widely implemented, and BP control in clinical practice is much worse than that attained in clinical trials. Insufficient awareness or poor application of hypertension guidelines by physicians may be an impediment to achieving adequate BP control rates in clinical practice. Therefore, both the initiation of antihypertensive medication and the intensification of treatment to therapeutic goals in those with hypertension have been identified as evidence practice gaps (therapeutic inertia). Identifying the barriers that prevent the best use of evidence is an important first step in designing an intervention to close that evidence practice gap. The practical value of any therapy depends on a combination of effectiveness and the extent to which the patient adheres to the prescribed treatment. Even in highly developed countries only half of the patients treated for hypertension adhere to the prescribed treatment. The consequence of the low rates of adherence to BP-lowering therapy is the increasing clinical and economic burden of those conditions. Targeting therapeutic inertia and adherence to medication through a variety of strategies may help in reducing lost therapeutic benefit. Copyright Sociedad Iberoamericana de Informacion Cientifica (SIIC), 2013.
Publication Types: Review
PMID:2013726475

Are Australian sexual health clinics attracting priority populations?
(Ali, Donovan, O’Connor, Grulich, Kaldor, Guy) Kirby Institute, University of New South Wales, Sydney, NSW 2052, Australia (Donovan, McNulty) Sydney Sexual Health Centre, Sydney Hospital, Macquarie Street, Sydney, NSW 2000, Australia (Fairley, Chen) Melbourne Sexual Health Centre, 580 Swanston Street, Carlton, VIC 3053, Australia (Fairley, Chen) Melbourne School of Population and Global Health, University of Melbourne, Parkville, VIC 3010, Australia (Ryder) Clinic 34, 87 Mitchell St,
To answer a key question ('Are Australian sexual health clinics attracting priority populations?'), we used data from 44 Australian sexual health clinics between 2004 and 2011. We assessed the proportion of patients that were from priority populations (deemed to be at risk of sexually transmissible infections) and compared this to their proportions in the general population using data from Australian Bureau of Statistics and the Australian Study of Health and Relationships. A chi2-test was used. A total of 278154 new patients attended during 2004-2011. The proportions from each priority population were significantly higher (P<0.01 for all) than for the general population: young people aged 15-29 years (58.1% v. 20.1%), men who have sex with men (26.0% v. 6.0%), female sex workers (10.8% v. 0.5%), and Aboriginal and Torres Strait Islander people (4.2% v. 2.3%). This study confirms that Australian sexual health clinics attract higher proportions of priority populations and are thus meeting their mandate as defined in the 2010-2013 National Sexually Transmissible Infections Strategy. 2013 CSIRO.

PMID:2013663069

Sexually Transmitted Infections. 2013; 89.

High rates of chlamydia positivity in aboriginal and torres strait islander people attending australian sexual health services; the australian collaboration for chlamydia enhanced sentinel surveillance (ACCESS).


Introduction Australia has a widely dispersed network of public sexual health services that see large numbers of people at risk of genital Chlamydia trachomatis infection. ACCESS was established to monitor chlamydia testing and positivity rates nationally and to assist the interpretation of chlamydia diagnoses reported through passive surveillance. We report on chlamydia testing and positivity in Aboriginal and Torres Strait Islander (hereafter Aboriginal) people attending 18 sexual health services participating in ACCESS between 2006 and 2011. Methods: Using line-listed data, we analysed Aboriginal status reporting, testing rates based on first visits and chlamydia positivity in those tested. Outcomes were stratified by age group, sex, and year of attendance and were compared with non-Indigenous clients using a chi-square test and multivariate logistic regression (p < 0.05). Results: From 2006 to 2011, 7,103 (4.2%) Aboriginal people and 161,626 (95.8%) non-Indigenous people attended participating sexual health services for an initial visit. Of the Aboriginal people 5,280 (74%) were tested for chlamydia. The positivity rates in Aboriginal people were 17.0% in women (23.3% in 15-19 year olds and 18.9% in 20-24 year olds) and 17.3% in men (20.2% in 15-19 year olds and 24.3% in 20-24 year olds). There were increasing trends seen in chlamydia positivity in Aboriginal and Torres Strait Islander females and non-Indigenous males and females between 2006 and 2011 (p-trend < 0.01). On multivariate analysis, positivity was associated with younger age, being heterosexual and living in Queensland in both Aboriginal men and women. In addition, in Aboriginal men, positivity was
associated with not living in a remote area, and not having sex overseas; and in Aboriginal women, it was associated with attending in 2010 or 2011. Conclusion: The high Chlamydia positivity rates and increases over time highlight the need for enhanced prevention and screening programmes in Aboriginal people in Australia.

