CONCLUSIONS: The results of this study have demonstrated for the first time that tympanic membrane (TM) structure is preserved following removal of fresh, normal tissue from patients undergoing surgery. Greater clarity has been demonstrated using resin sections than in previous studies on paraffin sections. Of particular note, cytokeratin (CK) immunocytochemistry was successfully performed on resin sections, which has not been previously reported. This may have potential applications for future work involving tissues that express CKs.

OBJECTIVES: To analyse the structure of normal, fresh human TM specimens after surgical removal and to evaluate their CK immunocytochemistry using resin techniques, neither of which have been demonstrated previously.

MATERIAL AND METHODS: Seven TM specimens were removed during surgery and then preserved in a modified Karnovsky’s fixative. Semi-thin and thin sections were examined by means of light and electron microscopy, respectively. For comparison purposes, paraffin block-embedded specimens were also sectioned. CK immunocytochemistry was performed on semi-thin sections using standard immunoperoxidase techniques, with expression being demonstrated using light microscopy.

RESULTS: The three-layer architecture of the TM was preserved. The morphology of the TM was vastly superior in the semi-thin resin sections than in the thicker paraffin sections. The outer, middle and inner layers were clearly demonstrated. The integrity of the outer epithelial layer was maintained, with an outer keratinizing stratum corneum and underlying stratum granulosum, stratum spinosum and stratum basale layers resting on the basal lamina. The thin inner mucosal layer was also viable, consisting of simple squamous or cuboidal cells. Preservation of the middle lamina propria was achieved, with demonstration of the outer radial and inner circular fibres. CK immunocytochemistry utilizing resin techniques provided excellent staining of CK 7 and 8 in the inner layer, with positive staining of CK 5 and 10 in the outer layer.

Evidence for undetected malaria infection in non-immune Australian travellers not taking chemoprophylaxis.
Australian Red Cross Blood Service, 97 Great Eastern Highway Rivervale, Western Australia 6103, Australia. cseed@arcs.redcross.org.au
To determine whether travellers from malaria-free countries can develop unrecognised or asymptomatic malaria after visiting endemic areas, we analysed data from 751 prospective blood donors who had visited or resided in malaria-risk areas in the previous 3 years. Malarial antibodies were measured using an established commercial enzyme-linked immunoassay incorporating four recombinant blood-stage plasmodial antigens and with published sensitivity >
or =83% and specificity 100%. Details of countries visited and antimalarial chemoprophylaxis used were obtained by questionnaire. Among the 606 subjects resident in malaria-free countries and with no past history of malaria, 176 had visited high-risk countries as categorised by the World Health Organisation (WHO). Of these, 89 took no chemoprophylaxis including 6 (6.7%) who were antibody-positive; there were no antibody-positive subjects in the 87 who took chemoprophylaxis (P=0.029), which was that recommended by WHO in 84% of cases. These data underscore the value of effective antimalarial prophylaxis in non-immune travellers visiting high malaria-risk areas but also suggest that unrecognised infections can occur in those unprotected by chemoprophylaxis.

PMID:16916494

**The management of acute endocarditis.**
Wells TA.
T.A. Wells, Fremantle Cardiac Unit, Fremantle Hospital, Perth, WA 6160; Australia. E-Mail: timwells@doctors.org.uk.
Infective endocarditis (IE) is an infection, usually of bacterial aetiology, which can affect any part of the endovascular surface of the heart or large intrathoracic vessels but most commonly affects cardiac valves. Without treatment this condition is invariably fatal and even with treatment is associated with a high incidence of morbidity and mortality. This article looks at the difficulties in diagnosing IE and the investigations used to confirm the diagnosis. It also lists the major causes of IE and its management.
Publication Types: Review
PMID:2006518337

**Quantitative MR imaging R2 relaxometry in elderly participants reporting memory loss.**
House MJ, St Pierre TG, et al.
School of Physics, University of Western Australia
BACKGROUND AND PURPOSE: In Alzheimer disease (AD), elevated brain iron concentrations in gray matter suggest a disruption in iron homeostasis, while demyelination processes in white matter increase the water content. Our aim was to assess whether the transverse proton relaxation rate, or R2, an MR imaging parameter affected by changes in brain iron concentration and water content, was different in elderly participants with mild to severe levels of cognitive impairment compared with healthy controls. METHODS: Twelve elderly participants reporting memory problems and 11 healthy volunteers underwent single-spin-echo MR imaging in a 1.5T scanner, with subsequent neuropsychological testing. R2 data were collected from 14 brain regions in cortical and subcortical gray and white matter. Those with memory complaints were separated into 2 further subgroups: MC1 (no objective cognitive impairment) and MC2 (mild to severe objective cognitive impairment). RESULTS: Mean brain R2 values from the 11 controls correlated strongly (r = 0.94, P < .0001) with reference brain iron concentrations for healthy adults. R2 values in the MC1 and MC2 subgroups were significantly higher in the right temporal cortex and significantly lower in the left internal capsule, compared with healthy controls. R2 values in the MC2 subgroup were significantly lower in the left temporal and frontal white matter, compared with healthy controls. CONCLUSIONS: R2 differences between both subgroups and the healthy controls suggest iron has increased in the temporal cortex, and myelin has been lost from several white matter regions in those with memory complaints, consistent with incipient AD pathogenesis and biochemical data.
Venom immunotherapy: an Australian perspective.

Brown SGA.

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Background: Australia has a diversity of stinging insects that presents unique clinical problems. Many species are found nowhere else in the world and management is problematic due to limited availability of venom extracts and potential for crossreactivity between venoms.

Methods/Data base: This article reviews published Australian research on this topic and discusses current research and development priorities. Results: Stinging insect species responsible for causing anaphylaxis in Australia include the honeybee, yellow jacket, native and introduced paper wasps (genera Polistes and Ropalidia), solitary wasps and native bees, and a variety of ants including the red imported fire ant Solenopsis invicta, the greenhead ant Rhytidoponera metallica, and jumper ants and bull dog ants of the genus Myrmecia. Little is known about the patterns of crossreactivity between the venoms of these many species. Biting insects also cause anaphylaxis, including the paralysis ticks (Ixodes spp.) and march flies (family Tabanidae). The most important species appear to be the honeybee and the jack jumper ant (JJA, Myrmecia pilosula). JJA allergy is remarkable for its severity, high re-sting reaction rates, and the high efficacy of venom immunotherapy proven by the only double-blind, randomized, placebo-controlled trial of venom immunotherapy published to date. Conclusion: Further work is required to improve our understanding of venomous and biting insect allergy in Australia. Of the many insects causing anaphylaxis in Australia, the JJA has thus far provided a unique model that, clearly demonstrates the impressive benefit of immunotherapy for insect venom allergy, and may be used to test novel approaches to treatment in the future. copyright 2006 Hogrefe & Huber Publishers.

Alzheimer's Care Quarterly. 2006; 7(2): 115-121.

Evaluation of a carer training project for the management of behavioral and psychological symptoms of dementia by home-based carers.

Dicker BS, Chawla S, et al.

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Sudarshan Chawla, MBBS, MRS, Psych MD, is consultant, Old Age Psychiatry, Fremantle Seniors Mental Health Service, Fremantle Hospital & Health Service, Fremantle, Western Australia, Australia.

Neil Preston, PhD, is senior research psychologist at the Fremantle Seniors Mental Health Service, Fremantle Hospital & Health Service, Fremantle, Western Australia, Australia.

Behavioral and psychological symptoms of dementia (BPSD) have been identified in several studies as the single largest contributor to caregiver stress. A training package that focuses specifically on the management of BPSD was developed and trialed with 50 home-based carers. The package uses a one-to-one, customized (modular) approach and can be delivered in the carer's home. Carers made statistically significant gains in knowledge of dementia and BPSD, management of BPSD, caregiving ability, and stress reduction. With the exception of stress reduction, these gains were maintained 6 and 12 months posttraining. (C)2006 Lippincott Williams & Wilkins, Inc.
Asymptomatic long-term survivors of coronary artery bypass surgery enjoy a quality of life equal to the general population.

Bradshaw PJ, Jamrozik KD, et al. 

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Department of Cardiothoracic Surgery, Fremantle Hospital, Fremantle, Western Australia, Australia (Gilfillan) 

Medicine and Population Health, University of Western Australia and Cardiologist, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia 

BACKGROUND: Health-related quality of life (HRQOL) among long-term survivors of coronary artery bypass surgery is an important outcome that has been little studied at the population level. 

METHODS: A postal survey was conducted in 1999 to 2000 in patients 6 to 20 years after coronary artery bypass graft (CABG) surgery in Western Australia. A random stratified sample of 2500 was drawn from 8910 patients who had their first CABG surgery in 1980 to 1993. Health-related quality of life was measured with Short Form 36 and EuroQol visual analogue scale. 

RESULTS: Response was 82% (n = 2061). Health-related quality of life declined with age and was similar for men and women, although scores for women were worse for physical functioning. Compared with Australian population norms, the age- and sex-standardized scores of survivors of CABG were generally worse, mainly in the physical domain. Reported angina at the time of follow-up (33%), symptoms of heart failure equivalent to New York Heart Association (NYHA) classes II to IV (34%), and comorbidities such as diabetes and hypertension were associated with poorer HRQOL. For both men and women without angina or heart failure at follow-up, HRQOL was no different from that of the general population. 

CONCLUSION: Overall, the quality of life among long-term survivors of CABG is worse than that of the general population, the difference being mainly attributable to recurrent symptoms and comorbidities. Quality of life for those without angina or heart failure at follow-up was equivalent to the population norms, providing an incentive to maximize efforts to abolish angina and ameliorate heart failure symptoms.
depression, global cognitive deficits, and elevated mood are the main psychiatric correlates of paranoid misidentification and expansive delusions in AD, whereas overt aggression and agitation are the most frequent behavioral concomitants of psychosis in AD.

Successful resuscitation of an ASA 3 patient following ropivacaine-induced cardiac arrest.
Khoo LP, Corbett AR.
Department of Anaesthesia, Fremantle Hospital, Fremantle, Western Australia, Australia.
A patient with severe myocardial disease and acute-on-chronic renal failure was undergoing a brachial plexus block for formation of an arteriovenous fistula when accidental intravascular injection of ropivacaine resulted in ventricular fibrillation. Cardiopulmonary resuscitation was instituted immediately and the advanced life support algorithm was followed until the return of sinus rhythm. Although, in comparison with bupivacaine, ropivacaine appears to be a safer local anaesthetic agent in the setting of intravenous injection, the emphasis on safety should remain a priority. Awareness of the risk of central nervous system and cardiovascular toxicity and preparation for immediate commencement of resuscitation in the event of toxicity remain of paramount importance.

Second symposium on the definition and management of anaphylaxis: summary report--second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium.
Fremantle Hospital, Fremantle, WA, Australia (SG Brown)
There is no universal agreement on the definition of anaphylaxis or the criteria for diagnosis. In July 2005, the National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network convened a second meeting on anaphylaxis, which included representatives from 16 different organizations or government bodies, including representatives from North America, Europe, and Australia, to continue working toward a universally accepted definition of anaphylaxis, establish clinical criteria that would accurately identify cases of anaphylaxis with high precision, further review the evidence on the most appropriate management of anaphylaxis, and outline the research needs in this area.

Role of P glycoprotein in absorption of novel antimalarial drugs.
Crowe A, Ilett KF, et al.
Curtin University of Technology, School of Pharmacy, Perth, Western Australia, Australia.
A.P.Crowe@curtin.edu.au
Bidirectional transport of four novel antimalarial compounds was determined using Caco-2 cell monolayers. P glycoprotein-mediated efflux was greatest for pyronaridine (5 to 20 microM) and low for naphthoquine (5 microM). With 20 microM naphthoquine, net efflux was blocked, suggesting saturation of the transporter. Piperaquine and dihydroartemisinin were not transported by the system.

In vitro interactions between piperaquine, dihydroartemisinin, and other conventional and novel antimalarial drugs.

Davis TME, Hamzah J, et al.
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In an in vitro assessment of antimalarial combinations, dihydroartemisinin (DHA) showed no interaction or was mildly antagonistic when combined with piperaquine, pyronaridine, or naphthoquine. Interactions between 4-aminoquinolines and related drugs were also indifferent/antagonistic. The clinical significance of mildly antagonistic DHA combinations is uncertain but may become important if parasite drug sensitivity declines. Copyright copyright 2006, American Society for Microbiology. All Rights Reserved.
PMID:2006382176


Karunajeewa HA, Reeder J, et al.
Medicine Unit Fremantle, School of Medicine and Pharmacology, University of Western Australia, Crawley
Drug treatment of severe malaria must be rapidly effective. Suppositories may be valuable for childhood malaria when circumstances prevent oral or parenteral therapy. We compared artesunate suppositories (n = 41; 8 to 16 mg/kg of body weight at 0 and 12 h and then daily) with intramuscular (i.m.) artemether (n = 38; 3.2 mg/kg at 0 h and then 1.6 mg/kg daily) in an open-label, randomized trial with children with severe Plasmodium falciparum malaria in Papua New Guinea (PNG). Parasite density and temperature were measured every 6 h for >/=72 h. Primary endpoints included times to 50% and 90% parasite clearance (PCT(50) and PCT(90)) and the time to per os status. In a subset of 29 patients, plasma levels of artemether, artesunate, and their common active metabolite dihydroartemisinin were measured during the first 12 h. One suppository-treated patient with multiple complications died within 2 h of admission, but the remaining 78 recovered uneventfully. Compared to the artemether-treated children, those receiving artesunate suppositories had a significantly earlier mean PCT(50) (9.1 versus 13.8 h; P = 0.008) and PCT(90) (15.6 versus 20.4 h; P = 0.011). Mean time to per os status was similar for each group. Plasma concentrations of primary drug plus active metabolite were significantly higher in the artesunate suppository group at 2 h postdose. The earlier initial fall in parasitemia with artesunate is clinically advantageous and mirrors higher initial plasma concentrations of active drug/metabolite. In severely ill children with malaria in PNG, artesunate suppositories were at least as effective as i.m. artemether and may, therefore, be useful in settings where parenteral therapy cannot be given.
PMID:16495259


Clinical significance of marrow micrometastases on outcome in operable non-small-cell lung cancer [Letter].
Tacrolimus ointment does not affect the immediate response to vaccination, the
generation of immune memory, or humoral and cell-mediated immunity in children.
Hofman T, Cranswick N, et al. 
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Background: Concern exists that the prolonged application of immunomodulators to treat atopic dermatitis may cause systemic immunosuppression. Aims: In a 7-month, multicentre, randomised, controlled trial, we investigated the equivalence of response to vaccination against meningococcal serogroup C disease with a protein-conjugate vaccine in children (2-11 years) with moderate to severe atopic dermatitis, by applying either 0.03% tacrolimus ointment (TAC-O; n = 21) or a hydrocortisone ointment regimen (HC-O; n = 111). Methods: TAC-O was applied twice daily (bid) for 3 weeks, and thereafter daily until clearance. 1% hydrocortisone acetate (HA) for head/neck and 0.1% hydrocortisone butyrate ointment for trunk/limbs was applied bid for 2 weeks; thereafter HA was applied bid to all affected areas. At week 1, patients were vaccinated with protein-conjugate vaccine against meningococcal serogroup C, and challenged at month 6 with low dose meningococcal polysaccharide vaccine. The control group (44 non-atopic dermatitis children) received the primary vaccination and challenge dose. Assessments were made at baseline, weeks 1 and 5, and months 6 and 7. The primary end point was the percentage of patients with a serum bactericidal antibody (SBA) titre >=8 at the week 5 visit. Results: The response rate (patients with SBA titre >=8) was 97.5% (95% CI approximately 97.3 to 100), 99.1% (94.8 to 100) and 97.7% (93.3 to 100) in the TAC-O, HC-O and control groups, respectively. Conclusions: The immune response to vaccination against meningococcal serogroup C in children with atopic dermatitis applying either 0.03% TAC-O or HC is equivalent. Ointment application does not affect the immediate response to vaccination, generation of immune memory or humoral and cell-mediated immunity. 

