**H1-antihistamines for the treatment of anaphylaxis: Cochrane systematic review.**
Sheikh A, Broek Vt, et al.

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**Background:** Anaphylaxis is an acute systemic allergic reaction, which can be life-threatening. H1-antihistamines are commonly used as an adjuvant therapy in the treatment of anaphylaxis. We sought to assess the benefits and harm of H1-antihistamines in the treatment of anaphylaxis.

**Methods:** We searched the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library); MEDLINE (1966 to June 2006); EMBASE (1966 to June 2006); CINAHL (1982 to June 2006) and ISI Web of Science (1945 to July 2006). We also contacted pharmaceutical companies and international experts in anaphylaxis in an attempt to locate unpublished material. Randomized and quasi-randomized-controlled trials comparing H1-antihistamines with placebo or no intervention were eligible for inclusion. Two authors independently assessed articles for inclusion.

**Results:** We found no studies that satisfied the inclusion criteria.

**Conclusions:** Based on this review, we are unable to make any recommendations for clinical practice. Randomized-controlled trials are needed, although these are likely to prove challenging to design and execute.

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**Myrmecia pilosula (Jack Jumper) ant venom: identification of allergens and revised nomenclature.**
Wiese MD, Brown SGA, et al.

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**Background:** The 'Jack Jumper Ant' (JJA; Myrmecia pilosula species complex) is the major cause of ant sting anaphylaxis in Australia. Our aims were to determine the allergenicity of previously described venom peptides in their native forms, identify additional allergens and if necessary, update nomenclature used to describe the allergens according to International Union of Immunological Societies criteria.

**Methods:** Various polyacrylamide gel electrophoresis methods were used to separate JJA venom. Gel resolved venom was Western-blotted and probed with individual sera taken from patients with a history of JJA sting anaphylaxis and immunoglobulin E radioallergosorbent test (IgE RAST) tracer uptakes of >1% to whole venom.

**Results:** Of 67 available sera, 54 had RAST uptakes >1%. Thirteen IgE binding bands were identified using these sera. Pilosulin 3, [Ile5]pilosulin 1, and pilosulin 4.1 were recognized by 42 (78%), 18 (33%) and nine (17%) of the 54 sera that were tested. Immunoglobulin E-binding proteins with estimated molecular masses of 6.6, 22.8, 25.6, 30.4, 32.1, 34.4 and 89.8 kDa were each recognized by three or more individual sera. Two of these (25.6 and 89.8 kDa) were recognized by 46% and 37% of sera, respectively.

**Conclusion:** Nomenclature used to describe
JJA venom allergens has been revised. Pilosulin 3 (Myr p 2) is the only major allergen, whilst [Ile5]pilosulin 1 (Myr p 1), and pilosulin 4.1 (Myr p 3) are minor allergens. There are an additional five IgE-binding proteins that require further characterization before they can be named as allergens. These findings provide a framework for standardizing venom extracts for diagnosis and immunotherapy., Copyright (C) 2007 Blackwell Publishing Ltd.

The construct of generalized anxiety disorder in Alzheimer disease.
Starkstein SE, Jorge R, et al.
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OBJECTIVES: The objectives of this study were to examine the criterion validity in Alzheimer disease (AD) of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) and the International Classification of Diseases, 10th Revision (ICD-10) criteria for generalized anxiety disorder (GAD), to clarify the symptoms associated with excessive anxiety and worry in AD, to examine the co-occurrence of GAD and depression in these patients, and to determine the neuropsychologic and functional impact of GAD in AD. RESULTS: One hundred forty-four of a consecutive series of 552 patients with probable AD (26%) reported excessive anxiety and worry difficult to control for most of the 6 months before the psychiatric evaluation. Excessive anxiety and worry were significantly associated with restlessness, irritability, muscle tension, fears, and respiratory symptoms of anxiety. Using these symptoms as diagnostic criteria, 56 of the 552 patients (10%) met revised diagnostic criteria for GAD as compared with 15% when using DSM-IV criteria and 9% when using the ICD-10 criteria. GAD was present in 38 of the 144 patients (26%) with major depression and in 12 of the 261 patients (5%) without depression. Patients with both GAD and depression showed more severe cognitive deficits than patients with either GAD or depression only. CONCLUSION: The authors validated a set of diagnostic criteria for anxiety in dementia. These criteria include restlessness, irritability, muscle tension, fears, and respiratory symptoms in the context of excessive anxiety and worry. Anxiety in AD is a frequent comorbid condition of major depression.
Publication Types: Comparative Study
Evaluation Studies
Research Support, Non-U.S. Gov't
PMID:17194814

Iron absorption and hepatic iron uptake are increased in a transferrin receptor 2 (Y245X) mutant mouse model of hemochromatosis type 3.
Drake SF, Morgan EH, et al.
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Hereditary hemochromatosis type 3 is an iron (Fe)-overload disorder caused by mutations in transferrin receptor 2 (TfR2). TfR2 is expressed highly in the liver and regulates Fe metabolism. The aim of this study was to investigate duodenal Fe absorption and hepatic Fe uptake in a TfR2 (Y245X) mutant mouse model of hereditary hemochromatosis type 3. Duodenal Fe absorption and hepatic Fe uptake were measured in vivo by 59Fe-labeled ascorbate in TfR2 mutant mice, wild-type mice, and Fe-loaded wild-type mice (2% dietary carbonyl Fe). Gene expression was measured by real-time RT-PCR. Liver nonheme Fe concentration increased progressively with age in TfR2 mutant mice compared with wild-type mice. Fe absorption (both duodenal Fe uptake and transfer) was increased in TfR2 mutant mice compared with wild-type
mice. Likewise, expression of genes participating in duodenal Fe uptake (Dcytb, DMT1) and transfer (ferroportin) were increased in TfR2 mutant mice. Nearly all of the absorbed Fe was taken up rapidly by the liver. Despite hepatic Fe loading, hepcidin expression was decreased in TfR2 mutant mice compared with wild-type mice. Even when compared with Fe-loaded wild-type mice, TfR2 mutant mice had increased Fe absorption, increased duodenal Fe transport gene expression, increased liver Fe uptake, and decreased liver hepcidin expression. In conclusion, despite systemic Fe loading, Fe absorption and liver Fe uptake were increased in TfR2 mutant mice in association with decreased expression of hepcidin. These findings support a model in which TfR2 is a sensor of Fe status and regulates duodenal Fe absorption and liver Fe uptake.


Post-transplant HLA class II antibodies and high soluble CD30 levels are independently associated with poor kidney graft survival.
Langan LL, Park LP, et al.
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HLA-specific antibodies (HSA) and soluble CD30 (sCD30) were measured in 208 renal transplant recipients with functioning grafts at least 1 year after transplantation (median 8.2 years) to investigate the predictive value of HSA and sCD30 on subsequent graft outcome. HSA (class I and class II) were detected by both ELISA LAT-M and Luminex LabScreen assays. Data on graft outcome was collected with a median follow-up time of 3.5 years after antibody and sCD30 measurement. Recipients with post-transplant HLA class II antibodies had particularly poor graft outcome with a hazard ratio (HR) of 7.8 (p < 0.0001) when detected by ELISA, and a HR of 6.0 (p < 0.0001) when detected by Luminex. A high post-transplant sCD30 level >=100 U/mL was associated with increased risk of subsequent graft failure (HR 2.7, p = 0.03). sCD30 and HSA had an independent and additive association with graft outcome. Recipients with HLA class II antibody and high sCD30 had the highest risk of subsequent graft failure (HR 43.4, p < 0.0001 and HR 18.1, p = 0.0008 for ELISA and Luminex, respectively). These data show that detection of HSA and serum sCD30 measured at least 1-year post-transplant provides valuable and predictive information regarding subsequent graft outcome., Copyright (C) 2007 Blackwell Publishing Ltd.

Levosimendan in acute pulmonary embolism.
Powell BP, Simes D.
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Levosimendan has been used successfully in the treatment of ischaemic cardiac failure and myocardial stunning. There is growing evidence from both human and animal experiments that levosimendan has particularly favourable effects on the right ventricle. We describe a case of life-threatening pulmonary embolus supported by the use of levosimendan.
activated charcoal decreases the risk of QT prolongation after citalopram overdose.
Isbister GKMDF, Friberg LEP, et al.
From the Menzies School of Health Research, Charles Darwin University, Darwin, Australia (Isbister); the School of Pharmacy, University of Queensland, Brisbane, Australia (Isbister, Friberg, Duffull); the Discipline of Clinical Pharmacology, University of Newcastle, Newcastle, Australia (Isbister, Stokes); the Department of Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden (Friberg); the Department of Clinical Pharmacology and Toxicology, The Canberra Hospital, Canberra and Australian National University, Canberra, Australia (Buckley, Lee); the Department of Clinical Pharmacology and Toxicology, Westmead Hospital, Sydney, Australia (Gunja); the Emergency Department, Liverpool Hospital, Sydney, Australia (Gunja, Holdgate); the Emergency Department, Fremantle Hospital, Perth and University of Western Australia, Perth, Australia (Brown, MacDonald); the Clinical Toxicology Unit, Prince of Wales Hospital and Prince of Wales Clinical School, University of NSW, Randwick, Australia (Graudins); and the School of Pharmacy, University of Otago, New Zealand (Duffull).

Study objective: We determine whether single-dose activated charcoal (SDAC) administration after citalopram overdose reduces the proportion of patients developing abnormal QT prolongation. Methods: Data were collected retrospectively for citalopram overdose patients presenting to 8 emergency departments. Demographics, dose, coingested drugs, SDAC administration, and serial ECGs were extracted from medical records. The primary outcome was the proportion of patients who had an observed QT, RR combination at any time above an abnormal threshold, established as a predictor of torsade de pointes. We compared the proportion of patients with QT prolongation who received or did not receive SDAC. These data were analyzed within a Bayesian framework, using probabilities of abnormal QT, RR combinations with and without derived from a previous single-center study. WinBUGS was used to generate posterior estimates and credible intervals of the relative risk by combining the prior probabilities and the study data. Results: SDAC was administered on average 2.1 hours (range, 0.5 to 6.25 hours) after ingestion in 48 of 254 admissions, and abnormal QT, RR combinations occurred in 2 cases (4.2%), compared with 23 of 206 (11.2%) cases not receiving SDAC. There did not appear to be any clinically important difference in age, sex, dose, and cardiotoxic coingestants between the 2 groups. No cases of torsade de pointes occurred. The estimated relative risk of having an abnormal QT, RR combination for SDAC compared to no SDAC was 0.28 (0.06 to 0.70) (median with 2.5% and 97.5% credible limits). The probability that the relative risk was less than 1.0 was 0.99, which can be interpreted as very strong evidence in favor of a beneficial effect of SDAC. The absolute risk difference was estimated as 7.5% and the median number needed to treat as 13.3. Conclusion: SDAC may be effective in reducing the risk of a prolonged QT in patients after citalopram overdose. Current trends toward nonuse of activated charcoal should be evaluated to determine whether patients poisoned by specific agents may benefit from activated charcoal administration. (C) Mosby-Year Book Inc. 2007. All Rights Reserved.

nonalcoholic fatty liver disease.
Adams LA, Lindor KD.
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Nonalcoholic fatty liver disease (NAFLD) refers to the presence of hepatic steatosis not associated with a significant intake of ethanol. Insulin resistance is central to the pathogenesis of NAFLD; thus obesity, diabetes, and the metabolic syndrome are frequently associated with the disease. Consequently, as these metabolic conditions emerge as major health problems in Western society, it is now recognized that NAFLD is the most common chronic liver condition in the Western world. NAFLD is generally asymptomatic, although a minority of patients may present with evidence of progressive liver injury with complications of cirrhosis, liver failure, and hepatocellular carcinoma. Despite being common and potentially serious, relatively little is known about the natural history or prognostic significance of NAFLD. Although diabetes, obesity, and age are recognized risk factors for advanced liver disease, other significant factors leading to progressive liver injury remain to be identified. The treatment of NAFLD focuses upon modifying metabolic risk factors. Insulin-sensitizing and hepatoprotective drugs have been subjected to study trials, but as yet, no agent has conclusively been demonstrated to prevent disease progression. Management is further complicated by the inability to predict which patients will develop liver-related morbidity and thus benefit from treatment. copyright 2007 Elsevier Inc. All rights reserved.

Publication Types: Review
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Hypersensitivity reaction to amiodarone in a patient with a previous reaction to an iodinated radiocontrast agent.
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OBJECTIVE: To describe a case of a hypersensitivity reaction to oral amiodarone in a patient with a previous reaction to an iodinated radiocontrast agent. CASE SUMMARY: A 55-year-old man experienced facial urticaria after intraarterial injection of iohexol, an iodinated radiocontrast agent, during coronary angiography, which was successfully treated with intravenous hydrocortisone and promethazine. The procedure revealed significant triple vessel disease, and the patient subsequently underwent coronary artery bypass grafting in October 2006. Postoperatively, the patient experienced 2 episodes of fast atrial fibrillation, the first of which was treated successfully with intravenous amiodarone. The second episode resulted in the commencement of therapy with oral amiodarone 400 mg 3 times daily. Within one hour after the first dose, the patient experienced lip swelling and tingling, which was again treated with intravenous promethazine. Amiodarone was stopped; the patient remained in sinus rhythm and was discharged without further incident. DISCUSSION: Amiodarone is a class III antiarrhythmic agent frequently used in the management of atrial fibrillation after cardiac surgery. The approved product information lists known hypersensitivity to iodine as a contraindication to its administration, but no other cases of amiodarone hypersensitivity in a patient with a previous reaction to an iodinated radiocontrast agent have been published. Conversely, it has been suggested that the drug may be safely used in such patients. The Naranjo probability scale supported a probable adverse reaction of hypersensitivity associated with amiodarone therapy in this patient. CONCLUSIONS: Prescribers should exercise caution in the administration of amiodarone to patients with a true, documented history of hypersensitivity to an iodinated compound.
PMID:17609235
Assessment of the effect of mefloquine on artesunate pharmacokinetics in healthy male volunteers.
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The effect of mefloquine on artesunate pharmacokinetics was assessed in 20 volunteers given artesunate for 3 days, followed > or =21 days later by combination therapy for 3 days. The areas under the concentration-time curve from 0 h to infinity for dihydroartemisinin, the active metabolite of artesunate, were similar on day 3 of the two dosing periods (P = 0.12), implying no interaction.
PMID:17178798

