Catastrophic failure of 4 cobalt-alloy Omnifit hip arthroplasty femoral components.
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Background Femoral component neck fracture is an uncommon type of failure in total hip arthroplasty. We present a report on 4 retrieved cobalt-chrome femoral components that fractured at the neck, where we investigated the mechanisms of failure. Methods The 4 retrieved implants were analyzed with regard to their macro- and microstructures and the fracture surfaces were examined using electron microscopy. The medical record of each patient was also examined for any history of complications prior to failure of the implant. Results These fractures occurred immediately adjacent to the base of the modular head. Skirted modular heads were used in 3 of the 4 failed components. This constructs promotes corrosion. Cyclic fatigue-loading in combination with the material factors of course grain microstructure and extensive carbide precipitation along the grain boundaries were also identified as the cause of implant failure. Interpretation Our findings suggest that a solution annealing step could be introduced into the manufacturing process to improve the microstructure of the cobalt chrome alloy. We also advise caution in using a skirted modular head in combination with a device of known suboptimum microstructure, for a greater margin of safety.

Rectal tacrolimus in the treatment of resistant ulcerative proctitis.
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BACKGROUND: Resistant ulcerative proctitis can be extremely difficult to manage. Oral tacrolimus can be effective, but may have numerous adverse effects. Topically administered tacrolimus, however, may also be effective in proctitis. Aim To undertake a pilot study to assess a potential role for topical tacrolimus in the management of resistant ulcerative proctitis. METHODS: Patients with resistant ulcerative proctitis were assessed prospectively by the colitis activity index (CAI) and Modified Mayo score. Topical rectal tacrolimus ointment was commenced at 0.3 mg/mL 3 mL b.d. and increased depending on clinical response. CAI and modified Mayo scores were assessed at 0 and 8 weeks, as were steroid usage and adverse effects. RESULTS: Eight patients (five male/three female) with inflammation to a maximum of 30 cm from the anus were included. All patients had failed disease control with 5-aminosalicylic acids, steroids, immunosuppressants and infliximab therapy. The mean initial CAI was 12.1 (range 9-16) and the mean modified Mayo score was 8.0 (range 6-9). After 8 weeks, six of eight patients achieved remission with steroids reduced or ceased in five of six. There were no significant adverse effects. CONCLUSIONS: This prospective pilot study demonstrated that topical rectal tacrolimus ointment can be effective in ulcerative proctitis. The preparation was well tolerated with no significant adverse effects. Further controlled studies are required.

Mirtazapine associated with profound hyponatremia: Two case reports.
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Background: Depression is a common problem in the elderly, and the recognition and appropriate management of this illness are important aspects of geriatric medicine. Selective serotonin reuptake inhibitors have been associated with hyponatremia, but the association of mirtazapine with hyponatremia is less well documented. Objective: The goal of this research was to highlight and
characterize the association between mirtazapine and hyponatremia. We present here 2 case reports as well as the results of a literature review. Case summaries: Two patients, a 61-year-old man and a 79-year-old woman, developed profound hyponatremia (sodium levels, 112 and 113 mEq/L, respectively) 7 and 10 days after commencement of mirtazapine for symptoms of depression. Investigations excluded other causes, and cessation of mirtazapine was associated with recovery of sodium levels to [greater-than or equal to]132 mEq/L after 7 and 10 days, respectively. Conclusions: The likelihood of mirtazapine use causing hyponatremia in these 2 cases was "probable" according to criteria of the Naranjo Adverse Drug Reaction Probability Scale (score, 6). A review of published cases found that mirtazapine-associated hyponatremia occurred in patients aged >60 years, after a mean of 6.5 days and with doses as low as 7.5 mg daily. The mean sodium nadir was 117.2 mEq/L, but after stopping mirtazapine, the mean time to recovery was 11 days. Clinicians should be aware of the possibility of this reaction in elderly patients and should monitor sodium levels in high-risk patients if symptoms suggestive of hyponatremia develop. copyright 2008 Excerpta Medica Inc. All rights reserved.

PMID:2008359358

Prevalence and Risk Factor Correlates of Elevated C-Reactive Protein in an Adult Australian Population.
Hung J, Knuiman MW, et al.
(Hung) School of Medicine and Pharmacology, Sir Charles Gairdner Hospital Unit, University of Western Australia. Perth, WA, Australia. (Knuiman, Divitini) School of Population Health, University of Western Australia. Perth, WA, Australia. (Davis) School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia. Perth, WA, Australia. (Beilby) Clinical Biochemistry PathWest and School of Surgery and Pathology, University of Western Australia. Perth, WA, Australia. Measurement of the inflammatory biomarker C-reactive protein (CRP) is advocated for coronary heart disease risk assessment. The distribution and correlates of CRP in the general population should be known before it is used in clinical practice. CRP was measured in 1,761 men and 2,248 women aged 25 to 84 years who attended the 1994/1995 Busselton Health Survey. Prevalences of increased CRP >3 mg/L for age groups 25 to 39, 40 to 59, and 60 to 84 years were 15.7%, 20.6%, and 38.7%, respectively, in men and 21.2%, 22.1%, and 33.7%, respectively, in women not on hormone therapy. Logistic regression analysis identified independent predictors of increased CRP in men as obesity (odds ratio [OR] 3.5, 95% confidence interval [CI] 2.4 to 5.0), smoking (OR 3.1, 95% CI 2.1 to 4.5), hypertension (OR 1.6, 95% CI 1.1 to 2.3), and low high-density lipoprotein cholesterol (OR 1.4, 95% CI 1.0 to 1.8). In women, predictors were obesity (OR 7.8, 95% CI 5.8 to 10.6), hypertension (OR 1.4, 95% CI 1.0 to 1.9), high triglycerides (OR 1.6, 95% CI 1.1 to 2.4), vigorous exercise (OR 0.7, 95% CI 0.5 to 0.9), oral contraceptive use (OR 4.6, 95% CI 3.3 to 6.5), and hormone replacement therapy (OR 2.8, 95% CI 1.9 to 4.0). Overall, risks of increased CRP attributable to the presence of an abnormal or borderline coronary heart disease risk factor were 59% for men and 64% for women. In conclusion, despite gender-related differences in cardiovascular risk, increased CRP occurred commonly in men and women. Because increased CRP was largely attributable to conventional coronary heart disease risk factors, measurement of CRP may have limited utility for risk screening and primary prevention. copyright 2008 Elsevier Inc. All rights reserved.
PMID:2008002100

A survey was conducted to determine sedation and delirium practices in Australian and New Zealand intensive care units. The survey was in two parts, comprising an online survey of reported sedation and delirium management (unit survey) and a collection of de-identified data about each patient in a unit at a given time on a specified day (patient snapshot survey). All intensive care units throughout Australia and New Zealand were invited by email to participate in the survey. Twenty-three predominantly metropolitan, level III Australian and New Zealand intensive care units treating adult patients participated. Written sedation policies were in place in 48% of units, while an additional 44% of units reported having informal sedation policies. Seventy percent of units routinely used a sedation scale. In contrast, only 9% of units routinely used a delirium scale. Continuous intravenous infusion is the primary means of patient sedation (74% of units). While 30% of units reported routinely interrupting sedation, only 10% of sedated patients in the snapshot survey had had their sedation interrupted in the preceding 12 hours. Oversedation appears to be common (46% of patients with completed sedation scales). Use of neuromuscular blockade is low (10%) compared to other published studies. Midazolam and propofol were the most frequently used sedatives. The proportion of patients developing delirium was 21% of assessable patients. Failed and self-extubation rates were low: 3.2% and 0.5% respectively. In Australian and New Zealand intensive care units, routine use of sedation scales is common but not universal, while routine delirium assessment is rare. The use of a sedation protocol is valuable and should be encouraged.
median duration of 10.5 months in responders. Six of 13 reresponders had the same or a longer response and six more remain in complete response. The median event-free survival was not significantly different for the two treatments. There was no significant difference in the severity of myelosuppression. Four patients developed hypothyroidism with three requiring thyroxine. One patient developed AML, with no other cases of MDS. The actuarial progression-free survival rate at 12 months was 36%. Conclusions: Repeat 131I-rituximab induces high response rates, some of which result in durable remissions in patients who had previously responded. copyright The Author 2008. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. PMID:2008415395

Pharmacokinetics and efficacy of piperaquine and chloroquine in melanesian children with uncomplicated malaria.
Karunajeewa HA, Ilett KF, et al.
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The disposition of chloroquine (CQ) and the related 4-aminoquinoline, piperaquine (PQ), were compared in Papua New Guinean children with uncomplicated malaria. Twenty-two children were randomized to 3 days of PQ phosphate at 20 mg/kg/day (12 mg of PQ base/kg/day) coformulated with dihydroartemisinin (DHA-PQ), and twenty children were randomized to 3 days of CQ at 10 mg base/kg/day with a single dose of sulfadoxine-pyrimethamine (CQ-SP). After a 42-day intensive sampling protocol, PQ, CQ, and its active metabolite monodesethyl-chloroquine (DECQ) were assayed in plasma by using high-performance liquid chromatography. A two-compartment model with first-order absorption was fitted to the PQ and CQ data. There were no significant differences in age, gender, body weight, or admission parasitemia between the two groups. The PCR-corrected 42-day adequate clinical and parasitological responses were 100% for DHA-PQ and 94% for CQ-SP, but P. falciparum reinfections during follow-up were common (33 and 18%, respectively). For PQ, the median volume of distribution at steady state, allowing for bioavailability (V(ss)/F), was 431 liters/kg (interquartile range [IQR], 283 to 588 liters/kg), the median clearance (CL/F) was 0.85 liters/h/kg (IQR, 0.67 to 1.06 liters/h/kg), the median distribution half-life (t(1/2)(alpha)) was 0.12 h (IQR, 0.05 to 0.66 h), and the median elimination half-life (t(1/2)(beta)) was 413 h (IQR, 318 to 516 h). For CQ, the median V(ss)/F was 154 liters/kg (IQR, 101 to 210 liters/kg), the median CL/F was 0.80 liters/h/kg (IQR, 0.52 to 0.96 liters/h/kg), the median t(1/2)(alpha) was 0.43 h (IQR, 0.05 to 1.82 h), and the median t(1/2)(beta) was 233 h (IQR, 206 to 298 h). The noncompartmentally derived median DECQ t(1/2)(beta) was 290 h (IQR, 236 to 368 h). Combined molar concentrations of DECQ and CQ were higher than those of PQ during the elimination phase. Although PQ has a longer t(1/2)(beta) than CQ, its prompt distribution and lack of active metabolite may limit its posttreatment malaria-suppressive properties.
Publication Types: Journal Article
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Abdominal aortic aneurysm, inguinal hernias and emphysema.
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PMID:2008498243

**Trends in embolectomy of the extremities: a population-based study.**

Ponosh S, Broadhurst R, et al.

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**Background:** There is anecdotal evidence that fewer brachial and femoral embolectomies are being carried out. This may be because of the greater use of anticoagulation in patients with atrial fibrillation. The aim of the present study was to assess community-wide temporal trends in embolectomy of the extremities and of warfarin usage.

**Methods:** The Western Australian Linked Data System was used to identify cases of extremity embolectomy with a combination of diagnosis (upper or lower limb embolus) and procedure (embolectomy and revascularization) codes. Trends in age-specific and age-standardized rates were assessed over the period 1992-2003. Data regarding warfarin prescriptions were acquired from the Pharmaceutical Benefits Schedule database for the period 2000-2005.

**Results:** One thousand and five patients aged 30 years and more underwent an embolectomy of the extremity during the study period. The age-specific rate of embolectomy increased from 0.78 per 100 000 in the 30- to 49-year-old group to 46.1 per 100 000 for those aged 80 years and more. There was a significant downward trend between 1992 and 2003 (Cuzik's trend test P = 0.015). This pattern was seen for all age groups. Prescriptions for warfarin increased by 50.4% over the period 2000-2005.

**Conclusion:** The rates of embolectomy of the extremity appear to be falling. Although the cause for this trend is not known, one possible explanation is increasing prescription of warfarin. copyright 2008 The Authors.

PMID:2008292719


**Risk factors for Type II endoleaks after endovascular repair of abdominal aortic aneurysms.**


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**Background:** Endovascular repair has been shown to be superior to open repair of abdominal aortic aneurysm in terms of aneurysm-related survival. However, endovascular repair has its own unique complications such as endoleak. Type II endoleaks may be associated with aortic rupture. We attempt to identify patient variables associated with the development of endoleaks and hence facilitate their early identification.

**Methods:** Endovascular repair was carried out for non-ruptured, infrarenal abdominal aortic aneurysms. Patients underwent preoperative computed tomography and angiography and were followed up with computed tomography and/or ultrasound scan at 1, 3 and 6 months and yearly thereafter. Univariate and multivariate analysis was used to identify any patient factors associated with the risk for developing an endoleak.

**Results:** One hundred and one patients were included in the study (12 female: 89 male). Age 59-93 years. Mean follow up was 20.2 months. Type II endoleaks developed in 26 (25.7%) patients. Fifteen cases resolved during follow up, three of which required secondary intervention. Nine cases persist. No aneurysms ruptured. The presence of patent inferior mesenteric artery (P < 0.001) and sac enlargement (P = 0.001) were associated with development of endoleak as was diabetes in a multivariate model (P = 0.005). History of smoking (P = 0.01) was a protective factor. The presence of four or more lumbar arteries (P = 0.55) was not associated with increased risk.

**Conclusions:** It is possible to identify individual patient risk factors associated with risk for developing type II endoleaks and it may be possible to modify screening practice as a result. The association between patent inferior mesenteric artery preoperatively and endoleak is further confirmed. Spontaneous sealing of endoleaks is common and rupture is rare. Early intervention is not mandatory.

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Homocysteine and depression in later life.
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Context: The prevalence of depression in later life increases with plasma total homocysteine concentration (tHcy). High tHcy accounts for about 15% of prevalent cases, but observational studies are prone to confounding and bias. Genetic association studies are not prone to the same sources of error and offer an opportunity to explore the consistency and external validity of this association.,
Objective: To determine if tHcy is causally related to depression in later life., Design: Cross-sectional study (Health in Men Study), systematic review, and meta-analysis., Patients: Community sample of 3752 men aged 70 years or older (Health in Men Study)., Main Outcome Measures: Fifteen-Item Geriatric Depression Scale and self-reported past or current treatment for depression (Health in Men Study)., Results: In the Health in Men Study, the odds ratio (OR) of prevalent depression increased 4% (OR, 1.04; 95% confidence interval [CI], 1.02-1.05) with every unit increase of tHcy (micromoles per liter). The tHcy was 0.19 mg/L higher among participants with the MTHFR C677T TT genotype compared with the CC genotype. The meta-analysis showed that older adults with high tHcy had increased risk of depression (OR, 1.70; 95% CI, 1.38-2.08) and TT carriers were 22% more likely than CC carriers to have current depression or a history of depression (OR, 1.22; 95% CI, 1.01-1.47)., Conclusions: The triangular association between the MTHFR genotype, tHcy, and depression implies that higher concentrations of tHcy increase the risk of depression and that lowering tHcy by 0.19 mg/L could reduce the odds of depression by about 20%. Confirmatory data from sufficiently powered randomized trials of homocysteine-lowering therapy are now required to test if the relationship between tHcy and depression is truly causal., Copyright 2008 by the American Medical Association. All Rights Reserved. Applicable FARS/DFARS Restrictions Apply to Government Use. American Medical Association, 515 N. State St, Chicago, IL 60610.

Low free testosterone concentration as a potentially treatable cause of depressive symptoms in older men.
Almeida OP, Yeap BB, et al.
Western Australian Centre for Health and Ageing (Drs Almeida, Hankey, and Flicker) and Schools of Psychiatry and Clinical Neurosciences (Dr Almeida) and Medicine and Pharmacology (Drs Yeap, Hankey, and Flicker), University of Western Australia, Perth; Departments of Psychiatry (Dr Almeida) and Geriatric Medicine (Dr Flicker) and Stroke Unit (Dr Hankey), Royal Perth Hospital, Perth; Department of Endocrinology, Fremantle Hospital, Fremantle (Dr Yeap); and School of Population Health and Clinical Practice, University of Adelaide, Adelaide (Dr Jamrozik), Australia.
Context: Serum concentrations of gonadal hormones have been associated with various measures of well-being, but it is unclear whether their association with mood is confounded by concurrent physical morbidity., Objective: To determine whether the association between serum testosterone concentration and mood in older men is independent of physical comorbidity., Design: Cross-sectional study., Setting: Community of Perth, Western Australia., Participants: A community sample of men aged 71 to 89 years., Main Outcome Measures: We used the 15-item Geriatric Depression Scale (GDS-15) to assess depressed mood. Clinically significant depression was defined a priori as a GDS-15 score of 7 or greater. Physical health was assessed using the weighted Charlson index and the Physical Component Summary score of the 36-Item Short Form Health Survey., Results: Of 3987 men
included in the study, 203 (5.1%; 95% confidence interval [CI], 4.4%-5.8%) had depression. Participants with depression had significantly lower total and free testosterone concentrations than nondepressed men (P < .001 for both). However, they were also more likely to smoke and to have low educational attainment, a body mass index categorized as obese, a Mini-Mental State Examination score less than 24, a history of antidepressant drug treatment, and greater concurrent physical morbidity. After adjusting for these factors and for age, men with depression were 1.55 (95% CI, 0.91-2.63) and 2.71 (95% CI, 1.49-4.93) times more likely to have total and free testosterone concentrations, respectively, in the lowest quintile., Conclusions: A free testosterone concentration in the lowest quintile is associated with a higher prevalence of depression, and this association cannot be adequately explained by physical comorbidity. A randomized controlled trial is required to determine whether the link between low free testosterone level and depression is causal because older men with depression may benefit from systematic screening of free testosterone concentration and testosterone supplementation., Copyright 2008 by the American Medical Association. All Rights Reserved. Applicable FARS/DFARS Restrictions Apply to Government Use. American Medical Association, 515 N. State St, Chicago, IL 60610.