Abdominal aortic aneurysm: pathogenesis and implications for management. 
Golledge J, Muller J, et al. 
From the Vascular Biology Unit (J.G., J.M.), School of Medicine, James Cook University, Townsville, Australia; Cardiovascular Research Center (A.D.), Gill Heart Institute, University of Kentucky, Lexington; and the School of Surgery and Pathology (P.N.), University of Western Australia, Fremantle Hospital, Fremantle, Western Australia. 

Abdominal aortic aneurysm (AAA) affects approximately 5% of elderly men and is
responsible for a significant number of deaths in Western Countries. At present surgery by open or endovascular means is the only widely used therapy for this condition. In this review we examine the risk factors, serum, and genetic associations of AAA. Epidemiology studies suggest that smoking cessation and control of cholesterol and blood pressure should reduce the number of patients developing AAA. Natural history studies suggest that smoking cessation should reduce the rate of progression of AAA. Clear level 1 evidence for drug treatments of AAA are presently lacking; however, animal and human in vitro studies suggest that medication targeted at reducing inflammation and proteolysis are most likely to be beneficial, with limited data to support the use of statins, Angiotensin II inhibitors, and macrolides. Work has commenced in understanding which patients, identified by clinical, serum, and genotype, are more at risk of AAA progression and thus should be selected out for aggressive treatment. Well designed large multicenter randomized controlled trials are required to examine the medical treatment of AAA. (C) 2006 American Heart Association, Inc.


Restrictive physiology in tetralogy of fallot: exercise and arrhythmogenesis.
Rathore KS, Agrawal SK, et al.
Suite 15, Level 4, St. George Hospital, Sydney, NSW 2217, Australia.
kaushalendra_rathore@hotmail.com.
The effect of right ventricular restrictive physiology on exercise capacity and arrhythmogenesis after correction of tetralogy of Fallot was assessed in 80 patients aged 7.9 +/- 3.6 years. Right ventricular restrictive physiology was defined as the presence of an A wave across the pulmonary artery on 2-dimensional echocardiography. At the 6 month follow-up, 52 patients had restrictive physiology (group 1). A transannular patch was used in 36 patients in group 1 (62%) and in 19 (86%) of the 28 patients without restrictive physiology (group 2). Maximum heart rate attained (69% vs. 77%), maximum predicted heart rate (211 +/- 12.6 vs. 226 +/- 24.2 beats.min(-1)), and metabolic equivalents (7.6 +/- 3.2 vs. 8.1 +/- 2.6) were higher in group 2, but not significantly. The chronotropic index was similar in both groups. In group 1, 14% of patients presented with ventricular premature complexes at 6 months. No effect on exercise capacity and arrhythmogenesis could be attributed to restrictive physiology, but both groups had chronotropic incompetence compared to normal children.
PMID:16868099


Mechanisms underlying inhibition of androgen-insensitive prostate cancer cell proliferation by peroxisome proliferator-activated receptor gamma: 1816.
Chew A, Trinder D, et al.
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Two-year interim results from a 5-year study evaluating clinical recurrence of superficial basal cell carcinoma after treatment with imiquimod 5% cream daily for 6 weeks.
Quirk C, Gebauer K, et al.
Fremantle, Western Australia, Australia. chrisquirk@iinet.net.au
Imiquimod 5% cream is approved in the USA, Europe and Australia to treat superficial basal cell
carcinoma, using a regimen of once daily, 5 times per week for 6 weeks. Vehicle-controlled, phase III clinical trials show that imiquimod is safe and effective for treating superficial basal cell carcinoma with dosing 5 or 7 times per week for 6 weeks. This phase III, open-label study evaluates the long-term (5 years) clinical efficacy and safety of dosing once daily, for which this manuscript reports the 2-year time point in the follow-up period. For the 169 enrolled subjects, the tumour selected for treatment was assessed clinically to determine initial clearance at the 12-week post-treatment visit. If clinically clear of superficial basal cell carcinoma, subjects entered a 5-year, long-term follow-up period. Subjects were evaluated for recurrence at the 3-, 6-, 12- and 24-month follow-up visits. The initial clearance rate at 12 weeks post treatment was 94.1%. The proportion of subjects who were clinically clear at the 2-year follow-up visit was estimated to be 82.0%. Imiquimod was tolerated when applied daily, with erythema reported for all subjects participating in the study. The recurrence rate observed suggests that once daily dosing and 5x/week dosing yield similar clearance rates, but daily dosing increases local skin reactions.

PMID:17034468

64 slice multidetector CT (MDCT) of massive lower gastrointestinal haemorrhage: P20 - Educational Exhibit.
Fremantle Hospital, Wembley, Australia

ECHO: The Western Australia emergency care hospitalisation and outcome linked data project.
Sprivulis P, Da Silva JA, et al.
Department of Emergency Medicine, Fremantle Hospital, Western Australia.
Prof. I. Jacobs, School of Primary, Aboriginal and Rural Health Care, Faculty of Medicine and Dentistry, University of Western Australia (M516), 35 Stirling Highway, Crawley, WA 6009; Australia. E-Mail: ian.jacobs@uwa.edu.au.
Objective: To describe and assess the quality of the data resources linked for the Western Australian Emergency Care Hospitalisation and Outcome (ECHO) project. Methods: The ECHO project links electronic records from the WA Emergency Department Information System to the St John Ambulance Service Pre-Hospital Care Database, the WA Hospital Morbidity Data System and the WA Mortality Database. Linkages are created using standard probabilistic matching techniques with extensive clerical review. Commencing with all metropolitan Perth public emergency departments from July 2000, these linkages will be updated annually for at least five successive years. The proportion of actual linkages between emergency department records and ambulance, admission and death records was assessed in comparison to expected linkage rates. Results: Of 578,200 total emergency department records, there were 144,897 emergency presentations recorded as arriving by ambulance, of which 135,332 (93.4%) were linked to an ambulance record pertaining to the same episode. Of the 165,650 presentations recorded as admitted, 162,216 (97.9%) were linked to a hospital morbidity record relating to the same episode. Furthermore, 96.2% of the 2,084 cases recorded as 'dead on arrival' and 98.9% of the 624 cases recorded as 'died in emergency' were linked to a corresponding death record. Conclusions: Linkage quality consistent with international standards has been achieved, resulting in an information infrastructure capable of supporting an extensive research agenda focusing on the interaction and outcomes of both pre-hospital and within-hospital emergency medical care services.

Grey nomads--health and health preparation of older travellers in remote Australia.
Tate J, Mein J, et al.

BACKGROUND: Many older Australians now tour remote Australia (so called 'grey nomads'). Anecdote suggests they place a burden on limited remote health services, however, this burden is poorly documented. METHODS: Two groups were approached to participate in the survey: travellers aged 50 years or over and staying in caravans, motor homes or tents at Fitzroy Crossing, Western Australia; and local primary health care providers. RESULTS: All 260 travellers approached responded. The prevalence of chronic diseases in those aged 65 years or over was 68%; 57% had sufficient chronic medications for the entire trip; 19% had a list of long term medications; and 9% of those with chronic diseases had a health summary from their usual general practitioner. Sixty-four local health providers responded: 95% rated health summaries highly (particularly if they included an active problem list, past history, current medications, and allergies). DISCUSSION: Older patients are poorly prepared for travel in remote Australia. They have a chronic disease rate no less than the national prevalence and could represent a drain on local health resources. Solutions might include GP review before travel, bringing sufficient medication for the trip, review of vaccination requirements, and a health summary.

Australian Prescriber. 2006; 29(6): 150.

Managing painful paediatric procedures.
Douglas R.

R. Douglas, Rockingham-Kwinana District Hospital, Fremantle Hospital, Perth.
Publication Types: Letter
PMID:2007005144


Management of asymptomatic hypoglycaemia in healthy term neonates for nurses and midwives.
Hewitt V, Watts R.
Curtin University of Technology and The Western Australian Centre for Evidence-based Nursing and Midwifery (a collaborating centre of the Joanna Briggs Institute), Perth, Western Australia, Australia
Publication Types: Clinical Guideline

British Journal of Cancer. 2006; 94(8): 1116-21.

General practice vs surgical-based follow-up for patients with colon cancer: randomised controlled trial.
Department of Surgery, Fremantle Hospital, Fremantle, 6160 Western Australia (Platell)
This trial examined the optimal setting for follow-up of patients after treatment for colon cancer by either general practitioners or surgeons. In all, 203 consenting patients who had undergone potentially curative treatment for colon cancer were randomised to follow-up by general practitioners or surgeons. Follow-up guidance recommended three monthly clinical review and annual faecal occult blood tests (FOBT) and were identical in both study arms. Primary outcome
measures (measured at baseline, 12 and 24 months were (1) quality of life, SF-12; physical and mental component scores, (2) anxiety and depression: Hospital Anxiety and Depression Scale and (3) patient satisfaction: Patient Visit-Specific Questionnaire. Secondary outcomes (at 24 months) were: investigations, number and timing of recurrences and deaths. In all, 170 patients were available for follow-up at 12 months and 157 at 24 months. At 12 and 24 months there were no differences in scores for quality of life (physical component score, P=0.88 at 12 months; P=0.28 at 24 months: mental component score, P=0.51, P=0.47; adjusted), anxiety (P=0.72; P=0.11) depression (P=0.28; P=0.80) or patient satisfaction (P=0.06, 24 months). General practitioners ordered more FOBTs than surgeons (rate ratio 2.4, 95% CI 1.4-4.4), whereas more colonoscopies (rate ratio 0.7, 95% CI 0.5-1.0), and ultrasounds (rate ratio 0.5, 95% CI 0.3-1.0) were undertaken in the surgeon-led group. Results suggest similar recurrence, time to detection and death rates in each group. Colon cancer patients with follow-up led by surgeons or general practitioners experience similar outcomes, although patterns of investigation vary.

PMID:16622437


Surgeon experience and trends in intraoperative complications in laparoscopic cholecystectomy.
Hobbs MS, Mai Q, et al.
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Background: Intraoperative complications, particularly bile duct injuries (BDIs), have increased since the introduction of laparoscopic cholecystectomy (LC). This excess risk is expected to decline as surgeon experience in laparoscopic surgery increases., Methods: This was a population-based study of trends in intraoperative injuries in 33 309 cholecystectomies carried out in Western Australia between 1988 and 1998, based on hospital discharge abstracts. Endpoints were identified from diagnostic and procedure codes in index or postoperative readmissions, or a register of endoscopic retrograde cholangiopancreatography procedures, and validated using hospital records. Multivariate analysis was used to estimate the risk of complications associated with potential risk factors., Results: Following the introduction of LC in 1991, the prevalence of all complications doubled by 1994 then stabilized, whereas that of BDI declined after 1994. The risk of complications increased with age, was higher in men, teaching and country hospitals, and was higher for LC and more complicated operations. It was lower when intraoperative cholangiography was performed and with increasing surgeon experience. Approximately 20 per cent of all complications and 30 per cent of BDIs were attributable to surgeons who had performed 200 or fewer cholecystectomies in the previous 5 years., Conclusion: The risk of intraoperative complications declined with increasing surgical experience and use of intraoperative cholangiography., (C) 2006 John Wiley & Sons, Inc.


Authors' reply: Randomized clinical trial of bowel preparation with a single phosphate enema or polyethylene glycol before elective colorectal surgery (Br J Surg 2006; 93: 427-433).
Platell C, Barwood N, et al.
Prof. C. Platell, University Department of Surgery, Fremantle Hospital, PO Box 480, Fremantle, WA 6160; Australia. E-Mail: cplatell@cyllene.uwa.edu.au
PMID:16915585
Population-based study of prognostic factors in stage II colonic cancer.
School of Surgery and Pathology, University of Western Australia, Nedlands, Australia

BACKGROUND: Adjuvant chemotherapy in stage II colorectal cancer may be considered for patients whose tumours have poor prognostic features. The aim of this study was to evaluate the prognostic significance of commonly reported clinical and pathological features of stage II colonic cancer. METHODS: A population-based observational study of all patients with stage II colonic cancer diagnosed in the state of Western Australia from 1993 to 2003 was performed. A total of 1306 patients treated by surgery alone were identified, with a median follow-up of 59 (range 0-145) months. RESULTS: Multivariable analysis revealed that the only independent prognostic factors for disease-specific survival were stage T4 (hazard ratio (HR) 1.75 (95 per cent confidence interval (c.i.) 1.32 to 2.32); P < 0.001) and vascular invasion (HR 1.63 (95 per cent c.i. 1.15 to 2.30); P < 0.001). In younger patients (aged 75 years or less), who are more likely to be considered for chemotherapy, these two features showed independent prognostic significance but with higher HR values (1.96 for stage T4 and 2.73 for vascular invasion). Stage T4 and/or the presence of vascular invasion identified a 'poor' prognostic group, comprising 26.6 per cent of younger patients and with a 5-year survival rate of 71.2 per cent. The remaining 'good' prognostic group had a survival rate of 84.3 per cent at 5 years' follow-up.
CONCLUSION: This study highlights the importance of accurate pathological assessment of tumour stage and vascular invasion for the prognostic stratification of patients with stage II colonic cancer. The results provide clarification of guidelines for the management of stage II disease in relation to recommendations for chemotherapy. Copyright (c) 2006 British Journal of Surgery Society Ltd. Published by John Wiley & Sons, Ltd.

Randomized clinical trial of bowel preparation with a single phosphate enema or polyethylene glycol before elective colorectal surgery. [Miscellaneous Article].
Platell C, Barwood N, et al.
(1)Colorectal Surgical Unit, Fremantle Hospital, Fremantle, Western Australia, Australia
(2)Department of Surgery, University of Western Australia, Perth, Western Australia, Australia

Background: A recent meta-analysis has questioned the value of bowel preparation in patients undergoing colorectal resection. The aim of this clinical trial was to evaluate whether a single phosphate enema was as effective as oral polyethylene glycol (PEG) solution in preventing anastomotic leakage.

Methods: Patients were randomized to receive either a single phosphate enema or 3 litres of oral PEG solution before surgery. Patients were followed for a minimum of 6 weeks to detect anastomotic leakage.

Results: There were 147 patients in each group and the groups were evenly matched for putative risk factors at baseline. Patients in the enema group had more anastomotic leaks requiring reoperation than those in the PEG group (4[middle dot]1 versus 0 per cent, P = 0[middle dot]013; relative risk 2[middle dot]04 (95 per cent confidence interval (c.i.) 1[middle dot]82 to 2[middle dot]30)). The mortality rate was higher in the PEG group (2[middle dot]7 versus 0[middle dot]7 per cent, P = 0[middle dot]176; odds ratio 1[middle dot]01 (95 per cent c.i. 0[middle dot]45 to 36[middle dot]98)).