Findlay M, Storey D, et al.
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Background: With poor cure rates in gastric cancer using surgery alone, the safety, efficacy and feasibility of preoperative and postoperative chemotherapy was investigated.
Methods: Patients with advanced but operable gastric or cardio-oesophageal adenocarcinoma were staged using endoscopy, computed tomography scan and laparoscopy. If considered potentially resectable, they received chemotherapy (epirubicin, cisplatin and 5-fluorouracil) for 9 weeks before and after surgery.
Results: Of 59 participants entered, two were found to have metastatic disease and were excluded from the analysis. Of the participants, 10 were women and 47 men; their median age was 58 years (range 27-83 years) and median performance status 0 (range 0-1). Two of the 57 participants commencing chemotherapy did not undergo surgery (one sudden death, one new liver metastases). Grade 3 and 4 preoperative and postoperative toxicity rates were, respectively, neutropenia 22 and 18%, emesis 12 and 14% and other non-haematological toxicity <10 and <10%. Of the 55 who underwent surgery, 40 had apparently curative resections (clear or positive microscopic margins), 2 died after surgery (anastomotic leak, sepsis) and 16 had postoperative complications. Of these, 27 participants commenced postoperative chemotherapy and 21 completed it. Median progression-free survival and overall survival were 19.6 and 22 months, respectively.
Conclusion: Epirubicin, cisplatin and protracted venous infusion of 5-fluorouracil chemotherapy was well-tolerated in the preoperative setting and did not appear to increase complication rates of surgery for advanced and operable stomach cancer. These findings demonstrate the feasibility of this strategy in the Australasian clinical setting and are in keeping with the results of a recently reported randomized trial, which demonstrated a significant survival advantage using this chemotherapy regimen.
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Homocysteine and abdominal aortic aneurysms.
Moroz P, Le MTQ, et al.
School of Surgery and Pathology, University of Western Australia, Fremantle Hospital, Perth, Western Australia, Australia.
There is evidence to suggest that increased levels of homocysteine play a significant role in vascular disease. It has been suggested that lowering homocysteine levels by dietary folate supplementation may reduce the risk of stroke and coronary heart disease. It is plausible that homocysteine may also play a role in the pathogenesis of abdominal aortic aneurysms (AAA) and that patients with this disease may benefit from folate supplementation. Our objective was to review the published work with regard to the role of homocysteine in the pathogenesis of AAA. Searches were carried out in published work in English with the keywords 'abdominal aortic aneurysm' and 'homocysteine'. There is evidence from in vitro and animal model studies that activation of metalloproteinases by homocysteine can influence aortic wall structure. Several case-control studies report an association between increased levels of homocysteine and the presence of an AAA. There are conflicting genotypic data concerning the association between methylenetetrahydrofolate reductase gene variants and AAA. Although there is evidence for an association between homocysteine and AAA, it is not strong enough to conclude that it plays a causal role in the pathogenesis of AAA. Further research is needed, given the potential benefit that simple vitamin supplementation may have for patients with AAA.
PMID:17497968

Vs20p trends in embolectomy of the extremities: a population-based study.
Fremantle Hospital, Western Australia, Australia.
Objective To assess community-wide temporal trends in the rates of embolectomy of the extremities over the period 1992-2003. Design Population-based study. Methods The Western Australian Linked Data System was used to identify cases of extremity embolectomy with a combination of diagnosis (upper or lower limb embolus) and procedure (embolectomy and revascularization) codes. Trends in age-specific and age-standardised rates were assessed over the period 1992-2003. Data regarding warfarin prescriptions was acquired from a separate Commonwealth Government database for the period 2000-2005. Results 1005 patients aged 30 years were admitted for an embolectomy of the extremity during the study period. The age specific rate of embolectomy increased with age from 0.78 per 100,000 in the 30-49 year old group to 46.1 per 100 000 for those aged over 80 years and over. There was a significant downward trend between 1992 and 2003 (Cuzik's trend test p = 0.015). This pattern was seen for all age groups. Prescriptions for warfarin increased by 50.4% over the period 2000-5. Conclusions The rates of embolectomy of the extremity appear to be falling. Although the cause for this trend is not known, one possible explanation is increasing prescription of warfarin.
PMID:17490011

Choroidal neovascularization from a presumed subretinal nematode.
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Publication Types: Journal Article
PMID:17846381

**Association between osteopontin and human abdominal aortic aneurysm.**

Golledge J, Muller J, et al.

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Objectives-: In vitro and animal studies have implicated osteopontin (OPN) in the pathogenesis of aortic aneurysm. The relationship between serum concentration of OPN and variants of the OPN gene with human abdominal aortic aneurysm (AAA) was investigated., Methods and Results-: OPN genotypes were examined in 4227 subjects in which aortic diameter and clinical risk factors were measured. Serum OPN was measured by ELISA in two cohorts of 665 subjects. The concentration of serum OPN was independently associated with the presence of AAA. Odds ratios (and 95% confidence intervals) for upper compared with lower OPN tertiles in predicting presence of AAA were 2.23 (1.29 to 3.85, P=0.004) for the population cohort and 4.08 (1.67 to 10.00, P=0.002) for the referral cohort after adjusting for other risk factors. In 198 patients with complete follow-up of aortic diameter at 3 years, initial serum OPN predicted AAA growth after adjustment for other risk factors (standardized coefficient 0.24, P=0.001). The concentration of OPN in the aortic wall was greater in patients with small AAAs (30 to 50 mm) than those with aortic occlusive disease alone. There was no association between five single nucleotide polymorphisms or haplotypes of the OPN gene and aortic diameter or AAA expansion., Conclusions-: Serum and tissue concentrations of OPN are associated with human AAA. We found no relationship between variation of the OPN gene and AAA. OPN may be a useful biomarker for AAA presence and growth., (C) 2007 American Heart Association, Inc.


**Refining a pain assessment self report tool for use with older adults in residential aged care.**

Toye C, Kristjanson L, et al.

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**Measurement of oedema in chronic venous disease using high frequency ultrasound: O31.**

Volikova AI, Wallace HJ, et al.

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**How Western Australian registrars choose training practices.**

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BACKGROUND: While general practice registrars receive advice on how to choose a training practice, little is known about what underlies their decision. METHOD: A questionnaire was sent to all registrars in Western Australian General Practice Education and Training practices seeking information about the choice of their practice. RESULTS: Most registrars reported that they had chosen their practice. The supervisor was most commonly the person spoken to before the practice was chosen. DISCUSSION: The supervisor’s personality was an important influence on choice and the practice manager was an important contact for registrars who were parents, presumably to arrange a part time attachment. Those who reported speaking to the supervisor also reported that they subsequently received greater remuneration. Registrars from a rural background chose more often to have all their training in a rural area. (author abstract) PMID:87093186

Type 2 diabetes mellitus: guidelines for initiating insulin therapy.
Yeap BB.
MBBS, FRACP, PhD, is Senior Lecturer in Medicine, University of Western Australia, and Head, Department of Endocrinology and Diabetes, Fremantle Hospital, Western Australia. BACKGROUND: Insulin is often indicated for patients with suboptimally controlled type 2 diabetes mellitus, despite lifestyle modification and oral antidiabetic agents. OBJECTIVE: This article outlines the initiation of insulin therapy for patients with type 2 diabetes in the general practice context. DISCUSSION: Insulin initiation options are bed time basal insulin (NPH, glargine) 10 U for patients with fasting hyperglycaemia, or twice daily premixed insulin (eg. aspart 30%/NPH 70%) 6-10 U twice per day targeting day time or postprandial hyperglycaemia. Basal insulin should be titrated regularly on a prophylactic basis (eg. fasting glucose <4.4 mmol/L: -2U, 4.4-7.0: +0 U, 7.1-10.0: +2 U, >10.0: +4 U) or increased by 1 U/day until fasting glucose of 5.5 mmol/L is reached. HbA1c changes of -1.5 to -2.5% are achievable with potential weight gain around 3 kg over 6 months. Approximately 50% of patients can achieve HbA1c <=7% with insulin doses around 40-70 U/day. Glitazones are an alternative to insulin, but for HbA1c, >/=9.5% insulin results in greater improvement in fasting glucose and HbA1c. Patients require education for blood glucose monitoring, healthy diet, exercise and identifying and responding to hypoglycaemia.
PMID:17619673

Prevalence rate of delirium at two hospitals in Western Australia.
Speed G, Wynaden D, et al.
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Objective: To estimate the prevalence of delirium in patients on 15 medical and surgical wards at two hospitals in Western Australia. Design: Following a review of the literature on delirium a standardised data collection tool was developed and four prevalence audits were conducted over a four week period at the target hospitals. The nurse coordinator on each ward was asked to identify any patient who was experiencing a delirium or who was confused. These patient’s records were then examined for documentation that confirmed the presence of delirium or confusion. Main outcome measures: The audit measured those patients with a confirmed documented delirium and identified patients who had a possible delirium superimposed on a confirmed or suspected dementia or unconfirmed organic brain disorder. Patients with a known dementia or organic brain disorder who displayed symptoms of confusion but had no evidence of delirium were also identified. Results: Of 1209 patients surveyed in four prevalence audits, 132 patients (10.9%) displayed behaviours suggestive of the presence of delirium; however only
48 of the 132 patients had a confirmed diagnosis of delirium. The remaining 84 patients displayed features of delirium that were superimposed on symptoms of dementia (diagnosed/undiagnosed) or an organic brain disorder. An additional 51 (4.2%) of the 1209 patients were identified with confusion resulting from other causes. Conclusions: Accurate assessment of delirium is particularly important in elderly people where behaviours associated with delirium are often assumed to be caused by dementia. This may result in delirium going undiagnosed and untreated. (author abstract)

Brain. 2007; 130(12): 3075-3090.

Anosognosia for hemiplegia after stroke is a multifaceted phenomenon: a systematic review of the literature.
Orfei MD, Robinson RG, et al.
(1)IRCCS Santa Lucia Foundation, Laboratory of Clinical and Behavioural Neurology, Rome, Italy, (2)The University of Iowa Carver College of Medicine, Iowa City, IA, USA, (3)Barrow Neurological Institute, Phoenix, Rome, Italy, (4)University of Western Australia and Fremantle Hospital, Fremantle, Rome, Italy, (5)Catholic University of the Sacred Heart, Rome, Italy, (6)Department of Neuroscience, University of Rome "Tor Vergata", Rome, Italy
Anosognosia is the lack of awareness or the underestimation of a specific deficit in sensory, perceptual, motor, affective or cognitive functioning due to a brain lesion. This self-awareness deficit has been studied mainly in stroke hemiplegic patients, who may report no deficit, overestimate their abilities or deny that they are unable to move a paretic limb. In this review, a detailed search of the literature was conducted to illustrate clinical manifestations, pathogenetic models, diagnostic procedures and unresolved issues in anosognosia for motor impairment after stroke. English and French language papers spanning the period January 1990-January 2007 were selected using PubMed Services and utilizing research words stroke, anosognosia, awareness, denial, unawareness, hemiplegia. Papers reporting sign-based definitions, neurological and neuropsychological data and the results of clinical trials or historical trends in diagnosis were chosen. As a result, a very complex and multifaceted phenomenon emerges, whose variable behavioural manifestations often produce uncertainties in conceptual definitions and diagnostic procedures. Although a number of questionnaires and diagnostic methods have been developed to assess anosognosia following stroke in the last 30 years, they are often limited by insufficient discriminative power or a narrow focus on specific deficits. As a consequence, epidemiological estimates are variable and incidence rates have ranged from 7 to 77% in stroke. In addition, the pathogenesis of anosognosia is widely debated. The most recent neuropsychological models have suggested a defect in the feedforward system, while neuro-anatomical studies have consistently reported on the involvement of the right cerebral hemisphere, particularly the prefrontal and parieto-temporal cortex, as well as insula and thalamus. We highlight the need for a multidimensional assessment procedure and suggest some potentially productive directions for future research about unawareness of illness., (C) Guarantors of Brain 2007. Published by Oxford University Press. All righs reserved.


Levosimendan in septic shock: a case series.
Powell BP, De Keulenaer BL.
Publication Types: Letter
PMID:17702832
Schizophrenia outcome measures in the wider international community.
Isaac M, Chand P, et al.
Community, Culture and Mental Health Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, Australia. Mohan.Isaac@uwa.edu.au

BACKGROUND: Outcome of schizophrenia has been described as favourable in low- and middle-income countries. Recently, researchers have questioned these findings. AIMS: To examine the outcome studies carried out in different countries specifically looking at those from low- and middle-income countries. METHODS: Long-term course and outcome studies in schizophrenia were reviewed. RESULTS: A wide variety of outcome measures are used. The most frequent are clinical symptoms, hospitalisation and mortality (direct indicators), and social/occupational functioning, marriage, social support and burden of care (indirect indicators). Areas such as cognitive function, duration of untreated psychosis, quality of life and effect of medication have not been widely studied in low- and middle-income countries. CONCLUSIONS: The outcome of schizophrenia appears to be better in low- and middle-income countries. A host of sociocultural factors have been cited as contributing to this but future research should aim to understand this better outcome. There is a need for more culture-specific instruments to measure outcomes.

Identification of nestin-positive putative mammary stem cells in human breastmilk.
(Cregan, Appelbee, Brown, Koppen, Piper, Hartmann) School of Biomedical, Biomolecular and Chemical Sciences, Faculty of Life and Physical Sciences, M310, University of Western Australia. 35 Stirling Highway, Crawley, WA 6009, Australia.

Stem cells in mammary tissue have been well characterised by using the mammary stem cell marker, cytokeratin (CK) 5 and the mature epithelial markers CK14, CK18 and CK19. As these markers have never been reported in cells from breastmilk, the aim of this study has been to determine whether mammary stem cells are present in expressed human breastmilk. Cultured cells from human breastmilk were studied by using immunofluorescent labelling and reverse transcription/polymerase chain reaction (RT-PCR). We found a heterogeneous population of cells with differential expression of CK5, CK14, CK18 and CK19. Further, by using the multipotent stem cell marker, nestin, we identified cells in culture that were positive only for nestin or double-positive for CK5/nestin, whereas no co-staining was observed for CK14, CK18 and CK19 with nestin. When cells isolated from breastmilk were analysed by using RT-PCR prior to culture, only nestin and CK18 were detected, thereby indicating that breastmilk contained differentiated epithelial and putative stem cells. Furthermore, fluorescence-activated cell-sorting analysis demonstrated, in breastmilk, a small side-population of cells that excluded Hoechst 33342 (a key property of multipotent stem cells). When stained for nestin, the cells in the side-population were positive, whereas those not in the side-population were negative. The presence of nestin-positive putative mammary stem cells suggests that human breastmilk is a readily available and non-invasive source of putative mammary stem cells that may be useful for research into both mammary gland biology and more general stem cell biology. copyright 2007 Springer-Verlag.

Publication Types: Journal Article
PMID:2007219634
Obesity, adipokines, and abdominal aortic aneurysm: Health in Men Study.
Golledge JMFF, Clancy PP, et al.
From the Vascular Biology Unit, School of Medicine, James Cook University, Townsville, Australia (J.G., P.C.); School of Population Health, University of Queensland, Herston, Queensland, Australia (K.J.); and School of Surgery and Pathology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia (P.E.N.).