Publication Types: Conference Abstract
PMID:71442777

Assessing overweight and obesity across mental disorders: Personality disorders at high risk.
Stanley SH, Laugharne JD, et al.

Purpose: The aim of the present investigation is to assess the prevalence of obesity in people diagnosed as having a mental illness and to investigate differences between disorders. This adds to the paucity of research in this particular population of people and assists with preventative knowledge to obtain optimum physical health. Methods: Data were collected for all 508 male and female inpatients (new and already existing) in a public mental health service centre in Western Australia between January and December 2008. Current weight for all patients and weight gain for some patients were calculated to obtain a body mass index (BMI) value, and diagnostic information was aligned to one of the six major categories of mental illness. Results: The percentage of obese inpatients (30.3 %) was much higher than that of the general population (21.4 %), with females showing a higher propensity toward obesity than males. Most diagnostic categories had a mean BMI in the overweight range, whereas Personality Disorders had a mean BMI in the obese range (30.07). A gradual increase in weight over a 9-month time period can be seen in most patients who were assessed on more than one occasion. Conclusions: The proportion of obese people within the mental health system far exceeds that of the general population, with these people at a much greater risk of becoming obese. The highest level of obesity was found in people with a personality disorder rather than in people with psychosis. Further research is needed to ease out the mitigating factors behind weight gain occurring across disorders. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract).

Publication Types: Empirical Study; Quantitative Study
PMID:2013-04950-014

Early experience with mRI-directed implantable guide tube technique for deep brain stimulation.
Lind CRP, Thani NB, et al.

Introduction: The MRI-guided implantable guide tube technique (GT) of Gill is a completely stereotactic technique for deep brain stimulation (DBS). Methods: The GT technique was adopted for
the first time outside Bristol, UK with minor modifications. Accuracy and outcomes were assessed in a consecutive series of 36 patients undergoing GT DBS from April 2009 to December 2012. Results: In the early part of this series we published three-dimensional inaccuracy of delivering a carbothane stylette and thus DBS lead to the imaging target to be 1.8 mm (95% CI: 1.5 mm, 2.1 mm) and air entrainment median of 0.00 mL (range 0 - 2.52 mL). Safe trajectories providing the surgeon with 97.5% confidence of avoiding hazards could always be planned. Twenty seven posterior subthalamic area (PSA), 1 anterior GPI, 1 STN, and 7 postero-ventral GPI cases have been performed. Twenty six PD, 5 tremor, 1 Tourette’s, 4 dystonia cases were operated. In those with PD undergoing PSA DBS, unblinded MDS-UPDRS III improved from a mean of 48/22 without/with medications to 10 with both stimulation and medications at 6 months. There were associated marked improvements in quality ON-time in diaries and on standard quality of life measures with no decrement in neuropsychological performance or major psychiatric disorders. The smaller movement disorder groups improved well.

Conclusion: The GT technique has distinct advantages in an era of evolving stereotactic indications and brain targets: (1) it is optimized for general anesthesia during imaging and surgery facilitating accuracy and tolerability; (2) pull-out of DBS leads from the brain target is obviated by prevention of intracranial air entrainment; and (3) electrode positions can be safely and accurately documented without artifact using MRI. We have been able to achieve good clinical results without the patient being awake and without intra-operative neurological examination, stimulation or physiological recordings.