Conclusion: Bowel preparation with a phosphate enema was associated with an increased risk of anastomotic leakage requiring reoperation compared with oral PEG. These results do not support the routine use of a phosphate enema in patients undergoing elective colorectal surgery. Copyright (C) 2006 British Journal of Surgery Society Ltd. Published by John Wiley & Sons, Ltd., (C) 2006 John Wiley & Sons, Inc.
Hepatic oval cell response to the choline-deficient, ethionine supplemented model of murine liver injury is attenuated by the administration of a cyclo-oxygenase 2 inhibitor.

Davies RA, Knight B, et al.

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Oval cell proliferation precedes neoplasia in many rodent models of hepatocellular carcinoma and prevention of this proliferative response can reduce the risk of subsequent carcinoma. This study aimed to determine whether a selective cyclo-oxygenase-2 (COX-2) inhibitor, SC-236, affects (i) the oval cell response to liver injury in a mouse model of hepatocarcinogenesis and (ii) an oval cell line. Four-week-old mice were fed either normal chow or a choline deficient, ethionine supplemented (CDE) diet in the presence or absence of SC-236. Liver histology and oval cell numbers were determined after 2, 4, 12 and 52 weeks of treatment. Oval cells were scored using morphological criteria and positive immuno-staining for the M2-isozyme of pyruvate kinase (M2PK) or A6. An immortalized oval cell line (PIL-2) was used to study the in vitro effects of SC-236 on oval cell proliferation, apoptosis and Akt phosphorylation. The percentage of M2PK-positive oval cells and COX-2-positive cells was reduced by 80% and 45%, respectively, in CDE-fed mice receiving SC-236 compared with CDE-fed animals not receiving SC-236. Some M2PK-positive oval cells were also COX-2 positive. The percentage of A6-positive cells was not affected by SC-236 administration to CDE-fed mice. Administration of SC-236 increased apoptosis as evidenced by a 73% increase in the number of TUNEL-positive cells at 2 weeks in CDE-fed mice. Primary oval cells and PIL-2 cells expressed COX-2. In vitro treatment of PIL-2 cells with SC-236 resulted in a dose-dependent preferential death of A6-negative cells. Administration of 25 and 50 [μMJ] Prostaglandin E2 partially attenuated SC-236 induced cell death by 25%. In vitro oval cell death was associated with apoptosis and a 70% reduction in Akt phosphorylation. These results suggest that the SC-236 induced reduction of M2PK-positive oval cell numbers may be due to COX-2 dependent inhibition of Akt phosphorylation and induction of apoptosis.
percentage of M2PK-positive oval cells and COX-2 positive cells was reduced by 80% and 45%, respectively, in CDE-fed mice receiving SC-236 compared with CDE-fed animals not receiving SC-236. Some M2PK positive oval cells were also COX-2 positive. The percentage of A6-positive cells was not affected by SC-236 administration to CDE fed mice. Administration of SC-236 increased apoptosis as evidenced by a 73% increase in the number of TUNEL-positive cells at 2 weeks in CDE fed mice. Primary oval cells and PIL-2 cells expressed COX-2. In vitro treatment of PIL-2 cells with SC-236 resulted in a dose-dependent preferential death of A6-negative cells. Administration of 25 and 50 microM Prostaglandin E2 partially attenuated SC-236 induced cell death by 25%. In vitro oval cell death was associated with apoptosis and a 70% reduction in Akt phosphorylation. These results suggest that the SC-236 induced reduction of M2PK-positive oval cell numbers may be due to COX-2 dependant inhibition of Akt phosphorylation and induction of apoptosis.

Clinical Endocrinology. 2006; 64(4): 476-7. Subclinical hypothyroidism and mortality in women with type 2 diabetes. Chubb SA, Davis WA, et al. *Department of Biochemistry, PathWest Laboratory Medicine WA (Chubb) and †University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, Australia (WA Davis & TME Davis)

Clinical Otolaryngology. 2006; 31(4): 273-279. Patient's quality of life and hearing outcomes after stapes surgery. Subramaniam K, Eikelboom RH, et al. (*)School of Surgery and Pathology, The University of Western Australia, (+)Lions Ear and Hearing Institute Sir Charles Gairdner Hospital, Nedlands Australia, (++)Otolaryngology Department, Sir Charles Gairdner Hospital, Nedlands Australia, ([S])Otolaryngology Department, Fremantle Hospital, Fremantle, WA, Australia

Objectives: To determine the quality of life (QOL) after stapes surgery and whether audiological parameters for hearing correlate with specific QOL factors., Design: A retrospective cross-sectional study., Setting: A tertiary referral centre., Participants: A series of 35 patients who underwent stapes surgery of which three were excluded because they were <18 years of age, chronically or mentally ill, or in a dependant relationship. Response rate was 93% (30/32). Nine were further excluded because they had revision or bilateral surgery, or missing data. Twenty-one patients were included in this study., Main outcome measures: The Glasgow Benefit Inventory (GBI) was used to evaluate general QOL and the Hearing Disability and Handicap Scale (HDHS) was used as a disease-specific measure. The Belfast Rule of Thumb and Glasgow Benefit Plot assessed hearing outcomes., Results: Operative success was 86% using the Belfast Rule of Thumb and 95% had closure of the air-bone gap to within 20 dB. 81.8% of patients reported a better overall QOL as surgery. Glasgow Benefit Inventory Social and GBI Physical scores correlated positively with the HDHS speech component (P < 0.05). The duration of hearing loss correlated inversely with the average HDHS score (P < 0.05),. Conclusion: The majority of patients report a better QOL as undergoing stapes surgery. Speech impacts on people's physical and social QOL of patients. Quality of life tools, in addition to objective audiologic measurements can provide clinicians with patients' subjective perspective that helps guide clinical decision-making and counselling., Copyright (C) 2006 Blackwell Publishing Ltd.
Clinical Rheumatology. 2006; Epub ahead of print.
**Cytomegalovirus infection of a cutaneous ulcer in a patient with ANCA-positive vasculitis.**
Department of Immunology, Level 4 B Block, Fremantle Hospital, Alma Street, Fremantle, WA, 6160, Australia, rich@perthnolans.com.
This case describes a patient in whom cytomegalovirus (CMV) infected a preexisting ulcer. The patient was immune-suppressed because of treatment for Wegener's granulomatosis. Specific antiviral therapy was delayed because of uncertainty as to the role of CMV, but the infection cleared and the ulcer improved promptly on institution of valganciclovir.

**Reflections on mental health nursing education.**
Wynaden D.
Research & Development Director and Senior Lecturer (Mental Health), School of Nursing and Midwifery, Curtin University of Technology and Research and Development Consultant, Directorate of Mental Health, Fremantle Hospital and Health Services, Perth WA, Australia
Publication Types: Editorial

Cornea. 2006; 25(9): 1100-1.
**Corneal graft rejection precipitated by uveitis secondary to alendronate sodium therapy.**
Richards JC, Wiffen SJ.
Department of Ophthalmology Fremantle Hospital, Fremantle, WA, Australia.
PURPOSE: To report a case of corneal graft rejection precipitated by severe uveitis secondary to alendronate therapy and to review the literature of relevance to this case. METHODS: A 77-year-old woman with a hypopyon and corneal graft rejection was studied for possible precipitants, including herpes viral and bacterial infection. Results were negative. She was treated unsuccessfully with systemic and topical steroids, systemic antivirals, and intraocular antibiotic therapy. RESULTS: Withdrawal of alendronate resulted in rapid resolution of intraocular inflammation and corneal edema. CONCLUSION: We recommend vigilance in corneal transplant patients on simultaneous bisphosphonate therapy. Caution is advised in the extension to human trials of animal studies investigating the use of bisphosphonates in corneal transplantation.
Publication Types: Case Reports
PMID:17133063

**An unusual case of vascular catastrophe.**
Bloom B, Simes DC.
Fremantle Hospital, Fremantle, WA, Australia. benbloom@mail.com
Thrombotic thrombocytopenic purpura (TTP) has been recognised as an entity since 1924, and haemolytic uraemic syndrome (HUS) since 1955. The disease processes have generated new interest during the past two decades, and much progress has been made both in understanding and treating these diseases. They are best thought of as part of the same disease spectrum, characterised by thrombocytopenia and microangiopathic haemolytic anaemia on the blood film. We present a patient with HUS/ TTP who developed the macroangiopathic thrombotic complications of coronary occlusion causing myocardial infarction, and cerebral artery occlusion causing massive stroke. To our knowledge, this is the first published report of macroangiopathic
complications of this condition.
Publication Types: Case Reports
PMID:17227273

**Dissociative and conversion disorders: defining boundaries.**
Isaac M, Chand PK.
Dr. M. Isaac, Primary Care Mental Health Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, 16, The Terrace, Fremantle, WA 6160; Australia. E-Mail: misaac@cyllene.uwa.edu.au.
PURPOSE OF REVIEW: Although dissociative disorders have been described and diagnosed for some time, their aetiology, pathogenesis, phenomenology and management continues to arouse debate. It is only in recent times that researchers have made some progress by integrating trauma related theories with more contemporary cognitive theories and neurobiology.
RECENT FINDINGS: Dissociation as a phenomenon is reported to occur in a variety of disorders. This widespread occurrence has contributed to a better understanding of dissociation. An expansion of this concept may have contributed to the loss of its original significance. Recent studies in the field of dissociation that pertain to its aetiology, pathophysiology, neurobiology and management are critically reviewed. SUMMARY: Dissociative disorder is conceptually a difficult disorder to study. Apart from exposure to trauma, certain primary personality attributes may contribute to the propensity to develop dissociative disorder. Recent advances in functional neuroimaging facilitated by enhanced knowledge in the neural representation of body state have helped to improve our understanding of dissociation. There is confusion over the use of various terms such as sexual abuse and physical abuse in explaining causality. Current classificatory systems have not been found suitable when applied across cultures. In spite of all of these limitations, there has been recent progress toward a better understanding of dissociative disorders. copyright 2006 Lippincott Williams & Wilkins.
Publication Types: Review
PMID:2006457411

Der Anaesthesist. 2006.
**Entflammungs- und Brandverhalten von biologischem Gewebe bei In-vitro-Bestrahlung mit dem CO2-Laser** [Ignition and burning of biological tissue under simulated CO2-laser surgery conditions].
(1) Institut für Anästhesiologie, Universitätsspital, Zürich
(2) Institut für Anästhesiologie, Kantonsspital, Baden
(3) Dept. of Otolaryngology, Head & Neck Surgery, Lions Ear and Hearing Institute, University of Western Australia, Fremantle, Australia
(4) Institut für Anästhesiologie, Universitätsspital, Rämistr. 100, 8091 Zürich, Schweiz
Background Laser surgery in endoscopy has greatly enhanced the surgical armamentarium for treating various laryngeal and hypopharyngeal disorders, but harbours a risk of tissue ignition and inflammation of surgical and anaesthetic instrumentation. However, even if non-inflammable material is used, there is still a residual fire hazard from endogenous tissue that may develop an ignitable aerosol (so-called laser smog) as an effect of laser irradiation. The aim of this study was to investigate how tissue carbonisation and vaporisation contributes to the risk of airway fire.
Methods For the simulation of gas accumulation in the hypopharynx and larynx following the European standard ISO-11990, a cylindrical steel chamber with an open and a closed end has
been used to simulate the operative setting. Pork meat chunks with a tissue composition similar
to the larynx and hypopharynx such as fat, muscle, cartilage and bone were introduced into this
chamber. Ventilation was achieved through jet ventilation with disposable, non-inflammable
laser jet catheters. The tissue was then repeatedly exposed to a laser beam in super-pulse
mode (pulse rate 250 Hz) with various intensities and exposure lengths at an impact angle of
75°. The laser intensity was varied from 2 to 15 W. The type, duration, intensity and incidence of
tissue ignition were recorded and analysed.

Results  The degree of tissue ignition correlated with laser intensity. Low laser intensity caused
spark formation whereas high intensity resulted in sustained tissue fire. The type of tissue had
an impact on ignition intensity thereby showing lower ignition thresholds and higher ignition
susceptibility in fat-containing tissue compared to muscle. The most important factor for
occurrence of tissue ignition was the chamber oxygen concentration which displayed an inverse
correlation with the time until tissue ignition. Oxygen concentrations of 35% led to tissue ignition
in 42 s, 40% oxygen in 20 s. Oxygen concentrations higher than 60% resulted in immediate
tissue ignition.

Conclusions  Despite the use of non-inflammable materials in endoscopic laser surgery of the
upper airway and hypopharynx, the risk of tissue ignition remains due to the inflammable laser
smog which is easily ignited in an oxygen-rich environment. Hence to minimise this risk, we
recommend using oxygen concentrations lower than 40%, low laser intensities (<6 W) and
limiting continuous laser activation to periods shorter than 10 s.
[A$], excluding glucometers) was A$162 per type 2 diabetic patient or A$51 million when projected to the Australian diagnosed type 2 diabetic population. CONCLUSIONS - Neither SMBG testing nor its frequency was associated with glycemic benefit in type 2 diabetic patients regardless of treatment. Our data did not include methods of SMBG delivery and application, factors that require further assessment in the evaluation of SMBG utility in non-insulin-treated type 2 diabetes. SMBG may be still of value in the identification and prevention of hypoglycemia and in dose adjustment in insulin-treated patients. PMID:2006368337


Peripheral arterial disease and risk of cardiac death in type 2 diabetes: the Fremantle Diabetes Study.
Norman PE, Davis WA, et al.
OBJECTIVE: The purpose of this study was to examine the natural history of peripheral arterial disease (PAD) complicating type 2 diabetes, in particular the influence of PAD on the risk of cardiac death and the adequacy of PAD risk factor management. RESEARCH DESIGN AND METHODS: The Fremantle Diabetes Study (FDS) was a prospective community-based observational study of diabetic patients recruited between 1993 and 1996. The present sample comprised the 1,294 FDS type 2 diabetic patients and a subgroup of 531 of these who had valid data at baseline and five or more subsequent consecutive annual reviews. Assessments consisted of a range of clinical and biochemical variables including the ankle/brachial index (ABI). PAD was defined as an ABI < or =0.90 at two consecutive reviews or any PAD-related lower-extremity amputation. RESULTS: The prevalence of PAD at study entry was 13.6% and the incidence of new PAD was 3.7 per 100 patient-years. Both prevalent and incident PAD was strongly and independently associated with increasing age, systolic blood pressure, total serum cholesterol, and especially smoking. Risk factor management improved but remained suboptimal during follow-up. An ABI of < or =0.90 was independently associated with an increased risk of cardiac death of 67%. CONCLUSIONS: Measurement of the ABI is a simple means of identifying PAD in diabetic patients. PAD is common in diabetic patients and predicts cardiac death. These data further support the role of regular screening for PAD in diabetes so that intensive management of vascular risk factors can be pursued. PMID:16505509


Is the metabolic syndrome a predictor of cardiac and all-cause in type 1 diabetes? The Fremantle Diabetes study: P2101.
Bruce D, Davis W.
University of Western Australia, School of Medicine and Pharmacology, Fremantle, Australia