Background-: Obesity is associated with occlusive artery disease but is not considered a risk factor for abdominal aortic aneurysm (AAA). We investigated the association between anthropometric measures of obesity, serum adipokines, and AAA.

Methods and Results-: As part of a population study, we screened 12 203 men 65 to 83 years of age for AAA using ultrasound; 875 had an AAA (>=30 mm). Cardiovascular risk factors and waist and hip circumference were recorded. Serum adipokines were measured in 952 men, 318 of whom had an AAA. Waist circumference (odds ratio [OR], 1.14; 95% confidence interval [CI], 1.06 to 1.22) and waist-to-hip ratio (OR, 1.22; 95% CI, 1.09 to 1.37) were independently associated with AAA after adjustment for other known risk factors. The association was stronger for AAA >=40 mm (waist-to-hip ratio: OR, 1.53; 95% CI, 1.26 to 1.85). Serum resistin concentration was strongly independently associated with AAA (OR, 1.53; 95% CI, 1.32 to 1.76) and aortic diameter ([beta]=0.19, P<0.0001). Serum adiponectin was associated with AAA >=30 mm (OR, 1.26; 95% CI, 1.07 to 1.50) but not AAA >=40 mm (OR, 1.03; 95% CI, 0.77 to 1.39). Serum leptin was not associated with AAA.

Conclusions-: Measures of obesity are independently associated with AAA. Serum resistin concentrations were more strongly associated with aortic diameter than adipokines that are more intimately associated with adiposity. Further studies are required to investigate the mechanisms linking resistin and AAA.

Abdominal aortic aneurysm: the prognosis in women is worse than in men.
Norman PE, Powell JT.
Prof. P.E. Norman, School of Surgery and Pathology, Fremantle Hospital, PO Box 480, Fremantle, WA 6959; Australia. E-Mail: paul.norman@uwa.edu.au.

Clinical Biomechanics. 2007; 22(1): 100-5.
A comparison of conventional versus locking plates in intraarticular calcaneus fractures: a biomechanical study in human cadavers.
Fremantle Orthopaedic Unit, University of Western Australia, Alma Street, B. Block, Level 6, Fremantle, Western Australia 6160, Australia. nkstoffel@hotmail.com

BACKGROUND: Internal fixation of displaced intraarticular calcaneal fractures in patients older than 50 years remains controversial. This is, in many cases, due to fear of loss of fixation and the risk of implant failure in osteoporotic bone. It is the objective of this study to compare the fixation strength obtained using calcaneal plates with and without locking screws, in the fixation of osteoporotic cadaveric intraarticular calcaneal fractures. METHODS: In seven pairs of fresh frozen lower limbs cadavers, intraarticular calcaneal fractures were created with a dynamic single impact loading device and stabilized using either the low profile locking plate, or the conventional calcaneus plate. Radiographs were obtained to assess reduction. The specimens were then subjected to cyclic loading followed by loading to failure, using matched pairs of cadaveric lower limbs. The Wilcoxon signed rank test was used to test for differences in the
results. FINDINGS: The locking plate showed a significant lower irreversible deformation during cyclic loading and a significant higher load to failure. The difference between the ultimate displacement, and work to failure was not significant. A low bone mineral content in the area of the posterior facet correlated only in the conventional plate group with increased irreversible deformation. INTERPRETATION: This study supports the mechanical viability of using locking calcaneal plates for the fixation of intraarticular calcaneal fractures in elderly patients.

PMID:17007974


Changes in biochemical markers after lower limb fractures.
Department of Orthopaedic Surgery, University of Western Australia, Fremantle, Western Australia, Australia.

BACKGROUND: The bone remodeling sequence after bone fracture changes the concentrations of biochemical bone markers, but the relationships of fracture size and of healing time to changes in biomarkers are unclear. The present pilot study was undertaken to determine the changes found in serum bone markers after plate osteosynthesis of closed distal tibial and malleolar fractures during a study period of 24 weeks. METHODS: We measured tartrate-resistant acid phosphatase (TRACP 5b), collagen type I C-terminal telopeptide (ICTP), bone-specific alkaline phosphatase (bone ALP), osteocalcin (OC), procollagen type I C-terminal propeptide (PICP), procollagen type III N-terminal propeptide (PIIINP), and human cartilage glycoprotein 39 (YKL-40) in 20 patients with lower limb fractures (10 malleolar, 10 tibia). A physical examination and radiographs were completed to assess evidence of union. RESULTS: All malleolar fractures healed within 6 weeks, whereas 2 tibial fractures did not show complete bone healing after 24 weeks. Changes were comparable but more pronounced in the tibia group, and marker concentrations remained increased at the end of study (bone ALP, 86 vs 74 U/L; OC, 14.9 vs 7.7 microg/L; ICTP: 5.6 vs 3.3 microg/L at day 84 after osteosynthesis, P <0.05 in tibia; 80 vs 70 U/L, 8 vs 5.2 microg/L, and 3.5 vs 3.2 microg/L, respectively, in the malleolar fracture group). CONCLUSIONS: In normal bone healing, changes in bone turnover markers were primarily dependent on the fracture size. Delayed tibia fracture healing may involve a disturbance in bone remodeling.

PMID:17130179


Cryptococcal immune reconstitution inflammatory syndrome following alemtuzumab therapy.
Ingram PR, Howman R, et al.
Department of Infectious Diseases, Fremantle Hospital, Fremantle, Western Australia, Australia.
Alemtuzumab is a lymphocyte ablative agent that may cause susceptibility to severe opportunistic infections similar to those seen in AIDS. Pathogen-specific immune reconstitution syndromes can complicate antiretroviral therapy and immune recovery in HIV-infected patients. We present the first reported case of immune reconstitution syndrome associated with T lymphocyte recovery after alemtuzumab therapy.

Publication Types: Case Reports
PMID:17516390


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.
PMID:16804736

The incidence of anastomotic leaks in patients undergoing colorectal surgery.
Platell C, Barwood N, et al.
Colorectal Surgical Unit, Fremantle Hospital, Fremantle, WA, Australia.
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BACKGROUND: There is evolving interest in auditing and credentialling the performance of surgeons. The incidence of anastomotic leakage has been proposed as a measure of performance following colorectal surgery. The aim of this study was to evaluate the incidence and risk factors associated with anastomotic leakage in patients undergoing resections of the colon and rectum. METHODS: A prospective database was developed for all patients undergoing colorectal surgery. Anastomotic leakage was defined prior to the commencement of the study. A logistic regression analysis was performed to determine independent predictors of leakage. The variables analysed included age, sex, American Society of Anesthesiology (ASA) score, anatomical location, pathology, emergency surgery, type of anastomosis, a covering stoma and radiotherapy. Significance was defined as the probability of a type 1 error of < 5%. The results are presented as odds ratios (ORs) and 95% confidence intervals (95% CIs).
RESULTS: There were 1598 patients who underwent 1639 anastomoses. Their mean age was 63 years, 34% of patients were ASA 3 or 4, and 16% of the operations were emergencies. Anastomotic leaks occurred in 2.4% (40/1639) of anastomoses. The leak rate for intraperitoneal anastomoses was 1.5% (19/1283) vs 6.6% for extraperitoneal anastomoses (21/316). Half of these leaks (20/40) were managed with re-operation or percutaneous drainage procedures. Ultra-low anterior resections were associated with the highest leak rate (8%, 18/225). A logistic regression analysis identified a covering stoma (P = 0.0001, OR 5.078, 95% CI 2.527-10.23) and diverticular disease (P = 0.037, OR 2.304, 95% CI 1.053-5.042) as independent predictors of a leak. CONCLUSIONS: Within this surgical unit, the incidence of leaks from intraabdominal anastomoses was relatively low. However, leaks in patients undergoing extraperitoneal anastomoses continue to be a major cause of morbidity and mortality.
PMID:17181849

Matrix biology of abdominal aortic aneurysms in diabetes: mechanisms underlying the negative association.
Norman PE, Davis TME, et al.
School of Surgery and Pathology, University of Western Australia. Fremantle. Western Australia.
Several case-control studies have shown a significant negative association between diabetes and abdominal aortic aneurysm (AAA). This interaction has the potential to further our understanding of these two diseases but has attracted little research. The changes seen in the walls of aneurysmal aortas include inflammation and the activation of proteolytic pathways
resulting in loss of elastin and other structural proteins. In contrast, diabetes is associated with increased synthesis and reduced degradation of matrix. The deposition of advanced glycation end products also renders vascular matrix resistant to proteolysis in diabetic patients. The aim of our present minireview is to compare the changes in matrix biology seen in diabetes and AAA and to explore molecular mechanisms that may explain the negative association and identify possible therapeutic implications.

PMID:17522995

Is there a place for levosimendan in the intensive care unit?
Simes DC.
Intensive Care Unit, Fremantle Hospital, Fremantle, WA. David.Simes@health.wa.gov.au.
Publication Types: Journal Article
PMID:18052906

Nitrogen challenge: are we any closer to achieving a balance?
De Keulenaer BL, Jenkins I.
Dr. B.L. De Keulenaer, Intensive Care, Fremantle Hospital, Fremantle, WA; Australia.
Publication Types: Editorial
PMID:2007010941

The regulation of cellular iron metabolism.
Chua ACG, Graham RM, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle, Western Australia, Australia.
While iron is an essential trace element required by nearly all living organisms, deficiencies or excesses can lead to pathological conditions such as iron deficiency anemia or hemochromatosis, respectively. A decade has passed since the discovery of the hemochromatosis gene, HFE, and our understanding of hereditary hemochromatosis (HH) and iron metabolism in health and a variety of diseases has progressed considerably. Although HFE-related hemochromatosis is the most widespread, other forms of HH have subsequently been identified. These forms are not attributed to mutations in the HFE gene but rather to mutations in genes involved in the transport, storage, and regulation of iron. This review is an overview of cellular iron metabolism and regulation, describing the function of key proteins involved in these processes, with particular emphasis on the liver's role in iron homeostasis, as it is the main target of iron deposition in pathological iron overload. Current knowledge on their roles in maintaining iron homeostasis and how their dysregulation leads to the pathogenesis of HH are discussed.
Publication Types: Journal Article
PMID:17943492

Schimke K, Davis TME.
University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, PO
Daiichi Sankyo Inc is developing rivoglitazone, an insulin sensitizer with peroxisome proliferator-activated receptor gamma agonistic activity, for the potential treatment of type 2 diabetes. By March 2006, phase I/III clinical trials were underway in the US and the EU.

**Self-monitoring of blood glucose in type 2 diabetes: steps toward consensus.**
Bot S, Davis TME, et al.
(Davis) School of Medicine and Pharmacology, Fremantle Hospital. P.O. Box 480, Fremantle, WA 6959, Australia.
Publication Types: Letter
PMID:2007494291

**An assessment of eligibility for inhaled insulin (Exubera): the Fremantle Diabetes Study.**
Davis TME, Davis WA.
School of Medicine and Pharmacology, Fremantle Hospital, P.O. Box 480, Fremantle, WA 6959, Australia. tdavis@cyllene.uwa.edu.au
PMID:17259508

To determine whether the metabolic syndrome (MS) predicts fatal outcome in type 1 diabetes, we assessed prospective data from 127 patients from the observational community-based Fremantle Diabetes Study. Causes of death were classified as cardiac or other. The mean+/− S.D. age of the patients was 42.0+/−15.7 years and 57.5% were male. MS defined by the World Health Organisation (WHO), National Cholesterol Education Program's Adult Treatment Panel (ATP) III and the International Diabetes Federation (IDF) consensus definitions was present in 44.9, 42.1 and 39.4% of patients, respectively. There were 29 deaths (22.8%) during a mean of 11.0 years of follow-up, 55% of which were cardiac. In Cox proportional hazards models incorporating all plausible contributory variables (including individual MS components), none of the definitions was independently associated with cardiac or all-cause death (p>/=0.49 in each case). When component variables were removed, the WHO definition weakly predicted cardiac death (p=0.045). Microalbuminuria was a significant predictor of cardiac mortality (p</=0.001). A minority of our community-based type 1 patients had the MS and its presence did not add significant prognostic predictive value to conventional vascular risk factors.
PMID:17645979

**Cardiovascular risk factors in pre-pubertal Malays: effects of diabetic parentage.**
Choo KE, Lau KB, et al.
Faculty of Medicine and Health Sciences, Universiti Malaysia Sarawak, Kuching, Malaysia.
Diabetes prevalence is increasing rapidly in Asian populations but the influence of a family history of diabetes on cardiovascular risk is unknown. To assess this relationship, 120 urban-dwelling Malays were recruited to a cross-sectional case-control study. Sixty were pre-pubertal children, 30 of diabetic parentage (Group 1) and 30 with no diabetes family history (Group 2). Group 1 and 2 subjects were the offspring of adults with (Group 3) or without (Group 4) type 2 diabetes. Subjects were assessed for clinical and biochemical variables defining cardiovascular risk. Principal component analysis assessed clustering of variables in the children. Group 1 subjects had a higher mean waist:hip ratio, diastolic blood pressure and HbA(1c) than those in Group 2, and a lower HDL:total cholesterol ratio (P<0.03). Although there were no correlations between Group 1 and 3 subjects for cardiovascular risk variables, significant associations were found in Groups 2 and 4, especially HbA(1c) and insulin sensitivity (P< or =0.004). Of five separate clusters of variables (factors) identified amongst the children, the strongest comprised diabetic parentage, HbA(1c), insulin sensitivity and blood pressure. Features of the metabolic syndrome are becoming evident in the young non-obese children of diabetic Malays, suggesting that lifestyle factors merit particular attention in this group.

PMID:16979774


Monocyte-derived macrophages from men and women with Type 2 diabetes mellitus differ in fatty acid composition compared with non-diabetic controls.
School of Medicine and Pharmacology, University of Western Australia, Fremantle and Royal Perth Hospitals, Western Australia, Australia.

We examined whether macrophages from men and women with Type 2 diabetes mellitus (T2DM) exhibited differences in expression of key genes involved in fatty acid metabolism and in fatty acid composition compared with macrophages from non-diabetic controls. Peripheral blood monocytes from subjects with T2DM (n=9) and non-diabetic controls (n=10) were differentiated into macrophages in 10% autologous serum and normal (5mM) or high (22mM) glucose. Levels of PPARalpha, PPARgamma, LXRalpha, SCD and ABCA1 mRNAs were similar in macrophages from subjects with T2DM and controls. At 5mM glucose, macrophage stearic acid (C18:0) was 12.6+/−1.0% of total fatty acids for T2DM compared with 18.1+/−2.0% for controls (p=0.03). Macrophage linoleic acid (C18:2) was 15.5+/−0.8% for T2DM and 9.3+/−2.0% for controls (p=0.005). The ratio of macrophage stearic acid (C18:0)/oleic acid (C18:1) was 0.29 [0.25,0.48] for T2DM versus 0.54 [0.36,0.82] for controls (p=0.04). Compared with non-diabetic controls, macrophages from men and women with T2DM had significantly different fatty acid profiles consistent with increased stearoyl-CoA desaturase (SCD) activity and increased C18:2 accumulation. This pattern of altered macrophage fatty acid composition may be relevant to diabetic atherogenesis.