Publication Types: Conference Abstract
PMID:71073557

Stroke Research and Treatment. 2013; (362961).
Reducing haemorrhagic transformation after thrombolysis for stroke: A strategy utilising minocycline.
Blacker DJ, Prentice D, et al.
(Blacker) Department of Neurology and Clinical Neurophysiology, Sir Charles Gairdner Hospital, Nedlands, WA, Australia (Prentice, Kohler) Department of General Medicine, Royal Perth Hospital, Perth, WA 6000, Australia (Alvaro, Kelly) Department of Neurology, Fremantle Hospital, Fremantle, WA 6160, Australia (Bates, Kho) Stroke Unit, Swan District Hospital, Middle-Swan, WA 6056, Australia (Bynevelt, Thompson) Department of Neurological Intervention and Imaging Service of Western Australia, Sir Charles Gairdner Hospital, Nedlands, WA 6009, Australia (Hankey) Department of Neurology, Royal Perth Hospital, Perth, WA 6000, Australia (Major) Data Analysis Australia, Nedlands, WA 6009, Australia (Blacker, Bates, Hankey) School of Medicine and Pharmacology, University of Western Australia, Nedlands, WA 6009, Australia
D.J. Blacker, Department of Neurology and Clinical Neurophysiology, Sir Charles Gairdner Hospital, Nedlands, WA, Australia. E-mail: david.blacker@health.wa.gov.au
Haemorrhagic transformation (HT) of recently ischaemic brain is a feared complication of thrombolytic therapy that may be caused or compounded by ischaemia-induced activation of matrix metalloproteinases (MMPs). The tetracycline antibiotic minocycline inhibits matrix MMPs and reduces macroscopic HT in rodents with stroke treated with tissue plasminogen activator (tPA). The West Australian Intravenous Minocycline and TPA Stroke Study (WAIMATSS) aims to determine the safety and efficacy of adding minocycline to tPA in acute ischaemic stroke. The WAIMATSS is a multicentre, prospective, and randomised pilot study of intravenous minocycline, 200 mg 12 hourly for 5 doses, compared with standard care, in patients with ischaemic stroke treated with intravenous tPA. The primary endpoint is HT diagnosed by brain CT and MRI. Secondary endpoints include clinical outcome measures. Some illustrative cases from the early recruitment phase of this study will be presented, and future perspectives will be discussed. 2013 David J. Blacker et al.
PMID:2013291310
Control of major haemorrhage and damage control surgery.
Mylan KJ, Wyatt MG.
(Mylan) Department of Vascular and Endovascular Surgery, Fremantle Hospital, Perth, WA, Australia (Wyatt) Freeman Hospital, Newcastle upon Tyne, United Kingdom
Department of Vascular and Endovascular Surgery, Fremantle Hospital, Perth, WA, Australia
Major haemorrhage is defined as 'life-threatening bleeding'. It is associated with significant morbidity and mortality and prompt, expeditious control of haemorrhage is essential to improve patient outcome. Understanding the mechanism of injury in trauma and a systematic approach to clinical examination and assessment of blood loss are essential to identify the patient with a life-threatening bleed. Permissive hypotension, correction of coagulopathy and avoidance of hypothermia are important during the resuscitation phase. Special investigations for major haemorrhage are reserved for the haemodynamically stable patient. There are some generic surgical principles, which apply to all scenarios of major haemorrhage, and endovascular interventions have added a further dimension to this management strategy. Recent advances in survivability following polytrauma are credited to the modern concept of an integrated approach to damage control resuscitation and damage control surgery. This article aims to discuss some of these key principles that govern the management of the patient with major haemorrhage. 2013 Published by Elsevier Ltd.
PMID:2013670423