How prognostic are the UKPDS and DiaCard diabetes-specific risk engines for predicting 5-year risk of events in type 2 diabetic patients without prior cardiovascular disease? The Fremantle Diabetes Study: A691.
Colagiuri R, Colagiuri S, et al.
(*)Prince of Wales Hospital, Department of Endocrinology and Diabetes, Randwick NSW, Australia, (+)University of Sydney, Australian Health Policy Institute, Sydney NSW, Australia, (++ ) University of Western Australia, School of Medicine & Pharmacology, Fremantle WA, Australia
Diabetologia. 2006; 49(12): 2828-36.
Vascular depression in older people with diabetes.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, P.O. Box 480, Fremantle, Western Australia, 6959, Australia, dbruce@cyllene.uwa.edu.au
AIMS/HYPOTHESIS: Cerebrovascular disease may be causal or a vulnerability factor in late-onset depression and may explain the high rate of depression in older adults with diabetes. We explored a wide range of potential explanatory variables of depression in a longitudinal study of older diabetic subjects to investigate the vascular depression hypothesis in these patients.
METHODS: We recruited 207 subjects with diabetes selected for potential cognitive deficits from an existing observational cohort study (average age 75.7 +/- 4.6 years, 52.2% men) for an assessment of depression using a standardised diagnostic instrument (Cambridge Examination for Mental Disorders of the Elderly - Revised). All subjects underwent a detailed clinical assessment at baseline and at follow-up (after 7.5 +/- 1.1 years). RESULTS: Major depression was present in 45 subjects (21.7%) and minor depression in ten (4.8%). A positive history of strokes and the presence of peripheral arterial disease were significantly associated with depression at the time of diagnosis. In a subsample of 93 cases who underwent structural neuroimaging, the presence of cerebral infarcts was also significantly associated with depression. Treatment with glucose-lowering therapy, higher serum cholesterol levels and difficulties with activities of daily living at baseline were significant predictors of depression at follow-up. CONCLUSIONS/INTERPRETATION: A history of cerebrovascular disease was strongly associated with depression and cerebrovascular risk factors were significant predictors of depression in older diabetic patients. Our findings are consistent with the hypothesis that the excess risk of depression in older diabetic patients is related to underlying cerebrovascular disease.
PMID:17039347

Predictors, consequences and costs of diabetes-related lower extremity amputation complicating type 2 diabetes: The Fremantle Diabetes Study.
Davis WA, Norman PE, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, P.O. Box 480, Fremantle, WA, 6959, Australia, wdavis@cyllene.uwa.edu.au
AIMS/HYPOTHESIS: The aims of this study were to assess the incidence, predictors, consequences, and inpatient cost of lower extremity amputation (LEA) in a community-based cohort of type 2 diabetic patients. METHODS: Between 1993 and 1996, 1,294 patients with type 2 diabetes were recruited to the longitudinal, observational Fremantle Diabetes Study. LEAs and mortality from cardiac causes were monitored until 30 June 2005. Inpatient costs (in A$ in year 2000), derived using a case-mix approach, were available for the period from 1 July 1993 to 30 June 2000. RESULTS: During follow-up 44 patients without LEA at baseline had a first-ever diabetes-related LEA, an incidence of 3.8 per 1,000 patient-years. Independent predictors of first-ever LEA included foot ulceration (hazard ratio [95% CI]: 5.56 [1.24-25.01]), an ankle brachial index </=0.90 (2.21 [1.11-4.42]), HbA(1c) (increase of 1%: 1.30 [1.10-1.54]) and neuropathy (2.65 [1.30-5.44]). The risk of cardiac death was significantly increased in patients with LEA at baseline, although this was not an independent risk factor. The median (interquartile range) inpatient cost per LEA admission was A$12,485 (A$6,037-A$24,415), with a median length of stay of 24 (10-43) days. CONCLUSIONS/INTERPRETATION: First-ever LEAs in type 2 patients were associated with poor glycaemic control, foot ulceration and evidence of microvascular and macrovascular disease. Patients with LEA were at increased risk of cardiac death. LEAs contribute disproportionately to diabetes-related inpatient costs.
**Bone mineral density and its determinants in diabetes: the Fremantle Diabetes Study.**  
Rakic V, Davis WA, et al.  
T.M.E. Davis, University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, P.O. Box 480, Fremantle, WA 6959; Australia. E-Mail: tdavis@cyllene.uwa.edu.au  
Aims/hypothesis: We assessed the effects of type 1 and type 2 diabetes on bone density and metabolism. Materials and methods: We analysed bone mineral density (BMD) measured at the hip, spine and forearm using dual energy X-ray absorptiometry in 34 patients with type 1 and 194 patients with type 2 diabetes. Patients were from the community-based Fremantle Diabetes Study, and findings for them were compared with those from normal age- and sex-matched control subjects from the local community. Biochemical and hormonal markers of bone metabolism were measured in a subset of 70 patients. Results: After adjusting for age and BMI, there was a lower BMD at total hip (p<0.001) and femoral neck (p=0.012) in type 1 men vs control subjects, but type 1 women and matched controls had similar BMD at each site. There was a higher BMD at total hip (p=0.006), femoral neck (p=0.026) and forearm (p<0.001) in type 2 women vs control subjects, but diabetes status was not associated with BMD in type 2 men after adjustment for age and BMI. Serum oestradiol, BMI, C-terminal telopeptide of collagen type 1 and male sex were consistently and independently associated with BMD at forearm, hip and femoral neck and explained 61, 55 and 50% of the total variance in BMD, respectively, at these sites. Spine BMD was independently associated with BMI and ln(oestradiol). Conclusions/interpretation: Men with type 1 diabetes may be at increased risk of osteoporosis, while type 2 women appear to be protected even after adjusting for BMI. Low serum oestradiol concentrations may predispose to diabetes-associated osteoporosis regardless of sex.  
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PMID:2006217689
In(oestradiol). CONCLUSIONS/INTERPRETATION: Men with type 1 diabetes may be at increased risk of osteoporosis, while type 2 women appear to be protected even after adjusting for BMI. Low serum oestradiol concentrations may predispose to diabetes-associated osteoporosis regardless of sex.
PMID:16518589

**Decompression sickness following breath-hold diving.**
Wong R.
R. Wong, Department of Diving and Hyperbaric Medicine, Fremantle Hospital, Fremantle, WA; Australia. E-Mail: robert.wong@health.wa.gov.au.
Publication Types: Letter
PMID:2007077050

Diving & Hyperbaric Medicine. 2006; 36(3): 139-144.
**Decompression sickness in breath-hold diving.**
Wong RM.
R.M. Wong, Department of Diving and Hyperbaric Medicine, Fremantle Hospital and Health Service, Alma Street, Fremantle, WA 6160; Australia. E-Mail: robert.wong@health.wa.gov.au.
Decompression sickness (DCS) in breath-hold (BH) diving has long been disputed as a distinct clinical entity. However, there has been a flurry of case reports describing various symptoms arising in BH divers. Since the 1950s, Taravana has been described in French Polynesia, where divers suffered from paralysis, vertigo and nausea. Prior hyperbaric exposure followed by BH dives also led to symptoms and Paulev, a submarine medical officer, described his personal experience of DCS after a series of BH dives. Three similar cases have been described. The Ama divers of Japan and Korea have long been studied, but in the early days no confirmed cases of DCS had been recorded, although Doppler ultrasound had detected circulating bubbles and cerebral injuries have been documented in them. Other BH divers have also been studied, including recreational sports divers and diver fishermen. In all these groups symptoms have been recorded after repetitive deep dives. Theoretical calculations by various authors have concluded that repetitive deep BH dives could give rise to symptoms of DCS. The clinical entity of DCS in BH divers is distinctive in that it tends to affect mainly the brain. Symptoms, even without treatment, tend to subside over time, in many cases without sequelae. Although the aetiological factors causing DCS in BH dives have not been elucidated, there is no doubt that such a clinical entity does exist. Hyperbaric oxygen therapy should be offered to divers with symptoms. Preventive measures are suggested.
Publication Types: Review
PMID:2006551714

**Taking emergency medicine international: What can we learn and teach?**
Curry C.
Prof. C. Curry, Department of Emergency Medicine, Fremantle Hospital, Fremantle, WA; Australia
Publication Types: Editorial
PMID:2006313105
Responding to the Boxing Day tsunami disaster in Aceh, Indonesia: Western and South Australian contributions.
Pearce A, Mark P, et al.
Dr. C. Curry, Emergency Department, Fremantle Hospital, Alma Street, Fremantle, WA 6160; Australia. E-Mail: chriscurry1@compuserve.com
Objective: To describe the Western and South Australian response to the Boxing Day tsunami disaster in Aceh, Indonesia. Method: Reports from three of the responders. Results: Comment has been made on organising a response, the first team to Banda Aceh, the second team to Banda Aceh, and lessons learned. Conclusions: These experiences have identified areas in which we could be better prepared for the next international disaster response. copyright 2006 Australasian College for Emergency Medicine and Australasian Society for Emergency Medicine. PMID:2006135586

Color atlas of emergency department procedures.
Banham N.
Director, Emergency Department, Rockingham/Kwinana District Hospital, Emergency Physician, Fremantle Hospital, Western Australia, Australia
Publication Types: Book Review

Anaphylaxis: clinical concepts and research priorities.
Brown SGA.
Discipline of Emergency Medicine, The University of Western Australia and Fremantle Hospital, Fremantle, Western Australia, Australia
Anaphylaxis is a severe immediate-type hypersensitivity reaction characterized by life-threatening upper airway obstruction bronchospasm and hypotension. Although many episodes are easy to diagnose by the combination of characteristic skin features with other organ effects, this is not always the case and a workable clinical definition of anaphylaxis and useful biomarkers of the condition have been elusive. A recently proposed consensus definition is ready for prospective validation. The cornerstones of management are the supine position, adrenaline and volume resuscitation. An intramuscular dose of adrenaline is generally recommended to initiate treatment. If additional adrenaline is required, then a controlled intravenous infusion might be more efficacious and safer than intravenous bolus administration. Additional bronchodilator treatment with continuous salbutamol and corticosteroids are used for severe and/or refractory bronchospasm. Aggressive volume resuscitation, selective vasopressors, atropine (for bradycardia), inotropes that bypass the [beta]-adrenoreceptor and bedside echocardiographic assessment should be considered for hypotension that is refractory to treatment. Management guidelines continue to be opinion- and consensus-based, with retrospective studies accounting for the vast majority of clinical research papers on the topic. The clinical spectrum of anaphylaxis including major disease subgroups requires clarification, and validated scoring systems and outcome measures are needed to enable good-quality prospective observational studies and randomized controlled trials. A systematic approach with multicentre collaboration is required to improve our understanding and management of this disease., Copyright (C) 2006 Blackwell Publishing Ltd. Publication Types: Review
**Refuge from the Lord's Resistance Army in Uganda: a report from a Medecins Sans Frontieres team leader.**
Caruso N.
Emergency Department, Fremantle Hospital, Fremantle, Western Australia, Australia.
In 2005 the author worked for Medecins Sans Frontieres (MSF, or Doctors without Borders) in northern Uganda. This short report shares some background information on MSF, the situation in northern Uganda as a consequence of the activities of the Lord's Resistance Army (LRA), the work of the MSF project and the personal experience of being there.
PMID:16712541

**Anaphylaxis to bull dog ant and jumper ant stings around Perth, Western Australia.**
Gilhotra Y, Brown SG.
Department of Emergency Medicine, Fremantle Hospital, Fremantle, Western Australia, Australia
Abstract Objective: To determine the main causative species, reaction characteristics and geographical locations of ant sting anaphylaxis around Perth, Western Australia (WA). Methods: Structured interviews were performed on a cohort of 10 patients referred to our Anaphylaxis Clinic who were allergic to ant venom, followed by field trips to collect ant specimens. A descriptive analysis of clinical data was performed. Results: Around Perth, Myrmecia gratiosa, a bull dog ant, was the only species of stinging ant found around the locations where reactions had occurred (eight patients). To the south-west of Perth, species implicated were another bull dog ant Myrmecia nigriscapa (one patient), and a jumper ant Myrmecia ludlowi (one patient). Twelve reactions were documented as mild (one), moderate (seven) and severe with hypotension (four). In three bull dog ant venom allergic patients, specific IgE was analysed, demonstrating substantial cross-reactivity with other bull dog ant species. Clinical patterns of reaction severity and response to repeated stings were consistent with known features of insect sting allergy. Conclusions: A single species of bull dog ant, M. gratiosa, appears to be responsible for ant sting anaphylaxis around Perth. Further investigation is required for other regions of WA. The provision of effective immunotherapies for people allergic to native Australian ants might be simplified by the dominance of a limited number of ant species and IgE binding cross-reactivity between venoms, as was evident in this study.
PMID:16454770

**Case of the month: Complete transection of the trachea and oesophagus in a 10 year old child: a difficult airway problem.**
O'Connor AE, Cooper J.
(1)Senior Lecturer in Emergency Medicine, Peel Health Campus, University of Western Australia, Australia, (2)Fremantle Hospital, Australia

**The prevalence, clinical correlates and treatment of apathy in Alzheimer's disease.**
Starkstein SE, Jorge R, et al.
Dr. Prof. S.E. Starkstein, Education Building T-7, Fremantle Hospital, Fremantle, WA 6959; Australia. E-Mail: ses@cyllene.uwa.edu.au.
The aim for this article is to review the frequency, clinical correlates and treatment of apathy in
Alzheimer's disease. Apathy is currently defined as diminished motivation as expressed in poor goal-oriented behaviours and cognitions. A structured clinical interview and a specific set of diagnostic criteria to diagnose apathy in dementia have been recently validated. There are several valid and reliable scales to measure the severity of apathy in adults with neuropsychiatric disorders. Apathy is present in about 20% of patients with mild dementia and in 60% of those with severe dementia. Among patients with Alzheimer's disease, apathy is significantly associated with older age, the presence of depression, and more severe cognitive and functional deficits, and also predicts a faster cognitive and functional decline. The mechanism of apathy in neuropsychiatric disorders is still unknown, but several studies suggest an important role for frontal lobe and basal ganglia dysfunction. There are no specific randomized controlled trials of psychoactive compounds to treat apathy in neuropsychiatric disorders. Evidence from case reports and small case series suggest the usefulness of psychostimulants to treat apathy in traumatic brain injury, whereas pharmacological trials for behavioural and psychological problems in dementia suggest that anticholinesterases may have some efficacy.

Publication Types: Review
PMID:2006493763

**Screening for abdominal aortic aneurysms: more benefit than cost.**
Norman PE, Golledge J.
P.E. Norman, School of Surgery and Pathology, University of Western Australia, Fremantle Hospital, Fremantle, WA 6959; Australia. E-Mail: pnorman@cyllene.uwa.edu.au.
Publication Types: Editorial
PMID:2006268974

**Depression in Alzheimer's disease.**
Starkstein SE, Mizrahi R.
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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 poorer 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 marked under-diagnosed and most patients with depression are either not treated or are on subclinical doses of antidepressants. Recent randomized controlled trials have 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.

**Fecal incontinence related to pregnancy.**
Chong AK, Hoffman B.
Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia.
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Fecal incontinence related to pregnancy is an underreported and debilitating physical problem that has psychosocial ramifications. Disruption of the external and internal anal sphincters,
which may occur during vaginal delivery, is the most common etiologic factor. Endoanal ultrasound is a minimally invasive, simple, and accurate diagnostic tool used to confirm and guide management of sphincter complex disruption.