PMID:16908084


Common infections in diabetes: Pathogenesis, management and relationship to glycaemic control.
Peleg AY, Weerarathna T, et al.
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Specific defects in innate and adaptive immune function have been identified in diabetic patients in a range of in vitro studies. However, the relevance of these findings to the integrated response to infection in vivo remains unclear, especially in patients with good glycaemic control.
Vaccine efficacy seems adequate in most diabetic patients, but those with type 1 diabetes and high glycosylated haemoglobin levels are most likely to exhibit hyporesponsiveness. While particular infections are closely associated with diabetes, this is usually in the context of extreme metabolic disturbances such as ketoacidosis. The link between glycaemic control and the risk of common community-acquired infections is less well established but could be clarified if infection data from large community-based observational or intervention studies were available. The relationship between hospital-acquired infections and diabetes is well recognized, particularly among post-operative cardiac and critically ill surgical patients in whom intensive insulin therapy improves clinical outcome independent of glycaemia. Nevertheless, further research is needed to improve our understanding of the role of diabetes and glycaemic control in the pathogenesis and management of community- and hospital- acquired infections.

Copyright 2006 John Wiley & Sons, Ltd.
Publication Types: Review
PMID:2007053110

Silent myocardial infarction is an independent risk factor for fatal myocardial infarction in patients with Type 2 diabetes: A39.
Cull CA, Davis TM, et al.
(*)Diabetes Trials Unit, University of Oxford, Oxford, UK, (+)School of Medicine and Pharmacology, University of Western Australia, Fremantle, Western Australia

Davis WA, Bruce DG, 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: To assess whether self-monitoring of blood glucose (SMBG) is an independent predictor of improved outcome in a community-based cohort of type 2 diabetic patients. MATERIALS AND METHODS: We used longitudinal data from (1) 1,280 type 2 diabetic participants in the observational Fremantle Diabetes Study (FDS) who reported SMBG and diabetes treatment status at study entry (1993-1996), and (2) a subset of 531 participants who attended six or more annual assessments (referred to as the 5-year cohort). Diabetes-related morbidity, cardiac death and all-cause mortality were ascertained at each assessment, supplemented by linkage to the Western Australian Data Linkage System. RESULTS: At baseline, 70.2% (898 out of 1,280) of type 2 patients used SMBG. During 12,491 patient-years of follow-up (mean 9.8 +/- 3.5 years), 486 (38.0%) type 2 participants died (196 [15.3%] from cardiac causes). SMBG was significantly less prevalent in those who died during follow-up than in those who were still alive at the end of June 2006 (65.4 vs 73.0%, p = 0.005). In Cox proportional hazards modelling, after adjustment for confounding and explanatory variables, SMBG was not independently associated with all-cause mortality, but was associated with a 79% increased risk of cardiovascular mortality in patients not treated with insulin. For the 5-year cohort, time-dependent SMBG was independently associated with a 48% reduced risk of retinopathy. CONCLUSIONS/INTERPRETATION: SMBG was not independently associated with improved survival. Inconsistent findings relating to the association of SMBG with cardiac death and retinopathy may be due to confounding, incomplete covariate adjustment or chance. PMID:17237940

**Botulinum toxin injection to facilitate rehabilitation of muscle imbalance syndromes in sports medicine.**

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Intramuscular injection of Botulinum toxin to produce reduction of focal muscle overactivity, and localized muscle spasm, has been utilized therapeutically for almost two decades. Muscle overactivity in neurologically normal muscle, where an imbalance exists between a relatively overactive muscle and its less active synergist or antagonist, can inhibit control of the antagonist producing a functional muscle imbalance. This brief review provides an overview of the role of muscle imbalance in sports-related pain and dysfunction, and outlines the potential for intramuscular injection of Botulinum toxin to be used as an adjunct to specific muscle re-education and functional rehabilitation in this patient group. A comprehensive understanding of normal movement and the requirements of the sporting activity are essential to allow accurate diagnosis of abnormal motor patterns and to re-educate more appropriate movement strategies. Therapeutic management of co-impairments may include stretching of tight soft tissues, specific re-education aimed at isolation of the non-dominant weak muscles and improvement in their activation, 'unlearning' of faulty motor patterns, and eventual progression onto functional exercises to anticipate gradual return to sporting activity. Intramuscular injection of Botulinum toxin, in carefully selected cases, provides short term reduction of focal muscle overactivity, and may facilitate activation of relatively 'inhibited' muscles and assist the restoration of more appropriate motor patterns. [References: 56]

Publication Types: Review
PMID:18033608


**Fluid skills: drinking games and alcohol consumption among Australian university students.**

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The objective of this study was to assess participation in drinking games among Australian university students; to determine the range of games played, their context and participant motivations; and to analyse the impact of games on alcohol consumption and its adverse consequences. We used a cross-sectional survey incorporating structured interviews and a self-administered questionnaire with students between 18 and 25 years of age at the University of Western Australia. This was a qualitative assessment of drinking game typology and contexts and participant motivation. Quantitative outcomes were rate and frequency of participation in drinking games; amount and rate of alcohol consumption during games; incidence of adverse outcomes following participation. Twenty-seven interview responses and 256 questionnaire responses were analysed for qualitative and quantitative outcomes, respectively. The qualitative analysis enabled categorisation of drinking games by skill and competitive nature, with varying influence on hazardous drinking. Common reported motivations for play included boredom, social pressure and social unease. The associated heavy drinking and possible hazards were well recognised but did not affect the decision to play. In the quantitative arm, most drinkers (74%) reported having participated in a drinking game. Game players reported playing an average of four drinking games in the previous 6 months. An average of six standard drinks was consumed during the most recent game. Pressure to participate from others was reported by 60% of game participants, while 50% reported that they had placed pressure on others to
participate. Half (51%) reported an adverse outcome following participation. Loss of consciousness due to drinking was experienced or witnessed by 89% of game players, of whom 63% reported that the person was put to bed, while 54% reported that the person was watched. Participation in drinking games was common, and plays an important social role in this group. Drinking games were associated commonly with binge drinking and adverse outcomes. Future harm minimisation strategies targeting this group should address the particular risks of these games. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract). PMID: Peer Reviewed Journal: 2007-12973-002


Flexible low-intensity combination chemotherapy for elderly patients with acute myeloid leukaemia: a multicentre, phase II study.
Manoharan A, Reynolds J, et al.
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Objective: To evaluate the efficacy of a flexible low-intensity combination chemotherapy (FLICC) protocol in a multicentre, phase II study of elderly patients with acute myeloid leukaemia (AML).

The median durations of significant neutropenia (<0.5 x 10^9/L) and thrombocytopenia (<20 x10^9/L) with the first course of treatment in the 19 evaluable patients were 19 days (range 12-26) and 11 days (range 1-25), respectively. The median duration of stay in the hospital was 27 days (range 14-42). These values were much shorter for the second course of treatment: 6 days, 5 days and 15 days, respectively.

Method: Twenty-five patients aged 61-78 years (median 70 years) with de novo (n = 17) or secondary (n = 8) AML (cytogenetic risk: favourable 2, intermediate 18, adverse 2, unknown 3) from eight Australian centres were enrolled. Treatment comprised mitoxantrone 6 mg/m2 intravenously daily for 3 days, cytarabine 10mg/m2 subcutaneously every 12 hours for 7-14 days and etoposide 100mg orally for 7-14 days.

The median durations of significant neutropenia (<0.5 x 10^9/L) and thrombocytopenia (<20 x10^9/L) with the first course of treatment in the 19 evaluable patients were 19 days (range 12-26) and 11 days (range 1-25), respectively. The median duration of stay in the hospital was 27 days (range 14-42). These values were much shorter for the second course of treatment: 6 days, 5 days and 15 days, respectively.

Results: The treatment was generally well tolerated, and 13 patients (52%) achieved a complete remission (CR). One patient achieved a partial remission but died on day 28 due to pneumonia. Five patients (20%) had no response, whilst six (24%) died on or before day 30 and so were not evaluable. The median overall survival (OS) was 6.5 months, and the median remission duration was 7.7 months. Estimated 1-year survival was 32%, but patients achieving CR had an estimated 1-year survival of 64%, whereas none in the non-CR group survived to 1 year. Two of the CR patients have survived beyond 2 years. OS was significantly shorter in the adverse cytogenetic risk group of patients compared with the favourable- and intermediate-risk groups, with the rates of death relative to the adverse group being 0.02 and 0.08 in the favourable- and intermediate-risk groups, respectively. There was no significant association between CR rate and pre-existing myelodysplasia or the presence of multilineage dysplasia.

The median durations of significant neutropenia (<0.5 x 10^9/L) and thrombocytopenia (<20 x10^9/L) with the first course of treatment in the 19 evaluable patients were 19 days (range 12-26) and 11 days (range 1-25), respectively. The median duration of stay in the hospital was 27 days (range 14-42). These values were much shorter for the second course of treatment: 6 days, 5 days and 15 days, respectively.

Conclusion: The findings of this multicentre, phase II study validate the previously reported single-institution experience with the FLICC protocol in elderly patients with AML. The clinical outcome with this protocol is
comparable to those reported with more aggressive anti-leukaemia protocols., Copyright 2007 Adis Data Information BV

Drugs & Aging. 2007; 24(7): 547-554.

Epidemiology and management of apathy in patients with Alzheimer's Disease.
Mizrahi R, Starkstein SE.
(1) PET Center, Centre for Addiction and Mental Health (CAMH), Toronto, Ontario, Canada, (2) Department of Psychiatry, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada, (3) School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, Western Australia, Australia, (4) Fremantle Hospital, Fremantle, Western Australia, Australia

Although apathy is a diagnostic term used with increasing frequency in both neurology and psychiatry, confusion still exists as to its proper definition and assessment, and whether apathy should be considered a symptom of major psychiatric diseases or an independent syndrome in its own right. Moreover, critical questions regarding the phenomenology and clinical correlates of apathy and the syndromic validity of this construct still exist. Despite these nosological concerns, there is strong evidence that apathy is a common finding in Alzheimer's disease (AD). However, the treatment of apathy is still elusive. Current data are obtained from randomised controlled trials that did not investigate apathy per se, but rather a number of other behavioural and psychological variables. In this context, acetylcholinesterase inhibitors and psychosocial interventions are the only available modalities for treating apathy in AD with some efficacy., Copyright 2007 Adis Data Information BV


Surviving atlanto-occipital dislocation.
Bloom BM, Powell BP.
Intensive Care Unit, Fremantle Hospital, Alma Street, Fremantle, West Australia, Australia.

Traumatic atlanto-occipital dislocation carries a significant mortality and morbidity. We present the clinical and radiological features of a case of traumatic skeletal and central nervous system disunion. Thanks to a combination of early resuscitation and luck, the patient survived an improbably severe injury to leave hospital and enjoy a degree of independent life. Such severe injuries are usually fatal and the literature on such extensive cervical disruption is often confined to postmortem evidence.

Publication Types: Journal Article
PMID:17655644


Route of administration of redback spider bite antivenom: Determining clinician beliefs to facilitate Bayesian analysis of a clinical trial.
Brown SGA, Isbister GK, et al.
Discipline of Emergency Medicine, University of Western Australia and Fremantle Hospital, Fremantle, West Australia, Australia.

Objective: To determine current beliefs of Australasian emergency physicians, to form the basis of 'stopping rules' for a clinical trial of intravenous (i.v.) versus intramuscular (i.m.) redback spider antivenom. Methods: An email survey of fellows and trainees of the Australasian College for Emergency Medicine. Results: There were 218 responses; 30% used the i.v. route exclusively, 16% used the i.m route exclusively, 17% used i.m. followed by i.v. if there was a poor initial clinical response, and 38% stated that they had no particular preference. The probability given by respondents that the i.v. route is superior allowed us to differentiate 'i.v.
enthusiasts' from 'i.v. sceptics'. Median predicted response rates were 90% versus 80% for the i.v. route and 60% versus 75% for the i.m. route in the enthusiastic and sceptical groups, respectively. The median expected absolute advantage of i.v. compared with i.m. antivenom was 20% versus 5%, respectively. The median number-needed-to-treat threshold that would lead respondents to choose the i.v. route in preference to the i.m. was 5. Conclusion: Australasian emergency physicians have polarized views on the optimal route for administering redback spider antivenom. We were therefore able to define both sceptical and enthusiastic priors for a fully Bayesian trial analysis. Our findings support using a number needed to treat of 5 (20% absolute advantage) for powering a clinical study and for determining the point at which it should be stopped.

Conclusion: A conclusion is provided about the polarized views of Australasian emergency physicians on the optimal route for administering redback spider antivenom. The study supports using a number needed to treat of 5 (20% absolute advantage) for powering a clinical study and for determining the point at which it should be stopped.

Publication Types: Journal Article
PMID:17919219

Electronic injury surveillance in Perth emergency departments: validity of the data.
Gillam CMPH, Meuleners LP, et al.
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Objective: To assess the validity of data collected by a new injury surveillance system in metropolitan public hospital ED in Western Australia.
Methods: A reference group of four experts used text descriptions recorded in the injury surveillance system to independently assign codes for intent and cause of injury for each case in the sample. These codes were then compared with the intent and cause codes which triage nurses had assigned to these cases. The level of agreement between these codes were assessed by means of descriptive statistics. Systematic coding errors were also identified and analysed.
Results: Of the 419 cases with adequate text descriptions, triage nurses agreed with the reference group of experts in 91.9% (intent) and 79.2% (cause) of cases. Falls accounted for 28.6% (n = 120) of cases and falls code agreement was 86.7%. Self-harm accounted for 5.3% (n = 22) of cases and self-harm code agreement was 77.3%. Systematic errors were detected in the coding of agent of injury, the underlying mechanism of injury and falls involving a mode of transport.
Conclusions: The new injury surveillance system can be successfully used in ED and provides a valid mechanism for monitoring injuries. Refinements to reduce systematic coding errors might improve the validity and quality of the data. A larger sample is needed to assess the validity of the self-harm code.