Peri-operative third party red blood cell transfusion in renal transplantation and the risk of antibody-mediated rejection and graft loss.
Fidler S, Swaminathan R, et al.
(Fidler, Witt, Christiansen, D'Orsogna) Department of Clinical Immunology, PathWest, Royal Perth Hospital, WA, Australia (Fidler, Witt, Christiansen, D'Orsogna) School of Pathology and Laboratory Medicine, University of Western Australia, Australia (Swaminathan, Irish) Medical Renal Transplant Unit, Royal Perth Hospital, WA, Australia (Swaminathan, Irish) School of Medicine and Pharmacology, University of Western Australia, Australia (Lim) Department of Nephrology Sir Charles Gairdner Hospital, Perth, WA, Australia (Ferrari) Department of Nephrology Fremantle Hospital, Fremantle, WA, Australia
A.B. Irish, Medical Renal Transplant Unit, Royal Perth Hospital, GPO Box X2213, Perth, WA 6847, Australia. E-mail: Ashley.Irish@health.wa.gov.au
Historic red blood cell transfusion (RBCT) may induce anti-HLA antibody which, if donor specific (DSA), is associated with increased antibody-mediated rejection (AMR). Whether post-operative RBCT influences this risk is unknown. We examined the RBCT history in 258 renal transplant recipients stratified according to prevalent recipient HLA antibody (DSA, Non-DSA or No Antibody). AMR occurred more frequently in patients who received RBCT both pre and post transplant compared with all other groups (Pre. +. Post-RBCT 21%, Pre-RBCT 4%, Post-RBCT 6%, No-RBCT 6%, HR 4.1 p = 0.004). In the 63 patients who received Pre. +. Post-RBCT, 65% (13/20) with DSA developed AMR compared with 0/6 in the Non-DSA group and 2/37 (5%) in the No-Antibody group (HR 13.9 p < 0.001). In patients who received No-RBCT, Pre-RBCT or Post-RBCT there was no difference in AMR between patients with DSA, Non-DSA or No-Antibody. Graft loss was independently associated with Pre. +. Post-RBCT (HR 6.5, p = 0.001) AMR (HR 23.9 p < 0.001) and Non-AMR (6.0 p = 0.003) after adjusting for DSA and delayed graft function. Re-exposure to RBCT at the time of transplant is associated with increased AMR only in patients with preformed DSA, suggesting that RBCT provides additional allostimulation. Patients receiving Pre. +. Post-RBCT also had an increased risk of graft loss independently of AMR or DSA. Both pre and post procedural RBCT in renal transplantation is associated with modification of immunological risk and warrants additional study. 2013.
PMID:2014213112
Pre-transplant donor specific anti-HLA antibody is associated with antibody-mediated rejection, progressive graft dysfunction and patient death.

Fidler SJ, Irish AB, et al. (Fidler) Department of Clinical Immunology, PathWest, Royal Perth Hospital, University of Western Australia, Australia (Fidler) School of Pathology and Laboratory Medicine, University of Western Australia, Australia (Irish, Witt, Christiansen) Department of Nephrology, Royal Perth Hospital, University of Western Australia, Australia (Irish, Witt, Christiansen) School of Medicine and Pharmacology, University of Western Australia, Australia (Lim) Department of Nephrology, Sir Charles Gairdner Hospital, University of Western Australia, Australia (Ferrari) Department of Nephrology, Fremantle Hospital, University of Western Australia, Australia

S.J. Fidler, Department of Clinical Immunology, PathWest, Royal Perth Hospital, Wellington Street, Perth, WA 6000, Australia. E-mail: Samantha.Fidler@health.wa.gov.au