Australasian Journal of Dermatology. 2008; 49(1): 30-34. Complete resolution of recurrent calciphylaxis with long-term intravenous sodium thiosulfate. Subramaniam K, Wallace H, et al. Departments of (1)Nephrology and Renal Transplantation and (3)Pathology, PathWest, Royal Perth Hospital, Perth, and (2)School of Surgery and Pathology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia SUMMARY: A 35-year-old morbidly obese woman on home haemodialysis presented with painful indurated subcutaneous nodules histologically characteristic of calciphylaxis. After failing to respond to conventional treatment, she was commenced on an intravenous infusion of 25 g of sodium thiosulfate three times per week. Two weeks after commencing sodium thiosulfate, the pain resolved completely. By 12 weeks, the lesions had healed and the infusions were ceased. Two months later, skin lesions recurred, but resolved again within 3 months of recommencement of sodium thiosulfate treatment, which was continued for 8 months. The treatment was well tolerated. There has been no recurrence of lesions in the 18 months since the cessation of sodium thiosulfate. Clinical trials to determine the optimum dose and duration of therapy for sodium thiosulfate treatment of calciphylaxis should be given priority because of its high rate of success in treating what is otherwise a severe and mostly lethal condition., Copyright (C) 2008 Blackwell Publishing Ltd.

Australasian Journal on Ageing. 2008; 27(3): 134-142. Antipsychotic use in the elderly: What doctors say they do, and what they do. Tiller J, Ames D, et al. Albert Road Clinic, The University of Melbourne, Melbourne, Victoria, Australia (Tiller), National Ageing Research Institute, The University of Melbourne, Melbourne, Victoria, Australia (Ames), Primary Dementia Collaborative Research Centre, School of Psychiatry, University of New South Wales, Sydney, New South Wales, Australia (Brodaty), Royal Brisbane and Women's Hospital, The University of Queensland, Brisbane, Queensland, Australia (Byrne), Fremantle Hospital, Fremantle, Western Australia, Australia (Halliday) (Snowdon), Statistical Consulting Centre, The University of Melbourne, Melbourne, Victoria, Australia (Hepworth), Albert Road Clinic, Melbourne, Victoria, Australia (McArdle), The Melbourne Clinic, The University of Melbourne, Melbourne, Victoria, Australia (Schweitzer) Objective: To review psychiatrists' attitudes and actual practice on the use of typical and atypical antipsychotics in the elderly., Methods: Audit data were collected from 18-old-age psychiatry units across Australia. The attitudes of old age psychiatrists and their perceptions of the efficacy, tolerability and clinical usefulness of antipsychotics were examined., Results: The medications used for 321 patients were audited, and the attitudes of the 57 prescribing doctors were assessed. All available
atypicals were prescribed and reported as more efficacious and clinically useful than typicals. Adverse events perceived by doctors as an obstacle to prescribing were more frequent than reported adverse event rates in product information. All diagnostic groups improved. Off-label use comprised almost 22% in this sample.
Conclusions: Adverse events are impediments to prescribing, more so with typical than atypical antipsychotics. All available atypicals were used and appeared effective in this elderly population., Copyright (C) 2008 Blackwell Publishing Ltd.


Record linkage of hospital and death data increased identification of dementia cases and death rate estimates.
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Medicinal mishap: Severe hyponatraemia due to mirtazapine.
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PMID:2008377888


Fc-Based Cytokines: Prospects for Engineering Superior Therapeutics.
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The application of Fc (fragment crystallizable)-based cytokines (the fusion of the constant region of IgG to a cytokine of interest) as biotherapeutic agents to modulate inflammatory and immune responses has become increasingly popular in recent years. This is because in their monomeric form, cytokines are relatively small molecules with short serum half-lives, which necessitates frequent administration and thus limits their clinical utility. To rectify the problem, attempts have been made to improve the stability of these agents in vivo. This has been achieved through diverse strategies such as modification with polyethylene glycol (PEGylation) or by ligating the cytokine to protein moieties such as the constant heavy chain of IgG, known as the Fc fragment. The construction of Fc chimeric proteins has been shown to improve pharmacokinetics. However, since there is an inverse relationship between the size of molecules and the rate at which they diffuse through mucus, Fc fusion constructs potentially have a lower rate of diffusion. Consequently, a compromise is reached whereby Fc constructs are engineered to incorporate ligated cytokines in a monomeric form (one molecule of cytokine fused to a single Fc dimer) rather than in a dimeric form (two molecules of cytokine fused to a single Fc dimer). A recent and novel approach to improve stability in serum is a procedure that involves sheathing cytokines in protective protein covers called latency peptides. The enclosed cytokine is protected from degradation and allowed to act where needed when the outer peptide cover is removed. For some applications, a reduced serum half-life is desirable; for example, where there is a need to reduce IgG levels in antibody-mediated diseases. To achieve this goal, a strategy called AbDeg, which involves enhanced Ig degradation, has been devised. This article provides an overview of the design and construction of Fc-based cytokines, in both dimeric and monomeric forms. Several examples of recent applications of such constructs, which include cytokine antagonism, cytokine traps, gene therapy and drug delivery, are also discussed. Other antibody-engineered constructs such as Fab (fragment, antigen binding) and single chain Fv (fragment, variable) fusions are also briefly covered., Copyright 2008 Adis Data Information BV
Laparoscopic radical prostatectomy: the WA experience: 090.
Dyer J, Shannon T, et al.
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Publication Types: Abstract

Effects of self-management, education and specific exercises, delivered by health professionals, in patients with osteoarthritis of the knee.
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(Coleman, McQuade) Arthritis Foundation of Western Australia, PO Box 34, Wembley, WA 6914, Australia. (Coleman, Briffa) Department of Physiotherapy, Curtin University of Technology, Bentley, WA 6102, Australia. (Carroll) Department of Rheumatology, Fremantle Hospital, University of Notre Dame Australia, WA 6055, Australia. (Inderjeeth) Gerontology, Sir Charles Gairdner Hospital, Verdun St, Nedlands, WA 6009, Australia. (Cook) Rheumatology, Royal Perth Hospital, Wellington St, Perth, WA 6001, Australia.

Background. An education self-management program for people with osteoarthritis (OA) of the knee was designed to be delivered by health professionals, incorporating their knowledge and expertise. Improvement in quality of life, health status and pain in response to this program has previously been demonstrated in an uncontrolled pilot study. To more rigorously test the effectiveness of the program we will undertake a randomised controlled trial of people with OA of the knee offering specific self-administered exercises and education, in accordance with the principles of self-management. Aim: To determine whether an education self-management program for subjects with Osteoarthritis (OA) of the knee (OAK program) implemented by health professionals in a primary health care setting can achieve and maintain clinically meaningful improvements compared standard medical management in a control group. Methods. The effects of standard medical management will be compared with the effects of the OAK program in a single-blind randomized study. Participants: 146 male and female participants with established OA knee will be recruited. Volunteers with coexistent inflammatory joint disease or serious co-morbidities will be excluded. Interventions: Participants will be randomized into either intervention or control groups (delayed start). The intervention group will complete the OA knee program and both groups will be followed for 6 months. Measurements: Assessments will be at baseline, 8 weeks and 6 months. SF-36, WOMAC and VAS pain questionnaires will be completed. Isometric quadriceps and hamstring strength will be measured using a dynamometer; knee range of movement using a goniometer; and physical function will be determined by a modified timed up and go test. Data will be analysed using repeated measures ANOVA. Discussion. While there is evidence to support the effectiveness of SM programs for people with hypertension, diabetes and asthma, the evidence available for treatment of arthritis remains equivocal. The aim of this study is to determine the effectiveness of a disease specific self-management program for people with OA knee. The study design includes all the important features of a clinical experimental study to minimize bias so the results of the study will provide a high level of evidence. People with OA of the knee have identified pain and problems with daily activities as the most important problems associated with their condition. The outcome measures selected specifically address these issues and have demonstrated validity and are responsive within the range of change expected in response to the intervention. Hence the results of the study will reflect their priorities. The results of the study will provide evidence to guide clinicians and funding bodies seeking to establish priorities regarding the provision of this disease specific program. Trial registration. ACTR number: 12607000080426. copyright 2008 Coleman et al; licensee BioMed Central Ltd. PMID:2008480893
Oxpentifylline versus placebo in the treatment of erythropoietin-resistant anaemia: A randomized controlled trial.
Johnson DW, Hawley CM, et al. (Johnson, Hawley, Rosser, Beller, Thompson, Fassett, Ferrari, MacDonald, Pedagogos, Cass) Australian Kidney Trials Network, School of Population Health, University of Queensland, Brisbane, QLD, Australia. (Johnson, Hawley) Department of Nephrology, Princess Alexandra Hospital, Brisbane, QLD, Australia. (Fassett) Department of Nephrology, Launceston Hospital, Launceston, TAS, Australia. (Ferrari) Department of Renal Medicine, Fremantle Hospital, Fremantle, WA, Australia. (MacDonald) Department of Nephrology and Transplantation Services, University of Adelaide, Queen Elizabeth Hospital, Adelaide, SA, Australia. (Pedagogos) Department of Nephrology, Royal Melbourne Hospital, Melbourne, VIC, Australia. (Cass) George Institute for International Health, Sydney, NSW, Australia.

Background. The main hypothesis of this study is that Oxpentifylline administration will effectively treat erythropoietin- or darbepoietin-resistant anaemia in chronic kidney disease patients. Methods/design. Inclusion criteria are adult patients with stage 4 or 5 chronic kidney disease (including dialysis patients) with significant anaemia (haemoglobin [less-than or equal to] 110 g/L) for at least 3 months for which there is no clear identifiable cause and that is unresponsive to large doses of either erythropoietin ([greater-than or equal to] 200 IU/kg/week) or darbepoetin ([greater-than or equal to] 1 mug/kg/week). Patients will be randomized 1:1 to receive either placebo (1 tablet daily) or oxpentifylline (400 mg daily) per os for a period of 4 months. During this 4 month study period, haemoglobin measurements will be performed monthly. The primary outcome measure will be the difference in haemoglobin level between the 2 groups at the end of the 4 month study period, adjusted for baseline values. Secondary outcome measures will include erythropoiesis stimulating agent dosage, Key's index (erythropoiesis stimulating agent dosage divided by haemoglobin concentration), and blood transfusion requirement. Discussion. This investigator-initiated multicentre study has been designed to provide evidence to help nephrologists and their chronic kidney disease patients determine whether oxpentifylline represents a safe and effective strategy for treating erythropoiesis stimulating agent resistance in chronic kidney disease. Trial Registration. Australian New Zealand Clinical Trials Registry Number ACTRN12608000199314. copyright 2008 Johnson et al; licensee BioMed Central Ltd. PMID:2008406264

Abdominal aortic aneurysm in postmenopausal women.
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Screening for type 2 diabetes: Screen women with gestational diabetes for type 2 diabetes.
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Screening for type 2 diabetes: Screen women with gestational diabetes for type 2 diabetes.
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Amiodarone-induced pulmonary toxicity.

Ernawati DK, Stafford L, et al.

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AIMS: A number of factors have been hypothesized to increase the risk of amiodarone-induced pulmonary toxicity (AIPT). This study aimed to confirm these risk factors and determine whether a cohort of tertiary hospital patients diagnosed with AIPT demonstrated comparable characteristics.

METHODS: Phase I of this study involved compilation of a database of adverse reactions to amiodarone reported to the Australian and US drug agencies, and identification of risk factors for AIPT using logistic regression analysis. In Phase II, AIPT cases were identified via a retrospective review of medical records of patients discharged from Fremantle Hospital and Health Service, Western Australia (FHHS) between 2000 and 2005 with diagnosed interstitial lung disease. Data were collected regarding these patients’ risk factors for AIPT and compared with those previously identified in Phase I.

RESULTS: A total of 237 cases of AIPT were identified from agency data. Patients aged > 60 years and those on amiodarone for 6-12 months (odds ratio 18.28, 95% confidence interval 6.42, 52.04) were determined to be at the highest risk of AIPT. Australian data also suggested increased risk in patients who had received cumulative doses of 101-150 g. The seven AIPT cases identified among the FHHS patients were all at high risk of AIPT based on their age and duration of amiodarone therapy.

CONCLUSION: Contrary to previous findings, only patient age and the duration of amiodarone therapy were confirmed as significant risk factors for AIPT. Targeted monitoring of these patients may facilitate early identification and management of AIPT.

Publication Types: Research Support, Non-U.S. Gov't
PMID:18460037

A comparison of serum antivenom concentrations after intravenous and intramuscular administration of redback (widow) spider antivenom.

Isbister GK, O'Leary M, et al.

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT: * Widow spider antivenoms, including redback spider antivenom, are often given by the intramuscular route., * No studies have measured widow spider antivenom following intramuscular or intravenous antivenom., WHAT THIS STUDY ADDS: * Intramuscular redback spider antivenom is not detectable in serum for at least 3-5 h after treatment. Intravenous antivenom is detectable 30 min after intravenous infusion., * Intramuscular antivenom may not be an effective administration route., AIMS: There are no studies measuring antivenom concentrations following intramuscular administration. This study aimed to compare antivenom concentrations following intravenous and intramuscular administration of redback spider antivenom (RBSAV)., METHODS: Twenty patients recruited to a controlled trial comparing intramuscular and intravenous administration of antivenom had serial blood samples collected at 30 min intervals for 2 h after the administration of one or two doses of antivenom. Antivenom concentration was measured using an enzyme immunoassay., RESULTS: Ten patients received intramuscular antivenom but
antivenom could not be detected in serum after either one or two vials, at any time point. The median time of the final sample after commencement of antivenom treatment in these patients was 3.2 h (1.8-5 h). Ten patients received intravenous antivenom (three one vial and seven two or more vials) and antivenom was detected in all patients. CONCLUSIONS: RBS AV given by the intramuscular route is unlikely to be effective in the treatment of redback (widow) spider bite. Copyright (C) 2008 Blackwell Publishing Ltd.

Polymorphisms of the matrix metalloproteinase 9 gene and abdominal aortic aneurysm.
Schools of Surgery, University of Western Australia, Fremantle, Western Australia.
BACKGROUND:: Increased matrix metalloproteinase (MMP) 9 activity has been implicated in the formation of abdominal aortic aneurysm (AAA). The aim was to explore the association between potentially functional variants of the MMP-9 gene and AAA. METHODS:: The - 1562C > T and - 1811A > T variants of the MMP-9 gene were genotyped in 678 men with an AAA (at least 30 mm in diameter) and 659 control subjects (aortic diameter 19-22 mm) recruited from a population-based trial of screening for AAA. Levels of MMP-9 were measured in a random subset of 300 cases and 84 controls. The association between genetic variants (including haplotypes) and AAA was assessed by multivariable logistic regression. RESULTS:: There was no association between the MMP-9 - 1562C > T (odds ratio (OR) 0.70 (95 per cent confidence interval (c.i.) 0.27 to 1.82)) or - 1811A > T (OR 0.71 (95 per cent c.i. 0.28 to 1.85)) genotypes, or the most common haplotype (OR 0.81 (95 per cent c.i. 0.62 to 1.05)) and AAA. The serum MMP-9 concentration was higher in cases than controls, and in minor allele carriers in cases and controls, although the differences were not statistically significant. CONCLUSION:: In this study, the genetic tendency to higher levels of circulating MMP-9 was not associated with AAA. Copyright (c) 2008 British Journal of Surgery Society Ltd. Published by John Wiley & Sons, Ltd.
PMID:18763261

CT angiography as a first line investigation in the management of massive lower gastrointestinal bleeding.
Koong D, Thirumalai T, et al.
Fremantle Hospital, Fremantle, Australia

Peer support shows promise in helping persons living with mental illness address their physical health needs.
Bates A, Kemp V, et al.
Bates, Ann: Community, Culture and Mental Health Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, WAU, Australia Kemp, Vivien: Community, Culture and Mental Health Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, WAU, Australia Isaac, Mohan: Community, Culture and Mental Health Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, WAU, Australia The physical health of individuals with long-term mental illnesses has long been of concern. In Western Australia, the overall mortality rate from preventable causes of people living with mental illness was reported to be 2.5 times greater than that of the general population. A trial peer support service was initiated to assist people with mental illness to attend to their physical health needs. This paper presents the planning, implementation, and results of this collaborative initiative involving non-government agencies, the public mental health service, consumers of mental health services, and the

**Circulating markers of abdominal aortic aneurysm presence and progression.**
Golledge JMFF, Tsao PSP, et al.
From the Vascular Biology Unit, School of Medicine and Dentistry, James Cook University, Townsville, Queensland, Australia (J.G.); Divisions of Vascular Surgery (R.L.D.) and Cardiovascular Medicine (P.S.T.), Stanford University, San Francisco, Calif; and School of Surgery, University of Western Australia, Fremantle Hospital, Fremantle, WA Australia (P.E.N.).