**Antiproliferative effects of interferon alpha on hepatic progenitor cells in vitro and in vivo.**  
Lim R, Knight B, et al.  
J.K. Olynyk, School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital Campus, PO Box 480, Fremantle, WA 6959; Australia. E-Mail: jolynyk@cyllene.uwa.edu.au  
Hepatic progenitor cells (called oval cells in rodents) proliferate during chronic liver injury. They have been suggested as targets of malignant transformation in chronic liver diseases, including chronic hepatitis C. Interferon alpha therapy reduces the risk of hepatocellular carcinoma (HCC) in chronic hepatitis C regardless of viral clearance. The aim of this study was to determine whether interferon alpha could reduce the risk of HCC by modifying preneoplastic events in the hepatic progenitor cell population. Pre- and post-treatment liver biopsies were evaluated for changes in the hepatic progenitor cell population in 16 patients with non-responding chronic hepatitis C. Interferon alpha-based treatment significantly reduced the numbers of c-kit-positive hepatic progenitor cells by 50%. To determine the mechanism of cell number reduction, the effects of interferon alpha on murine hepatic progenitor cells were studied in vitro. MTT (3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide) proliferation assay and proliferating cell nuclear staining showed that interferon alpha had a dose-dependent, anti-proliferative effect. Interferon alpha stimulated hepatocytic and biliary differentiation of the oval cell lines reflected by increased expression of albumin and cytokeratin19 accompanied by decreased expression of alphafetoprotein and Thy-1. To validate these results in vivo, mice were placed on the choline-deficient, ethionine-supplemented diet to induce liver injury and oval cell proliferation and treated with pegylated interferon alpha 2b for 2 weeks. This resulted in a significant four-fold reduction in the number of oval cells (P < .05). In conclusion, interferon alpha-based treatment reduced the number of hepatic progenitor cells in chronic liver injury by modulating apoptosis, proliferation, and differentiation. Copyright copyright 2006 by the American Association for the Study of Liver Diseases.

PMID:2006230808

**Outcomes with Toronto stentless porcine aortic valve: the Australian experience.**  
S. Yadav, Departments of Cardiothoracic Surgery, Fremantle Hospital, Fremantle, WA 6160; Australia. E-Mail: s_yadava@rediffmail.com.  
The purpose of this study is to describe the Australian experience with TSPV in the aortic position in 543 patients followed for up to 8 years. Prospectively collected data were reviewed. The average age was 73.5 years, with 74.4% older than 70 years. Eighty-five percent of valves were calcified and 79.5% stenotic. Most valves implanted (79.3%) were sizes 25, 27, or 29 mm. Concomitant coronary bypass was performed in 45.3% of patients. Total cumulative follow-up for the 543 patients was 2131 patient years. At 6 years, 82.1% and at 8 years, 76.3% were in New York Heart Association class I, 55% had no aortic insufficiency. The average mean systolic gradient for all valves at 6 years was 7.4 mmHg. The effective orifice area varied from 1.7 cm<sup>2</sup> (23-mm valve) to 1.96 cm<sup>2</sup> (29-mm valve). Actuarial survival at 8
years was 79.3%. Freedom from valve-related deaths was 93.2%. There was one instance of primary tissue valve failure during follow-up, with 93.3% freedom from explant. The early hemodynamic benefits of the TSPV are well maintained during more than 8 years of followup, without evident significant valvular dysfunction. Longer follow-up time is required to validate durability. copyright 2006 Published by European Association for Cardio-Thoracic Surgery. All rights reserved.

Publication Types: Conference Paper
PMID:2006607741

**Australian ant venom allergy study: P60.**
MacDonald E, Hudson P.
Emergency Medicine, Fremantle Hospital, Western Australia Dept of Resp & Allergy Medicine, Flinders Medical Centre, SA

**Rest myocardial perfusion (‘hot’ MIBI) scans in patients with acute chest pain: follow-up study over 12 month period: 308.**
Macdonald WBG, Gawthrope IC, et al.
Fremantle Hospital, Australia (Macdonald) (Gawthrope), University of Western Australia, Australia (Turner)

**Rapid one-day myocardial rest-stress perfusion scans with TC-99M agents: feasibility using a cardiac phantom model: 307.**
Macdonald WBG, Hindley KL.
Fremantle Hospital, Australia (Macdonald), Princess Margaret Hospital for Children, Australia (Hindley)

**Sarcoid arthropathy: scintigraphic appearance: 468.**
Macdonald WBG, Thompson J.
Fremantle Hospital, Australia

**The obesity-driven rising costs of type 2 diabetes in Australia: projections from the Fremantle Diabetes Study.**
Davis WA, Knuiaman MW, et al.
University of Western Australia, School of Medicine and Pharmacology, Western Australia, Australia. wdavis@cyllene.uwa.edu
BACKGROUND: The cost of diabetes is high for both the individual and society. Future health-care planning requires patient-level diabetes-attributable health-care cost data that have not previously been available for Australia. AIM: To determine Australian national direct diabetes-attributable health-care costs for known type 2 diabetes in 2000 and project these to 2051. METHODS: A total of 1294 patients with type 2 diabetes was recruited to the Fremantle Diabetes Study between 1993 and 1996. A bottom-up, prevalence-based approach using
diabetes-attributable costs provided average annual per patient health-care costs (in year 2000 A$). Costs were extrapolated to 2051 using Australian type 2 diabetes prevalence figures and Australian Bureau of Statistics population projections, assuming that prevalence rates (i) remain at current levels and (ii) rise steadily.

RESULTS: Total annual direct diabetes-attributable health-care costs in 2000 in Australia for people > or =25 years with known type 2 diabetes were estimated at A$636 million. As a result of ageing, the number of people with type 2 diabetes will double between 2000 and 2051 with a 2.5-fold increase in diabetes-attributable health-care costs. If obesity and inactivity prevalence rates continue to rise, prevalence rates of type 2 diabetes will further increase. The number of people with type 2 diabetes in 2051 may be 3.5 times higher than in 2000 with a 3.7-fold cost increase.

CONCLUSIONS: The financial burden of treating type 2 diabetes could quadruple by 2051 unless more is done to prevent type 2 diabetes and its complications. A smaller proportion of the population will have the capacity to fund these rising health-care costs.


Medications and green urine.
Gillett MJ, Burnett JR.
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Chronic hepatitis C infection and sex hormone levels: effect of disease severity and recombinant interferon-alpha therapy.
Nguyen HV, Mollison LC, et al.
Department of Endocrinology, Fremantle Hospital, Fremantle, WA, Australia.

BACKGROUND: We aimed to investigate the associations between androgen status and markers of liver disease severity and to determine the effect of interferon-alpha (IFN-alpha) treatment on sex hormone levels in the context of hepatitis C infection. METHODS: We audited liver biopsy and sex hormone data from 35 men with chronic hepatitis C and a separate group of 11 men with hepatitis C who received IFN-alpha treatment at Fremantle Hospital. RESULTS: We found that men with low fibrosis scores (0-2) on the modified Knodell histological activity index were more likely to have lower sex hormone-binding globulin (SHBG) levels (38.2 +/- 13.2 vs 66.6 +/- 43.3 nmol/L, P < 0.001) and higher free testosterone levels (380.4 +/- 102.0 vs 255.9 +/- 83.0 pmol/L, P = 0.01) than those with higher fibrosis scores (3-6). SHBG directly correlated with fibrosis scores (r = 0.37, P = 0.032). Free testosterone levels inversely correlated with liver fibrosis scores (r = -0.43, P = 0.011). A transient reduction in total testosterone of 5.7 +/- 4.2 nmol/L (P = 0.014) occurred within the first 6 months of IFN-alpha therapy although free testosterone was unaffected. CONCLUSION: More severe liver disease was associated with lower free testosterone and higher SHBG. IFN-alpha therapy reduced total testosterone but not to hypogonadal levels, with no decline in free testosterone. These data suggest that liver disease in hepatitis C infection modulates androgen status indirectly via increased SHBG. Screening for androgen deficiency in the context of hepatitis C infection should selectively target men with more severe liver disease or documented higher grade fibrosis.

Publication Types: Journal article
PMID:16732861
Can epidemiological studies assist in the evaluation of community treatment orders? - The experience of Western Australia and Nova Scotia.
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Epidemiological studies using administrative databases have several advantages over other methodologies in studying the effectiveness of compulsory community treatment such as community treatment orders (CTOs). We compared patients placed on CTOs in Western Australia with controls drawn from both within the jurisdiction and from another without this measure (Nova Scotia). Although in different countries, the mental health services in both jurisdictions share common characteristics. Notably, we were able to control for forensic history in our comparison within Western Australia. We analysed predictors of admission and number of bed-days using multiple, logistic or Cox regression as appropriate. Of the 274 subjects placed on a CTO, we were able to find controls for up to 96% (n=265). CTO placement was not associated with reduced admissions or mean bed-days, although there was a threshold effect with a reduced risk of inpatient stays exceeding 100 days. Outpatient contacts were significantly greater for the CTO group. However, we do not know whether the intensity of treatment, or its compulsory nature, effected outcome.

Challenging the smoking culture within a mental health service supportively.
Reilly P, Murphy L, et al.
Alma Street Centre, Fremantle Hospital and Health Service, South Metropolitan Health Service, Fremantle, WA, Australia
Smoking is an entrenched part of the culture of mental health care services. This paper discusses the smoking culture in mental health care settings and demonstrates a supportive model to engage staff to actively address their tobacco use and to influence a change in smoking-related workplace policy, practice, and culture. With management endorsement, two 9-week staff smoking cessation support groups were implemented and subsidized nicotine replacement therapy was provided to staff within the Alma Street Mental Health Service, Fremantle Hospital, Western Australia. Eighteen staff members from nursing, social work, administration staff, and patient care assistants participated in the group programme. At the conclusion of the programme, 61% (n = 11) of participants had quit as a result of the groups. Furthermore, a 3-month follow-up evaluation revealed that 39% (n = 7) of the group had abstained from smoking because of the programme. More importantly, the groups engaged staff to discuss workplace smoking issues and produced five recommendations to review policy and practice to further influence a change in the smoking culture of the mental health care service. The groups also provided the opportunity to develop a model of intervention to address smoking in a mental health setting and to raise the public health role of mental health nurses.

Best practice guidelines for the administration of intramuscular injections in the mental health setting.
Wynaden D, Landsborough I, et al.
Wynaden, Dianne: School of Nursing and Midwifery, Curtin University of Technology, GPO Box U1987, Perth, WAU, Australia, 6845, d.wynaden@curtin.edu.au
Intramuscular injections are administered to mental health consumers in both the community and hospital settings. Medications delivered by the intramuscular route assist consumers to live in the community and enhance their ability to integrate and engage in community life. Although the practice of giving intramuscular injections is routine for mental health nurses, the process is invasive and best practice guidelines are not well developed. The aim of this study was to identify a best practice technique for the administration of intramuscular injections in the mental health setting based on: (i) the identification of 300 abstracts and a systematic review of 150 articles in the subject area; (ii) an evaluation of current practice of 93 nurses; and (iii) the use of the newly developed technique with 96 consumers. The findings add significantly to the knowledge base on administering intramuscular injections in the mental health setting. The identified best practice technique provides mental health nurses with evidence-based guidelines, thus ensuring that the medication administered by intramuscular injection provides the best possible outcomes for consumers. (PsycINFO Database Record (c) 2006 APA, all rights reserved) (journal abstract).

Towards better understanding and management of somatoform disorders.
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Much research has recently been conducted on somatoform disorders demonstrating their clinical importance, associated health-service burden and economic cost. These conditions are often comorbid with other mental and physical disorders and particularly prevalent in primary care and general medical settings. Although culture-specific manifestations and variations of somatization occur— it is now accepted that medically unexplained somatic symptoms are a universal phenomenon. The management of somatoform disorders is generally a complex and lengthy process; however, a number of recent studies have demonstrated the effectiveness of short-term treatments such as cognitive behaviour therapy and educational interventions. Despite advances in their understanding and treatment, debate still surrounds the conceptualization and categorization of somatoform disorders, with a number of experts proposing a complete re-evaluation and reassignment of this diagnostic classification category. The following paper represents a review of recently published literature on frequency, characteristics, conceptualization, impact and management of somatoform disorders.

Limited iron export by hepatocytes contributes to hepatic iron-loading in the Hfe knockout mouse.
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School of Medicine and Pharmacology, Fremantle Hospital, The University of Western Australia, Fremantle, WA 6160, Australia.
BACKGROUND/AIMS: In hereditary hemochromatosis, iron-loading of hepatocytes is associated with increased iron uptake while little is known about iron release. This study aims to characterise iron release and ferroportin expression by Hfe knockout hepatocytes to determine if they contribute to iron overload in haemochromatosis. METHODS: Iron release by hepatocytes from Hfe knockout, non-iron-loaded and iron-loaded wild-type mice was measured after incubation with nontransferrin-bound iron as iron-citrate. RESULTS: Iron release and ferroportin expression by hepatocytes from Hfe knockout, non-iron-loaded and in vivo iron-
loaded wild-type mice were similar although, nontransferrin-bound iron uptake was significantly increased in Hfe knockout hepatocytes and decreased in iron-loaded wild-type hepatocytes compared with non-iron-loaded wild-type cells. When expressed as a percentage of total iron uptake, iron release was decreased in Hfe knockout hepatocytes (4.6±0.7 versus 13.7±1.2%, P<0.0001) and increased in iron-loaded wild-type hepatocytes (29.5±0.5 versus 13.5±0.7%; P<0.0001) compared with wild-type hepatocytes. In contrast, in vitro iron-loading increased iron release and ferroportin expression by both Hfe knockout and wild-type hepatocytes.

CONCLUSIONS: Hfe knockout hepatocytes accumulate iron as a result of limited iron export and enhanced iron uptake. The correlation between iron release and ferroportin expression suggests that iron export in hepatocytes is mediated by ferroportin.

PMID:16271796


A prospective longitudinal study of apathy in Alzheimer's disease.
Starkstein SE, Jorge R, et al.
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BACKGROUND: Apathy and depression are the most frequent behavioural and psychiatric disorders in Alzheimer's disease, and may both have a negative impact on the progression of the illness. OBJECTIVES: To examine the clinical correlates of apathy in Alzheimer's disease (AD), and to determine whether apathy is a significant predictor of more rapid cognitive, functional and emotional decline. METHODS: Using a structured psychiatric evaluation, we examined a consecutive series of 354 subjects meeting clinical criteria for AD. Apathy was assessed by the Apathy Scale, and diagnosed using standardised criteria. Additional measurements included scales for depression, functional impairment, and global cognitive functions. A follow up evaluation was carried out in 247 patients (70% of the total sample) between 1 and 4 years after the baseline evaluation. RESULTS: Apathy was significantly associated with older age (p = 0.009), and a higher frequency of minor and major depression (p < 0.0001). Apathy at baseline was a significant predictor of depression at follow up (p = 0.01), and was associated with a faster cognitive (p = 0.0007) and functional decline (p = 0.006). CONCLUSIONS: Apathy in AD is a behavioural marker of a more aggressive dementia, characterised by a faster progression of cognitive, functional, and emotional impairment.