Background: The long term effect of donor specific antibodies (DSA) detected by Luminex Single Antigen Bead (SAB) assay in the absence of a positive complement-dependant cytotoxicity (CDC) crossmatch is unclear. DSA at the time of transplant were determined retrospectively in 258 renal transplant recipients from 2003 to 2007 and their relationship with rejection and graft function prospectively evaluated. After a median of 5.6. years follow-up 9% of patients had antibody mediated rejection (AMR) (DSA 11/37 (30%), DSA-Neg 13/221 (6%), HR 6.6, p < 0.001). Patients with anti-HLA class II (HR 6.1) or both class I + II (HR 10.1) DSA had the greatest risk for AMR. The Mean Fluorescent Intensity (MFI) of the DSA was significantly higher in patients with AMR than those with no rejection (p. = 0.006). Moreover, the strength of the antibody was shown to be important, with the risk of AMR significantly greater in those with DSA > 8000 MFI than those with DSA < 8000 MFI (HR 23, p < 0.001). eGFR progressively declined in patients with DSA but was stable in those without DSA (35.7 +/- 20.4. mls/min vs 48.5 +/- 22.7) and composite patient and graft survival was significantly worse in those with class II (HR 2.9) or both class I + II (HR 3.7) but not class I DSA. Class II DSA alone, or in combination with class I DSA had the strongest association with graft loss and patient death. Patients with DSA not only have increased rates of acute AMR, but also chronic graft dysfunction, graft loss and death. Antibody burden quantified by SAB assay may identify patients at highest immunological risk and therefore influence patient management and improve long-term patient outcome. 2013 Elsevier B.V.

PMID:2013425770

Response to kute: 'facilitators to national kidney paired donation program'.
Ferrari P.
Department of Nephrology, Fremantle Hospital, Perth, WA, Australia; School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia; Australian Paired Kidney Exchange Program, Perth, WA, Australia. paolo.ferrari@health.wa.gov.au.
Publication Types: Letter
PMID:23437918

ABO-Incompatible Matching Significantly Enhances Transplant Rates in Kidney Paired Donation.
Ferrari P, Hughes PD, et al.
1 Department of Nephrology, Fremantle Hospital, Perth, Western Australia, Australia. 2 School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia. 3 Department of Nephrology, Royal Melbourne Hospital, Parkville, Victoria, Australia. 4 Department of Nephrology, Western Hospital, Footscray, Victoria, Australia. 5 University of Melbourne, Melbourne, Victoria, Australia. 6 Department of Immunology, PathWest, Royal Perth Hospital, Perth, Western
Australia, Australia. 7 School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia, Australia. 8 Address correspondence to: Paolo Ferrari, M.D., Australian Paired Kidney Exchange Program, Department of Nephrology, Fremantle Hospital, School of Medicine and Pharmacology, University of Western Australia, Perth WA 6160, Australia.

BACKGROUND: Although preformed donor-specific anti-human leukocyte antigen antibodies (DSA) can be overcome by plasmapheresis-based strategies with some success in renal transplantation, kidney paired donation (KPD) is a more effective strategy to avoid DSA. In contrast, ABO incompatibility can be crossed with outcomes equivalent to ABO-compatible transplantation. Here, we report the ability of accepting human leukocyte antigen-compatible but ABO-incompatible donors to increase the number of exchanges in a KPD program.

METHODS: In the Australian KPD program, virtual crossmatch is used to allocate suitable donors to recipients. Acceptance of ABO-incompatible donors is allowed in cases where anti-blood group antibody titres are deemed amenable to removal by apheresis or immunoabsorption. The number of matched recipients, identified chains, and transplants performed with and without acceptance of ABO incompatibility was analyzed.

RESULTS: In 2 years, 115 pairs were included in nine quarterly match runs. Incompatibility due to DSA accounted for 86% of the listed pairs and 52% were also blood group incompatible to their coregistered donor. Median calculated panel-reactive antibody in registered recipients was 83% (mean, 67%+/37%). ABO-incompatible donors were accepted for 36 patients. Two waitlist recipients and 48 KPD candidates were matched and transplanted. Ten recipients (20%) of an ABO-incompatible donor kidney were distributed across 8 chains that resulted in 21 recipients being transplanted. Thus, without ABO-incompatible matching, only 27 recipients in 12 chains would have been transplanted.