**Mutations in the HFE Gene and Cardiovascular Disease Risk: An Individual Patient Data Meta-Analysis of 53 880 Subjects.**
van der A DL, Rovers MM, et al.
From the National Institute for Public Health and the Environment, Bilthoven, the Netherlands (D.L.v.d.A., J.M.A.B.); Julius Center for Health Sciences and Primary Care (D.L.v.d.A., M.M.R., D.E.G., Y.T.v.d.S.) and Eijkman Winkler Institute for Microbiology, Infectious Diseases, and Inflammation (J.J.M.M.), University Medical Center Utrecht, Utrecht, the Netherlands; Department of Molecular and Experimental Medicine, Scripps Research Institute, La Jolla, Calif (J.W.); Department of Clinical Biochemistry, Herlev University Hospital, University of Copenhagen, Herlev, Denmark (C.E., B.G.N.); Copenhagen City Heart Study, Bispebjerg University Hospital, University of Copenhagen, Copenhagen, Denmark (B.G.N.); School of Medicine and Pharmacology, Faculty of Medicine, University of Western Australia and the Department of Gastroenterology, Fremantle Hospital, Fremantle, Western Australia (J.K.O.); Gartnavel General Hospital, Glasgow, Scotland, UK (P.R.M.); Department of Vascular Biochemistry, University of Glasgow, Glasgow, Scotland, UK (J.S.); INSERM U773 and Universite Denis Diderot, Paris, France, and AP-HP Service de Genetique et Biochimie Hormonale, Hospital Xavier Bichat, Association Claude Bernard, Paris, France (B.G.); Department of Pathobiology and Biomedical Methodologies, University of Palermo, Palermo, Italy (C.C.); Department of Clinical and Applied Medical Therapy, University of Rome La Sapienza, Rome, Italy (M.A.); and Cardiovascular Center (CVC-Lindenhofspital), Bern University, Bern, Switzerland (B.J.M.).

Background-: Whether mutations in the hemochromatosis (HFE) gene increase cardiovascular disease risk is still undetermined. The main reason is the low frequency of the mutations, in particular of the compound C282Y/H63D genotype. We combined the data of 11 observational studies for an individual patient data meta-analysis. Methods and Results-: Individual patient data were obtained from published as well as unpublished studies that had information available on the C282Y mutation as well as the H63D mutation in relation to coronary heart disease risk. Individual records were provided on each of the 53 880 participants in 11 studies. In total, 10 541 patients with coronary events were documented, of whom 5724 had an acute myocardial infarction. The crude and adjusted association between HFE genotypes and coronary events was examined by logistic regression analysis. We explored potential effect modification of the association between traditional cardiovascular risk factors and coronary events by HFE genotypes. After full adjustment, the odds ratio for coronary heart disease was 1.12 (95% CI, 0.92 to 1.37) for subjects with the compound heterozygous (C282Y/H63D) genotype relative to those with the wild-type/wild-type genotype. The odds ratios for C282Y/C282Y, C282Y/wild-type, H63D/H63D, and H63D/wild-type were 0.78 (95% CI, 0.49 to 1.26), 0.98 (95% CI, 0.90 to 1.07), 1.16 (95% CI, 0.97 to 1.38), and 1.07 (95% CI, 1.00 to 1.14), respectively. There was no evidence for effect modification. Conclusions-: The results of this large individual patient data meta-analysis do not support the view that HFE gene mutations are associated with an increased risk of coronary heart disease or acute myocardial infarction. (C) 2008 American Heart Association, Inc.
A new technique for cement augmentation of the sliding hip screw in proximal femur fractures.
Stoffel KK, Leys T, et al.
Fremantle Orthopaedic Unit, The University of Western Australia, Fremantle 6160, Australia; Department of Orthopaedic Surgery, The University of Western Australia, Fremantle Hospital, Fremantle 6160, Australia.

BACKGROUND: Fractures of the osteoporotic proximal femur are a significant source of mortality and morbidity in today's ageing population. Even with modern fixation techniques such as the sliding hip screw, a certain percentage of fixations will fail due to cut-out of the screw. This study presents a new method for augmenting hip screws with cement to reinforce the fixation. METHODS: Unstable pertrochanteric fractures were created in paired osteoporotic cadaver femora (n=10). The fractures were fixed using either standard fixation techniques (dynamic hip screw), or using a dynamic hip screw augmented with cement. Cement was introduced using a customised jig to guide cement into a region superior to the screw in the femoral head. Cut-out resistance was assessed using a biaxial material testing machine, with loading applied in compression until failure. FINDINGS: The new cement augmentation technique significantly improved the cut-out strength of the fixation (mean 42%; P=0.032). The failure mechanism for both groups was the same, with failure occurring through compression of the cancellous bone superior to the screw. The mean increase in temperature at the femoral neck was 3.7 degrees C in augmented bones, which is much lower than values previously reported for polymethylmethacrylate cements. INTERPRETATION: Several benefits with this technique have emerged. The method is technically straightforward. The risk of cement penetration into the joint is reduced, and cement is targeted to the areas of the femoral head where it is most needed. The exothermic reaction is minimised by reducing the volume of cement used. The first clinical results are promising.

Higher serum free testosterone is associated with better cognitive function in older men, while total testosterone is not. The Health In Men Study.
Yeap BB, Almeida OP, et al.
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Objective: To determine the relationship of total and free serum testosterone to cognitive performance in older men.
Design: Cross-sectional study of a population-based sample.
Participants: A total of 2932 men aged 70-89 years.
Measurements: Cognitive function was assessed using the Standardized Mini-Mental State Examination (SMMSE). Early morning sera were assayed for total testosterone, SHBG and LH. Free testosterone was calculated using the Vermeulen method.
Results: There were weak positive correlations between SMMSE score and serum free testosterone (Spearman's rho = 0.06, P = 0.001) and total testosterone (r = 0.04, P = 0.027), and a weak negative correlation with LH (r = -0.07, P < 0.001). Men with SMMSE scores in the top quintile had higher serum free testosterone compared with those in the lowest quintile [median (interquartile range, IQR): 278 (228-335) vs. 262 (212-320) pmol/l, P = 0.003], but similar total testosterone [15 (11-19) vs. 14 (11-18) nmol/l, P = 0.13]. Increasing age, non-English-speaking background, lower educational attainment, presence of clinically significant depressive symptoms, and cardiovascular morbidity were associated with the lowest cognitive performance quintile. After their effects were taken into account in a multivariate analysis, serum free testosterone >= 210 pmol/l was associated with reduced likelihood of poor cognitive performance on
the SMMSE [odds ratio (OR) 0.71, 95% confidence interval (CI) 0.52-0.97]. Conclusions: In community-dwelling older men, serum free testosterone ≥ 210 pmol/l is associated with better cognitive performance. In this context, calculated free testosterone seems to be a more informative measure of androgen status than total testosterone. Studies examining the contribution of androgens to age-related cognitive decline should incorporate an assessment of free testosterone concentration., Copyright (C) 2008 Blackwell Publishing Ltd.


Plasmodium knowlesi malaria in humans is widely distributed and potentially life threatening.
Cox-Singh J, Davis TME, et al.
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Background. Until recently, Plasmodium knowlesi malaria in humans was misdiagnosed as Plasmodium malariae malaria. The objectives of the present study were to determine the geographic distribution of P. knowlesi malaria in the human population in Malaysia and to investigate 4 suspected fatal cases. Methods. Sensitive and specific nested polymerase chain reaction was used to identify all Plasmodium species present in (1) blood samples obtained from 960 patients with malaria who were hospitalized in Sarawak, Malaysian Borneo, during 2001-2006; (2) 54 P. malariae archival blood films from 15 districts in Sabah, Malaysian Borneo (during 2003-2005), and 4 districts in Pahang, Peninsular Malaysia (during 2004-2005); and (3) 4 patients whose suspected cause of death was P. knowlesi malaria. For the 4 latter cases, available clinical and laboratory data were reviewed. Results. P. knowlesi DNA was detected in 266 (27.7%) of 960 of the samples from Sarawak hospitals, 41 (83.7%) of 49 from Sabah, and all 5 from Pahang. Only P. knowlesi DNA was detected in archival blood films from the 4 patients who died. All were hyperparasitemic and developed marked hepatorenal dysfunction. Conclusions. Human infection with P. knowlesi, commonly misidentified as the more benign P. malariae, are widely distributed across Malaysian Borneo and extend to Peninsular Malaysia. Because P. knowlesi replicates every 24 h, rapid diagnosis and prompt effective treatment are essential. In the absence of a specific routine diagnostic test for P. knowlesi malaria, we recommend that patients who reside in or have traveled to Southeast Asia and who have received a "P. malariae" hyperparasitemia diagnosis by microscopy receive intensive management as appropriate for severe falciparum malaria. copyright 2007 by the Infectious Diseases Society of America. All rights reserved.
PMID:2008089497


Management of peripheral arterial disease in the elderly: focus on cilostazol.
School of Surgery, University of Western Australia, Fremantle Hospital, Western Australia, Australia.
Symptomatic and asymptomatic peripheral arterial disease (PAD) is a common problem in the elderly. The management of PAD includes the prevention of cardiovascular events and relief of symptoms—most commonly intermittent claudication (IC). Both require treatment of the causes and consequences of atherothrombosis, but some strategies are more effective for prevention of cardiovascular events and others are more effective for the relief of symptoms. Priorities for the prevention of cardiovascular events include smoking cessation, exercise, antiplatelet therapy, and the treatment of dyslipidemia, hypertension, and diabetes. Walking time and ability are improved by exercise. The benefit of
numerous drugs in the treatment of IC has been assessed. The results have generally been disappointing, but there is some evidence that statins and cilostazol (an inhibitor of phosphodiesterase 3) are of benefit. Meta-analyses suggest that cilostazol increases maximum walking distance by 40%-50% and improves other objective measures of walking. The safety profile of cilostazol in patients with PAD appears to be acceptable although the mechanism for its effect on IC is unclear. In addition to risk factor management, treatment with cilostazol should be considered in patients with disabling IC. PMID:18488875

**A questionnaire to determine nurses' knowledge of delirium and its risk factors.**
Hare M, Wynaden D, et al.
Delirium is a frequent complication of hospital admission, especially among the elderly. It can have serious consequences in terms of morbidity, mortality and decreased quality of life. Nevertheless, an extensive literature review found that it is poorly recognised and poorly managed by medical and nursing staff. Although some researchers have found that education programs for nurses can improve outcomes for patients with delirium, no research assessing nurses' knowledge was found. The objective of this research was to determine nurses' level of knowledge regarding delirium and its risk factors. A questionnaire survey sent to nurses at a teaching hospital found that nurse's knowledge of delirium was generally inadequate, although one ward which had had in-service education attained better results. It is recommended that cognitive assessment in general and delirium in particular be incorporated into nursing education. Improved education could potentially lead to improved health outcomes and considerable cost savings.
Publication Types: Journal Article, Research, Tables/Charts
PMID:2010045203

**The case for levosimendan.**
De Keulenaer BL.
Publication Types: Editorial
PMID:18798714

**Burkholderia pseudomallei sepsis presenting with pericardial effusion and tamponade.**
De Keulenaer BL, Hooland SR, et al.
Intensive Care Unit, Fremantle Hospital, Fremantle, WA. bdekeul@hotmail.com.
Severe septicaemia secondary to melioidosis carries a high mortality. Although melioidosis can involve most tissues and organs, pericardial involvement is rare. We report a 40-year-old woman with melioidosis with pericardial involvement but no contiguous pulmonary involvement. She developed acute pericardial tamponade but was successfully treated with surgery and medical therapy. This is the first case in Australia or New Zealand of melioid sepsis presenting with pericarditis and subsequent cardiac tamponade. We review the literature on cardiac involvement in melioidosis.
PMID:18522528

**Burkholderia pseudomallei sepsis presenting with pericardial effusion and tamponade.**
De Keulenaer BL, Van Hooland SR, et al.
Intensive Care Unit, Fremantle Hospital, Fremantle WA bdekeul@hotmail.com
Severe septicaemia secondary to melioidosis carries a high mortality. Although melioidosis can involve most tissues and organs, pericardial involvement is rare. We report a 40 year old woman with
melioidosis with pericardial involvement but no contiguous pulmonary involvement. She developed acute pericardial tamponade but was successfully treated with surgery and medical therapy. This is the first case in Australia or New Zealand of melioid sepsis presenting with pericarditis and subsequent cardiac tamponade. We review the literature on cardiac involvement in melioidosis.


Enrollment of intensive care unit patients into clinical studies: A trinational survey of researchers’ experiences, beliefs, and practices *.
Cook DJ, Blythe D, et al.
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Background: As critical care practice increases in scope, size, and complexity, enrollment of critically ill patients into clinical studies is increasing.

Objective: To understand the experiences, beliefs, and practices of the Canadian Critical Care Trials Group and Australian and New Zealand Intensive Care Society Clinical Trials Group regarding enrollment of critically ill children and adults into clinical studies.

Methods: Survey items generated by the research team were formatted in four domains: experiences, beliefs, practices, and demographics. Five research coordinators and five physicians pretested the survey, providing feedback on clarity and completeness. Intrarater reliability (16 participants, 2 wks apart) was very good.

Results: The response rate was 284 of 322 (88.2%). Respondents worked in intensive care units with a mean of 20.5 (sd 10) beds, caring for adults (72.2%), pediatric (18.8%), and both groups (9%) of critically ill patients. Clinical research was considered key to the future of improved clinical care. To enhance recruitment efficiency, respondents widely endorsed the effectiveness of increasing participating centers, after-hours, and weekend enrollment (all 3 scores 7 [6-7 sqb], reflecting median [interquartile range] on 1-7 scale). Overall, the effectiveness (6 [4-7]), feasibility (5 [4-6]) and ethics (5 [4-7]) of coenrollment into more than one randomized trial was endorsed. Half of respondents have adopted coenrollment with scientific and psychosocial provisos. Alternative designs, such as factorial and cluster randomized trials, were considered when suitable. Modifications to consent approaches (deferred consent (7 [6-7]), waived consent (7 [6-7]), or consent from two physicians in the absence of a substitute decision maker (6 [5-7])) were considered effective, but beliefs about the feasibility and ethics of some of these approaches varied.

Conclusions: Clinical research is highly valued by these intensive care unit communities. Strategies to increase capacity involve enhancing recruitment efficiencies, considering alternative study designs and expanding consent procedures. Thoughtfully implementing these strategies may advance the care of critically ill adults and children.


Clinical perspectives on hereditary hemochromatosis.
Ayonrinde OT, Milward EA, et al.
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Hereditary hemochromatosis (HH) comprises a group of inherited disorders of iron metabolism that can result in progressive iron overload, morbidity, and mortality, generally in adulthood. HFE-related HH is the most common type of HH and will form the core of this discussion. The discovery of new proteins and gene mutations has defined other types of HH, termed non-HFE HH. The regulatory protein hepcidin has a central role in iron homeostasis in these disorders. While the liver is the predominant organ of iron deposition and iron-overload-related disease in HFE-related HH, involvement of extrahepatic tissue can also result in morbidity and mortality if the disorder is not diagnosed before organ damage develops. This review traverses the road from HFE genotype to phenotype with a focus on clinical penetrance, modifier factors for disease expression, and current thoughts and controversies on HH diagnosis and screening. Copyright © 2008 Informa Healthcare USA, Inc.


**Editorial introductions.**

Fleischhacker WW, DeLisi LE, et al.

Publication Types: Editorial
PMID:2008115087


**Predictors of cognitive decline in older individuals with diabetes.**

Bruce DG, Davis WA, et al.
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OBJECTIVE: The purpose of this study was to determine longitudinal predictors of cognitive decline in older individuals with diabetes who did not have dementia.

RESEARCH DESIGN AND METHODS: Cognitive assessments were performed in 205 subjects with diabetes (mean age 75.3 years) and repeated a median 1.6 years later. The sample was drawn from an existing cohort study, and data on diabetes, cardiovascular risk factors, and complications were collected 7.6 +/- 1.1 years before and at
the time of the initial cognitive assessment. Cognitive status was defined using the Clinical Dementia Rating (CDR) scale, and cognitive decline was defined by change in CDR.

RESULTS: The sample included 164 subjects with normal cognition (CDR 0) and 41 with cognitive impairment without dementia (CDR 0.5). At follow-up, 33 (16.1%) had experienced cognitive decline (4 new cases of dementia and 29 cognitive impairment without dementia). Only educational attainment predicted cognitive decline from the data collected 7.6 years before cognitive assessment. Univariate predictors of cognitive decline at the time of the first cognitive assessment included age, education, urinary albumin-to-creatinine ratio (ACR), and treatment with either ACE inhibitors (ACEIs) or angiotensin receptor blockers (ARBs). With multiple logistic regression controlling for age and education, cognitive decline was predicted by natural logarithm ACR (odds ratio 1.37 [95% CI 1.05-1.78], P = 0.021), whereas treatment with either ACEIs or ARBs was protective (0.28 [0.12-0.65], P = 0.003).

CONCLUSIONS: In this sample of older patients with diabetes, microalbuminuria was a risk factor for cognitive decline, whereas drugs that inhibit the renin-angiotensin system were protective. These observations require confirmation because of their considerable potential clinical implications.

Prevalence, characteristics, and prognostic significance of HFE gene mutations in type 2 diabetes: the Fremantle Diabetes Study.

Davis TM, Beilby J, et al.
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OBJECTIVE: To examine the relationship between iron status, hereditary hemochromatosis (HFE) gene mutations, and clinical features and outcomes of type 2 diabetes in a well-characterized representative sample of community-based patients. RESEARCH DESIGN AND METHODS: HFE genotype data were available for 1,245 type 2 diabetic patients from the longitudinal observational Fremantle Diabetes Study (FDS), representing 96.2% of the total FDS type 2 diabetes cohort. Data were collected at recruitment between 1993 and 1996 and annually until the end of June 2001. Hospitalization and mortality data were available until the end of June 2006. The presence of the C282Y HFE mutation was determined in all subjects and H63D in C282Y heterozygotes. Fasting serum iron, transferrin, and ferritin were measured in all C282Y homozygotes and C282Y/H63D heterozygotes and in 286 randomly selected wild-type subjects. Multiple logistic regression analysis was performed to determine independent baseline associates of prevalent complications (myocardial infarction, cerebrovascular disease, retinopathy, neuropathy, and nephropathy), as was Cox proportional hazards modeling to determine predictors of incident complications and mortality. RESULTS: Although there were expected positive associations between HFE gene mutations and serum iron and transferrin saturation, there were no independent positive associations between HFE gene status and either microvascular or macrovascular complications in cross-sectional and longitudinal analyses. HFE gene status did not independently predict cardiac or all-cause mortality. Measures of iron metabolism including serum ferritin were not associated with combined microvascular or macrovascular end points. CONCLUSIONS: Directed screening for iron overload and/or HFE mutations appears unwarranted in patients with type 2 diabetes.