PMID:16361584


A diagnostic formulation for anosognosia in Alzheimer's disease.
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OBJECTIVE: To determine the earliest symptoms of anosognosia in people with Alzheimer's disease and to validate a criteria-guided strategy to diagnose anosognosia in dementia. METHODS: A consecutive series of 750 patients with very mild or probable Alzheimer's disease attending a memory clinic, as well as their respective care givers, was assessed using a comprehensive psychiatric evaluation. RESULTS: The factors of anosognosia for (1) basic activities of daily living (bADL), (2) instrumental activities of daily living (iADL), (3) depression and (4) disinhibition were produced by a principal component analysis on the differential scores (ie, caregiver score minus patient score) on the anosognosia questionnaire for dementia. A discrepancy of two or more points in the anosognosia-iADL factor was found to have a high sensitivity and specificity to identify clinically diagnosed anosognosia in people with Alzheimer's
disease. By logistic regression analysis, the severity of dementia and apathy were both shown to be noticeably associated with anosognosia in people with Alzheimer's disease.

CONCLUSION: Anosognosia in those with Alzheimer's disease is manifested as poor awareness of deficits in iADL and bADL, depressive changes and behavioural disinhibition. The frequency of anosognosia is found to increase considerably with the severity of dementia. The validity of a specific set of criteria to diagnose anosognosia in people with Alzheimer's disease was shown, which may contribute to the early identification of this condition.

Publication Types: Validation Studies
PMID: 16549411


Primary osteoarthritis in the ankle joint is associated with finger metacarpophalangeal osteoarthritis and the H63D mutation in the HFE gene: evidence for a hemochromatosis-like polyarticular osteoarthritis phenotype.

Carroll GJ.
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BACKGROUND AND AIM:: Osteoarthritis (OA) can occur in the ankle joint. It also occurs in an appreciable proportion of subjects with hereditary hemochromatosis (HH). Might these conditions have common genetic characteristics? The aim of this study was to test the hypothesis that HFE gene mutations are associated with primary osteoarthritis in the ankle joint.

METHODS:: Consecutive referred patients who had primary or secondary (posttraumatic) OA of the ankle joint were assessed by a single rheumatologist and had a full physical and joint examination. Plain x-rays of the ankle joint, other clinically involved osteoarthritic joints, iron studies, HFE genotyping, and Hb electrophoresis were performed. The significance of differences was evaluated by 2-tailed Fisher exact test.

RESULTS:: Fourteen patients met the inclusion criteria for primary ankle OA and 6 met the criteria for secondary ankle OA. One of the 14 had had a previous subtalar joint fusion and was excluded. Among the remaining 13, 7 had OA in the index and/or middle finger metacarpophalangeal joints (MCP2,3 OA) with radiologic features similar to those found in hemochromatotic arthropathy (HA). Furthermore, 11 of the 13 had at least one HFE mutation, one subject in this group was homozygous for H63D, one was compound heterozygous for C282Y and S65C, and one was compound heterozygous for H63D and S65C. Eight were heterozygous for H63D. The 13 subjects were compared with the 6 secondary ankle OA subjects and with a previously studied population cohort (n = 3011) from the town of Busselton in whom HFE genotyping had been performed. A statistically significant increase in the frequency of HFE gene mutations was observed in the group with primary OA of the ankle joint compared with that with secondary ankle joint OA (P = 0.0095) and compared with the Busselton cohort (P = 0.0008). Furthermore, a statistically significant association between finger MCP joint OA and primary ankle joint OA was observed (P = 0.0436). Iron studies were normal in the 13 primary and 6 secondary ankle OA subjects. None of the subjects with ankle OA had clinical signs of hemochromatosis or abnormal liver function tests.

CONCLUSIONS:: A strong and statistically significant association was observed between HFE gene mutations and primary OA in the ankle joint. The frequent presence of MCP2,3 OA in these patients suggests the existence of a type 2 polyarticular OA phenotype that closely resembles the arthropathy of HH and which appears to be clinically differentiable from type 1 OA or nodal generalized OA (NGOA). HFE gene mutations may be a marker for the type 2 polyarticular OA phenotype and a clue to OA pathogenesis.

PMID: 16755236
We reviewed 142 consecutive primary total hip replacements implanted into 123 patients between 1988 and 1993 using the Exeter Universal femoral stem. A total of 74 patients (88 hips) had survived for ten years or more and were reviewed at a mean of 12.7 years (10 to 17). There was no loss to follow-up. The rate of revision of the femoral component for aseptic loosening and osteolysis was 1.1% (1 stem), that for revision for any cause was 2.2% (2 stems), and for re-operation for any cause was 21.6% (19 hips). Re-operation was because of failure of the acetabular component in all but two hips. All but one femoral component subsided within the cement mantle to a mean of 1.52 mm (0 to 8.3) at the final follow-up. One further stem had subsided excessively (8 mm) and had lucent lines at the cement-stem and cement-bone interfaces. This was classified as a radiological failure and is awaiting revision. One stem was revised for deep infection and one for excessive peri-articular osteolysis. Defects of the cement mantle (Barrack grade C and D) were found in 28% of stems (25 hips), associated with increased subsidence (p = 0.01), but were not associated with endosteal lysis or failure. Peri-articular osteolysis was significantly related to the degree of polyethylene wear (p < 0.001), which was in turn associated with a younger age (p = 0.01) and male gender (p < 0.001). The use of the Exeter metal-backed acetabular component was a notable failure with 12 of 32 hips (37.5%) revised for loosening. The Harris-Galante components failed with excessive wear, osteolysis and dislocation with 15% revised (5 of 33 hips). Only one of 23 hips with a cemented Elite component (4%) was revised for loosening and osteolysis. Our findings show that the Exeter Universal stem implanted outside the originating centre has excellent medium-term results. copyright 2006 British Editorial Society of Bone and Joint Surgery.

Iontophoresis of antibiotics into segmental allografts.
Khoo PPC, Michalak KA, et al.
From Royal Perth Hospital, Perth, Australia, P. P. C. Khoo, MBBS (Hons), Orthopaedic Registrar; Department of Orthopaedic Surgery; K. A. Michalak, BSc/BE (Hons), Bioengineer; R. E. Day, MBmedEng, Project Bioengineer; Bioengineering Division, Medical Engineering and Physics Department; Royal Perth Hospital, Wellington Street Campus, Box X2213 GPO, Perth, Western Australia 6847, Australia., P. J. Yates, FRCS(Tr & Orth), Consultant Senior Lecturer; Department of Orthopaedics and Trauma, Fremantle Hospital & The University of Western Australia, Fremantle Hospital, Level 6, Block B, Alma Street, Fremantle, Western Australia 6160, Australia., S. M. Megson, FRACS(Orth), Orthopaedic Surgeon; Pioneer Valley Private Hospital, Norris Road, Mackay, Queensland 4740, Australia., D. J. Wood, FRACS(Orth), FRCS, Professor of Orthopaedic Surgery; Unit of Orthopaedic Surgery; University of Western Australia, Gate 3, Verdun Street, Nedlands, Western Australia 6009, Australia.
Iontophoresis is a novel technique which may be used to facilitate the movement of antibiotics into the substance of bone using an electrical potential applied externally. We have examined the rate of early infection in allografts following application of this technique in clinical practice. A total of 31 patients undergoing revision arthroplasty or surgery for limb salvage received 34 iontophoresed sequential allografts, of which 26 survived for a minimum of two years. The mean serum antibiotic levels after operation were low (gentamicin 0.37 mg/l (0.2 to 0.5); flucloxacillin 1 mg/l (0 to 1) and the levels in the drains were high (gentamicin 40 mg/l (2.5 to 131); flucloxacillin
17 mg/l (1 to 43). There were no early deep infections. Two late infections were presumed to be haemotogenous; 28 of the 34 allografts were retained. In 12 patients with pre-existing proven infection further infection has not occurred at a mean follow-up of 51 months (24 to 82)., (C) 2006 British Editorial Society of Bone and Joint Surgery

Iontophoresed segmental allografts in revision arthroplasty for infection.  
Michalak KA, Khoo PPC, et al.  
From the Royal Perth Hospital, Perth, Western Australia, K. A. Michalak, BE, Bioengineer; R. E. Day, CP Eng(Biomed), Bioengineer; Medical Engineering and Physics Department Royal Perth Hospital, Wellington Street, Perth, Western Australia 6847, Australia., P. P. C. Khoo, MB BS, Orthopaedic Registrar; P. J. Yates, MRCS, FRCS(Tr & Orth), Consultant Orthopaedic Surgeon and Senior Lecturer; Department of Orthopaedics and Trauma; Fremantle Hospital, Alma Street, Fremantle, Western Australia 6160, Australia., D. J. Wood, MS, FRCS, FRACS, Professor of Orthopaedic Surgery; Perth Orthopaedic Institute, Verdun Street, Nedlands, Perth, Western Australia 6009, Australia.  
Revision arthroplasty after infection can often be complicated by both extensive bone loss and a relatively high rate of re-infection. Using allograft to address the bone loss in such patients is controversial because of the perceived risk of bacterial infection from the use of avascular graft material. We describe 12 two-stage revisions for infection in which segmental allografts were loaded with antibiotics using iontophoresis, a technique using an electrical potential to drive ionised antibiotics into cortical bone., Iontophoresis produced high levels of antibiotic in the allograft, which eluted into the surrounding tissues. We postulate that this offers protection from infection in the high-risk peri-operative period. None of the 12 patients who had two-stage revision with iontophoresed allografts had further infection after a mean period of 47 months (14 to 78)., (C) 2006 British Editorial Society of Bone and Joint Surgery

Unusual positron emission tomography findings in pulmonary amyloidosis: a case report.  
Yadav S, Sharma S, et al.  
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ABSTRACT: Positron emission tomography (PET) has come to play an increasingly important role in the evaluation of pulmonary lesions, which are suspicious of malignancy. As is true for other techniques, PET gives false positive and negative results. We report a case of pulmonary amyloidosis with multiple pulmonary nodules showing different uptake of 18 F-fluorodeoxyglucose (FDG) on PET. There are limitations of specificity of FDG-PET in characterising pulmonary nodules and it is important to confirm a suspected malignancy with histology before potentially curative treatment is undertaken.  
PMID:17020625

A multi-step approach in anti-calcification of glutaraldehyde-preserved bovine pericardium.  
Fremantle Heart Institute, Fremantle Hospital, School of Surgery and Pathology, University of Western Australia, Fremantle, Western Australia
AIM: Bioprosthetic cardiovascular substitutes, manufactured from glutaraldehyde-preserved bovine or porcine tissues, are prone to calcification after implantation. The aim of the study was to evaluate the ultrastructure, material stability and calcification behaviour of glutaraldehyde-preserved bovine pericardium, treated with a multi-step anti-calcification process which addresses each of the major causes of calcification and tissue degeneration. METHODS: Bovine pericardium samples were divided into 2 groups. Group I (control) consisted of tissue fixed with 0.625% glutaraldehyde and Group II (study group) consisted of tissue fixed with 0.625% glutaraldehyde and exposed to a multi-step anti-calcification process. Ultrastructure was examined by scanning electron microscopy and material stability was assessed by mechanical testing, shrinkage temperature and enzymatic degradation. Calcification was assessed by histology (Von Kossa stain) and by atomic absorption spectrophotometry in the subcutaneous rat model. RESULTS: Bovine pericardium in the study group revealed less visible changes in the ultrastructure of the collagen matrix, improved material stability (P<0.05) and significantly (P<0.001) reduced calcification compared to control tissues (4.5+/−1.2 versus 136.03+/−11.39 ug/mg tissue). CONCLUSIONS: In conclusion, results demonstrate that the multi-step anticalcification process improved the material stability and reduced the calcification potential of bovine pericardial tissue. These improvements in the quality of the bovine pericardium should enhance the long-term durability of the tissue as a bioprosthetic substitute for cardiovascular application.

PMID:17043620


Diagnostic evaluation of nonalcoholic fatty liver disease.

Adams LA, Talwalkar JA.

Nonalcoholic fatty liver disease (NAFLD) is a diagnostic consideration among patients with asymptomatic elevated aminotransaminases, patients with radiologic findings of hepatic fatty infiltration, or occasionally in the patient with "cryptogenic" cirrhosis. The diagnosis of NAFLD requires evidence of fatty infiltration of the liver in the absence of excessive alcohol ingestion. Clinical evaluation should examine for metabolic risk factors (central obesity, glucose intolerance, hypertension, hypertriglyceridemia, and low HDL cholesterol), which are suggestive but not specific for the diagnosis of NAFLD. Secondary causes of NAFLD, such as medications and intestinal bypass surgery, should be excluded as management of these conditions may differ. Confirmation of hepatic steatosis can usually be done by imaging studies, although occasionally liver biopsy is required. Among suspected NAFLD patients with chronically elevated aminotransaminases, clinical evaluation and serological testing should be performed to exclude other causes of chronic liver disease. Liver biopsy is required to stage fibrosis and distinguish between nonalcoholic steatohepatitis and steatosis. This is valuable for providing prognosis, excluding other liver disease, monitoring response to therapy or evaluating disease progression over time. Clinical features, particularly diabetes, obesity, and older age, can aid in stratifying patients at risk for advanced fibrosis but are not sufficiently accurate to replace liver biopsy.


Multicenter phase II clinical study of iodine-131-rituximab radioimmunotherapy in relapsed or refractory indolent non-Hodgkin's lymphoma.

Leahy MF, Seymour JF, et al.

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PURPOSE: To evaluate efficacy and safety of iodine-131 (131I) -rituximab chimeric anti-CD20
antibody radioimmunotherapy in patients with relapsed or refractory indolent non-Hodgkin's lymphoma (NHL). PATIENTS AND METHODS: After a standard loading dose of rituximab 375 mg/m², individualized dosimetry was performed by whole-body gamma imaging of a tracer activity of 131I-rituximab followed by administration of a therapeutic activity of 131I-rituximab to deliver an estimated whole-body radiation absorbed dose of 0.75 Gy. RESULTS: Ninety-one patients were entered onto the trial: 78 patients (86%) had follicular lymphoma, six patients (7%) had mucosa-associated lymphoid tissue/marginal zone lymphoma, and seven patients (8%) had small lymphocytic lymphoma. The objective overall response rate (ORR) was 76%, with 53% attaining a complete response (CR) or CR unconfirmed (CRu). Median duration of response for patients achieving CR/CRu was 20 v 7 months for those with a partial response (P = .0121). Median progression-free survival for the entire cohort was 13 months, with 14% remaining relapse free beyond 4 years. Median follow-up was 23 months, with a 4-year actuarial survival rate of 59% +/- 10%. Toxicity was principally hematologic; grade 4 thrombocytopenia occurred in 4% and neutropenia occurred in 16% of patients, with nadirs at 6 to 7 weeks after treatment. CONCLUSION: 131I-rituximab radioimmunotherapy of relapsed or refractory indolent NHL achieves high ORR and CR rates with minimal toxicity.