CONCLUSION: Acceptance of blood group-incompatible donors for patients with low to moderate anti-blood group antibody significantly increases transplant rates for highly sensitized recipients.

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Modelling the benefits and costs of integrating an acceptable HLA mismatch allocation model for highly-sensitised patients.


(Nguyen, Lim) Department of Renal Medicine, Sir Charles Gairdner Hospital, Perth, Australia (Wong, Howard, Craig) Sydney School of Public Health, University of Sydney, Sydney, Australia (Wong, Craig, Chapman) Centre for Kidney Research, Children’s Hospital at Westmead, Westmead Hospital, Sydney, Australia (Clas) Eurotransplant Reference Laboratory, Department Immunohematology and Blood Transfusion, Leiden University Medical Centre, Leiden, Netherlands (Fidler, D’Orsogna, Christiansen) Department of Clinical Immunology, Royal Perth Hospital, Perth, Australia (Irish) Department of Renal Medicine, Royal Perth Hospital, Sydney, Australia (Ferrari) Department of Renal Medicine, Fremantle Hospital, Perth, Australia

W. Lim, Department of Renal Medicine, Sir Charles Gairdner Hospital, Perth, Australia

Background: The Eurotransplant acceptable mismatch program has improved transplantation access for highly-sensitised recipients. However, the benefits and costs of implementing such a program remain unknown. Methods: Using decision analytical modelling, we compared the average waiting time for transplantation, overall survival gains (in life-years and quality-adjusted life-years gained) and costs of integrating an acceptable mismatch allocation model compared with the current deceased-donor kidney allocation model in Australia. Results: Acceptable mismatches were identified in 12 of 28 (43%) highly-sensitised recipients using HLAMatchmaker. Inclusion of acceptable mismatches in the current allocation model improved the transplantation access for 4 (14%) highly-sensitised recipients, with an average reduction in waiting time of 34 months (from 86 to 52 months). Compared with the current allocation model, incorporating an acceptable mismatch allocation model achieved an overall lifetime gain of 0.034 quality-adjusted life-years and savings of over $4,000 per highly-sensitised patient, with a small consequential loss of 0.005 quality-adjusted life-years and extra costs of $800 for
every reallocated patient. Conclusions: Despite modest overall health gains, application of an acceptable mismatch allocation model is an equitable approach to improve transplantation access for highly-sensitised transplant candidates without compromising the overall health benefits among the other patients on the deceased-donor waitlist in Australia.
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**A developmental ontology for the mammalian brain based on the prosomeric model.**

(Puelles) Department of Human Anatomy, University of Murcia, Murcia 30003, Spain (Harrison) Fremantle Hospital, Fremantle 6160, Australia (Paxinos, Watson) Neuroscience Research Australia, Sydney 2031, Australia (Paxinos, Watson) University of New South Wales, Sydney 2052, Australia (Watson) Faculty of Health Sciences, Curtin University, Perth 6845, Australia  
C. Watson, Department of Human Anatomy, University of Murcia, Murcia 30003, Spain. E-mail: c.watson@curtin.edu.au  

In the past, attempts to create a hierarchical classification of brain structures (an ontology) have been limited by the lack of adequate data on developmental processes. Recent studies on gene expression during brain development have demonstrated the true morphologic interrelations of different parts of the brain. A developmental ontology takes into account the progressive rostrocaudal and dorsoventral differentiation of the neural tube, and the radial migration of derivatives from progenitor areas, using fate mapping and other experimental techniques. In this review, we used the prosomeric model of brain development to build a hierarchical classification of brain structures based chiefly on gene expression. Because genomic control of neural morphogenesis is remarkably conservative, this ontology should prove essentially valid for all vertebrates, aiding terminological unification. 2013.  
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