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Anaphylaxis update.
Brown SG.
University of Western Australia and Fremantle Hospital, Fremantle, WA

Emergency medicine in the developing world.
Curry C.
Fremantle Hospital, Fremantle, WA
Levosimendan: a new option in acute septic cardiac failure?
Powell BP, De Keulenaer B.
Intensive Care Unit, Fremantle, Western Australia, Australia.
PMID:17448109

Splenic artery aneurysm rupture: case report of this uncommon presentation.
Mattick A, Gawthrope I.
Dr Anthony Mattick, Department of Emergency Medicine, Fremantle Hospital, Alma Street, Fremantle, WA 6160, Australia; anthonymattick@hotmail.com.
Rupture of a splenic artery aneurysm remains an uncommon cause of hypovolaemic shock in the emergency department. This case report highlights that rapid resuscitation, diagnostic imaging, surgical consultation, and subsequent laparotomy remain the priorities in patient management.
PMID:18029530

An audit of compliance with motor traffic regulations and use of green warning lights by consultants recalled to hospital to attend emergencies.
Pring DW, Young RA, et al.
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Objectives: To determine consultants' compliance with motor traffic regulations on recall to hospital to attend emergencies, and ownership and use of green warning lights (GWLs). To determine the views of senior police officers on consultants complying with traffic regulations on emergency recall with and without GWLs., Method: Questionnaire survey of all consultants in obstetrics and gynaecology, paediatrics and emergency medicine in the Yorkshire Deanery, UK, and members of the Association of Chief Police Officers (ACPO)., Results: 220 consultant questionnaires were distributed and 166 replies were received; 21% of respondents owned a GWL. Almost 50% of consultants would consider exceeding speed limits when returning to an emergency. Between 43% and 80% consultants would cross red traffic lights; driving habits varied with usage and ownership of a GWL. 12.7% (21) of respondents had been stopped for traffic violations attending emergencies, 2.4% (4) had been prosecuted and 4.8% (8) had been involved in accidents. The ACPO advised that consultants should observe all traffic regulations at all times., Conclusion: Consultants recalled to their hospitals for emergencies disregard speed restrictions and traffic light signals both with and without GWLs and risk both accident and prosecution for ignoring traffic legislation. They should consider using a GWL to ease their progress through traffic when attending an emergency and observe all traffic laws., (C) 2007 BMJ Publishing Group Ltd, British Association for Accident and Emergency Medicine, & Faculty of Accident & Emergency Medicine

Insight and danger in Alzheimer's disease.
Starkstein SE, Jorge R, et al.
School of Psychiatry and Clinical Neurosciences University of Western Australia, WA, Australia. ses@meddent.uwa.edu.au
To determine the frequency, and demographic and clinical correlates of dangerous behaviours in Alzheimer's disease (AD). We assessed a consecutive series of 278 patients with AD and 45 age-comparable healthy controls with a comprehensive psychiatric and neuropsychological evaluation. Caregivers rated the frequency of patients' exposure to dangerous situations or commission of dangerous behaviours. The frequency of dangerous behaviours was 16% in the AD group and 2% in the healthy control group. The presence of anosognosia was associated with a threefold increase in the risk of dangerous behaviours, but there was no significant association between dangerous behaviours and patients' age, years of education, diagnosis of major or minor depression and presence of suicide ideation. Sixteen per cent of a consecutive series of patients with AD had dangerous behaviours during the month preceding the clinical evaluation. Anosognosia was the main clinical correlate of dangerous behaviours in this population.

PMID: 17388998


The Australian Vascular Quality of Life Index (AUSVIQUOL): an Improved Clinical Quality of Life Tool for Peripheral Vascular Disease.
Smith MJ, Borchard KLA, et al.
(Smith) Department of General Surgery, Sir Charles Gairdner Hospital. Perth, Australia.
Objectives: To validate the Australian Vascular Quality of Life Index (AUSVIQUOL) as a quality of life (QOL) tool appropriate for peripheral vascular disease patients in the clinical setting.
Design: Cross-sectional study. Materials: The study group consisted of 71 patients with vascular claudication of varying severity attending a tertiary hospital outpatient department. Methods: The results of the AUSVIQUOL and Medical Outcomes Short Form Health Survey (SF-36) were compared through factor and regression analyses. A group of 12 patients was then reassessed to compare the reliability and internal consistency of the two indices. Results: The AUSVIQUOL took less time to complete than the SF-36 (3.27 v 10.79 min; p < 0.0001) and fewer patients found the questions confusing (2% v 26%). The AUSVIQUOL was easier to administer and had a higher level of patient acceptance than the SF-36. The regression analysis showed that for each of the domains in the AUSVIQUOL there was a significant correlation with measures in the SF-36 (adjusted R-squared 0.420, 0.480 and 0.331). The AUSVIQUOL demonstrated a good level of internal consistency when compared to the SF-36 (Cronbach's alpha 0.8702 vs 0.6307). Conclusion: In comparison with the SF-36, the AUSVIQUOL is an improved tool for the QOL assessment of patients with peripheral vascular disease in the clinical setting. copyright 2007 Elsevier Ltd. All rights reserved.
Publication Types: Journal Article
PMID: 2007313341


Diagnostic performance of EUS for chronic pancreatitis: a comparison with histopathology.
Chong AKH, Hawes RH, et al.
Gastroenterology Department, Fremantle Hospital, University of Western Australia, Fremantle, Western Australia, Australia.
BACKGROUND: EUS has been proposed as a minimally invasive and accurate test to detect chronic pancreatitis (CP). OBJECTIVE: To investigate the correlation between EUS criteria and histopathology grading in patients with presumed CP. DESIGN: Retrospective study. SETTING AND PATIENTS: Patients who received pancreatic surgery according to presumed CP from the Medical University of South Carolina surgical database between 1995 and 2003 were identified.
and included if EUS was performed within 1 year before surgery. The number of EUS criteria for CP was compared with a histologic fibrosis score (FS). MAIN OUTCOME MEASUREMENTS: Sensitivity and specificity of number of EUS criteria compared with FS. RESULTS: Seventy-one patients were identified (38 women). Median FS was 7 (range, 0-12). Of the patients with calcifications: calcifications were detected by EUS in 30 (42%), 14 (47%) had calcifications missed by other imaging modalities, and 28 (93%) were confirmed to have abnormal histology (FS ≥ 2). Of the patients without calcifications: in the 41 patients without calcifications on EUS, 36 (88%) had FS ≥ 2; median FS was 5 (range, 0-12); the correlation between the number of EUS criteria and FS was low but statistically significant (r = 0.40; P = .01). Three or more EUS criteria provided the best balance of sensitivity (83.3%) and specificity (80.0%) for predicting abnormal histology. LIMITATIONS: Retrospective study. All patients were believed to need surgery. CONCLUSIONS: A threshold of 3 or more EUS criteria provides the best balance of sensitivity and specificity for histologic pancreatic fibrosis. Calcifications seen by EUS but missed by other imaging are common in this group of patients.

Publication Types: Journal Article
PMID:17466199

The risk of hepatocellular carcinoma and decompensation following hepatitis C treatment with interferon-based therapy.
(1)Gastroenterology and Hepatology, Royal Perth Hospital; (2)Gastroenterology and Hepatology, Sir Charles Gairdner Hospital; (3)Gastroenterology and Hepatology, Fremantle Hospital; (4)Microbiology, Royal Perth Hospital; (5)Pathology, Sir Charles Gairdner Hospital, Perth, Australia

The relationship between organised physical recreation and mental health.
PO Box 22, Fremantle WA 6959 streetgr@gmail.com
Issue addressed: The mental health benefit of participation in organised physical recreation is investigated as strategies aimed at enhancing mental health and wellbeing in the community have the potential to decrease social and economic costs. Methods: A literature review was undertaken to explore evidence relating to the mental health benefits of participation in organised physical recreation. Results: Regular physical activity is widely recognised as protective against the overall burden of disease. Evaluations by government departments in Australia and the United States (US) found that people who participate in sports clubs and organised recreational activity enjoy better mental health, are more alert, and more resilient against the stresses of modern living. Participation in recreational groups and socially supported physical activity is shown to reduce stress, anxiety and depression, and reduce symptoms of Alzheimer's disease, yet more than one-third of adult Australians report no participation in sports and physical recreation. Evaluations of some programs found that physical activity is increased when the social environment is supportive and that the mental and physical benefits of participating in organised recreational activity can be experienced by people other than those directly involved with the sport or activity. Conclusion: This review supports the development and maintenance of organised sport and recreational activities that are socially and culturally appropriate. An increase in valid and reliable evaluations of sport and physical recreation programs would contribute to the international body of evidence of the mental health benefits of organised physical recreation. (author abstract)
Clinical expression of hemochromatosis gene (HFE) variants.
Ayonrinde OT, Olynyk JK.
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Fremantle Hospital, Fremantle, Western Australia, Australia.
Publication Types: Comment
Editorial
PMID:17894321

Immunology & Allergy Clinics of North America. 2007; 27(2): 165-75.
The pathophysiology of shock in anaphylaxis.
Brown SGA.
Emergency Medicine Research Unit, The University of Western Australia and Fremantle Hospital, Alma Street, Fremantle, WA 6160, Australia.
The balance of evidence from human observations and animal studies suggests that the main pathophysiologic features of anaphylactic shock are a profound reduction in venous tone and fluid extravasation causing reduced venous return (mixed hypovolemic-distributive shock) and depressed myocardial function. Aggressive fluid resuscitation is required to ameliorate hypovolemic-distributive shock, and an intravenous infusion of epinephrine will increase vascular tone, myocardial contractility, and cardiac output in most cases. Where these measures fail, pathophysiologic considerations and anecdotal evidence support the consideration of selective vasoconstrictors as the next step in treatment.
PMID:17493496

Coronary veins and their role in current electrophysiology.
Kapoor A, Rowland E, et al.
Coronary Care Fremantle Hospital, Fremantle, Washington, USA. akapoor65@gmail.com
Publication Types: Review
PMID:19104134

Indian Heart Journal. 2007; 59((1 Suppl A)): A6-13.
Coronary veins and their role in current electrophysiology.
Kapoor A, Rowland E.
Coronary Care Fremantle Hospital, Fremantle, Washington, USA. akapoor65@gmail.com
Publication Types: Review
PMID:2008011697

The growth and shaping of a relationship.
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Pattison, Claire: South West CAMHS, 1 Stirling Street, Fremantle, WAU, Australia, 6160, claire.pattison@health.wa.gov.au
Despite the limitations of the observation role I developed a relationship with the baby, Sarah, whom I observed. This paper discusses my thoughts on the ways in which our relationship was developed and maintained. Sarah initiated and shaped our relationship using gaze, smile and other forms of nonverbal communication. Sharing experiences together further enhanced our relationship. I gained an understanding of her emotional world by attending to countertransference and reflecting on it in the seminar group. Finally, as I brought my own beliefs and experience to the observation this also impacted upon our relationship. My experience in this observation helped me to appreciate how patterns of relating begin from birth and are developed in the first months of life. (PsycINFO Database Record (c) 2007 APA, all rights reserved) (journal abstract).

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PMID:17160418

Swimming as a precipitating factor for ischaemic stroke and transient cerebral ischaemia.
Stroke Unit and Neurology Department, Fremantle Hospital, WA

Reply.
Davis TME, Davis WA.
School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia, Perth, Western Australia, Australia.
PMID:17640199

Internal Medicine Journal. 2007; 37(8): 582-583.
Characteristics and outcome of type 2 diabetes in urban Aboriginal people.
Davis TME, Davis WA.
School of Medicine and Pharmacology, Fremantle HospitalUniversity of Western Australia, PerthWestern Australia, Australia

Ant sting anaphylaxis in South Australia (SA): P05.
(1)Flinders Medical Centre, Adelaide, Australia, (2)Flinders University, Adelaide, Australia, (3)Fremantle Hospital, Fremantle, Australia, (4)University of Western Australia, Perth
(1)Princess Margaret Hospital for Children, (2)Dept. of Immunology, Fremantle Hospital, (3)Dept. of Immunology, Princess Margaret Hospital, (4)Department of Paediatrics, Fremantle Hospital

Thrombotic microangiopathy from Australian brown snake (Pseudonaja) envenoming.
Isbister GK, Little M, et al.
(1)Tropical Toxinology Unit and (11)Tropical and Emergency Infectious Disease Division, Menzies School of Health Research, Charles Darwin University, (7)Royal Darwin Hospital, (12)Northern Territory Clinical School, Flinders University, Royal Darwin Hospital, Darwin, Northern Territory, (2)Department of Clinical Toxicology and Pharmacology, Newcastle Mater Hospital, Newcastle, (8)Tamworth Base Hospital, Tamworth, New South Wales, Australia, (3)Sir Charles Gairdner Hospital, (4)University of Western Australia, (5)PathWest Laboratories, (6)Royal Perth Hospital, (9)Discipline of Emergency Medicine, The University of Western Australia and (10)Fremantle Hospital, Perth, Western Australia, Australia
Background: Australian brown snake (genus Pseudonaja) envenoming causes a venom-induced consumptive coagulopathy (VICC). A proportion of cases go on to develop thrombotic microangiopathy characterized by thrombocytopenia, microangiopathic haemolytic anaemia (MAHA) and acute renal failure (ARF). Aim: The aim of the study was to define better the natural history and empirical treatments for thrombotic microangiopathy in brown snake envenoming.
Methods: A review of brown snake bites recruited to the Australian Snakebite Project (ASP), a national multicentre study of snake envenoming was undertaken. Serial data are recorded on clinical effects and laboratory results, including measurement of venom concentrations. We describe cases of thrombotic microangiopathy and compare these to cases without thrombotic microangiopathy.
Results: From 32 cases of brown snake envenoming with severe VICC, four (13%) developed thrombotic microangiopathy, we also included two cases of thrombotic microangiopathy from prior to ASP. All six developed severe thrombocytopenia (<20 x 10^9/L), worst 3 days after the bite and resolving over a week, MAHA with fragmented red blood cells on the blood film and five developed anuric ARF requiring dialysis and lasting 2-8 weeks. All six received antivenom, which was delayed compared with other brown snake-envenoming cases. Four were treated with plasmapheresis. The severity and recovery of the thrombocytopenia, anaemia and renal function were similar with and without plasmapheresis.
The median length of stay for MAHA cases was 14 days (interquartile range (IQR) 12-14) compared to 1.8 days (IQR 1.3-2) for all other cases.
Conclusion: Thrombotic microangiopathy resulting from brown snake bite appears to have a good prognosis and management should focus on early antivenom therapy and supportive care including dialysis. The role of plasmapheresis is yet to be defined.