PMID:16940276

Champions for a good cause: Quality care. 
Haynes G. 
G. Haynes, Fremantle Trust 
PMID:2006239868

Iron uptake by transferrin receptor 1 is regulated by HFE in hepatocytes: 132. 
Chua AC, Herbison CE, et al. 
School of Medicine and Pharmacology, The University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia

The relationship between disease severity, quality of life and health care resource use in a cross-section of patients with Crohn's disease: 69. 
Gibson PR, Weston AR, et al. 
IBD-Australia, Melbourne, Brisbane and Fremantle, Australia

Poor correlation between clinical impression, the small colonic polyp and their neoplastic risk. 
Lawrance IC, Sherrington C, et al. 
I.C. Lawrance, Department of Gastroenterology, University Department of Medicine, Fremantle Hospital, Alma Street, Fremantle, WA 6159; Australia. E-Mail: ilawranc@cyllene.uwa.edu.au 
Background and Objectives: Significance of the small colonic polyp is unclear and its removal is frequently determined by the proceduralist's clinical impression. Our aims were to determine if clinical discernment is accurate, and the likelihood that lesions <10 mm are histologically advanced. Method: We prospectively collected 1988 lesions from 854 subjects (2215 consecutive colonoscopies). Lesion size, location, patient age, sex and the colonoscopist's
clinical impression was recorded. Results: Clinical assessment for neoplasia had a sensitivity of 87.4%, specificity of 65.0%, positive predictive value of 76.0% and negative predictive value of 80.2%, resulting in an accuracy of 73.4%. Factors predictive of correct clinical impression were polyp size, location in the rectum and being pedunculated, but not the patient’s age, sex or the endoscopist’s experience. Of the 1434 lesions <=5 mm in size, 44.5% were neoplastic and 3.5% were histologically advanced. Of the 266 lesions 6-9 mm, 79.3% were neoplastic, 19.9% were histologically advanced, five demonstrated high-grade dysplasia and three were malignant. Only two patients with an adenocarcinoma or high-grade dysplasia in a polyp <10 mm had a lesion >=10 mm elsewhere in the colon. Of the 288 lesions >=10 mm in size, 92.7% were neoplastic, 29.5% had a villous component, 6.9% demonstrated high-grade dysplasia and 29.2% were malignant. Factors predictive of neoplasia were patient age, polyp size and sessile nature of the lesion. Conclusion: Polyps <10 mm had a significant risk of neoplasia and advanced histology and, in general, clinical impression correlated poorly with neoplasia. Removal of all lesions proximal to the rectum, regardless of size, should therefore be considered. copyright Blackwell Publishing Asia Pty Ltd.

PMID:2006133426


**Randomized double blind placebo-controlled trial of a Chinese herbal therapy (CH100) in chronic hepatitis C.**

Mollison L, Totten L, et al.

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Background and Aim: Hepatitis C virus (HCV) is a common infection with serious health consequences. Alternative therapies are often used for hepatitis C. The aim of the present study was to examine CH100, a Chinese herbal remedy, for efficacy in therapy of chronic HCV.

Methods: A randomized double blind placebo-controlled study in a tertiary outpatient clinic of CH100 over 24 weeks with 24 weeks follow-up in patients with chronic HCV infection. Alanine aminotransferase (ALT), HCV-RNA, quality of life (by SF-36) and side-effects were examined regularly. Ninety-seven patients were enrolled of which 91 were suitable for analysis. Results: No significant differences were observed between patients receiving CH100 (n = 61) or placebo (n = 30) at baseline or during follow-up in either ALT or viral titer. However, patients receiving CH100 had a fall in mean ALT over time (P = 0.05 at week 4, P = 0.26 at week 12, and P = 0.04 at week 24), with reversion to baseline during post-treatment follow up. No significant side-effects were observed although mild complaints were common. Quality of life scores improved in both groups with time, and bodily pain significantly improved in CH100 recipients. Conclusion: CH100 appears to be no better than placebo in the treatment of patients with chronic HCV infection. copyright 2006 Journal of Gastroenterology and Hepatology Foundation and Blackwell Publishing Asia Pty Ltd.

PMID:2006291717


**MRI enteroclysis to distinguish fibrotic from inflammatory small bowel Crohn’s disease?**

Segarajasingam DS, Welman C, et al.

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Population-based study of the relationship between mutations in the hemochromatosis (HFE) gene and arthritis.

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BACKGROUND AND AIM: Mutations in the hemochromatosis (HFE) gene are carried by one in three individuals of British Isles descent and may result in increased iron stores. These increased iron stores could potentially induce or exacerbate diseases, such as arthritis, in which iron has a role in pathogenesis. Although arthritis is a well-known association of clinically overt hereditary hemochromatosis, controversy surrounds the role of mutations in the HFE gene as risk factors for arthritis. The aim of the present study was to determine whether mutations in the HFE gene are associated with an increased prevalence of arthritis. METHODS: A population-based study was conducted in Busselton, Western Australia, of the prevalence of arthritis in 1372 individuals of British Isles descent. Participants completed a questionnaire and general physical examination. Analysis for C282Y and H63D HFE mutations was undertaken. Unadjusted and adjusted odds ratios (OR) were calculated for the relationship between HFE mutations and the prevalence of self-reported, doctor-diagnosed arthritis. RESULTS: There was no association between the presence of HFE mutations and the prevalence of self-reported, doctor-diagnosed arthritis. RESULTS: There was no association between the presence of HFE mutations and the prevalence of self-reported, doctor-diagnosed arthritis (C282Y/wild type (WT) adjusted OR = 1.041 (95% confidence interval (CI) 0.68-1.61), H63D/WT OR = 0.76 (95% CI 0.53-1.08), C282Y/C282Y OR = 0.39 (95% CI 0.04-3.63), C282Y/H 63D OR = 0.808 (95% CI 0.27-2.42), H63D/H63D OR = 0.419 (95% CI 0.13-1.36)). Overall adjusted OR for arthritis in participants with one or more HFE mutations was 0.81 (95% CI 0.61-1.09). CONCLUSIONS: Mutations of the HFE gene are not risk factors for arthritis in populations of British Isles descent.

PMID:16638105

Volar versus dorsal locking plates with and without radial styloid locking plates for the fixation of dorsally comminuted distal radius fractures: a biomechanical study in cadavers.

Blythe M, Stoffel K, et al.

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PURPOSE: To compare the stability and stiffness of dorsal and volar fixed-angle distal radius constructs in a cadaveric model. METHODS: A locking distal radius system was used in a combination of a dorsal and styloid plate (group 1), a single volar plate (group 2), and a combination of a volar and styloid plate (group 3) configuration. In addition a single volar 3.5-mm steel locking plate was used in group 4. Each construct was tested on 6 fresh-frozen radii with simulated unstable dorsally comminuted extra-articular distal radius fractures. Specimens were tested on a material testing machine with an extensometer and subjected to axial compression fatigue and load-to-failure testing. RESULTS: No construct failed in fatigue testing of 250 N for 5,000 cycles. Two specimens in each group were tested for 20,000 cycles without failure. The plastic deformation in the double-plate groups was lower compared with the single-plate groups, although the difference was not statistically significant. Group 1 had the highest and group 4 the lowest failure load and stiffness, respectively. The differences between group 1 and the other groups, except failure load compared with group 3, were statistically significant. Groups 2 and 3 had a significantly higher load to failure and group 3 had a significantly higher stiffness compared with group 4. CONCLUSIONS: All constructs offer adequate stability with minimal deformation on fatigue testing under physiologic conditions. Dorsal fixed-angle constructs are stiffer and stronger than volar constructs. The addition of a styloid plate to a volar
plate did not significantly improve stability in this model of simulated extra-articular dorsal comminution loaded in axial compression. 
PMID:17145377

**Aim, design and methods of the ‘reasons for not intensifying antihypertensive treatment’ (RIAT): an international registry in essential hypertension.**
Department of Nephrology, Fremantle Hospital, Perth, Australia
Failure of physicians to adhere to hypertension guidelines may partly account for the failure to achieve blood pressure (BP) goals in clinical practice. The aim of this trial is a comprehensive description of the approach of physicians in the management of high BP among primary care patients. It will primarily assess what are the Reasons for not Intensifying an Antihypertensive Treatment (RIAT), when predefined individual BP goals are not achieved. Open intervention survey was conducted in 17 countries in Latin America, Eastern Europe, Africa and Asia in family practices, government and private clinics. The registry is based on a three-step epidemiological design. Step one shall identify guidelines and recommendations taken as reference in each country for the management of hypertension. Step two will assess the variance between individual targets defined by physicians in their practice compared to guidelines and recommendations. Step three is a prospective registry where physicians collect patient data at baseline; determine individual target BP values. Several follow-up visits are proposed to monitor achievement of these targets. Step three of RIAT aims at providing responses to several key objectives. Recruitment is under way aiming at enrolling 33 000 patients. To identify, what is the BP targeted according to the risk factor profile and what are the reasons for not modifying an antihypertensive treatment when BP goals are not reached, and to analyse the type of antihypertensive drugs prescribed according to compelling indications and to assess the percentage of patients reaching target figures. Journal of Human Hypertension (2006) 20, 31-36. doi:10.1038/sj.jhh.1001937; published online 27 October 2005. 
PMID:16252001

Journal of Investigative Dermatology. 2006; 126(Suppl 2 ): S34.
**MAL-PDT in "Difficult-to-Treat" basal cell carcinoma, an Australian study: 48 month follow-up data.**
Vinciullo C, Elliott T, et al.
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**Tumor necrosis factor-alpha gene polymorphism associated with increased susceptibility to venous leg ulceration.**
Wallace HJ, Vandongen YK, et al.
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PMID:16439968

**Antiplatelet and proton pump inhibitor prescribing in patients with acute coronary syndrome.**

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Publication Types: Letter
PMID:2006225998


**HFE Gene Mutations are associated with osteoarthritis in the index or middle finger metacarpophalangeal joints.**

Carroll GJ.

OBJECTIVE:. To test the hypothesis that possession of either C282Y or H63D mutations in the HFE gene is associated with primary osteoarthritis (OA) in joints commonly affected in hemochromatotic arthropathy. METHODS: HFE genotyping was performed in 87 patients with radiologically proven OA in 3 joint regions: index or middle finger metacarpophalangeal joints (MCP2,3; n = 52), elbow joints (n = 8), ankle, intertarsal or tarsometatarsal joints (ankle/IT/TMT; n = 27); and in 56 patients with radiologically proven OA in finger interphalangeal (IP) joints, but not MCP2,3 joints (IP OA control group). HFE mutation frequencies in these groups were also compared to those in a similar population (Busselton population control group). RESULTS: A statistically significant association between HFE mutations and OA was observed for the MCP2,3 joints (p = 0.0001) and the ankle/IT/TMT joint group (p = 0.002) as well as for the 3 joint regions collectively (p = 0.0001), but not for the elbow joints (p = 0.062). Comparison with the Busselton population controls showed similar statistically significant associations, except for the elbow and ankle/IT/TMT groups, where similar trends were observed. CONCLUSION: HFE gene mutations are associated with OA in the MCP2,3 joints. These mutations may be markers for a polyarticular OA phenotype.
PMID:16583477


**Apparent mineralocorticoid excess: report of six new cases and extensive personal experience.**

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In mineralocorticoid target tissues such as the cortical collecting duct in the kidney, the enzyme 11beta-hydroxysteroid dehydrogenase type 2 (11betaHSD2) is responsible for the peripheral inactivation of cortisol to cortisone, thereby protecting the mineralocorticoid receptor from inappropriate activation by cortisol. Mutations in the HSD11B2 gene cause the syndrome of apparent mineralocorticoid excess, an autosomal recessive form of inherited hypertension in which cortisol acts as a potent mineralocorticoid. Herein are described six new families with mutations in the HSD11B2 gene causing the syndrome of apparent mineralocorticoid excess, an autosomal recessive form of inherited hypertension in which cortisol acts as a potent mineralocorticoid. Herein are described six new families with mutations in the HSD11B2 gene causing hypokalemic hypertension, with low plasma aldosterone and low renin levels in affected individuals, indicating mineralocorticoid hypertension. Profiling of urinary steroid metabolites showed decreased cortisol inactivation, with urinary tetrahydrocortisol and tetrahydrocortisone ratio (THF + 5alphaTHF)/THE ranging 2.4 to 40 and nearly absent urinary free cortisone in all but one case. Genetic analysis of the HSD11B2 gene from these patients with apparent mineralocorticoid excess revealed distinct homozygous point mutations in four families, a compound heterozygous mutation in one family,
and a large 23-bp exonic insert with frameshift and disruption of the amino acid sequence in another family. Expression studies of mutants that were expressed in HEK-293 cells showed marked reduction or abolition of 11betaHSD2 enzymatic activity. These cases are reviewed along with previous ones from the authors' extensive personal experience to highlight the importance of 11betaHSD2 in the understanding of a new biologic principle in hormone action, demonstrating that local metabolism of the glucocorticoid hormones into inactive derivatives by the enzyme 11betaHSD2 is one of the mechanisms that intervene to allow specific aldosterone regulatory effects.

PMID:17035606

The effect of the metabolic syndrome, hepatic steatosis and steatohepatitis on liver fibrosis in hereditary hemochromatosis.
OBJECTIVES: The variability in phenotypic expression of hereditary hemochromatosis (HH) is not fully understood. We sought to examine whether the metabolic syndrome, hepatic steatosis or steatohepatitis influenced hepatic fibrosis among patients with HH and iron overload.
METHODS: We identified 86 patients with C282Y/C282Y or C282Y/H63D HH and iron overload (hepatic iron concentration (HIC) >2,200 microg/g for males, >1,600 microg/g for females). Features of the metabolic syndrome were assessed at the time of liver biopsy. Biopsies were scored by a blinded pathologist. Significant fibrosis was defined as peri-portal fibrosis or greater.
RESULTS: The mean (+/-SD) age of the study population was 53+/-12 years and 68 (79%) were male. The median (range) values of ferritin and HIC were 1,125 (253-9,530) microg/l and 9963 (1926-50 887) microg/g, respectively. The metabolic syndrome was present in 23 (27%), hepatic steatosis in 43 (50%), steatohepatitis in 18 (21%) and significant fibrosis in 38 (44%). Overall, neither the metabolic syndrome nor any of its components were associated with significant fibrosis or a higher mean fibrosis stage. Hepatic steatosis but not steatohepatitis was associated with a lower fibrosis stage. C282Y/H63D compound heterozygous individuals who had glucose intolerance had more severe fibrosis compared with those without glucose intolerance (1.0+/-1.0 vs. 0.1+/-0.3, P=0.01). CONCLUSIONS: Overall, the metabolic syndrome and fatty liver were not associated with hepatic fibrosis among individuals with HH and iron overload. However, glucose intolerance may be important risk factor for the development of hepatic fibrosis in subjects with the C282Y/H63D HFE genotype.

Differential findings for CD14-positive hepatic monocytes/macrophages in primary biliary cirrhosis, chronic hepatitis C and nonalcoholic steatohepatitis.
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BACKGROUND AND AIMS: Endotoxin-responsive monocytes/macrophages (CD14-positive) are potential sources of profibrogenic factors. The aims of this study were to determine (1) whether hepatic CD14-positive cells are present in various forms of chronic liver disease, and (2) the relationship between CD14-positive cells, myofibroblasts, and fibrosis in these diseases.
METHODS: Liver specimens from control subjects (n = 12) and those with primary biliary cirrhosis (n = 18), chronic hepatitis C (n = 13), or nonalcoholic steatohepatitis (n = 13) were immunostained for CD14, CD68, and alpha-smooth muscle actin (SMA) and the number of cells expressing these antigens was determined. Fibrosis and inflammation were also assessed.
RESULTS: The total number of hepatic CD68-positive cells was similar in diseased and control livers. The number of CD14-positive cells was increased in advanced fibrosis in primary biliary
cirrhosis and hepatitis C but not in nonalcoholic steatohepatitis. The number of CD14-positive cells was also increased in hepatitis C specimens with high inflammatory activity. CD14-positive cells were often associated with alpha-SMA-positive myofibroblasts in fibrous septa.