Incidence and determinants of carpal tunnel decompression surgery in type 2 diabetes: the Fremantle Diabetes Study.

Makepeace A, Davis WA, et al.
University of Western Australia, Fremantle Hospital, P.O. Box 480, Fremantle, Western Australia 6959, Australia.

To examine the incidence and predictors of carpal tunnel decompression (CTD) in community-based
patients with type 2 diabetes, we studied 1,284 type 2 diabetic participants (mean +/- SD age 64.1 +/- 6.1 years, 49.1% male) in the longitudinal observational Fremantle Diabetes Study who had no history of CTD. A total of 67 participants (5.8%) had a first CTD during 12,109 years (mean 9.4 +/- 3.7) of follow-up, an incidence of 5.5 per 1,000 patient-years. This was at least 4.2 times the incidence in the general population (P < 0.001). In Cox proportional hazards analysis, significant independent determinants of first-ever CTD were higher BMI, taking lipid-lowering medication, and being in a stable relationship (P < 0.021). The crude incidence of first CTD is increased in type 2 diabetes and is associated with obesity and sociodemographic/treatment factors that could indicate treatment-seeking behavior including CTD in symptomatic patients.


A cardiac magnetic resonance imaging study of electrocardiographic Q waves in type 2 diabetes: The Fremantle Diabetes Study.

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To investigate the evolution and significance of Q waves in type 2 diabetes, we studied 36 patients of mean (+/-S.D.) age 69.9 +/- 7.1 years from the longitudinal observational Fremantle Diabetes Study (FDS). All had (i) neither history/symptoms of coronary heart disease (CHD) nor pathological Q waves at FDS recruitment between 1993 and 1996, (ii) five consecutive annual assessments by FDS close-out in 2001, and (iii) contrast-enhanced cardiac magnetic resonance imaging in 2005. At this latter assessment, there were (i) 9 with no history of CHD or Q waves during follow-up (Group 1), (ii) 13 with Q waves on [greater-than or equal to]1 electrocardiogram but no CHD history/symptoms (Group 2), and (iii) 14 with CHD history/symptoms irrespective of electrocardiographic status (Group 3). Of 20 episodes of new Q waves in 17 Group 2 or Group 3 patients during FDS follow-up, 17 (85%) resolved within 2 years. A myocardial infarction (MI) was detected by CMR in three patients (8.3%; one subendocardial in Groups 1 and 3, one non-full-thickness in Group 3) but these did not correlate with electrocardiographic appearances. Q waves may have unreliable pathological significance in type 2 diabetes, including as a marker of silent MI. copyright 2008 Elsevier Ireland Ltd. All rights reserved.

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Ethnic diversity in type 2 diabetes.

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BACKGROUND AND METHODS: The present review assesses published data relating to the main ethnic groups in the UK Prospective Diabetes Study (UKPDS), namely White Caucasians (WC; 82% of the cohort), Indian-Asians (IA; 10%) and Afro-Caribbeans (AC; 8%). RESULTS: At entry, the IA patients were younger than WC and AC patients, had a greater waist-hip ratio and more sedentary lifestyle, but had the lowest prevalence of hypertension and current smoking. The AC patients had the poorest glycaemic control but the most favourable lipid profile. The differences in modifiable vascular risk factors did not change over 9 years of follow-up. Consistent with UKPDS exclusion criteria, few patients had complications at baseline and there were no between-group differences. An interim analysis of incident fatal/non-fatal myocardial infarction (median follow-up 8.7 years) showed that the AC patients had a 70% lower risk than WC after adjustment for explanatory variables and that IA patients had a similar risk to WC. An analysis of complete albuminuria and renal failure data (median follow-up 15 years) showed that IA ethnicity was independently associated with an increased risk.
CONCLUSIONS: There are sustained ethnic differences in the nature of diabetes, including vascular risk factors. AC patients had a substantially reduced risk of myocardial infarction that was not explained by their more favourable lipid profile, while IA patients were more likely to develop nephropathy than WC and IA patients. Longer follow-up is needed to determine whether the increased macrovascular risk observed in IA patients in other studies is replicated in the UKPDS cohort.


Chronic complications and mortality in community-based patients with latent autoimmune diabetes in adults: The Fremantle Diabetes Study.
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Aims: To compare (i) the prevalence and incidence of chronic complications and (ii) cardiac and all-cause mortality in community-based patients with latent autoimmune diabetes in adults (LADA) with those in Type 2 diabetic patients without antibodies to glutamic acid decarboxylase (GAD). Methods: Of the 1294 patients with clinically-defined Type 2 diabetes recruited to the longitudinal, observational Fremantle Diabetes Study between 1993 and 1996, 1255 (97%) had GAD antibodies measured at baseline. Complications were ascertained using standard criteria in patients returning for annual assessments until November 2001. Data on hospital admissions and mortality were available to the end of June 2006. Cox proportional hazards modelling was used to determine independent predictors of first occurrence of complications and cardiac and all-cause mortality. Results: Forty-five (3.6%) subjects had LADA. Compared with the GAD antibody-negative patients, they had a similar prevalence and incidence of coronary heart (P = 0.48 and 0.80, respectively) and cerebrovascular (P = 0.64 and 0.29) disease and cardiac and all-cause mortality (P = 0.62 and 0.81, respectively). There was also a similar prevalence and incidence of retinopathy (P = 0.22 and 0.64, respectively) and neuropathy (P = 0.25 and 0.95), but microalbuminuria was less frequent both at baseline and during follow-up in the LADA subgroup in unadjusted models (P = 0.046) and after adjustment for other risk factors (P = 0.014 and 0.013). Conclusions: Except for a lower prevalence and incidence of nephropathy, LADA patients have a similar risk of complications and death to patients with clinically-diagnosed Type 2 diabetes without GAD antibodies. Cardiovascular risk factor management in LADA should, therefore, be as intensive as that for GAD antibody-negative patients. copyright 2008 The Authors.


Prevalence and associations of psychological distress in young adults with Type 1 diabetes.
Hislop AL, Fegan PG, et al.
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AIMS: To determine the prevalence of psychological distress in young adults with Type 1 diabetes and to explore associated factors. METHODS: Ninety-two participants with Type 1 diabetes (46 male, 46 female) attending a young adult clinic completed two psychological self-report assessments; the Centre for Epidemiological Studies-Depression Scale (CES-D) and Adult Self-Report Scale (ASR). The mean age was 21.6 +/- 2.8 years (sd) and mean duration of diabetes was 9.3 +/- 5.4 years. A questionnaire identified the method of insulin delivery, the frequency of blood glucose monitoring and hypoglycaemia requiring third-party assistance. HbA(1c) was measured. RESULTS: Of the participants, 35.2% reported depressive symptoms (CES-D > or = 16), 23.1% indicating severe depressive symptoms (CES-D > or = 24), and 32.2, 40.4 and 35.5% of participants reported significant
distress (ASR > or = 60) on the ASR total problem scales, ASR internalizing and ASR externalizing scores, respectively. Mean HbA(1c) levels were higher in participants with depressive symptoms compared with those with normal scores (CES-D > or = 16, HbA(1c)= 9.4% vs. CES-D < 16, HbA(1c)= 8.4%, P = 0.01). Factors associated with psychological distress included use of continuous subcutaneous insulin infusion (CSII) (P = 0.02) and increased frequency of hypoglycaemic episodes (P = 0.03). CSII users had higher CES-D (21.3 vs. 11.9, P = 0.001) and ASR-Total (59.7 vs. 53.0, P = 0.02) scores than non-CSII users.

CONCLUSIONS: Approximately one-third of young adults with Type 1 diabetes experience psychological distress, which is associated with poorer glycaemic control. Psychological distress was related to frequency of hypoglycaemic episodes and method of insulin administration, with significantly greater distress being observed in those using CSII. These findings support inclusion of a psychologist in the diabetes team.

Publication Types: Journal Article
PMID:18199136


Predictors of cognitive impairment and dementia in older people with diabetes.
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Aims/hypothesis: Diabetes is associated with an increased risk of dementia but the reasons for this association are unclear because there are many potential mechanisms. We explored the relative contribution of diabetes-related variables as predictors of dementia in older individuals with diabetes.

Methods: Survivors, aged [greater-than or equal to]70 or more, were recruited from an existing observational cohort study 7.6+/-1.0 years after baseline, when they underwent a comprehensive assessment of diabetes, complications and cardiovascular risk factors. Dementia, probable Alzheimer's disease and cognitive impairment without dementia were diagnosed clinically. Logistic regression modelling determined independent predictors of cognitive diagnoses. Results: Of 302 participants, aged 75.7+/-4.6 years, 28 (9.3%) had dementia (16 with probable Alzheimer's disease) and 60 (19.9%) had cognitive impairment without dementia. The major independent longitudinal predictors of dementia were older age (per decade; odds ratio 4.0, 95% CI 1.59-10.10), diabetes duration (for each 5 years; odds ratio 1.69, 95% CI 1.24-2.32), peripheral arterial disease (odds ratio 5.35, 95% CI 2.08-13.72) and exercise (which was protective; odds ratio 0.26, 95% CI 0.09-0.73). For Alzheimer's disease, diabetes duration was an independent predictor in addition to age and diastolic blood pressure. The results of the cross-sectional analyses were similar with respect to diabetes duration and peripheral arterial disease. Conclusions/interpretation: Peripheral arterial disease is a strong independent risk factor for dementia in diabetes. After adjustment for a wide range of potential risk factors, diabetes duration remains independently associated with dementia and probable Alzheimer's disease, indicating that factors not measured in this study may be important in the pathogenesis of dementia in diabetes. copyright 2007 Springer-Verlag.

PMID:2008008596


Lipid-lowering therapy and peripheral sensory neuropathy in type 2 diabetes: the Fremantle Diabetes Study.
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AIMS/HYPOTHESIS: The aim of this study was to assess the relationships between lipid-lowering therapy and the prevalence and incidence of peripheral sensory neuropathy in type 2 diabetes mellitus. METHODS: We analysed data from an observational cohort study, the Fremantle Diabetes Study (FDS), specifically, (1) a cross-sectional sample comprising 1,237 FDS participants with type 2 diabetes mellitus, and (2) a longitudinal subgroup of 531 individuals who had attended six consecutive annual assessments. Neuropathy was identified using the clinical portion of the Michigan Neuropathy Screening Instrument. RESULTS: At entry, the cross-sectional sample had a mean +/- SD age of 63.8 +/- 11.3 years, 48.7% were men, median (interquartile range) diabetes duration was 4.0 (1.0-9.0) years, and 30.9% had peripheral neuropathy. Fibrates and statins were used by 3.5 and 6.8%, respectively. Multiple logistic regression analysis showed that older age, longer diabetes duration, central adiposity, increased height, higher fasting serum glucose, albuminuria and aboriginality were significant independent positive predictors of prevalent neuropathy, while systolic blood pressure and fibrate use (odds ratio 0.30, 95% CI 0.10-0.86; p = 0.025) were negatively associated. In the longitudinal subgroup, fibrate and statin use increased to 10.4 and 36.5%, respectively, over 5 years. In time-dependent Cox proportional hazards modelling, fibrate use [hazard ratio (HR) 0.52, 95% CI 0.27-0.98] and statin use (HR 0.65, 95% CI 0.46-0.93) were significant determinants of incident neuropathy (p </= 0.042). CONCLUSIONS/INTERPRETATION: These preliminary observational data suggest that therapy with a statin or a fibrate may protect against the development of diabetic peripheral sensory neuropathy, but there is a need for additional confirmatory evidence, preferably from randomised clinical trials.

PMID:18193189


Indomethacin and retinoic acid modify mouse intestinal inflammation and fibrosis: a role for SPARC.


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The mouse model of 2,4,6-Trinitrobenzene Sulfonic Acid (TNBS)-induced intestinal fibrosis allows for detailed study of the extracellular matrix changes that complicate Crohn's disease. Indomethacin induces intestinal fibrosis, while retinoic acid (RA) reduces liver fibrosis. Secreted protein acidic and rich in cysteine (SPARC), an extracellular matrix-modifying agent, may potentially link these opposing effects. Our aim was to determine the effects of indomethacin and RA and to evaluate their correlation to SPARC expression in the TNBS mouse model. CD-1 mice were randomised to TNBS enemas weekly for 2 or 8 weeks with or without indomethacin (0.2 mg/kg per day) or RA (100 microg/kg per day). At 2 weeks, indomethacin/TNBS enhanced and RA reduced inflammation, tissue destruction and fibrosis. The expression of SPARC was inversely related to fibrosis, but not to inflammation, in the TNBS-alone groups at 2 weeks; these differences were lost by 8 weeks. The results demonstrate that indomethacin increases TNBS-induced fibrosis in mice, while RA reduces it, and that SPARC may link these opposing effects.

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

PMID:17994277


Rapid risk stratification in suspected acute coronary syndrome using serial multiple cardiac biomarkers: A pilot study.

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Objective: To determine the feasibility of using a biomarker panel of myoglobin, creatinine kinase MB (CK-MB) and cardiac troponin I (cTnI) to identify patients with suspected acute coronary syndrome...
ACS who are suitable for discharge within 2 h. Methods: We took blood at presentation and at 2 h from patients with suspected ACS and non-diagnostic electrocardiogram who were admitted to the ED short stay ward for serial electrocardiogram and troponin testing. We used a point-of-care device that gives rapid estimation of myoglobin, CK-MB and cTnI (Triage cardiac panel). These results were compared with the results of our standard hospital cardiac troponin T assay. Patients were followed up by telephone at 30 days. Results: The study group comprised 100 patients (61 men) with mean age of 58 years. Six had a troponin-positive ACS during their ED stay. One additional patient died of a myocardial infarction within the follow-up period. The Triage panel at 2 h after presentation predicted 12-h cardiac troponin T elevation (sensitivity 100%, negative predictive value 99%) and 30-day events (sensitivity 86%, negative predictive value 97%). The majority of patients were ultimately suitable for discharge. Conclusion: Serial myoglobin, CK-MB and cTnI have the potential to identify patients who are suitable for early discharge and outpatient work-up. A large multicentre study is required.

PMID:2008489340
The pharmacokinetics of intramuscular adrenaline in patients with anaphylaxis: a preliminary analysis.
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Publication Types: Abstract

The use of total lymphocyte counts (TLC) and clinical staging to initiate antiretroviral therapy (ARV) for human immunodeficiency virus (HIV) infections in resource poor settings.
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 Publication Types: Abstract

Molecular typing of Australian Scedosporium isolates showing genetic variability and numerous S. aurantiacum.
One hundred clinical isolates from a prospective nationwide study of scedosporiosis in Australia (2003-2005) and 46 additional isolates were genotyped by internal transcribed spacer-restriction fragment length polymorphism (ITS-RFLP) analysis, ITS sequencing, and M13 PCR fingerprinting. ITS-RFLP and PCR fingerprinting identified 3 distinct genetic groups. The first group corresponded to Scedosporium prolificans (n = 83), and the other 2 comprised isolates previously identified as S. apiospermum: one of these corresponded to S. apiospermum (n = 33) and the other to the newly described species S. aurantiacum (n = 30). Intraspecies variation was highest for S. apiospermum (58%), followed by S. prolificans (45%) and S. aurantiacum (28%) as determined by PCR fingerprinting. ITS sequence variation of 2.2% was observed among S. apiospermum isolates. No correlation was found between genotype of strains and their geographic origin, body site from which they were cultured, or colonization versus invasive disease. Twelve S. prolificans isolates from 2 suspected case clusters were examined by amplified fragment length polymorphism analysis. No specific clusters were confirmed.


Reduced expansion rate of abdominal aortic aneurysms in patients with diabetes may be related to aberrant monocyte-matrix interactions.


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Aims: Diabetes increases the risk of atherothrombosis, but reduces the risk of abdominal aortic aneurysm (AAA). The reason for this difference is unknown. We examined the role of diabetes and glycation on AAA expansion and extracellular matrix-monocyte interactions.

Methods and results: We followed 198 patients (20 with diabetes) who had 30-45 mm AAAs with yearly aortic ultrasound for 3 years. Diabetes was independently associated with reduced AAA growth ([beta]=-0.17, P=0.01; OR for expansion above median 0.18, 95% confidence interval 0.06-0.57). In vitro incubation of resting human monocytes with glycated bovine serum albumin or monomeric type I collagen increased matrix metalloproteinase (MMP) secretion. In contrast, exposure of activated monocytes to glycated type I collagen lattices induced a marked reduction in MMP and interleukin-6 secretion. This de-activating effect was also demonstrated in cross-linked non-glycated collagen lattices, healthy decellularized aortic media, and decellularized aortic media from diabetes patients with atherosclerosis. In contrast, decellularized aortic media from patients with atherosclerosis, but no diabetes, induced increased MMP secretion.

Conclusion: These findings confirm that the progression of AAA is slower in patients with diabetes and suggest a mechanism by which the aortic media may be protected from degradation in these individuals. (C) Copyright Oxford University Press 2008.


Athletic induced iron deficiency: new insights into the role of inflammation, cytokines and hormones.