Characteristics and outcome of type 2 diabetes in urban Aboriginal people.
Morton AP, Davis TM, et al.
Endocrinology and Obstetric Medicine, Mater Hospital, Brisbane QLD
The author compares the characteristics and outcomes of type 2 diabetes in urban Aboriginal people in Fremantle with those seen at an indigenous health service in South Brisbane. The authors of the original paper provide a response. (non-author abstract)

Takotsubo cardiomyopathy.
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Characteristics and outcome of type 2 diabetes in urban Aboriginal people: the Fremantle Diabetes Study.[see comment].
Davis TME, McAullay D, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Western Australia, Australia. tdavis@cyllene.uwa.edu.au
We analysed data from Aboriginal patients with type 2 diabetes recruited to the community-based Fremantle Diabetes Study and compared them with those from the Anglo-Celt participants. Diabetes prevalence among Aboriginal people in the Fremantle area was more than double that of Anglo-Celts and the average age at diagnosis was 14 years or younger. Glycaemic control, urinary albumin : creatinine and the proportion of smokers were all higher in the Aboriginal group and there was evidence of lower diabetes-related quality of life and high rates of disability at a young age. The Aboriginal patients died 18 years or younger than their Anglo-Celt counterparts. Specialized, culturally-sensitive and sustainable programmes are urgently needed to improve the management of diabetes in urban Aboriginal communities.


Retinol supplementation in murine Plasmodium berghei malaria: effects on tissue levels, parasitaemia and lipid peroxidation.
Hamzah J, Batty KT, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.
Reduced plasma retinol concentrations occur in human malaria but the benefits of supplementation remain uncertain. We assessed the in vivo efficacy of retinol administration, and its effect on lipid peroxidation, in a Plasmodium berghei murine model. Animals received vehicle (n=17) or retinol (i) before P. berghei inoculation (four doses), (ii) at parasitaemia 10-15% (three to four doses) or (iii) before and after inoculation (six to seven doses; n=15 in each group), with euthanasia on day 8 post-inoculation or when the parasitaemia exceeded 50%. Multiple-dose pre-inoculation retinol reduced endpoint parasitaemia by 24% (P=0.001 versus controls). A reduction of 18% (P=0.042) was observed when retinol was given to parasitaemic animals. Retinol was ineffective when given both before and after infection (11% reduction; P=0.47). Although retinol supplementation did not change plasma retinol concentrations, liver retinol content increased and correlated inversely with endpoint parasitaemia (r=-0.45, P=0.001). Malaria infection augmented concentrations of the free radical lipid peroxidation end-product F(2)-isoprostanes in plasma, erythrocytes and liver by 1.8-, 2.8- and 4.9-fold,
respectively, but retinol supplementation had no effect on these increases. Consistent with some human malaria studies, prophylactic retinol reduces P. berghei parasitaemia. This effect relates to augmentation of tissue retinol stores rather than to retinol-associated changes in oxidant status.

PMID:17157853

Isolation, culture and immortalisation of hepatic oval cells from adult mice fed a choline-deficient, ethionine-supplemented diet.
Tirnitz-Parker JE, Tonkin JN, et al.
School of Biomedical, Biomolecular and Chemical Sciences, University of Western Australia, Crawley, Australia. tirnitz@cyllene.uwa.edu.au
Oval cells have great potential for use in cell therapy to treat liver disease, however this cannot be achieved until the factors which govern their proliferation and differentiation are better understood. We describe a method to establish primary cultures of murine oval cells, and the derivation of two novel lines from these. Primary cultures from the livers of wildtype or TAT-GRE lacZ transgenic mice subjected to a choline-deficient, ethionine-supplemented diet comprised up to 80% oval cells at day 7 based on A6 or CK19 staining. Cell lines were clonally derived, which underwent spontaneous immortalisation following prolonged maintenance in culture. Immunostaining and RT-PCR demonstrated they express hepatocytic and biliary markers and they were therefore termed "bipotential murine oval liver" (BMOL) cells. Under proliferating culture conditions, BMOL or BMOL-TAT cells abundantly expressed oval cell and biliary markers, whereas mature hepatocytic markers were upregulated when the growth conditions were changed to facilitate differentiation. Hepatic differentiation of BMOL-TAT cells could be traced by measuring the expression of their lacZ transgene, which is driven by a promoter element from tyrosine aminotransferase (TAT), a marker of adult hepatocytes. Interestingly, haematopoietic markers were upregulated in super confluent cultures, indicating a possible multipotentiality. None of the cell lines grew in semi-solid agar, nor did they form tumours in nude mice, suggesting they are non-tumourigenic. These novel murine oval cell lines, together with a reliable method for isolation and culture of primary oval cells, will provide a useful tool for investigating the contribution of oval cells to liver regeneration.
Publication Types: Research Support, Non-U.S. Gov't
PMID:17693121

Percutaneous coronary intervention through a Cabrol composite graft.
Wells TA, Kapoor A.
Fremantle Cardiac Unit, Fremantle Hospital, Alma Road, Fremantle, Western Australia, 6160, Australia
There are several different surgical techniques used to repair acute type-A aortic dissections. One such technique is called the Cabrol procedure which uses a Dacron tube graft to re-attach the native coronary arteries. Stenosis of this graft-native coronary anastomosis is a recognized complication of the procedure and one amenable to percutaneous intervention. However, knowledge of the complex anatomy involved with the Cabrol repair is required in order to potentially carry out successful intervention. We report one such case involving a critical stenosis at the anastomosis of the Cabrol graft with the native left main stem.
Publication Types: Case Reports Letter
PMID:17126935
Recurrent exercise-induced syncope and failed sudden cardiac death.
Wells TA, Peebles CR, et al.
Publication Types: Case Reports
Letter
PMID:17056138

Research, empiricism and clinical practice in low-income countries.
Isaac M, Chand P, et al.
Community, Culture and Mental Health Unit, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, Western Australia.
Mental health problems are relevant for every country. They are particularly important for low-income countries which face a high burden of illness due to infectious disease, greater socio-economic disparities, and have limited resources for mental health care. There is a great mismatch in the areas of mental health research, practice, policy and services in comparison to developed countries. There have been a few studies that have investigated major mental health problems prevailing in these countries but missed out significant health problems. Studies have tended to be more donor driven and conducted in tertiary centres. The low priority accorded to mental health by the policy makers, scarcity of human resources, lack of culture-specific study instruments, lack of support from scientific journals have been some of the impediments to mental health research in these countries. In addition, lack of community participation and absence of sound mental health policies have deprived the vast majority of the benefit of modern psychiatric treatments. Recently, with increase in collaboration in research, availability of treatment including low-priced psychotropics, and a growing emphasis on the need for mental health policy in some low-income countries, the bleak scenario is expected to change.
Publication Types: Journal Article
PMID:17896235

Saddle pulmonary embolus successfully treated with unfractionated heparin.
Wells T, Kapoor A, et al.
Antemortem diagnosis of a saddle thromboembolus at the bifurcation of the main pulmonary artery (MPA) is rare. Such proximally located thrombi are regarded as unstable, and may fragment spontaneously or following treatment, leading to obstruction of distal pulmonary arteries. We describe a case of a saddle embolus of the MPA successfully treated with intravenous unfractionated heparin (UFH), followed by oral anticoagulation for three months with complete resolution of the thrombus.
Publication Types: Journal Article, Case Study, Diagnostic Images
PMID:2009560357

The small abdominal aortic aneurysm.
Golledge J, Muller J, et al.
(Golledge, Muller) Vascular Biology Unit, James Cook University. Townsville, QLD, Australia.
Small abdominal aortic aneurysms (AAAs) are increasingly being identified in developed countries with widespread use of abdominal imaging. In this review we describe the epidemiology, pathogenesis, natural history and management of this problem. Present evidence
suggests that small aortic aneurysms should be managed conservatively with ultrasound surveillance and cardiovascular risk factor reduction. Trials of endovascular treatment of small AAAs are underway but equally important are studies of drug-based therapies for AAA which are presently deficient.

Publication Types: Review
PMID:2007590063


Rectal administration of artemisinin derivatives for the treatment of malaria.
Karunajeewa HA, Manning L, et al.

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

CONTEXT: Rectal administration of artemisinin derivatives is a potentially lifesaving emergency treatment of severe malaria. Many different preparations are marketed in tropical countries, but their pharmacokinetic disposition and clinical efficacy may vary. OBJECTIVE: To review the pharmacokinetics, efficacy, and safety of rectally administered artesunate, artemisinin, dihydroartemisinin, and artemether. DATA SOURCES: We searched the MEDLINE, EMBASE, Cochrane Database of Clinical Reviews, Global Health, Web of Science, and CINAHL computerized databases up to December 2006, along with reviewing unpublished data from conference proceedings, pharmaceutical companies, and regulatory applications. Studies in languages other than English were translated. STUDY SELECTION: Studies were included involving rectal administration of an artemisinin derivative to healthy volunteers or patients with measurement of plasma drug concentrations or rates of initial parasite clearance. Both single-arm and comparative trials were included. DATA EXTRACTION: Forty-five studies were identified, of which 39 eligible studies were included in the review. Primary efficacy outcome measures included parasite density as a percentage of baseline at 12 and 24 hours following the first dose. Pharmacokinetic variables included maximum plasma concentration (C(max)), time to C(max) (T(max)), and area under the plasma concentration-time curve. Weighted means were calculated from available data. DATA SYNTHESIS: Thirty-two studies provided valid clinical efficacy data: 19 of artesunate, 10 of artemisinin, 2 of dihydroartemisinin, and 1 of artemether. All demonstrated prompt parasite clearance, with evidence of a dose-dependent effect for artesunate. Mortality rates in severe malaria (weighted means, 0%-13%) were consistent with those expected. Eight studies compared rectal artemisinin with conventional parenteral treatment (quinine, artemether, or artesunate) for severe malaria. Despite similar clinical outcomes, rectal artemisinin derivatives initiated parasite clearance more rapidly than parenteral treatment (percentage of baseline at 12 hours, < or =27% vs > or =56%, respectively). Eighteen pharmacokinetic studies were identified, including 13 of artesunate. There was marked interindividual variability in most pharmacokinetic variables, but artesunate achieved an earlier T(max) and higher C(max) and area under the plasma concentration-time curve than other artemisinin derivatives. CONCLUSIONS: Available rectal preparations of artemisinin derivatives differ in their pharmacokinetic disposition. Most available evidence pertains to artesunate and artemisinin. Despite marked interindividual variability in bioavailability, rectal preparations appear to have acceptable therapeutic efficacy, including in severe illness. [References: 59]

Publication Types: Research Support, Non-U.S. Gov't Review
PMID:17551131
The variation in medial and lateral collateral ligament strain and tibiofemoral forces following changes in the flexion and extension gaps in total knee replacement: a laboratory experiment using cadaver knees.


From Fremantle Hospital, Fremantle, Australia, B. Jeffcote, BMBS, FRACS(Orth), Orthopaedic Surgeon; Department of Orthopaedic Surgery; R. Nicholls, PhD, Research Fellow; University of Western Australia, Fremantle Orthopaedic Unit, Fremantle Hospital, Alma Street, Fremantle, Western Australia., A. Schirm, MD, Orthopaedic Surgeon; M. S. Kuster, MD, PhD, FRACS(Orth), Chairman, Professor; Klinik fur Orthopadische Chirurgie, Kantonsspital 9007, St. Gallen, Switzerland.

Achieving deep flexion after total knee replacement remains a challenge. In this study we compared the soft-tissue tension and tibiofemoral force in a mobile-bearing posterior cruciate ligament-sacrificing total knee replacement, using equal flexion and extension gaps, and with the gaps increased by 2 mm each. The tests were conducted during passive movement in five cadaver knees, and measurements of strain were made simultaneously in the collateral ligaments. The tibiofemoral force was measured using a customised mini-force plate in the tibial tray. Measurements of collateral ligament strain were not very sensitive to changes in the gap ratio, but tibiofemoral force measurements were. Tibiofemoral force was decreased by a mean of 40% (SD 10.7) after 90[degrees] of knee flexion when the flexion gap was increased by 2 mm. Increasing the extension gap by 2 mm affected the force only in full extension. Because increasing the range of flexion after total knee replacement beyond 110[degrees] is a widely-held goal, small increases in the flexion gap warrant further investigation., (C) 2007 British Editorial Society of Bone and Joint Surgery

The effect of surgical approach on blood flow to the femoral head during resurfacing.


The Avon Orthopaedic Centre, The University of Western, Australia, Fremantle, Perth, Western Australia.

We determined the effect of the surgical approach on perfusion of the femoral head during hip resurfacing arthroplasty by measuring the concentration of cefuroxime in bone samples from the femoral head. A total of 20 operations were performed through either a transgluteal or an extended posterolateral approach. The concentration of cefuroxime in bone was significantly greater when using the transgluteal approach (mean 15.7 mg/kg; 95% confidence interval 12.3 to 19.1) compared with that using the posterolateral approach (mean 5.6 mg/kg; 95% confidence interval 3.5 to 7.8; p < 0.001). In one patient, who had the operation through a posterolateral approach, cefuroxime was undetectable. Using cefuroxime as an indirect measure of blood flow, the posterolateral approach was found to be associated with a significant reduction in the blood supply to the femoral head during resurfacing arthroplasty compared with the transgluteal approach.

Exercise alone reduces insulin resistance in obese children independently of changes in body composition.


Telethon Institute for Child Health Research, Centre for Child Health Research (L.M.B., K.W.,
A.T., N.R., M.B., T.W.J., E.A.D.), and Schools of Population Health (L.M.B., M.B., J.F.) and Human Movement and Exercise Science (K.W., G.O.), University of Western Australia, Crawley, Western Australia 6009, Australia; Department of Endocrinology and Diabetes (L.M.B., A.S., A.T., T.W.J., E.A.D.), Princess Margaret Hospital, Subiaco, Western Australia, Australia 6008; Advanced Heart Failure and Cardiac Transplant Service (G.O.), Royal Perth Hospital, Perth, Western Australia 6001, Australia; and School of Medicine (G.O.), University of Notre Dame, Fremantle, Western Australia 6959, Australia; and Research Institute for Sport and Exercise Sciences (D.J.G.), Liverpool John Moores University, Liverpool L3 5UX, United Kingdom

Context: The number of obese children with insulin resistance and type 2 diabetes is increasing, but the best management strategy is not clear.

Objective: The objective of this study was to assess the effect of a structured 8-wk exercise training program on insulin resistance and changes in body composition in obese children.

Design: The study was 8 wk of structured supervised exercise intervention with outcome measures before and after the exercise period.

Subjects: Fourteen obese children (12.70 +/- 2.32 yr; eight male, six female) with high fasting insulin levels were enrolled into the study.

Intervention: Intervention consisted of 8 wk of supervised circuit-based exercise training, composed of three fully supervised 1-h sessions per week.