CONCLUSIONS: The number of hepatic CD14-positive cells is increased in advanced fibrosis in subjects with primary biliary cirrhosis and hepatitis C but not in nonalcoholic steatohepatitis. In primary biliary cirrhosis and hepatitis C, CD14-positive macrophages are found in close proximity to fibrous septa and myofibroblasts. In hepatitis C, an increased number of CD14-positive cells are associated with high inflammatory activity.

Polyarticular osteoarthritis - Two major phenotypes hypothesized.
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Osteoarthritis is the commonest form of arthritis, at least amongst Caucasians and is frequently polyarticular. Genetic factors are now considered pivotal in the aetiopathogenesis of polyarticular osteoarthritis (POA). This document proposes a nexus between the gene most commonly mutated amongst Caucasian peoples, notably the HFE gene and an appreciable subset of POA patients who have a clinically recognisable OA phenotype. It is hypothesised that there are at least 2 major POA phenotypes each of which is associated with discrete genotypes. Type 1 POA characterized by Heberden's or Bouchard's nodes with prominent DIP, PIP, knee joint (medial compartment) and Great toe MTP joint involvement corresponds to the putative nodal generalized form of OA or NGOA (proposed Type 1 POA phenotype). As yet no genetic marker has been defined for this POA subset. The second is a hitherto less well recognized phenotype characterized by involvement of the index and/or middle finger metacarpophalangeal (MCP2,3) joints and the elbows, ankles and possibly the intertarsal and tarsometatarsal joints. The hip and knee joints may sometimes also be involved. This different joint distribution corresponds closely to the pattern observed in the arthropathy that often accompanies hereditary haemochromatosis. It is predicted that mutations in the HFE gene will associate strongly with the proposed Type 2 POA phenotype and serve as a genetic marker for this clinically recognisable subset.
PMID:16213101

National exit exam needed to test core knowledge.
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Publication Types: Letter

MJA Practice Essentials — Allergy 2. Anaphylaxis: diagnosis and management.
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Anaphylaxis is a serious, rapid-onset, allergic reaction that may cause death. Severe anaphylaxis is characterised by life-threatening upper airway obstruction, bronchospasm and/or
hypotension. Anaphylaxis in children is most often caused by food. Bronchospasm is a common symptom, and there is usually a background of atopy and asthma. Venom- and drug-induced anaphylaxis are more common in adults, in whom hypotension is more likely to occur. Diagnosis can be difficult, with skin features being absent in up to 20% of people. Anaphylaxis must be considered as a differential diagnosis for any acute-onset respiratory distress, bronchospasm, hypotension or cardiac arrest. The cornerstones of initial management are putting the patient in the supine position, administering intramuscular adrenaline into the lateral thigh, resuscitation with intravenous fluid, support of the airway and ventilation, and giving supplementary oxygen. If the response to initial management is inadequate, intravenous infusion of adrenaline should be commenced. Use of vasopressors should be considered if hypotension persists. The patient should be observed for at least 4 hours after symptom resolution and referred to an allergist to assist with diagnosis, allergen avoidance measures, risk assessment, preparation of an action plan and education on the use of self-injectable adrenaline. Provision of a MedicAlert bracelet should also be arranged.

PMID:16948628


Glycaemic levels triggering intensification of therapy in type 2 diabetes in the community: the Fremantle Diabetes Study.

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OBJECTIVE: To assess the effectiveness of the management of type 2 diabetes in an urban Australian setting. DESIGN AND SETTING: The Fremantle Diabetes Study (FDS), a community-based longitudinal observational study. PATIENTS: 531 FDS participants with type 2 diabetes, with mean age, 62.4 years (95% CI, 40.9-79.3 years), 54% male, median diabetes duration 3.0 years (interquartile range [IQR], 0.7-7.0 years), with valid data from the baseline FDS assessment and five subsequent annual reviews between 1993 and 2001. MAIN OUTCOME MEASURES: Glycated haemoglobin (HbA(1c)) levels at annual review visits before and after change in blood glucose-lowering therapy. RESULTS: Over 2893 patient-years of follow-up, 97 patients (18%) progressed from dietary management to therapy with oral hypoglycaemic agents (OHA), and 45 (9%) progressed from OHA to insulin therapy, after a median duration of diabetes of 4.0 years (IQR, 2.9-5.5 years) and 8.1 years (IQR, 5.5-13.0 years), respectively. Median HbA(1c) concentrations (IQR) at the review before OHA or insulin were started were 7.7% (6.9%-8.8%) and 9.4% (8.0%-10.7%), respectively. At the next annual review, HbA(1c) levels in the two groups had fallen to 7.4% (6.5%-8.1%) and 7.9% (7.2%-9.5%), respectively (P < or = 0.001). Intensification of therapy was associated with beneficial changes in serum lipid profiles, but not with an increase in frequency of hypoglycaemia. CONCLUSIONS: Most Australian patients with type 2 diabetes may be spending most of the duration of their disease with suboptimal glycaemic control (HbA(1c) > 7.0%), despite the availability of a range of effective therapies, including insulin.

PMID:16584365


High rate of immediate systemic hypersensitivity reactions to tiger snake antivenom.

Isbister GK, Tankel AS, et al.
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2 Emergency Department, Coffs Harbour Base Hospital, NSW.
3 Women's and Children's Hospital, Adelaide, SA.
Predicting commercial success for Australian medical inventions patented in the United States: a cross sectional survey of Australian inventors.
Mattes E, Stacey MC, et al.
University of Western Australia, Perth, WA.
Michael C Stacey, DS, FRACS, Professor of Surgery.
OBJECTIVES: To examine the commercial development of Australian medical patents and identify the determinants of their being used in innovations (new or improved products or production processes). DESIGN: Cross-sectional survey with a nested case-control study.
PARTICIPANTS AND SETTING: 177 inventors listed as the first Australian on medical patents granted in the United States between 1 January 1984 and 30 December 1994, and surveyed in 1998-1999. MAIN OUTCOME MEASURE: A series of predictor variables (including characteristics of the patents; characteristics of the inventors; ideas, advice and funding during commercialisation; and the process of commercialisation) for whether or not a patent became an innovation. RESULTS: Half (89/177) of the medical patents became innovations, with 34% generating a total of A $287 million (13% over $1 million) in annual sales a median of 8 years after the patent had been granted. A patent was more likely to become an innovation if the inventor was employed by industry at the time of invention (odds ratio [OR], 3.2; 95% CI, 1.1-9.2), had invested their own finances (OR, 2.8; 95% CI, 1.0-7.4), and if the patent had been licensed (OR, 4.6; 95% CI 1.7-12.7), led to further patents (OR, 3.2; 95% CI, 1.0-10.4) and involved an industry partner in its commercial development (OR, 10.1; 95% CI, 3.6-27.7). It was less likely to become an innovation if finance came from a research funding agency (OR, 0.3; 95% CI, 0.1-0.8) and if interest from Australian industry was judged by inventors as "poor" (OR, 0.6; 95% CI, 0.4-0.9). CONCLUSIONS: Medical patents in the US listing Australian inventors are more likely to become innovations if they originate from industry rather than the public sector, and if inventors are willing to invest their own finances.

Inspection time in non-demented older adults with mild cognitive impairment.
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The aim of this study was to examine inspection time (IT) performance in older adults with mild cognitive impairment (MCI), who are at higher risk of developing further cognitive decline or dementia. IT is described as an index of speed of informational intake. IT correlates with measures of fluid intelligence and is possibly a marker for the integrity of the cholinergic system of the brain. IT may therefore be useful in aiding the diagnosis of early-stage progressive cognitive impairment. The current study compares IT in 28 people with MCI to 28 age, gender and education-matched controls. The computer-based, visual IT task required participants to discriminate between two visual stimuli that were presented for brief periods. Participants' IT performance was compared to their performance on cognitive and memory tasks. Group comparison showed that participants with MCI performed significantly worse on IT than controls and was not affected by years of education. In combination with other clinical,
the identification of older adults at risk for clinically relevant cognitive decline.

**Sutureless technique for repair of traumatic iridodialysis.**  
Richards JC, Kennedy CJ.  
Department of Ophthalmology, Fremantle Hospital, Fremantle, Western Australia, Australia.  
A technique for repair of traumatic iridodialysis that avoids the need for iris sutures is described. Following a limbal peritomy, sclerostomy sites level with the iris base are created at each clock hour of the iridodialysis using a microvitreoretinal blade. Vitreoretinal forceps passed through these ports are used to incarcerate the peripheral iris. No suture material is used to secure the iris. The conjunctiva is closed with absorbable sutures. The technique is suitable for use in simple iridodialysis repair and in conjunction with intraocular procedures.  
PMID:17152550

**Treatment of non-alcoholic fatty liver disease.**  
Adams LA, Angulo P.  
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(2)Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, USA  
Non-alcoholic fatty liver disease (NAFLD) is common and may progress to cirrhosis and its complications. The pathogenesis of steatosis and cellular injury is thought to be related mostly to insulin resistance and oxidative stress. Therefore, management entails identification and treatment of metabolic risk factors, improving insulin sensitivity, and increasing antioxidant defences in the liver. Weight loss and exercise improve insulin sensitivity. Bariatric surgery may improve liver histology in patients with morbid obesity. Insulin sensitising drugs showed promise in pilot trials as have a number of hepatoprotective agents. Further randomised, well controlled trials are required to determine the efficacy of these drugs., (C) 2006 The Fellowship of Postgraduate Medicine

Primary Intention. 2006; 14(3): 122.  
**Case study: neuropathic heel ulcer.**  
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PMID:2009288600

**Differential modulation of cell cycle, apoptosis and PPARgamma2 gene expression by PPARgamma agonists ciglitazone and 9-hydroxyoctadecadienoic acid in monocytic cells.**  
School of Medicine and Pharmacology, University of Western Australia, Fremantle and Royal Perth Hospitals, Australia.  
We sought to compare the effects of the thiazolidinedione ciglitazone with the endogenous fatty
acid PPARgamma agonists 9- and 13-hydroxyoctadecadienoic acid (9- and 13-HODE), in U937 mononuclear cells. Ciglitazone and 9-HODE inhibited cell proliferation and all three agonists increased cellular content of C18:0 fatty acids. Ciglitazone and 13-HODE resulted in an increased percentage of cells in S phase and ciglitazone reduced the percentage of cells in G2/M phase of cell cycle, whilst 9-HODE increased the percentage of cells in G0/G1 and reduced the fraction in S and G2/M phases. 9-HODE selectively induced apoptosis in U937 cells, and increased PPARgamma2 gene expression. Induction of apoptosis by 9-HODE was not abrogated by the presence of the PPARgamma antagonist GW9662. Synthetic (TZD) and endogenous fatty acid ligands for PPARgamma, ciglitazone and 9- and 13-HODE, possess differential, ligand specific actions in mononuclear cells to regulate cell cycle progression, apoptosis and PPARgamma2 gene expression.

PMID: 16647253


**Men's voices: postnatal depression from the perspective of male partners.**
Davey SJ, Dziurawiec S, et al.
South Metropolitan Child and Adolescent Mental Health Service, Fremantle, Australia.
Postnatal depression (PND) is a serious and debilitating condition that is recognized as being disruptive to women's lives at a time when they are already under stress adapting to the demands that a new baby creates. What has not always been fully acknowledged is that PND is linked with elevated levels of depression in male partners. In this article, the authors report on men's experiences of PND and of participation in a 6-week group treatment program specifically designed for male partners. The men experienced their partners' PND as overwhelming, isolating, stigmatizing, and frustrating. Coping with PND was assisted by participation in the men's group. Men reported lowered levels of depression and stress, and higher levels of social support, as a result of their participation. The men valued highly the opportunity to share experiences with peers, to hear strategies for engaging in their relationship, and to gain factual information.

PMID: 16394210


**Physical disability contributes to caregiver stress in dementia caregivers.**
Bruce DG, Paley GA, et al.
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Background: There have been few studies on the impact of physical illness on caregiver health. We wished to determine whether physical disability, as determined by the SF-12 survey contributes to caregiver stress. Methods: We interviewed 91 primary caregivers of dementia sufferers, aged 38-85 years old. Caregivers completed the SF-12 version of the Medical Outcomes Study Short Form Health Survey and reported on caregiver stress and concurrent medical conditions. Results: Most caregivers reported stress (76.9%), having medical conditions (72.4%) or taking medications (67.0%). The SF-12 data demonstrated that mental health problems were common and that 40.7% of the sample had some degree of physical disability. Using multiple logistic regression analysis, both SF-12 mental and physical component scores were independently associated with caregiver stress. Conclusion: Chronic disability and mental health problems were independently associated with caregiver stress. These data suggest that reducing the impact of physical disability could help ameliorate caregiver stress.

PMID: 2007091290
Enzyme immunoassays in brown snake (Pseudonaja spp.) envenoming: Detecting venom, antivenom and venom-antivenom complexes.

O'leary MA, Isbister GK, et al.

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Although a commercial snake venom detection kit (SVDK) is available to distinguish between the five major snake groups in Australia, there is no assay for quantifying venom or antivenom concentrations in envenomed patients. Serum samples were obtained from patients with brown snake (Pseudonaja spp.) envenoming before and after the administration of antivenom and patients with suspected brown snake bites but no evidence of envenoming. Enzyme immunoassays (EIAs) were developed for free venom, free antivenom and the venom-antivenom complex. Standard samples measured in duplicate had a coefficient of variation of less than 10%. The EIA for venom was able to detect brown snake venom down to concentrations of 3ng/mL. A high baseline absorbance was measured in some patients that did not change with the addition of excess antivenom to the samples. In these patients, the baseline absorbance was subtracted from all measurements to calculate the true venom concentration. The EIA for brown snake antivenom had a limit of detection of 20µg/mL, but 50µg/mL was used as a cut-off based on assays in patients who had not received antivenom. The EIA for venom-antivenom complexes was unable to detect these at the low venom concentrations that occurred in patients. Quantification of venom and antivenom will help to determine the dose of antivenom required to bind venom and to establish appropriate end points for antivenom treatment.

Proteomic analysis of Myrmecia pilosula (jack jumper) ant venom.

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Ant sting allergy in Australia is predominantly due to the Myrmecia pilosula species complex. Gel separation of M. pilosula venom is necessary so that the allergenic importance of each component can be defined by western blotting. However, previous PAGE methods produced suboptimal resolution and the components of each band were not precisely defined. Venom was resolved in both non-reduced and reduced form by one-dimensional acid urea PAGE, SDS-PAGE and two-dimensional acid urea-SDS PAGE. Resolved peptides were extracted and analysed by HPLC-MS. Acid urea PAGE and acid urea-SDS PAGE proved more effective than SDS-PAGE for resolution of peptides smaller than 10 kDa. All of the major peptides previously observed in M. pilosula venom were observed in gel resolved venom. Venom was found to primarily consist of peptides with molecular weight <10 kDa, most of which contain disulfide bridges. SDS-PAGE of non-reduced venom clearly defined six higher molecular weight proteins between 26 and 90 kDa. An 8546 Da dimer named pilosulin 5 was observed, but pilosulin 4, a peptide recently proposed to be present in venom was not. A variant of pilosulin 4 here named pilosulin 4.1a, existing as an 8198 Da dimer, was observed and has been characterised.