Byline: Peter Peeling (1,4), Brian Dawson (1), Carmel Goodman (2), Grant Landers (1), Debbie Trinder (3) Keywords: Iron deficiency; Interleukin-6; Hepcidin; Athlete Abstract: Iron is utilised by the body for oxygen transport and energy production, and is therefore essential to athletic performance. Commonly, athletes are diagnosed as iron deficient, however, contrasting evidence exists as to the
severity of deficiency and the effect on performance. Iron losses can result from a host of mechanisms during exercise such as hemolysis, hematuria, sweating and gastrointestinal bleeding. Additionally, recent research investigating the anemia of inflammation during states of chronic disease has allowed us to draw some comparisons between unhealthy populations and athletes. The acute-phase response is a well-recognised reaction to both exercise and disease. Elevated cytokine levels from such a response have been shown to increase the liver production of the hormone Hepcidin. Hepcidin up-regulation has a negative impact on the iron transport and absorption channels within the body, and may explain a potential new mechanism behind iron deficiency in athletes. This review will attempt to explore the current literature that exits in this new area of iron metabolism and exercise.

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Lower sex hormone-binding globulin is more strongly associated with metabolic syndrome than lower total testosterone in older men: the Health in Men Study.
Chubb SA, Hyde Z, et al.
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BACKGROUND: Reduced circulating testosterone and sex hormone-binding globulin (SHBG) are implicated as risk factors for metabolic syndrome. As SHBG increases with age while testosterone declines, we examined the relative contributions of SHBG and testosterone to the risk of metabolic syndrome in older men. METHODS: We conducted a cross-sectional study of 2502 community-dwelling men aged > or = 70 years without known diabetes. Metabolic syndrome was defined using the National Cholesterol Education Program-Third Adult Treatment Panel (NCEP-ATPIII) criteria. Early morning fasting sera were assayed for total testosterone, SHBG and LH. Free testosterone was calculated using mass action equations. RESULTS: There were 602 men with metabolic syndrome (24.1%). The risk of metabolic syndrome increased for total testosterone < 20 nmol/l, SHBG < 50 nmol/l and free testosterone < 300 pmol/l. In univariate analyses SHBG was associated with all five components of metabolic syndrome, total testosterone was associated with all except hypertension, and free testosterone was associated only with waist circumference and triglycerides. In multivariate analysis, both total testosterone and especially SHBG remained associated with metabolic syndrome, with odds ratios of 1.34 (95% confidence interval (CI): 1.18-1.52) and 1.77 (95% CI: 1.53-2.06) respectively. Men with hypogonadotrophic hypogonadism (total testosterone < 8 nmol/l, LH < or = 12 IU/l) had the highest prevalence of metabolic syndrome (53%, P<0.001). CONCLUSIONS: Lower SHBG is more strongly associated with metabolic syndrome than lower total testosterone in community-dwelling older men. SHBG may be the primary driver of these relationships, possibly reflecting its relationship with insulin sensitivity. Further studies should examine whether measures that raise SHBG protect against the development of metabolic syndrome in older men.
Publication Types: Research Support, Non-U.S. Gov't PMID:18505902


Antidepressant therapy in post-stroke depression.
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Background: About 40% of patients with stroke will develop depression at some stage after the acute event. Post-stroke depression (PSD) is associated with a poor prognosis. Depressed patients have more severe deficits in activities of daily living, a worse functional outcome, more severe cognitive deficits and increased mortality as compared to stroke patients without depression. Objective: This review will focus on available controlled trials of treatment for PSD. Methods: An unsystematic review of recent studies for the treatment of PSD. Results: Randomized controlled trials have demonstrated the efficacy of sertraline, citalopram and nortriptyline to treat post-stroke depression. Whether antidepressant medication may help to prevent post-stroke depression and decrease post-stroke mortality will require further controlled studies. copyright 2008 Informa UK Ltd.

Inhaled human insulin (Exubera): Its pharmacologic profile, efficacy and safety in the treatment of adults with diabetes mellitus.
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Exubera (EXU, insulin human (rDNA origin)) is the first inhaled insulin approved for the treatment of diabetes in adults. Its pharmacokinetic properties make it suitable as therapy for postprandial glycemia. Clinical trials have demonstrated equal efficacy with short-acting subcutaneous regular and analog insulin in both Type 1 and 2 diabetes, and have also shown that it has value as adjunctive therapy in Type 2 patients inadequately controlled on maximal doses of oral hypoglycemic agents. EXU is well tolerated and associated with a high level of patient satisfaction. Hypoglycemia is the most common adverse event but its incidence does not exceed that expected for the degree of glycemic improvement. Minor reductions in some measures of pulmonary function have been observed in EXU-treated patients but safety studies of up to 2 years duration reveal that they occur early, do not progress and resolve quickly after treatment cessation. Longer-term postregistration pulmonary function studies that include assessment of insulin antibodies and the associated risk of allergic/immune disorders are in progress. EXU overcomes problems associated with the invasive nature of subcutaneous injection without loss of efficacy. Depending on cost and confirmation of safety, it could be a valuable part of future treatment strategies for both Type 1 and 2 diabetes.
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Role of testosterone in older men: recent advances and future directions.
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Publication Types: Editorial
PMID:2008526391

C-kit inhibition by imatinib mesylate attenuates progenitor cell expansion and inhibits liver tumor formation in mice.[see comment].
Knight B, Tirnitz-Parker JE, et al.
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BACKGROUND & AIMS: Numerous studies have linked the proliferation of liver progenitor cells (LPCs) during chronic liver disease to the risk for development of hepatocellular carcinoma. Thus, selective inhibition of LPC growth during preneoplastic injury may prevent or delay the onset of liver cancer. Rats carrying a germ-line mutation in c-kit have an impaired LPC response to liver injury. Therefore, we hypothesized that the c-kit inhibitor imatinib mesylate (IM) would suppress LPC growth and, therefore, may exert antitumorigenic effects in the liver. METHODS: Expression of IM target proteins was examined in chronically injured rodent and human livers. The effect of IM was examined in vitro using LPC lines and in vivo in mice fed a choline-deficient, ethionine-supplemented (CDE) diet. Livers were examined following short-term (up to 1 month) or long-term (up to 14 months) feeding of CDE diet and drug treatments. RESULTS: C-kit was significantly up-regulated in chronic injury and expressed by LPCs. IM was antiproliferative to LPC lines, and knockdown of c-kit reduced this response. IM treatment inhibited the LPCs response and early fibrogenesis induced by a short-term CDE diet. On the longer term, IM treatment reduced the extent of fibrosis and significantly inhibited tumor formation. CONCLUSIONS: Tyrosine kinase inhibitors, such as IM, may be suited for the prevention of hepatocellular carcinoma in the setting of chronic liver injury via antiproliferative effects on c-kit-expressing LPCs.

Publication Types: In Vitro
Research Support, Non-U.S. Gov't
PMID:18602920


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Publication Types: Editorial
PMID:2007625613


Multiple cavernous hemangiomas with iron deficiency anemia successfully treated with double-balloon enteroscopy.
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PMID:18155208


Thymic cyst causing superior venacava syndrome relieved by mediastinoscopy: a rare presentation.
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Superior venacava obstruction is most often caused by intrathoracic malignant masses. The commonest cause of benign superior venacava obstruction is fibrosing mediastinitis. A thymic cyst causing marked superior venacava obstruction is very rare and has not been reported. We hereby present a case of a 40-year-old man with such a finding who presented with chest pain and facial congestion. Evaluation revealed a mediastinal mass causing marked superior venacaval obstruction. He underwent a mediastinoscopy, which showed a cyst. It was drained following which there was
complete resolution of symptoms post-operatively. Histopathology of the lesion confirmed a thymic cyst. copyright 2007 Australasian Society of Cardiac and Thoracic Surgeons and the Cardiac Society of Australia and New Zealand.


**Hereditary hemochromatosis in the post-HFE era.**
Olynyk JK, Trinder D, et al.
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Following the discovery of the HFE gene in 1996 and its linkage to the iron overload disorder hereditary hemochromatosis (HH) there have been profound developments in our understanding of the pathogenesis of the biochemical and clinical manifestations of a number of iron overload disorders. This article provides an update of recent developments and key issues relating to iron homeostasis and inherited disorders of iron overload, with emphasis on HFE-related HH, and is based on the content of the American Association for the Study of Liver Diseases Single-Topic Conference entitled "Hemochromatosis: What has Happened After HFE?" which was held at the Emory Convention Center in Atlanta, September 7-9, 2007.

Publication Types: Research Support, N.I.H., Extramural
Research Support, Non-U.S. Gov't
PMID:18752323


**The role of Hfe in transferrin-bound iron uptake by hepatocytes.**
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HFE-related hereditary hemochromatosis results in hepatic iron overload. Hepatocytes acquire transferrin-bound iron via transferrin receptor (Tfr) 1 and Tfr1-independent pathways (possibly Tfr2-mediated). In this study, the role of Hfe in the regulation of hepatic transferrin-bound iron uptake by these pathways was investigated using Hfe knockout mice. Iron and transferrin uptake by hepatocytes from Hfe knockout, non-iron-loaded and iron-loaded wild-type mice were measured after incubation with 50 nM (125)I-Tf-(59)Fe (Tfr1 pathway) and 5 microM (125)I-Tf-(59)Fe (Tfr1-independent or putative Tfr2 pathway). Tfr1 and Tfr2 messenger RNA (mRNA) and protein expression were measured by real-time polymerase chain reaction and western blotting, respectively. Tfr1-mediated iron and transferrin uptake by Hfe knockout hepatocytes were increased by 40% to 70% compared with iron-loaded wild-type hepatocytes with similar iron levels and Tfr1 expression. Iron and transferrin uptake by the Tfr1-independent pathway was approximately 100-fold greater than by the Tfr1 pathway and was not affected by the absence of Hfe. Diferric transferrin increased hepatocyte Tfr2 protein expression, resulting in a small increase in transferrin but not iron uptake by the Tfr1-independent pathway. Conclusion: Tfr1-mediated iron uptake is regulated by Hfe in hepatocytes. The Tfr1-independent pathway exhibited a much greater capacity for iron uptake than the Tfr1 pathway but it was not regulated by Hfe. Diferric transferrin up-regulated hepatocyte Tfr2 protein expression but not iron uptake, suggesting that Tfr2 may have a limited role in the Tfr1-independent pathway.

Publication Types: Research Support, Non-U.S. Gov't
PMID:18393371


**Relationship between two sequence variations in the gene for peroxisome proliferator-activated receptor-gamma and plasma homocysteine concentration. Health in men study.**
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The concentration of circulating homocysteine has been associated with a variety of diseases, including myocardial infarction, stroke, venous thrombosis and cognitive decline. Genetic variation has been demonstrated to play an important role in determining plasma homocysteine, however, the genes involved are incompletely understood. Ligation of the transcription factor peroxisome proliferator-activated gamma (PPARG) has been demonstrated to lower plasma homocysteine. We examined the association of two sequence variations in PPARG with plasma concentrations of homocysteine in a population-based study of 3,875 elderly men. PPARG c.34G > C and PPARG c.1347C > T sequence variations were determined by real-time quantitative PCR and related to logarithm transformed homocysteine concentrations using linear regression, adjusting for the co-variants age, renal function, smoking, coronary heart disease, waist to hip ratio, diabetes, hypertension and MTHFR g.677C > T sequence variation. Median plasma homocysteine concentration was 10% higher in men who were homozygous for the rare allelic variation in PPARG c.34G > C and PPARG c.1347C > T by comparison to those who had wild type sequence variation. PPARG c.1347C 5> T (beta = 0.038, P = 0.01 recessive model; beta = 0.036, P = 0.02 dominant model) sequence variation was positively associated with homocysteine concentration after adjusting for co-variants. The two PPARG sequence variations were in linkage disequilibrium and the common haplotype was associated with lower plasma homocysteine (P = 0.005). Our findings demonstrate a new genotypic association with plasma homocysteine. Replication will be required in other cohorts.
PMID:2008059953

Infection Control and Hospital Epidemiology. 2008; 29(9): 859-865.

Outbreak of invasive methicillin-resistant Staphylococcus aureus infection associated with acupuncture and joint injection.
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OBJECTIVE. To describe an outbreak of invasive methicillin-resistant Staphylococcus aureus (MRSA) infection after percutaneous needle procedures (acupuncture and joint injection) performed by a single medical practitioner.
SETTING. A medical practitioner's office and 4 hospitals in Perth, Western Australia.
PATIENTS. Eight individuals who developed invasive MRSA infection after acupuncture or joint injection performed by the medical practitioner.
METHODS. We performed a prospective and retrospective outbreak investigation, including MRSA colonization surveillance, environmental sampling for MRSA, and detailed molecular typing of MRSA isolates. We performed an infection control audit of the medical practitioner's premises and practices and administered MRSA decolonization therapy to the medical practitioner.
RESULTS. Eight cases of invasive MRSA infection were identified. Seven cases occurred as a cluster in May 2004; another case (identified retrospectively) occurred approximately 15 months earlier in February 2003. The primary sites of infection were the neck, shoulder, lower back, and hip: 5 patients had septic arthritis and bursitis, and...
3 had pyomyositis; 3 patients had bacteremia, including 1 patient with possible endocarditis. The medical practitioner was found to be colonized with the same MRSA clone [ST22-MRSA-IV (EMRSA-15)] at 2 time points: shortly after the first case of infection in March 2003 and again in May 2004. After the medical practitioner's premises and practices were audited and he himself received MRSA decolonization therapy, no further cases were identified. CONCLUSIONS. This outbreak most likely resulted from a breakdown in sterile technique during percutaneous needle procedures, resulting in the transmission of MRSA from the medical practitioner to the patients. This report demonstrates the importance of surveillance and molecular typing in the identification and control of outbreaks of MRSA infection. copyright 2008 by The Society for Healthcare Epidemiology of America. All rights reserved. PMID:2008439938

Inflammatory Bowel Diseases. 2008; 14 Supplement(3): S1.

CIMZIA (Certolizumab Pegol) is effective in the treatment of Crohn's Disease patients with open fistulas: O-0003.

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Panaccione R, Colombel J, et al.
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Publication Types: Abstract (Oral Presentation)


Introduction: This feasibility study aimed to establish if retrieval physicians can overcome the transport environment and obtain F.A.S.T. (focused assessment by sonography in trauma) images of suitable quality during patient retrieval in rotary wing aircraft such that diagnostic interpretation of free intra-abdominal fluid or pericardial fluid would be possible. Materials and methods: During a 6-month trial period, one of three retrieval physicians attempted to obtain the standard four quadrant F.A.S.T. views
using a portable ultrasound on patients they retrieved. Ultrasound images where obtained whilst in-flight in a rotary wing aircraft. Image adequacy was assessed by the retrieval physician and by an independent blinded physician using strict clinical criteria. Results: Thirty-eight patients were enrolled. Thirty-six patients had a complete F.A.S.T. scan attempted whilst a further two patients had their abdominal quadrants scanned without a pericardial view being attempted. Independent blinded physician review of scans agreed with the scanning retrieval physician that images were adequate for showing the F.A.S.T. quadrants appropriately in 143 of 150 quadrants imaged and inadequate in two. Blinded physician review disagreed with scanning physician regarding adequacy of image in 5 of 150 quadrants imaged. Scanning physicians were happy with adequacy of the view in all F.A.S.T. quadrants in 34 of the 36 patients in whom a complete F.A.S.T. was performed. Blinded physician review agreed in 30 of those cases. Discussion: The physicians performing the F.A.S.T. examination, all incorporate ultrasound into their daily clinical practice thereby maintaining their skill level. This is likely to contribute to the high level of view adequacy. Independent blinded image review controlled for bias regarding view adequacy. Disagreement between scanning physician and reviewing physician assessment of view adequacy in 5 of the 150 views obtained is likely to relate to the difficulties in interpreting still ultrasound images, compared to interpreting real time images at point-of-care. There were no machine limitations. Conclusion: This study demonstrates that it is possible for critical care retrieval physicians to obtain adequate ultrasound F.A.S.T. images on patients using a portable ultrasound machine en-route to definitive care, in a rotary wing aircraft. Crown Copyright copyright 2007.

PMID:2008151619


The effect of different reference transducer positions on intra-abdominal pressure measurement: A multicenter analysis.

De Waele JJ, De Laet I, et al.