Outcome Measures: Outcome measures were assessed pretraining program and posttraining program and included insulin sensitivity (euglycemic-hyperinsulinemic clamp studies), fasting insulin and glucose levels, body composition using dual energy x-ray absorptiometry scan, lipid profile, and liver function tests.

Results: Insulin sensitivity improved significantly after 8 wk of training (MbLm 8.20 +/- 3.44 to 10.03 +/- 4.33 mg/kg[dot]min, P < 0.05). Submaximal exercise heart rate responses were significantly lower following the training (P < 0.05), indicating an improvement in cardiorespiratory fitness. Dual energy x-ray absorptiometry scans revealed no differences in lean body mass or abdominal fat mass.

Conclusion: An 8-wk exercise training program increases insulin sensitivity in obese children, and this improvement occurred in the presence of increased cardiorespiratory fitness but is independent of measurable changes in body composition.

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The prevalence and phenotypic characteristics of Western Australian adolescents with nonalcoholic fatty liver disease.
Ayonrinde OT, Adams LA, et al.
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How common is tissue transglutaminase positivity in Australia.
Chin MW, Mallon DF, et al.
Departments of (1)Gastroenterology and (2)Immunology, Fremantle Hospital, and (3)Department of Medicine, University of Western Australia, Australia

HLA, TPMT and ITPA genotypes and susceptibility to azathioprine hypersensitivity reactions (HSR) in inflammatory bowel disease (IBD) patients.
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Relationship between disease severity, quality of life and health-care resource use in a cross-section of Australian patients with Crohn's disease.
Gibson PR, Weston AR, et al.
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Background and Aim: New treatments for Crohn's disease are expensive and place economic strain upon health-care systems, and 'value-for-money' needs to be confirmed. This study aimed to correlate disease severity with health-related quality of life and with health-care resource use, to allow evaluation of the cost effectiveness of these treatments.
Methods: A cross-sectional, non-interventional, pharmacoeconomics study was performed with patients completing questionnaires comprising demographic, disease and health-care utilization questions, together with the disease-specific Inflammatory Bowel Disease Questionnaire (IBDQ)
and the Assessment of Quality of Life (AQoL) multi-attribute utility instrument. The Crohn's Disease Activity Index (CDAI) was used to assess disease severity.

Results: 143 patients with a broad range of disease severity (CDAI 36-446, fistulae 23%) were recruited from referral centers. Stepwise regression analyses demonstrated a negative correlation between disease severity and both IBDQ and AQoL (both P < 0.0001). Age, gender and years since diagnosis did not impact upon either of the quality-of-life outcomes. Mean utility score for non-fistulizing patients with moderate-severe active disease (CDAI >= 220) was 0.45, mild disease (CDAI 150-219) was 0.68 and for remission (CDAI < 150) was 0.77. Health-care resource utilization increased with increasing CDAI (P < 0.001), with hospital admissions being the largest component cost. Twenty-seven percent of patients (mean age 38 year) received a government benefit, 51% primarily due to their Crohn's disease.

Conclusion: Crohn's disease severity correlates with poor quality of life. Utility scores determined will permit cost-utility analyses to be made in order to best allocate limited health resources.

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Iron uptake by transferrin receptor 2 in human hepatoma cells.
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Use of a high-resolution miniature endoscope in the investigation of murine models of intestinal inflammation?
Lawrance IC, Klopcic B, et al.
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Percutaneous endoscopic gastrostomy: an eight-year prospective follow up.
Paramsothy S, Mollison LC, et al.
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Careful patient selection may improve response rates to infliximab in inflammatory bowel disease.
Pearce CB, Lawrance IC.
Department of Gastroenterology, Fremantle Hospital, Fremantle, Western Australia, Australia.
Background and Aim: The use of infliximab in the treatment of Crohn's disease (CD) is acceptable and appears to be effective in ulcerative colitis (UC). Careful patient selection, resulting in infliximab only for truly refractory inflammatory bowel disease (IBD), may improve its efficacy. The present study aimed to determine if careful patient selection improved infliximab efficacy in IBD. Methods: CD or UC/IBD unclassified patients (Montreal classification) were considered for infliximab treatment only after failure of disease control with conventional therapies and confirmation of active disease. Patients with purely luminal IBD received a single infliximab dose. Patients with fistulizing disease (with or without luminal disease) received...
infliximab at 0, 2 and 6 weeks. Changes to Harvey Bradshaw (HBI) for inflammatory CD and Colitis Activity Index (CAI) for UC/IBDU were used to determine the response and remission rates. In fistulizing CD, a remission was sustained cessation of drainage and resolution of the fistula. Response was correlated to inflammatory marker levels. Results: Seventy IBD patients were treated. In CD, 85.2% (46/54) had active luminal and 40.7% (22/54) had fistulizing disease. In luminal CD, at 8 weeks a single infliximab dose induced remission in 75% (24/32) of patients compared to 92.9% (13/14) after infliximab at 0, 2 and 6 weeks. Fistulizing disease responded in 77.2% (17/22) and remitted in 50% (11/22) of patients at 8 weeks. In UC/IBDU, 75% (12/16) responded and 43.8% (7/16) of patients were in remission at 8 weeks. Conclusion: Careful patient selection may improve infliximab's efficacy and clinical remission appears greater after induction with three infliximab doses in CD. Clinical efficacy is suggested for UC/IBDU.


Secreted protein acidic and rich in cysteine (SPARC): prognostic marker in colorectal cancer?
Robbshaw A, Lloyd F, et al.
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Light and lymphotoxin-fi acting via the lymphotoxin-fi receptor are able to modulate the expression of key profibrogenic mediators in the hepatic stellate cell.
Ruddell RG, Knight B, et al.
1 The Hepatic Fibrosis Group, The Queensland Institute of Medical Research, Brisbane, QLD, (2)School of Medicine and Pharmacology, The University of Western Australia Fremantle Hospital, WA, Australia


Sustained virological response (SVR) with combination pegylated interferon/ribavirin (PEG/RBV) in chronic hepatitis C patients failing to respond to standard interferon based regimes.
Studd CR, Mollison L, et al.
Fremantle Hospital, Western Australia, Australia


Characterising the clinical spectrum of hepatic iron loading using MRI ferriscan in suspected HFE and non-HFE iron overloaded patients.
Tan TC, Olynyk JK.
Department of Gastroenterology, Fremantle Hospital, Fremantle WA & School of Medicine and Pharmacology, University of Western Australia, Australia
The use of mycophenolate mofetil and tacrolimus in the treatment of resistant IBD.
Tan TC, Philpott J, et al.
(1)Department of Gastroenterology, Fremantle Hospital, WA, (2)University Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia

Reasons for non-compliance with five-yearly screening flexible sigmoidoscopy.
Viiala CH, Olynyk JK.
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Oral peppermint oil does not reduce pain associated with screening flexible sigmoidoscopy.
Viiala CH, Olynyk JK.
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The use of infliximab in the prevention of colectomy in severe and refractory ulcerative colitis.
Willert RP, Lawrance IC.
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A biomechanical comparison of scaphoid fixation with bone grafting using iliac bone or distal radius bone.
Jarrett P, Kinzel V, et al.
Fremantle Orthopaedic Unit, The University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.
PURPOSE: Although many scaphoid fractures may be treated by immobilization, complex scaphoid fractures generally require bone grafting with internal fixation. A preferred source of bone graft for scaphoid grafting is the iliac crest. Donor site morbidity from iliac crest harvest, however, is a known complication, and the comparable strength and osteogenic properties of bone harvested from other sites are unclear. To this end, we have conducted a cadaveric comparative investigation of the strength of scaphoid nonunions with bone graft and internal fixation using either iliac crest bone or distal radius bone.
METHODS: Ten paired, human, fresh-frozen cadaveric wrists were used to create a standard midwaist wedge osteotomy into which identically shaped distal radius or iliac crest bone wedges were internally fixed using headless compression screws. After bone density and computed tomography assessment of the bones, benchtop biomechanical testing was conducted to compare the strength of the scaphoids after iliac and distal radius grafting, at 2-mm displacement, and at failure.
RESULTS: Analysis of scaphoid length, width, height, weight, density, and screw placement revealed no statistical differences between both bone graft groups. Although not significant, scaphoid nonunions grafted with distal radius bone evidenced a reduced load (3.23 +/- 0.26 Nm) to 2-mm
displacement compared with iliac crest bone (5.97 +/- 0.68 Nm). Similarly, though not significant, scaphoids grafted with distal radius bone showed a reduced load (4.18 +/- 0.30 Nm) to failure compared with iliac crest bone grafting (6.42 +/- 0.66 Nm). Although no significance was found between the 2 grafting methods, a trend toward greater strength in the iliac crest graft group was observed. CONCLUSIONS: Given the comparable biomechanical strength shown between iliac and distal radius bone in this study and the simplified surgical technique of distal radius harvesting, the data justify use of distal radius bone as a viable alternative donor source in scaphoid fracture treatment.

PMID: 17996771


Interferon-gamma exacerbates liver damage, the hepatic progenitor cell response and fibrosis in a mouse model of chronic liver injury.

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BACKGROUND/AIMS: Several previous studies have suggested that interferon gamma (IFNgamma) may play a key role during hepatic progenitor cell (HPC) mediated liver regeneration. However to date, no studies have directly tested the ability of IFNgamma to mediate the HPC response in an in vivo model. METHODS/RESULTS: Administration of IFNgamma to mice receiving a choline deficient, ethionine (CDE) supplemented diet to induce chronic injury resulted in an augmented HPC response. This was accompanied by increased inflammation, altered cytokine expression and hepatic fibrosis. Serum alanine aminotransferase activity, hepatocyte apoptosis and Bak staining were significantly increased in IFNgamma-treated, CDE-fed mice, demonstrating that liver damage was exacerbated in these animals. Administration of IFNgamma to control diet fed mice did not induce liver damage, however it did stimulate hepatic inflammation. CONCLUSIONS: Our results suggest that IFNgamma increases the HPC response to injury by stimulating hepatic inflammation and aggravating liver damage. This is accompanied by an increase in hepatic fibrogenesis, supporting previous reports which suggest that the HPC response may drive fibrogenesis during chronic liver injury.

PMID: 17923165


Attenuated liver progenitor (oval) cell and fibrogenic responses to the choline deficient, ethionine supplemented diet in the BALB/c inbred strain of mice.

Knight B, Akhurst B, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Alma Rd., Fremantle, WA 6101, Australia; School of Biomedical and Chemical Sciences, University of Western Australia, Australia.

BACKGROUND/AIMS: Liver regeneration following chronic injury is associated with inflammation, the proliferation of liver progenitor (oval) cells and fibrosis. Previous studies identified interferon-gamma as a key mediator of oval cell proliferation. Interferon-gamma is known to regulate Th1 cell activities during immune challenge. Therefore, we hypothesised that progenitor cell-mediated regeneration is associated with a Th1 immune response. METHODS: C57Bl/6 (normal Th1 response) and BALB/c mice (deficient in Th1 signalling) were placed on a carcinogenic diet to induce liver injury, progenitor cell proliferation and fibrosis. RESULTS: Serum transaminases and mortality were elevated in BALB/c mice fed the diet. Proliferation of liver progenitor cells was significantly attenuated in BALB/c animals. The pattern of cytokine
expression and inflammation differed between strains. Liver fibrosis and hepatic stellate cell activation were significantly inhibited in BALB/c mice compared to C57Bl/6. In addition, interferon-gamma knockout mice also showed reduced fibrosis compared to wild type. These findings are in contrast to published results, in which interferon-gamma is shown to be anti-fibrogenic. CONCLUSIONS: Our data demonstrate that the hepatic progenitor cell response to a CDE diet is inhibited in mice lacking Th1 immune signalling and further show that this inhibition is associated with reduced liver fibrosis.

PMID:17112626

The challenge of renal cystic disease and its association with hypertension, age and abnormal potassium handling.
Ferrari P.
Publication Types: Comment
Editorial
PMID:17563553

Generation of mutant leukaemia inhibitory factor (LIF)-IgG heavy chain fusion proteins as bivalent antagonists of LIF.
Department of Pharmaceutical Biology, Victorian College of Pharmacy, Monash University, Parkville, Victoria 3051, Melbourne, Australia, and Department of Rheumatology, Fremantle Hospital, Perth, Western Australia, Australia.
Two leukaemia inhibitory factor (LIF) mutants, designated MH35-BD and LIF05, have been shown to have a capacity to inhibit the biological activities of not only human LIF (hLIF) but also other interleukin-6 (IL-6) subfamily cytokines such as human oncostatin M (hOSM). These cytokines share the same receptor complex in which the glycoprotein 130 (gp130) subunit is a common constituent. However, at low concentrations and in their monomeric forms, such molecules have a relatively short plasma half-life due to rapid clearance from the kidneys. Here, to prolong their serum half-lives, we have used a multi-step polymerase chain reaction (PCR) to fuse each of the LIF05 and MH35-BD cDNA fragments to a sequence encoding the Fc portion, and the hinge region, of the human immunoglobulin G (hIgG) heavy chain. The linking was achieved through an oligomer encoding a thrombin-sensitive peptide linker thus generating MH35-BD:Fc and LIF05:Fc, respectively. Both Fc fusion constructs were expressed in insect cell Sf21 and the proteins were purified by two successive affinity chromatography steps using nickel-nitritotriacetic acid (Ni-NTA) agarose and protein A beads. The Ba/F3 cell-based proliferation assay was used to confirm that the proteins were biologically active. In addition, preliminary pharmacokinetics indicates that the Fc fusion constructs have a longer serum half-life compared to their non-fusion counterparts.
PMID:17408687

In vitro evaluation of leukemia inhibitory factor receptor antagonists as candidate therapeutics for inflammatory arthritis.
Department of Pharmaceutical Biology, Victorian College of Pharmacy, Monash University, Parkville, Victoria 3051, Melbourne, Australia, and Department of Rheumatology, Fremantle...
Leukemia inhibitory factor (LIF) and oncostatin M (OSM) are found in appreciable concentrations in synovial fluid from patients with rheumatoid arthritis (RA) but not osteoarthritis. Accordingly, both are potential therapeutic targets in inflammatory diseases of the joints. Several LIF antagonists have been developed. They have the capacity to inhibit the biologic activities of not only LIF but also other interleukin-6 (IL-6) subfamily cytokines, including OSM. Both LIF and OSM share the same receptor, which is part of a cytokine receptor super family in which the glycoprotein 130 (gp130) subunit is a common constituent. The aim of this study was to evaluate the antagonistic potentials of two LIF mutants, LIF05 and MH35-BD. Both are mutant forms of human LIF with reduced affinity for gp130 and greater LIF receptor (LIFR) binding affinity. The results, using Ba/F3 cell proliferation assay, acute-phase protein (haptoglobin) induction analysis in HepG2 human hepatoma cells, a porcine cartilage glycosaminoglycan release assessment for proteoglycan degradation, and a collagen release assay, show that these antagonists inhibit relevant LIF, OSM, and other IL-6 subfamily cytokines in vitro albeit with differential potencies and have, therefore, therapeutic potential for treatment of RA and perhaps other diseases.