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Objective: To investigate the effect of different reference transducer positions on intra-abdominal pressure (IAP) measurement. Three reference levels were studied: the symphysis pubis; the phlebostatic axis; and the midaxillary line at the level of the iliac crest. Design: Prospective cohort study. Setting: The intensive care units of participating hospitals. Patients and participants: One hundred thirty-two critically ill patients at risk for intra-abdominal hypertension (IAH). Interventions: In each patient, three sets of IAP measurements were obtained in the supine position, using the different reference levels. The IAP measurements obtained at the different reference levels were compared using a paired t-test and Bland-Altman statistics were calculated. Measurements and results: IAPphlebostatic (9.9 +/- 4.67 mmHg) and IAPpubis (8.4 +/- 4.60 mmHg) were significantly lower than IAPmidax (12.2 +/- 4.66 mmHg; p < 0.0001 for both comparisons). The bias between the IAPmidax and IAPpubis was 3.8 mmHg (95% CI 3.5-4.1) and 2.3 mmHg (95% CI 1.9-2.6) between the IAP midax and the IAPphlebostatic. The precision was 3.03 and 3.40, respectively. Conclusions: In the supine position, IAPmidax is higher than both IAPphlebostatic and IAPpubis, differences found to be
clinically significant; therefore, the symphysis pubis or phlebostatic axis reference lines are not interchangeable with the midaxillary level. copyright 2008 Springer-Verlag. PMID:2008313252


Internal Medicine Journal. 2008; 38 Suppl.(4): A101. **Impact of ambulance diversion strategy on delivery of patients to stroke units.** Blacker D, Jacobs I, et al. (1)Department of Neurology, Sir Charles Gairdner Hospital, Nedlands, WA; (2)School of Medicine and Pharmacology, University of WA, WA; (3)Discipline of Emergency Medicine, University of WA, WA; (4)ST John's Ambulance Service, WA; (5)Department of Neurology, Fremantle Hospital, WA; (6)Department of Emergency Medicine, Sir Charles Gairdner Hospital, WA

Internal Medicine Journal. 2008; 38 Suppl.(4): A111. **Embolic stroke caused by carbamazepine induced myocarditis.** Cunningham J, Lai M, et al. (1)Neuro-rehabilitation Unit, Ward 2, Shenton Park Campus (SPC) of Royal Perth Hospital, Shenton Park, WA; (2)Stroke Unit, Fremantle Hospital (FH), Fremantle, WA

Internal Medicine Journal. 2008; 38 Suppl(5): A135. **Intracerebral haemorrhage in older patients: a retrospective review.** Geddes J, Alvaro T, et al. (1)Fremantle Hospital, Fremantle, WA, (2)University of Western Australia, Perth, WA

Internal Medicine Journal. 2008; 38 Supplement(6): A153. **Jack jumper ant (JJA) sting anaphylaxis in South Australia (SA).** Heddle RJ, Hudson P, et al. (1)Department of Respiratory Medicine, Flinders Medical Centre and Flinders University of South Australia, Adelaide, South Australia, (2)Emergency Medicine Research Unit, Fremantle Hospital and University of Western Australia, Fremantle, Western Australia

Urinary incontinence: type, cause and effect.
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(2)Department of Rehabilitation and Aged Care, Sir Charles Gairdner Hospital, Perth, WA,
(3)Corporate Nursing, Sir Charles Gairdner Hospital, Perth, WA

Prevalence of food allergies in Western Australian schoolchildren: a Busselton study.
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Co-registered Gallium-67 SPECT/CT imaging of infection.
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SPECT has no role in tertiary memory clinic setting.
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Synovial fluid ferritin is higher in osteoarthritis subjects heterozygous for the C282Y or H63D mutations in the FHE gene compared to wild type subjects: AR16.
Carroll GJ.
Fremantle Hospital and the Universities of Notre Dame and Western Australia

Outcomes for women in a flexible sigmoidoscopy-based colorectal cancer screening programme.
Viiala CH, Olynyk JK.
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BACKGROUND: There are concerns that technical and anatomical factors can reduce the potential benefit of flexible sigmoidoscopy (FS) as a colorectal cancer (CRC) screening tool in women compared with men. Our aim was to review the outcomes for female participants in a community-based CRC screening project using FS. METHODS: In 1995, a programme of unsedated FS-based screening of asymptomatic average-risk individuals aged 55-64 years was established at Fremantle Hospital, Western Australia. Insertion depths, pathological findings and site of adenomas and subject-rated pain scores have been prospectively recorded. Later diagnoses of malignancy were determined by linkage of the cohort with the West Australian Cancer Registry. RESULTS: Between 1995 and 2005, 3402 primary screening FS examinations had been carried out (women 41%). Mean age of participants was 59.6 years. Women were more likely to undergo a FS with insertion depth less than 40 cm (17 vs 6%, P < 0.0001). Mean pain score was 2.9 for men and 4.0 for women (P < 0.0001). Women were less likely to have any neoplasia detected, independent of pain score or insertion depth
(odds ratio 0.5, 95% confidence interval 0.4-0.6). Increasing insertion depth from 50 to 60 cm in a woman would only have a 0.4% chance of detecting any additional neoplasia. An insignificant trend to higher incidence of later interval CRC was observed in women with normal sigmoidoscopy. CONCLUSION: Women probably undergo FS with more discomfort and lesser insertion depth than men. It is unlikely that moderate increases in insertion depth would have a substantial benefit.
Publication Types: Comparative Study
PMID:17916176

*Assessing cognition in elderly patients presenting to the emergency department.*
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INTRODUCTION AND BACKGROUND: Delirium occurs frequently among elderly patients in the Emergency Department (ED), and accurate assessment is difficult without knowledge of the patient's usual cognitive functioning. This audit was designed to determine whether routine cognitive screening of elderly patients in ED could lead to early identification of delirium. METHODOLOGY: An audit using the abbreviate mental test (AMT) and Confusion Assessment Method (CAM) tools assessed 28 elderly ED patients for the presence of delirium. RESULTS: Fourteen (50%) of the 28 patients had no cognitive deficit on admission. Eleven (39.3%) displayed a cognitive deficit other than delirium and three (10.7%) had delirium, but only one had been diagnosed prior to the audit. DISCUSSION: The prevalence rate of delirium in elderly ED patients was similar to those reported in the literature. The audit demonstrated the importance of cognitive assessment, as cognitive changes can be an early and sensitive indicator of physiological dysfunction. However, the AMT had limitations which inhibited its use in ED. A four question version known as the AMT4 may be more suitable. RECOMMENDATIONS: ED nurses should routinely establish baseline cognitive functioning and assess for delirium. The AMT4 may be more suitable because of its brevity, but requires further research.
PMID:18519057

*Evaluating nurses’ knowledge and skills in the detection of child abuse in the Emergency Department.*
Fremantle Hospital, P.O. Box 480, Fremantle, W.A. 6959, Australia. carolyn.keane@health.wa.gov.au
This commentary paper highlights the issue of child abuse and the important role that nursing staff working in the Emergency Department (ED) can play in halting the cycle of abuse. Child abuse is a worldwide problem that is occurring with increasing frequency. In fact, in Australia over the last 5 years the number of child protection referrals has more than doubled. As well as the immediate physical damage child abuse causes, it can also escalate to result in more serious injury and death. Furthermore, children who are abused in their early years of life are at increased risk of a range of adverse long-term developmental problems. Research has demonstrated that there is a significant lack of detection of suspected cases of child abuse in the ED. In fact the true incidence of children presenting to hospital EDs with abuse is difficult to determine, and many cases remain undetected. Nursing staff are perfectly positioned to detect the signs that a child may be at risk of abuse. However, in order to identify these signs it is essential that ED nurses have the knowledge and skills necessary to do so. Failure to consider the possibility of abuse will mean that the appropriate diagnosis is not made and the child is returned to an abusive environment. Therefore, this paper offers ED nurses recommendations for future directions in research and interventions to improve the detection of child abuse in Western Australia.
PMID:18519048
Successful aspiration of an LAD thrombus 'cast' using an Export catheter.
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The use of a mechanical device to aspirate thrombus prior to stent deployment during primary angioplasty is currently not routinely recommended as results are often disappointing. However, we report a remarkable case during which we were able to successfully aspirate a 31 mm continuous length of thrombus using an Export catheter with subsequent dramatic improvement in both TIMI-flow and ST-segment resolution. copyright 2007.

Colonic endometriosis with malignant transformation mimicking a diverticular abscess.
Wong DD, Havlat MF, et al.
(Wong) PathWest Laboratory Medicine, Sir Charles Gairdner Hospital. Hospital Avenue, Nedlands, WA 6009, Australia. (Havlat) St. John of God Pathology, University of Notre Dame. Fremantle, WA, Australia. (Thin) Fremantle Hospital. Alma St., Fremantle, WA 6959, Australia.

A perspective on developing emergency medicine as a specialty.
Curry C.
Emergency Department, Fremantle Hospital, Alma St, Fremantle, Western Australia, 6160, chris@chriscurry.com.au.

Molecular insights into the pathophysiology of iron metabolism: 44.
Olynyk JK.
School of Medicine and Pharmacology, University of Western Australia and the Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia.

Mental status assessment: the current focus of this vital sign in nursing curricula.
Wynaden D, Hare M, et al.
(1)Curtin University of Technology, Perth, (2)Fremantle Hospital, Fremantle, WA, Australia

Hyperbaric oxygen treatment of chronic refractory radiation proctitis: a randomized and controlled double-blind crossover trial with long-term follow-up: in regard to Clarke et al. (Int J

**Depression in Alzheimer's disease: Phenomenology, clinical correlates and treatment.**
Starkstein SE, Mizrahi R, et al.
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Depression is one of the most frequent comorbid psychiatric disorders in Alzheimer's disease and other dementias, and is associated with worse quality of life, greater disability in activities of daily living, a faster cognitive decline, a high rate of nursing home placement, relatively higher mortality, and a higher frequency of depression and burden in caregivers. Depression in Alzheimer's disease is markedly under-diagnosed, and most patients with depression are either not treated or are on subclinical doses of antidepressants. This is related to the lack of validated diagnostic criteria and specific instruments to assess depression in dementia. Apathy and pathological affect-crying are the main differential diagnoses of depression in Alzheimer's disease. Left untreated, major depression in Alzheimer's disease may last for about 12 months. Recent randomized controlled trials demonstrated the efficacy of sertraline and moclobemide to treat depression in Alzheimer's disease. Other psychoactive compounds may be useful as well, but careful consideration must be given to potentially serious side-effects. copyright 2008 Informa Healthcare USA, Inc.

Publication Types: Review
PMID:2008493733


**Induction of MMP-1, MMP-3 and TIMP-1 in normal dermal fibroblasts by chronic venous leg ulcer wound fluid.**
School of Surgery and Pathology, The University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.

In the wound bed of chronic venous leg ulcers, an imbalance of matrix metalloproteinases (MMPs) and tissue inhibitor of metalloproteinases (TIMPs) may cause excessive proteolysis and impair wound granulation. Soluble mediators in the wound environment may be responsible for this imbalance. The in vitro effect of wound fluid from venous leg ulcers on dermal fibroblast production of MMP-1, MMP-3 and TIMP-1 was compared with the effect of acute wound fluid from two different sources: fluid from post-mastectomy axillary drains and fluid from skin graft donor sites. Significantly higher MMP-1 and MMP-3 levels were induced by chronic venous leg ulcer wound fluid compared with both types of acute wound fluid (P < 0.005). Chronic venous ulcer wound fluid reduced TIMP-1 protein levels significantly more than acute graft fluid (P < 0.05). Venous ulcer wound fluid significantly increased MMP-1 and MMP-3 production in dermal fibroblasts and reduced TIMP-1 production, confirming that mediators in the leg ulcer microenvironment can potentially induce excessive proteolysis in the ulcer dermis by altering the balance between MMPs and TIMPs. Inflammatory mediators including interleukin-1beta and tumour necrosis factor-alpha can induce these MMPs. Further work is required to confirm the factors responsible for the induction of a high MMP and low TIMP profile in fibroblasts by venous ulcer wound fluid.

Publication Types: Research Support, Non-U.S. Gov't
Luteinizing hormone levels are positively correlated with plasma amyloid-beta protein levels in elderly men.
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Dhaliwal, Satvinder: School of Public Health, Curtin University, Bentley, WAU, Australia
Burkhardt, Melanie S.: Sir James McCusker Alzheimer's Disease Research Unit, Hollywood Private Hospital, Nedlands, WAU, Australia
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Dysregulation of the hypothalamic pituitary gonadal (HPG) axis during aging has been associated with increased risk of cognitive decline and developing dementia. Compared to controls, men with Alzheimer's disease (AD) have been shown to have lower serum testosterone levels and higher serum luteinizing hormone (LH) levels. As serum free testosterone concentration is negatively correlated with LH in older men, the independent contributions of these hormones to the pathogenesis of AD warrants further clarification. To explore this notion, we measured plasma amyloid-beta (Abeta ), serum testosterone, serum LH and other biochemical parameters in 40 cognitively normal elderly men. Multiple linear regression analysis revealed that serum LH concentration is the only parameter that significantly correlates with plasma Abeta levels in these men (r = 0.5, p = 0.041). These results suggest that increased serum LH concentration, rather than lower serum free testosterone, is associated with the accumulation of Abeta in plasma. Larger, longitudinal human studies are needed to determine the significance of LH in the pathogenesis of AD. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract).

Microstructural features in fractured high nitrogen stainless steel hip prostheses: A retrieval study of polished, tapered femoral stems.
Swarts E, Kop A, et al.
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Six fractured high nitrogen stainless steel (HNSS), polished, tapered hip stems have been reviewed for analysis. Clinical data suggests that poor proximal support (loosening), varus positioning, and canal morphology are implicated in the failure of these stems. Metallurgical assessment reveals a number of microstructural deficiencies contributing to failure. Of significance is poor grain homogeneity and larger grain size near the surface of the fractured stems. It appears some polished, tapered HNSS stems are at risk when combinations of these clinical and metallurgical features occur. As the control of grain size, microstructural uniformity, and inclusion content are critical for optimum mechanical performance, it is important the manufacturers review processing methods to further minimize the risk of component failure. Copyright 2007 Wiley Periodicals, Inc.

PMID:2008078405


Collarless polished tapered stem: clinical and radiological results at a minimum of ten years' follow-up.
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We retrospectively reviewed 175 patients (191 hips) who had undergone primary cemented total hip replacement between November 1992 and November 1995 using a collarless polished double-tapered femoral component after a minimum of ten years (mean 11.08; 10 to 12.8). All stems were implanted using contemporary cementing techniques with a distal cement restrictor, pressurised lavage, retrograde cementing with a gun and proximal pressurisation. Clinical outcome was assessed using the Harris Hip score. Radiological analysis was performed on calibrated plain radiographs taken in two planes. Complete radiological data on 110 patients (120 hips) and clinical follow-up on all the surviving 111 patients (122 hips) was available. The fate of all the hips was known. At final follow-up, the mean Harris Hip score was 86 (47 to 100), and 87 of 116 patients (75%) had good or excellent scores. Survival with revision of the stem for aseptic loosening as the endpoint was 100%; and survival with revision of the stem for any reason was 95.9% (95% confidence interval 87.8 to 96.8) at ten years. All the stems subsided vertically at the stem-cement interface in a predictable pattern, at an overall mean rate of 0.18 mm per year (0.02 to 2.16), but with a mean rate of 0.80 mm (0.02 to 2.5) during the first year. The mean total subsidence was 1.95 mm (0.21 to 24). Only three stems loosened at the cement-bone interface. There was excellent preservation of proximal femoral bone stock. There was a high incidence of Brooker III and IV heterotopic ossification affecting 25 patients (22%). The collarless polished tapered stem has an excellent clinical and radiological outcome at a minimum of ten years' follow-up. The pattern and magnitude of subsidence of the stem within the cement mantle occurred in a predictable pattern, consistent with the design philosophy.
Publication Types: Journal Article
PMID:18160493


Body mass index is a stronger predictor of alanine aminotransaminase levels than alcohol consumption.
Adams LA, Knuiman MW, et al.
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BACKGROUND AND AIMS: The relative effects of obesity compared to alcohol on liver injury are uncertain. We examined their effects on alanine aminotransferase (ALT) and gamma glutamyltransferase (GGT) levels in a population-based cohort. METHODS: Adult residents (2610: 1326 males, 1284 females) from Busselton, Australia, participated in a cross-sectional survey determining alcohol intake as determined by a validated questionnaire, anthropometric measurements and serum analysis. Alcohol consumption was classified as never, light (<140 g/week), moderate...
RESULTS: The majority of subjects were either overweight (41%) or obese (17%). A minority of subjects were moderate (25%) or heavy drinkers (4%). Body mass index (BMI) and waist circumference were strongly associated with ALT and GGT (P < 0.0001 for all tests). Alcohol consumption was modestly associated with ALT in females (P = 0.01) but not in males (P = 0.9). In contrast, GGT was significantly associated with alcohol in both genders (P < 0.0005). The risk of an elevated ALT was seven-fold higher with obesity but only two-fold higher with moderate or heavy alcohol use. Obesity accounted for half of all elevated ALT levels in the cohort, whereas alcohol excess was responsible for less than 10%. No synergistic effect was observed between BMI or waist circumference and alcohol on ALT or GGT (P > 0.2 for all tests).

CONCLUSIONS: Excess weight is more common than excessive alcohol consumption in the community and confers a greater risk of elevated aminotransaminase levels.

PMID: 18557801


Reasons for failure to attend hepatitis clinics: results from a survey.
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An Australian experience with biological agents for perianal Crohn's disease.
Burger DC, Lawrence IC, et al.
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Prevalence of thyroid dysfunction in patients with chronic hepatitis C infection receiving pegylated interferon alpha 2a versus alpha 2b, plus ribavirin.
Gan EK, Miczkova S, et al.
Hepatitis Services, Fremantle Hospital, Alma St, Fremantle, Western Australia, Australia


Co-localisation of hepatitis C virus drug-resistant mutations and immune-driven adaptations for genotype 1 and 3: relevance to therapy outcome.
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Serious infective complications associated with anti-TNF[alpha] therapy in inflammatory bowel disease.
The use of topical tacrolimus in the treatment of resistant ulcerative proctitis.
Lawrance IC, Copeland T, et al.
(1)Department of Gastroenterology, Fremantle Hospital, WA, (2)University Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia

An audit of adherence to screening guidelines for early detection of hepatocellular carcinoma in cirrhotic patients.
Li WD, Miczkova S, et al.
Fremantle Hepatitis Services, Fremantle Hospital, Alma St, Fremantle, WA, Australia

Stevens-Johnson syndrome complicating adalimumab therapy: a case report.
Salama M, Lawrance IC.
(1)Department of Gastroenterology, Fremantle Hospital, WA, (2)University Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia

Hepatitis C treatment and the elderly: one centre perspective.
Tate J, Miczkova S, et al.
Fremantle Hospital, Western Australia

Observed and expected age-related mortality outcomes 5 years post colonoscopy +/- polypectomy.
Thin LW, Lawrance IC.
(1)Centre for Inflammatory Bowel Diseases, Fremantle Hospital, WA, (2)University Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia

Initial experience of adalimumab efficacy in the management of IBD in the clinical setting.
Trinder M, Lawrance IC.
(1)Centre for Inflammatory Bowel Diseases, Fremantle Hospital, WA, (2)University Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia

Comparing outcomes in hepatitis C virus infected patients treated with pegasys or pegatron and ribavirin.
Comparing outcomes in patients with treatment naive chronic hepatitis C, treated with two different types of Pegylated Interferon molecules, when matched for age, gender, BMI, genotype and fibrosis scores.
Venugopal K, Miczkova S, et al.
(1)Hepatitis Unit, Fremantle Hospital, WA, (2)School of Population Health, WA, (3)Royal Perth Hospital, WA, Australia

A prospective audit of tolerability and mucosal cleansing efficacy with orally administered colon cleansing preparations for colonoscopy.
(1)Department of Gastroenterology, Fremantle Hospital, WA, Centre for inflammatory Bowel diseases, Fremantle Hospital, WA, (3)University Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia

Enhanced biostability and biocompatibility of decellularized bovine pericardium, crosslinked with an ultra-low concentration monomeric aldehyde and treated with ADAPT.
Neethling WM, Yadav S, et al.
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BACKGROUND AND AIM OF THE STUDY: Matrix preparation remains controversial due to incomplete cell removal, inflammatory responses, reabsorption and thrombocyte activation. Previously, crosslinked matrices have been considered unsatisfactory due to cytotoxicity. In the present study, the biostability, biocompatibility and calcification potential of a decellularized matrix crosslinked with a low concentration of monomeric glutaraldehyde (GA) and treated with the ADAPT anti-calcification process were examined. METHODS: Bovine pericardium was decellularized with Triton X-100, deoxycholate, IgePal CA-630 and ribonuclease. The resulting matrices were allocated to either group I (control, n = 5), crosslinked in 0.2% polymeric GA + ADAPT, or to group II (treatment, n = 5), crosslinked in 0.05% monomeric GA + ADAPT. The physical properties, enzymatic degradation, histology and immunohistochemical staining of the tissues were monitored. The matrices were also implanted in the jugular vein of juvenile sheep for 200 days. RESULTS: Complete acellularity was achieved. Biostability was significantly (p <0.01) enhanced in group II, but inflammatory responses were limited in both groups. Host fibroblasts infiltrated the periphery in group I and the entire matrix in group II. The luminal surfaces were free from thrombotic depositions and covered with endothelial cells. Both groups tested positive for Factor VIII, smooth muscle alpha-actin and vimentin. Tissue extractable calcium levels were low (group I = 1.02 +/- 0.39, group II = 0.86 +/- 0.22 microg Ca/mg tissue). CONCLUSION: Low-concentration GA-crosslinked matrices proved to be stable. The immunoreactivity of both groups was low, with host cell infiltration, migration and trans-differentiation being optimized in those grafts crosslinked with an ultra-low monomeric GA concentration. Calcification levels were close to zero in both groups. Enhanced crosslinking and effective anti-calcification produce a biomaterial with advanced in-vivo tissue-engineering properties.
PMID:18751476
Transferrin receptor 2 mediates uptake of transferrin-bound and non-transferrin-bound iron.

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BACKGROUND/AIMS: Transferrin receptor 2 appears to have dual roles in iron metabolism; one is signalling, the other is iron transport. It is sensitive to high levels of diferric transferrin, which is associated with disorders of iron overload. Also present in these disorders are increased levels of plasma non-transferrin-bound iron. This study sought to clarify the role of transferrin receptor 2 in the uptake of transferrin-bound and non-transferrin-bound iron.

METHODS: Variant Chinese Hamster Ovary (CHO) cells, transfected with transferrin receptor 2, were incubated with radio-labelled transferrin-bound or non-transferrin-bound iron. Competition studies were performed in the presence of unlabelled dimetallic transferrin; knockdown was performed using specific siRNA.

RESULTS: Cells expressing transferrin receptor 2 bound and internalised transferrin and transferrin-bound iron. Transferrin recycling occurred with an average cycling time of 11-15min. Interestingly, the presence of transferrin receptor 2 was also associated with uptake of non-transferrin-bound iron which was inhibited by unlabelled transferrin-bound metals. Knockdown reduced transferrin-bound and non-transferrin-bound iron uptake by approximately 60%.

CONCLUSIONS: Transferrin receptor 2 mediates transferrin-bound iron uptake by receptor-mediated endocytosis. It is also involved in the uptake of non-transferrin-bound iron and the inhibition of non-transferrin-bound iron uptake by diferric transferrin in CHO cells.

The nosological position of apathy in clinical practice.

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Apathy is increasingly recognised as a common behavioural syndrome in psychiatric disorders, but it is conceptually ill defined. The aim of this study was to examine the concept of apathy as it is currently used in neurology and psychiatry, by review of the literature and conceptual analysis. There is no consensus on diagnostic criteria for apathy as a syndrome. Apathy is mostly defined as a disorder of motivation, and operationalised as diminished goal oriented behaviour and cognition. There is discussion about whether an emotional dimension should form part of the definition of apathy. Abulia is considered a more severe type of apathy, but its nosological position is still unclear. A structured clinical interview and a proposal for diagnostic criteria for apathy in dementia have been recently validated. There are several valid and reliable scales to measure the severity of apathy in patients with psychiatric and neurological disorders. In summary, apathy is increasingly recognised as a common behavioural syndrome associated with neuropsychiatric disorders. There is a need for consensus on diagnostic criteria to facilitate future research. From a nosological perspective, future studies should examine the overlap with other psychiatric and neurodegenerative conditions and further validate specific diagnostic and assessment tools.

Reduction in salivary cortisol concentration correlates with resolution of psychosis in Cushing's syndrome.

Myhill PC, Sillars BA, et al.
(Myhill, Sillars) Department of Endocrinology, Fremantle Hospital. WA, Australia. (Starkstein) Department of Psychiatry and Clinical Neurosciences, University of Western Australia.

Nicholls RL, Schirm AC, et al.
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Publication Types: Erratum
PMID:2008450970


Comparative stability of perpendicular versus parallel double-locking plating systems in osteoporotic comminuted distal humerus fractures.
Stoffel K, Cunneen S, et al.
Department of Orthopaedic Surgery, Level 6, B Block, Fremantle Hospital, Alma Street, The University of Western Australia, Fremantle, Western Australia 6160, Australia.
In distal humerus fractures, the restoration of stability is important to allow early mobilization and hence more favorable functional outcomes. In this article, we compare the biomechanical stability of perpendicular and parallel locking plating systems for the internal fixation of AO Type C2 distal humerus fractures in osteoporotic bone. Fractures were simulated in paired cadaveric bones and fixed using either the perpendicular 3.5 mm LCP distal humerus plating system (Synthes; Sydney, Australia) or the parallel Mayo Clinic Congruent elbow plate system (Acumed; Hillsboro, OR), using locking screws in both systems. Both systems were then tested for their stiffness (in compression and internal/external rotation), plastic deformation, and failure in torsion. Comparatively, the parallel locking plate system provided a significantly higher stability in compression (p = 0.005) and external rotation (p = 0.006), and a greater ability (p = 0.005) to resist axial plastic deformation. Stability for both constructs appeared to be dependent on bone quality, however the stability of the perpendicular system was generally more sensitive to bone mineral density, indicating a possible need for additional independent interfragmentary screws. A disadvantage of the parallel locking plate system was wear debris produced by its tapping system. In summary, the biomechanical findings of this study suggest that both locking plate systems allow early mobilization of the elbow in patients with osteoporotic bone following fixation of a comminuted distal humerus fracture. However, the parallel locking system
showed improved stability compared with the perpendicular locking system, and therefore may be more indicated. (c) 2008 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 26:778-784, 2008.
PMID:18203185

The Fremantle lead study part 2.
Guttinger R, Pascoe E, et al.
Princess Margaret Hospital for Children, Fremantle, Australia. robin.guttinger@health.wa.gov.au
AIM: A 1993 study of blood lead levels (BLLs) in pre-schoolers living in Fremantle showed 25% had BLLs >or= 10 microg/dL. This study compares the 1993 BLLs with a sample of contemporary Fremantle pre-schoolers. METHODS: Pre-schoolers (0-5 years) living in the Fremantle area were recruited from hospital and community settings during 2005. As in the 1993 study, guardians completed a questionnaire concerning demographic, environmental and behavioural variables. BLLs were determined by the same method used in 1993. Statistical analysis compared the 1993 and 2005 samples according to demographic variables and dichotomised BLL. Multivariate linear regression was used to control for confounding variables, and linear regression was used to identify risk factors in the 2005 sample. RESULTS: Community (40) and hospital (60) participants provided blood and completed questionnaires; none had BLLs >or=10 microg/dL. Compared with the 1993 sample, 2005 participants were younger, fewer were aboriginal, more had occupied their homes for over 6 months and more had a habit of putting soil in their mouths. After controlling for these variables, the geometric mean BLL in 2005 remained significantly lower than the 1993 value (1.83 and 6.82 microg/dL respectively). As in 1993, aboriginality, presence of participants during home renovation, occupancy of home less than 6 months and living <200 m from a main road were associated with higher mean BLLs. CONCLUSIONS: The reassuring decline in the mean BLL between the 1993 and 2005 samples is likely associated with the phasing out of leaded petrol. Future research should concentrate on monitoring groups at higher risk.
Publication Types: Research Support, Non-U.S. Gov't
PMID:19077066

Myrmecia pilosula (Jack Jumper) ant venom: Validation of a procedure to standardise an allergy vaccine.
Wiese MD, Milne RW, et al.
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Ant sting allergy is relatively common within south-eastern Australia and is predominantly due to Myrmecia pilosula (Jack Jumper Ant, JJA). Venom immunotherapy has been shown to be effective in preventing anaphylaxis to the sting of the JJA, but analytical techniques to standardise the venom have not been validated. The purpose of this study was to develop assays to analyse JJA venom and apply these to the standardisation of venom prior to new batches being used for the diagnosis and treatment of JJA sting allergy. Venom was analysed by protein content, HPLC-UV, enzyme-linked immunosorbent assay (ELISA) inhibition, sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and SDS-PAGE immunoblot. The protein content in JJA venom was adjusted so that all batches were equivalent. A HPLC-UV assay was used to quantify the relative amount of the major allergen Myr p 2 and two minor allergens Myr p 1 and Myr p 3 and allergenic potency was determined by ELISA inhibition. SDS-PAGE and SDS-PAGE immunoblot were used as qualitative tools to determine the protein profile and presence or absence of additional high molecular weight allergens not quantifiable by HPLC-UV. A standardisation procedure has been developed that complies with the requirements described in the European Pharmacopoeia. Techniques used to determine the content of some of the other minor allergens could be developed, which would further improve the
Development and testing of a modified version of the brief pain inventory for use in residential aged care facilities.
Auret KA, Toye C, et al.
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OBJECTIVES: A two-phase study was conducted to refine a version of Cleeland's Brief Pain Inventory (BPI, Short Form) for use in residential aged care facilities (RACFs)., DESIGN: The Australian Pain Society modified Cleeland's BPI by changing numerical response options to word descriptors. In Phase I, this version was tested in RACFs to determine the feasibility of its use, its stability over time, and its internal consistency reliability. Minor modifications resulted. In Phase II, the refined version was abbreviated, and the internal consistency reliability of this Modified Residents' Verbal BPI was examined., SETTING: RACFs., PARTICIPANTS: Thirty-three residents of RACFs in Phase I, 149 in Phase II., INTERVENTION: The study revised and abbreviated the BPI to better fit it for use in RACFs, examining the reliability of the tool., MEASUREMENTS: Mini-Mental State Examination, Global Deterioration Scale, modified BPI., RESULTS: The abbreviated tool comprises three items assessing pain intensity and three assessing pain interference. It also includes an item to specify pain location and a movement protocol. Cronbach alpha coefficient for six intensity and interference items was 0.72 (N=106)., CONCLUSION: This abbreviated tool requires further testing but has demonstrated adequate internal consistency reliability and is a brief, multidimensional tool that appears feasible for assessing pain in RACFs, including use with residents who have some cognitive impairment. It shows promise as a screening tool and may be useful to assess the effectiveness of pain relief interventions and to measure pain prevalence., (C) 2008 by the American Geriatrics Society

Noncitrus fruits as novel dietary environmental modifiers of iron stores in people with or without HFE gene mutations.
Milward EA, Baines SK, et al.
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OBJECTIVE: To investigate whether citrus fruit, noncitrus fruit, and other dietary factors act as
environmental modifiers of iron status in the absence or presence of hemochromatotic HFE gene mutations. PARTICIPANTS AND METHODS: Iron studies, HFE genotypic analyses, and dietary data from a survey conducted from March 21, 1994, through December 15, 1995, were analyzed for a group of 2232 residents (1105 men, 1127 women) aged 20 to 79 years recruited from the community electoral roll of Busselton in Western Australia. Data were analyzed by linear regression analysis and analysis of covariance. RESULTS: Higher levels of fresh fruit intake (excluding citrus fruits and citrus juices) had a significant protective effect (P=.002) against high body iron status as gauged by ferritin levels in men, irrespective of HFE genotype. Consumption of 2 or more pieces of fruit per day on average reduced mean serum ferritin levels by 20% compared with average consumption of less than 1 piece of fruit per day. This effect was not observed in women. Consumption of citrus fruits and citrus juices had no significant effects in either sex. No protective effects were observed for tea consumption or any other dietary factors studied. Red meat and alcohol consumption correlated with high body iron stores (P<.05), consistent with previous studies, but did not interact with fruit with regard to effects on serum ferritin (P>.05). CONCLUSION: Noncitrus fruits are environmental modifiers of iron status independent of HFE genotype. This could have important implications for the provision of evidence-based dietary advice to patients with other iron-storage disorders. 2008 Mayo Foundation for Medical Education and Research.

PMID:2008249638


Noncitrus fruits as novel dietary environmental modifiers of iron stores in people with or without HFE gene mutations.

Milward EA, Baines SK, et al.
School of Biomedical Sciences and Hunter Medical Research Institute, University of Newcastle, Callaghan, NSW, Australia.

OBJECTIVE: To investigate whether citrus fruit, noncitrus fruit, and other dietary factors act as environmental modifiers of iron status in the absence or presence of hemochromatotic HFE gene mutations. PARTICIPANTS AND METHODS: Iron studies, HFE genotypic analyses, and dietary data from a survey conducted from March 21, 1994, through December 15, 1995, were analyzed for a group of 2232 residents (1105 men, 1127 women) aged 20 to 79 years recruited from the community electoral roll of Busselton in Western Australia. Data were analyzed by linear regression analysis and analysis of covariance. RESULTS: Higher levels of fresh fruit intake (excluding citrus fruits and citrus juices) had a significant protective effect (P=.002) against high body iron status as gauged by ferritin levels in men, irrespective of HFE genotype. Consumption of 2 or more pieces of fruit per day on average reduced mean serum ferritin levels by 20% compared with average consumption of less than 1 piece of fruit per day. This effect was not observed in women. Consumption of citrus fruits and citrus juices had no significant effects in either sex. No protective effects were observed for tea consumption or any other dietary factors studied. Red meat and alcohol consumption correlated with high body iron stores (P<.05), consistent with previous studies, but did not interact with fruit with regard to effects on serum ferritin (P>.05). CONCLUSION: Noncitrus fruits are environmental modifiers of iron status independent of HFE genotype. This could have important implications for the provision of evidence-based dietary advice to patients with other iron-storage disorders.

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

PMID:18452683


Contemporary management of type 2 diabetes: blood glucose-lowering therapies and glycaemic targets.

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Recent trials and meta-analyses have raised questions about choice of therapy and use of strict glycaemic targets.


**Incidence of bariatric surgery and postoperative outcomes: A population-based analysis in Western Australia.**

Smith FJ, Holman CDJ, et al.

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**Objective:** To investigate the incidence of bariatric surgery and postoperative outcomes in a population-based cohort of patients in Western Australia over a 17-year period. **Design and setting:** A population-based incidence study of all bariatric procedures (n= 1403) performed in WA hospitals over the period 1988-2004, based on hospital morbidity and death data from the WA Data Linkage System. **Main outcome measures:** Changes in incidence of bariatric procedures over time; mortality and complications within 30 days after surgery; survival rates after surgery relative to age-, sex-, and period-matched survival rates in the general population; factors predictive of re-admission to hospital.

**Results:** The incidence of bariatric surgery increased from 1.2 procedures per 100 000 person-years in 1988 to 24.2 procedures per 100000 person-years in 2004. Although some of this was ascribed to a rising prevalence of obesity generally, there was a 13-fold increase in the bariatric procedure rate within the obese population itself. At 5 years, the relative survival rate in bariatric patients was the same as the survival rate in the general population. Within the 30-day postoperative period, mortality was low (0.07%) and 9.6% of patients experienced complications. Those who had bypass-type procedures were more likely to be re-admitted within 30 days than those who had gastric reduction procedures (adjusted hazard ratio, 5.80 [95% CI, 3.42-9.84]). **Conclusion:** The use of bariatric surgery increased 20-fold over the study period. Relative survival after surgery was in line with population norms. The observed low mortality rates and moderate level of complications are similar to findings in other studies in which the proportion of reduction procedures has been high.

**PMID:** 2008425450

**Medical Journal of Australia. 2008; 188(8): 446-9.**

**Metformin and lactic acidosis in an Australian community setting: the Fremantle Diabetes Study.**

Kamber N, Davis WA, et al.

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**OBJECTIVE:** To determine the incidence of lactic acidosis in community-based patients with type 2 diabetes, with special reference to metformin therapy. **DESIGN:** Substudy within a longitudinal observational study, the Fremantle Diabetes Study (FDS). **PARTICIPANTS AND SETTING:** 1279 patients from a postcode-defined population of 120 097 people in Western Australia. **MAIN OUTCOME MEASURES:** Confirmed hospitalisation with lactic acidosis identified through the WA Data Linkage System during two periods: (1) from study entry, between 1993 and 1996, and study close in November 2001; and (2) from study entry to 30 June 2006. **RESULTS:** At entry, 33.3% of patients were metformin-treated, and 23.1% of these had one or more contraindications to metformin (55.1% and 38.0%, respectively, after 5 years’ follow-up). Five confirmed cases of lactic acidosis were identified during 12 466 patient-years of observation; all had at least one other potential cause, such as cardiogenic shock or renal failure. From study entry to close, the incidence was 0/100 000 patient-years in both metformin-treated and non-metformin-treated patients. Between study entry and 30 June 2006, incidence was 57/100 000 patient-years (95% CI, 12-168) in metformin-treated patients and 28/100 000 patient-years (95% CI, 3-100) in the non-metformin-treated group, an incidence rate
difference of -30 (-105 to 46) (P = 0.4). CONCLUSION: The incidence of lactic acidosis in patients with type 2 diabetes is low but increases with age and duration of diabetes, as cardiovascular and renal causes become more prevalent. Metformin does not increase the risk of lactic acidosis, even when other recognised precipitants are present. PMID:18429709


Learning from error: identifying contributory causes of medication errors in an Australian hospital.
School of Medicine and Pharmacology, University of Western Australia, Fremantle, WA, Australia. dbruce@cyllene.uwa.edu.au.
OBJECTIVE: To study the clinical contexts contributing to harmful medication errors. DESIGN, SETTING AND PARTICIPANTS: A qualitative study using semi-structured interviews was conducted between March and August 2005 at Fremantle Hospital, a 450-bed metropolitan teaching hospital. Twenty-six of 46 staff members (57%) identified by pharmacy staff as having contributed to a significant medication error were interviewed. Interviews were recorded and transcribed for thematic analysis. RESULTS: Most errors were due to slips in attention that occurred during routine prescribing, dispensing or drug administration. Knowledge-based mistakes (eg, failure to follow a protocol) also contributed to prescribing errors. Errors were more likely to occur during tasks being carried out after hours by busy, distracted staff, often in relation to unfamiliar patients. Communication problems with senior staff and difficulty accessing appropriate drug dosing information contributed to knowledge-based prescribing errors. Several medical staff were unaware they had committed an error until their involvement with our study. CONCLUSIONS: Contextual factors that contributed to slips, lapses and knowledge-based mistakes in our sample are likely to be widespread in hospitals, and their impact on medication error may be substantial. Staff need training in how to recognise and deal with error-prone clinical situations. Safe prescribing practices (eg, the absolute requirement to acquire information before prescribing unfamiliar drugs) must be emphasised. Improved access to drug information at the point of prescribing, attention to communication barriers, and increasing staffing levels in particular areas are other potential strategies for reducing error.
Publication Types: Journal Article
PMID:18312190


Estimation of glomerular filtration rate in older individuals: does haemoglobin discriminate between ageing and true CKD?: 014.
Ferrari P, Xiao J, et al.
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Magnetic resonance imaging demonstrates iron overload in patients on long-term haemodialysis: 196.
Kulkarni H, Olynyk J, et al.
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Elevated TSH following iodinated radiocontrast media in patients on haemodialysis: 048.
Wright S, Yeap B, et al.
(1)Department of Nephrology, Royal Perth Hospital, WA, Australia; (2)Department of Endocrinology, Fremantle Hospital, WA, Australia; (3)Department of Nephrology, Fremantle Hospital, WA, Australia

High prevalence of ascorbate deficiency in an Australian peritoneal dialysis population.
Singer R, Rhodes HC, et al.
School of Medicine and Pharmacology, University of Western Australia and Department of Nephrology, Fremantle Hospital, Perth, Western Australia, Australia.
Background: An adequate total body pool of ascorbate is essential for optimum health in humans. Requirements for ascorbate are increased in peritoneal dialysis (PD) patients most likely due to a combination of poor nutrition and increased dialysate losses. Methods: We measured serum ascorbate levels in 45 clinically stable PD patients to assess the prevalence of ascorbate insufficiency (level between 2 and 4 mg/L) and deficiency (level <2 mg/L). We also assessed the efficacy of subsequent supplementation and patients' adherence to the prescribed supplementation. All patients were advised on commencement of dialysis to take a multivitamin tablet containing 100-120 mg ascorbate. Results: Eighteen (41%) PD patients were regularly taking ascorbate-containing multivitamins, while 27 (59%) patients did not take ascorbate supplements. Serum ascorbate levels ranged from <0.2 to 41 mg/L, with wide variations in serum ascorbate at any given intake level. Ascorbate deficiency was present in 1/3 of the current PD population (44% of patients not taking supplements and in 16% of those on supplements), although none of the patients demonstrated clinical manifestations of scurvy. Targeted supplementation of ascorbate insufficient patients increased the median serum ascorbate level from 1.7 mg/L (IQR 1.2-2.2) to 22.5 mg/L (IQR 16.7-32.9). Conclusion: Our results show that, in PD patients, ascorbate deficiency is common and can readily be identified with serum ascorbate measurements. Oral supplements in the form of inexpensive multivitamin preparations restore adequate serum ascorbate levels in the majority of these patients. We therefore suggest measurement of ascorbate levels in all PD patients at the commencement of dialysis with a target level in the normal range (4-14 mg/L).
Publication Types: Journal Article
PMID:18199096

Challenging cannulation in haemodialysis: 375.
Yung J, Yee H.
Fremantle Hospital Renal Unit, Western Australia
Publication Types: Conference Poster Abstract

Optimal Ultrafiltration Profiling In Hemodialysis.
Yung J.
John Yung, is a Clinical Nurse, Fremantle Hospital Renal Unit, Fremantle, Western Australia.

Treatment of hypertension in the elderly [3].
Cheah CY, Wilson MD.
(Cheah, Wilson) Fremantle Hospital, Perth, WA 6160, Australia.
Publication Types: Letter

A trial of combination antimalarial therapies in children from Papua New Guinea.

Karunajeewa HA, Mueller I, et al.

From the School of Medicine and Pharmacology, University of Western Australia, Crawley, WA, Australia (H.A.K., I.L., M.P.-S., R.W., S.S., K.F.I., T.M.E.D.); and the Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea (I.M., M.S., E.L., P.S.G., O.O., S.G., K.K., P. Suano, N.T., A.U., D.L., P. Siba). Address reprint requests to Dr. Davis at the University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, P.O. Box 480, Fremantle, WA 6959, Australia, or at tdavis@cyllene.uwa.edu.au., This article (10.1056/NEJMoa0804915) was published at www.nejm.org on December 8, 2008.

Background: Malaria control is difficult where there is intense year-round transmission of multiple plasmodium species, such as in Papua New Guinea., Methods: Between April 2005 and July 2007, we conducted an open-label, randomized, parallel-group study of conventional chloroquine-sulfadoxine-pyrimethamine and artesunate-sulfadoxine-pyrimethamine, dihydroartemisinin-piperaquine, and artemether-lumefantrine in children in Papua New Guinea 0.5 to 5 years of age who had falciparum or vivax malaria. The primary end point was the rate of adequate clinical and parasitologic response at day 42 after the start of treatment with regard to Plasmodium falciparum, after correction for reinfections identified through polymerase-chain-reaction (PCR) genotyping of polymorphic loci in parasite DNA. Secondary end points included the rate of adequate clinical and parasitologic response at day 42 with regard to P. vivax without correction through PCR genotyping., Results: Of 2802 febrile children screened, 482 with falciparum malaria and 195 with vivax malaria were included. The highest rate of adequate clinical and parasitologic response for P. falciparum was in the artemether-lumefantrine group (95.2%), as compared with 81.5% in the chloroquine-sulfadoxine-pyrimethamine group (P=0.003), 85.4% in the artesunate-sulfadoxine-pyrimethamine group (P=0.02), and 88.0% in the dihydroartemisinin-piperaquine group (P=0.06). The rate of adequate clinical and parasitologic response for P. vivax in the dihydroartemisinin-piperaquine group (69.4%) was more than twice that in each of the other three treatment groups. The in vitro chloroquine and piperaquine levels that inhibited growth of local P. falciparum isolates by 50% correlated significantly (P<0.001). Rash occurred more often with artesunate-sulfadoxine-pyrimethamine and dihydroartemisinin-piperaquine than with chloroquine-sulfadoxine-pyrimethamine (P=0.004 for both comparisons)., Conclusions: The most effective regimens were artemether-lumefantrine against P. falciparum and dihydroartemisinin-piperaquine against P. vivax. The relatively high rate of treatment failure with dihydroartemisinin-piperaquine against P. falciparum may reflect cross-resistance between chloroquine and piperaquine. (Australian New Zealand Clinical Trials Registry number, ACTRN12605000550606.), Copyright (C) 2008 Massachusetts Medical Society. All rights reserved.


Melanoma affinity in mice and immunosuppressed sheep of [125I]N-(4-dipropylaminobutyl)-4-iodobenzamide, a new targeting agent.


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The increasing incidence of melanoma and the lack of effective therapy have prompted the development of new vectors, more specific to the pigmented tumor, for early detection and treatment. Targeted agents have to exhibit a rapid, high tumor uptake, long tumor retention and rapid clearance
from nontarget organs. This joint work presents results obtained with a new melanoma targeting agent, \([125\text{I}]-\text{N-(4-dipropylaminobutyl)-4-iodobenzamide}\) or \([125\text{I}]\text{BZ18}\). After labeling with a high specific activity, the biodistribution of the compound was investigated in two animal models, the mouse and the sheep. Melanotic tumor retention was observed lasting several days. We visualized the internalization of the agent inside the melanosomes by secondary ion mass spectroscopy imaging, we measured the affinity constants of \([125\text{I}]\text{BZ18}\) on a synthetic melanin model and we demonstrated a radiotoxic effect of this labeled agent on B16F0 melanoma cell culture due to its cellular internalization. From this work, \([125\text{I}]\text{BZ18}\) appeared a promising melanoma targeting agent in the nuclear medicine field. copyright 2008 Elsevier Inc. All rights reserved.

PMID:2008468592

**Fish bone migration through the cervical spine.**
Bilish DP, Rajan GP, et al.
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Publication Types: Journal Article
PMID:18312896

**An exploratory study of changes in salivary cortisol, depression, and pain intensity after treatment for chronic pain.**
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Objective. To investigate the relationship between cortisol levels, pain intensity, and negative mood in chronic pain patients participating in a multidisciplinary pain management program. Patients. Eighteen chronic pain patients collected saliva samples over several days both directly before and after attending a 4-week multidisciplinary pain management program. Outcome Measures. Saliva samples were assayed for their cortisol concentration. Participants also completed self-report measures of pain intensity and depression. Results. Usual pain intensity and waking cortisol levels changed in parallel following treatment, as did changes in depression and cortisol levels late in the morning and in the evening. Depression did not mediate the association between cortisol and usual pain intensity; neither did pain intensity moderate the association between cortisol and depression. Conclusions. Changes in cortisol secretion may provide a useful biological marker of treatment outcome in chronic pain patients after their participation in a multidisciplinary pain management program. copyright 2008 by American Academy of Pain Medicine.
PMID:2008405222

**Endoscopic total retroperitoneal distal pancreatectomy in a large animal model.**
Ahmad H, Sandroussi C, et al.
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**Reasons for noncompliance with five-yearly screening flexible sigmoidoscopy.**
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OBJECTIVE: To determine factors influencing the low return rate observed in a program of flexible sigmoidoscopy for average risk screening for colorectal carcinoma. METHODS: Flexible sigmoidoscopy-based screening of average risk 55-64 yr olds has been ongoing since 1995. Greater than 3400 primary and 1000 follow up screening examinations have been performed. Participants with a primary screen in 1997-1999 and eligible for rescreening in 2002-2004 were studied. A questionnaire assessing possible reasons for noncompliance was sent to subjects who did not attend the five year repeat screening. RESULTS: 1672 primary screening flexible sigmoidoscopies were performed in 1997-1999 with 1362 being normal or having hyperplastic polyps only. The return rate was 45%: 48% of eligible males and 39% of eligible females had returned (p = 0.001 for difference). 709 questionnaires were mailed with a 50% response rate and 162 requests for repeat flexible sigmoidoscopy were generated. 27% of all respondents had undergone further bowel evaluation since the original normal sigmoidoscopy. Of eligible subjects who refused further screening, 65% did so because of concerns over procedural pain. CONCLUSIONS: Reasons for nonattendance relate to uptake of other bowel investigations and pain felt at initial screening. Return rate can be raised with ongoing prompting to attend screening.

PMID:19920941


A randomised controlled trial of intramuscular vs. intravenous antivenom for latroductism-the RAVE study.
Isbister GK, Brown SGA, et al.
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Background: Widow spider-bite causes latroductism and is associated with significant morbidity worldwide. Antivenom is given by both the intravenous (IV) and intramuscular (IM) routes and it is unclear which is more effective., Aim: To compare the effectiveness of IV vs. IM redback spider antivenom., Design: Randomized controlled trial., Methods: Patients with latroductism were given either IV or IM antivenom according to a randomized double-dummy, double-blind protocol. The first antivenom treatment was followed by another identical treatment after two hours if required. The primary outcome was followed by another identical treatment after two hours if required. The primary outcome was a clinically significant reduction in pain two hours after the last treatment. A fully Bayesian analysis was used to estimate the probability of the desired treatment effect, predetermined as an absolute difference of 20%. Results: We randomly allocated 126 patients to receive antivenom IV (64) and IM (62). After antivenom treatment pain improved in 40/64(62%) in the IV group vs. 33/62(53%) in the IM group (+9%; 95% Credible Interval [CrI]: -8% to +26%). The probability of a difference greater than zero (IV superior) was 85% but the probability of a difference >20% was only 10%. In 55 patients with systemic effects, these improved in 58% after IV antivenom vs. 65% after IM antivenom (-8%; 95% CrI: -32% to +17%). Twenty-four hours after antivenom pain had improved in 84% in the IV group vs. 71% in the IM group (+13%; 95% CrI: -2% to +27%). A meta-analysis including data from a previous trial found no difference in the primary outcome between IV and IM administration., Discussion: The difference between IV and IM routes of administration of widow spider antivenom is, at best, small and does not justify routinely choosing one route over the other. Furthermore, antivenom may provide no benefit over placebo., (C) Association of Physicians 2008. Published by Oxford University Press. All rights reserved.
**Limited role for outpatient parenteral antibiotic therapy for community-acquired pneumonia.**

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**Background and objective:** This study examined the potential utility of outpatient parenteral antibiotic therapy (OPAT) as a means of reducing the excessive number of patients hospitalized with low-risk community-acquired pneumonia (CAP).  

**Methods:** A prospective feasibility study was conducted, in which a selection algorithm was applied to a cohort of patients admitted with suspected CAP, to identify a group in whom admission may have been prevented by the use of OPAT. Numbers of potentially suitable patients, inpatient bed days saved and frequency of adverse events that may have led to readmission were measured.  

**Results:** There were 118 inpatients treated with confirmed CAP during the study period, of whom 27 had low-risk disease (Pneumonia Severity Index grades I-III). Application of the selection algorithm identified eight (30% of those with low-risk disease) patients who were potentially suitable for OPAT, and this group commonly experienced adverse events during follow up which may have resulted in readmission to hospital.  

**Conclusions:** In many hospitalized patients with CAP, outpatient therapy is precluded by either disease severity or active medical and psychosocial factors. This limits the role of OPAT as a tool for reducing the inpatient burden of CAP.  

PMID:2008426707

**The Western Australian experience of donation after cardiac death (DCD).**

Norman D, Byrne P.  
Since the introduction of the brain death criteria in the Human Tissue and Transplant Act 1982, Western Australia (WA) has only had one experience of donation after cardiac death (DCD). With the perceived potential pool of donors from brain death criteria in decline, the introduction of DCD in WA is seen as maximising the opportunity for donation. This case study will describe WA's first encounter with DCD in 2004 and the lessons learned from the experience.  

The DCD debate re-emerged with the establishment of the National Organ Donation Collaborative (NODC) in 2006, of which the three tertiary hospitals--Royal Perth, Fremantle and Sir Charles Gairdner--are participants. WA could potentially have a minimum of three to four DCD donors per year and the WA Department of Health is eager to support and encourage the implementation of DCD protocols across the State.

**Decline in native kidney function in liver transplant recipients is not associated with BKV virus infection: 1345.**  
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**Transient diabetes mellitus due to tacrolimus toxicity in a simultaneous pancreas-kidney transplant recipient: 1018.**  
Wright S, Jamboti J, et al.  
Fremantle Hospital
Use of infliximab in the prevention and delay of colectomy in severe steroid dependant and refractory ulcerative colitis.

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AIM: To determine if infliximab can prevent or delay surgery in refractory ulcerative colitis (UC).

METHODS: UC patients who failed to have their disease controlled with conventional therapies and were to undergo colectomy if infliximab failed to induce a clinical improvement were reviewed. Patients were primarily treated with a single 5 mg/kg infliximab dose. The Colitis Activity Index (CAI) was used to determine response and remission. Data of 8 wk response and colectomy rates at 6 mo and 12 mo were collected. RESULTS: Fifteen patients were included, 7 with UC unresponsive or intolerant to i.v. hydrocortisone, and 8 with active disease despite oral steroids (all but one with therapeutic dosage and duration of immunomodulation). All the i.v. hydrocortisone-resistant/intolerant patients had been on azathioprine/6-MP < 8 wk. At 8 wk, infliximab induced a response in 86.7% (13/15) with 40% in remission (6/15). Within 6 mo of treatment 26.7% (4/15) had undergone colectomy and surgery was avoided in 46.6% (7/15) at 12 mo. The colectomy rate at 12 mo in those on immunomodulatory therapy < 8 wk at time of infliximab was 12.5% (1/8) compared with 100% (7/7) in patients who were on long-term maintenance immunomodulators (P < 0.02). CONCLUSION: Infliximab prevented colectomy due to active disease in immunomodulatory-naive, refractory UC patients comparable to the use of Cyclosporine. In patients, however, on effective dosage and duration of immunomodulation at time of infliximab therapy colectomy was not avoided.

PMID:18442203

Chronic wound research: an integrated approach.

Wallace HJ, Stacey MC.

Publication Types: Journal Article, Pictorial, Tables/Charts

**Genes and venous leg ulcers - Homing in on Chromosome 6.**


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