Journal of Investigative Dermatology. 2007; 127(7): 1770-1771.
Tumor necrosis factor-a - 308 Gene polymorphism and venous leg ulceration - Comment on possible link with obesity.
Wallace HJ, Vandongen YK, et al.
H.J. Wallace, School of Surgery and Pathology, University of Western Australia, Fremantle Hospital, Fremantle, WA; Australia. E-Mail: hilary.wallace@uwa.edu.au.
Publication Types: Letter
PMID:2007294228

Tibiofemoral force following total knee arthroplasty: comparison of four prosthesis designs in vitro.
Nicholls RL, Schirm AC, et al.
Fremantle Orthopaedic Unit, The University of Western Australia, Fremantle, Australia 6160.
Despite ongoing evolution in total knee arthroplasty (TKA) prosthesis design, restricted flexion continues to be common postoperatively. Compressive tibiofemoral force during flexion is generated through the interaction between soft tissues and prosthesis geometry. In this study, we compared the compressive tibiofemoral force in vitro of four commonly used prostheses: fixed-bearing PCL (posterior cruciate ligament)-retaining (PFC), mobile-bearing posterior-stabilized (PS), posterior-stabilized with a High Flex femoral component (HF), and mobile-bearing PCL-sacrificing (LCS). Fourteen fresh-frozen cadaver knee joints were tested in a passive motion rig, and tibiofemoral force measured using a modified tibial baseplate instrumented with six load cells. The implants without posterior stabilization displayed an exponential increase in force after 90 degrees of flexion, while PS implants maintained low force throughout the range of motion. The fixed-bearing PFC prosthesis displayed the highest peak force (214 +/- 68 N at 150 degrees flexion). Sacrifice of the PCL decreased the peak force to a level comparable with the LCS implant. The use of a PCL-substituting post and cam system reduced the peak force up to 78%, irrespective of whether it was a high-flex or a standard PS knee. However, other factors such as preoperative range of motion, knee joint kinematics, soft tissue impingement, and implantation technique play a role in postoperative knee function. The present study suggests that a posterior-stabilized TKA design might be advantageous in
reducing soft tissue tension in deep flexion. Further research is necessary to fully understand all factors affecting knee flexion after TKA. (c) 2007 Orthopaedic Research Society. PMID:17568418


Biomechanical considerations in plate osteosynthesis: the effect of plate-to-bone compression with and without angular screw stability.
Fremantle Orthopaedic Unit, University of Western Australia, and Orthopaedic Department, Kantonsspital St.Gallen, Switzerland. nkstoffel@hotmail.com

OBJECTIVE: We compared the biomechanical stability of bone-plate constructs using a compression plate (CP), an internal fixator (IF), and a combination plate (CP/IF). METHODS: Standardized simulated shaft fractures with a segmental defect in composite bones (n=60) and intraarticular distal femur fractures with a comminuted supracondylar zone in fresh frozen cadaveric femurs (n=36) were stabilized by CP, IF, and CP/IF. Construct stiffness, plastic deformation, and fixation strength were measured under axial compression and torsion using a biaxial testing machine. RESULTS: The experimental results indicate for the distal femur fracture model that IF has less loss of reduction by plastic deformation under axial load compared to CP (IF 61% of CP). Under torsion, the CP showed significantly (P<0.05) decreased plastic deformation compared to the IF (CP 51% of IF). The combination (CP/IF) of the 2 fixation principles generally resulted in a higher load to failure under axial compression and torsion (145% failure load of CP and 118% of IF under axial compression, 88% of CP and 109% of IF under torsion). Results were similar between the 2 fracture models.
CONCLUSIONS: Under compression, IF provides similar fixation in comminuted fractures and was better than the CP for avoiding loss of reduction, whereas under torsional loading, CP was more important for stiffness, plastic deformation, and load to failure than IF. However, combination (CP/IF) fixation seems advisable in intraarticular and extraarticular fractures of long bones with a metaphyseal comminution. These data may be utilized by surgeons to build a more specific treatment plan in patients with these fracture types.
PMID:17620993


Fear of falling in older women: a longitudinal study of incidence, persistence, and predictors.
Austin N, Devine A, et al.
School of Medicine and Pharmacology, Sir Charles Gairdner Hospital Unit and Fremantle Hospital Unit, University of Western Australia, Perth, Western Australia, Australia.

OBJECTIVES: To determine longitudinal predictors of incident and persistent fear of falling (FOF) in older women. DESIGN: Longitudinal study. SETTING: Clinical research center based at a university hospital. PARTICIPANTS: One thousand two hundred eighty-two community-dwelling women aged 70 to 85. MEASUREMENTS: FOF at baseline and after 3 years of follow-up; a range of baseline demographic and clinical variables, including mobility, balance, and depression. RESULTS: FOF was present in 418 subjects (33%) at baseline, developed in 30% of women who had been free of the symptom at baseline, and was reported by a total of 46% of the sample after 3 years of follow-up. In cross-sectional multivariable analysis, baseline FOF was independently associated with a range of variables, including living alone, obesity, cognitive impairment, depression, and impairments in balance and mobility. Baseline predictors of FOF that persisted after 3 years were similar, whereas obesity and slower timed up and go test scores predicted new-onset FOF. CONCLUSION: FOF in older women is a common and
persistent complaint that is caused mainly by impairments of balance and mobility. A range of social, psychological, and physical risk factors for disability are associated with persistence of FOF. These results imply that early intervention may be important for the prevention of persistent FOF.

Publication Types: Journal Article
PMID:17908062

**Impaired protein stability of 11beta-hydroxysteroid dehydrogenase type 2: a novel mechanism of apparent mineralocorticoid excess.**

Atanasov AG, Ignatova ID, et al.
Address correspondence to: Dr. Alex Odermatt, Department of Nephrology and Hypertension, University of Berne, Freiburgstrasse 15, 3010 Berne, Switzerland. alex.dermatt@dkf.unibe.ch.

Apparent mineralocorticoid excess (AME) is a severe form of hypertension that is caused by impaired activity of 11beta-hydroxysteroid dehydrogenase type 2 (11beta-HSD2), which converts biologically active cortisol into inactive cortisone. Mutations in HSD11B2 result in cortisol-induced activation of mineralocorticoid receptors and cause hypertension with hypokalemia, metabolic alkalosis, and suppressed circulating renin and aldosterone concentrations. This study uncovered the first patient with AME who was described in the literature, identified the genetic defect in HSD11B2, and provided evidence for a novel mechanism of reduced 11beta-HSD2 activity. This study identified a cluster of amino acids (335 to 339) in the C-terminus of 11beta-HSD2 that are essential for protein stability. The cluster includes Tyr(338), which is mutated in the index patient, and Arg(335) and Arg(337), previously reported to be mutated in hypertensive patients. It was found that wild-type 11beta-HSD2 is a relatively stable enzyme with a half-life of 21 h, whereas that of Tyr(338)His and Arg(337)His was 3 and 4 h, respectively. Enzymatic activity of Tyr(338)His was partially retained at 26 degrees C or in the presence of the chemical chaperones glycerol and dexamethasone, indicating thermodynamic instability and misfolding. The results provide evidence that the degradation of both misfolded mutant Tyr(338)His and wild-type 11beta-HSD2 occurs through the proteasome pathway. Therefore, impaired 11beta-HSD2 protein stability rather than reduced gene expression or loss of catalytic activity seems to be responsible for the development of hypertension in some individuals with AME.

PMID:17314322

**No one is dead until warm and dead.**

Iyer A, Rajkumar V, et al.
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Publication Types: Journal Article
PMID:17903527

**Intraosseous blood flow of the everted or laterally-retracted patella during total knee arthroplasty.**

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Patellofemoral problems are relatively common sequelae of total knee arthroplasty (TKA), and many factors contribute to these complications. Vascular compromise has been identified as a possible contributing factor, and was selected for further investigation in the present study. Laser Doppler Flowmetry was used to quantify patella intraosseous blood flow in vivo during TKA surgery without the use of a tourniquet. Flow was measured after medial parapatellar arthrotomy, and compared to flow during patella eversion and lateral retraction. Patella blood flow during eversion was reduced to 13% of baseline values (p<0.05). A significantly greater proportion of flow was preserved during lateral retraction (53%), although the reduction from baseline was still significant (p<0.05). A statistically significant difference in flow (60% of baseline) was also noted when the leg was flexed from full extension to 90 degrees (p<0.05) with the patella in its normal anatomical alignment. In this study, we have demonstrated the sensitivity of the patella blood supply to knee flexion angle and patella dislocation technique, particularly to patella eversion. These may be important findings with regard to surgical technique for TKA.

PMID:17826095

Patellofemoral contact pressure following high tibial osteotomy: a cadaveric study.
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Patella infera is a known complication of high tibial osteotomy (HTO) that can cause anterior knee pain due to excessive stresses associated with abnormal patellofemoral (PF) joint biomechanics. However, the translation of these abnormal biomechanics to native cartilage pressure has not been explored. The present study was designed to compare the PF contact pressures of three different HTOs in a human cadaveric model of valgus tibiofemoral correction. Nine fresh cadaveric knees underwent (1) medial opening wedge (OWHTO) with a proximal tuberosity osteotomy (PTO), (2) OWHTO with a distal tuberosity osteotomy (DTO), and (3) a lateral closing wedge (CWHTO). The specimens were mounted in a custom knee simulation rig, with muscle forces being simulated using a pulley system and weights. The PF contact pressure was recorded using an electronic pressure sensor at 15 degrees, 30 degrees, 60 degrees, 90 degrees, and 120 degrees of knee flexion, with results of the intact knees obtained as relative control. Compared to the intact knee, the DTO OWHTO and CWHTO did not significantly (P > 0.05) influence PF pressure at any flexion angle. On the other hand, PTO OWHTO lead to a significant elevation in PF cartilage pressure at 30 degrees (P < 0.05), 60 degrees (P < 0.005), and 90 degrees (P < 0.0005) knee flexion. We conclude from these results that DTO OWHTO maintains normal joint biomechanics and has no significant effect on PF cartilage pressure. In patients who complain of pre-existing anterior knee pain, DTO OWHTO or CWHTO should be considered.
Publication Types: Journal Article
PMID:17342550

Eliminating the limitations of manual crimping in stapes surgery: mid-term results of 90 patients in the Nitinol stapes piston multicenter trial.
Rajan GP, Diaz J, et al.
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OBJECTIVE: To present our mid-term results of our multicenter study using the Nitinol self-
crimping stapes piston, focusing on the interindividual variations of postoperative air-bone gap closures (ABGC), postoperative hearing results, and postoperative recurrences of conductive hearing loss and to compare these findings with our pilot group of patients. STUDY DESIGN: Prospective, multicenter cohort study involving three academic tertiary care referral centers from Australia, Switzerland, and the United States. METHODS: Ninety patients with otosclerosis undergoing laser-stapedotomy with the Nitinol stapes piston were matched to reference patients from our titanium piston database. The effects of the self-crimping Nitinol piston on the postoperative ABGC, the postoperative interindividual air-bone gap (ABG) variations, and the postoperative hearing results were investigated 3, 6, 12, 18, and 24 months postoperatively. These data were statistically compared with the results of the control patients in our titanium stapes piston database and the results of our previously published pilot study. RESULTS: The mean postoperative ABG and the interindividual variations of the postoperative ABG continue to be significantly smaller in the Nitinol group; the extent of ABGC now is significantly larger in the Nitinol piston group. The postoperative mid-term stability of ABGC was similar in both groups. No adverse reactions occurred during follow-up. CONCLUSION: Our mid-term results continue to show that the self-crimping shape memory alloy Nitinol stapes piston overcomes the limitations of manual malcrimping in stapedotomy, thus simplifying and optimizing the surgical procedure. This so far has allowed reliable, safe, and consistent ABGC in patients with otosclerosis.

Publication Types: Multicenter Study
PMID:17603322

Potential protective effects of zinc in iron overload.
Delima R, Trinder D, et al.
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The difficulty with data: greater accuracy required for policy making.
Downes S, Roach SM.
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PMID:17576194

A treatable cause of aborted sudden cardiac death.
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PMID:17680751

Outcomes after 10 years of a community-based flexible sigmoidoscopy screening program for colorectal carcinoma.
Viitala CH, Olynyk JK.
Endoscopy Unit, Department of Gastroenterology, Fremantle Hospital, Fremantle, and School of
OBJECTIVE: To evaluate the outcomes 10 years after a flexible sigmoidoscopy colorectal cancer (CRC) screening program in asymptomatic average-risk individuals. DESIGN, SETTING AND PATIENTS: In 1995, a program of flexible sigmoidoscopy-based screening of asymptomatic average-risk individuals aged 55-64 years was established at Fremantle Hospital, Western Australia. Insertion depths, pathological findings and subject-rated pain scores have been prospectively recorded. A follow-up flexible sigmoidoscopy examination was offered to attendees 5 years after the initial screening. Post-screening malignancies were determined by linkage with the Western Australian Cancer Registry in September 2006. MAIN OUTCOME MEASURES: Yield of neoplasia at initial and follow-up sigmoidoscopy, and the incidence of CRC detected after screening. RESULTS: Between 1995 and 2005, 3402 people underwent an initial flexible sigmoidoscopy screening examination (mean age, 60 years; women, 41%) and 1025 had a 5-year recall examination. Mean insertion depth was greater in men than women (60 cm v 52 cm, P<0.001). The insertion depth in women was more likely to be <40 cm (17% v 6%, P<0.001). Mean pain score was 2.9 for men and 4.0 for women (P<0.001). Fourteen per cent of initial screenings detected at least one adenoma. Over a mean follow-up time of 8 years, invasive CRC was detected by flexible sigmoidoscopy screening in 0.4% of participants; 0.7% of those with a normal result of screening later developed CRC, with 75% of these found proximal to the splenic flexure. CONCLUSIONS: Flexible sigmoidoscopy is a viable screening method, with well defined utility and limitations, for CRC screening of asymptomatic people with average risk.


Waiting times for colonoscopy and colorectal cancer diagnosis.[see comment].
Viiala CH, Tang KW, et al.
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OBJECTIVE: To evaluate whether prolonged waiting times for colonoscopy in public hospitals could result in delayed diagnosis of colorectal carcinoma. DESIGN, SETTING AND PATIENTS: Analysis of all outpatient colonoscopies performed at a Western Australian tertiary teaching hospital, 1 November 2003 - 31 October 2005. Colonoscopy data, corresponding pathological findings, category of urgency at referral for colonoscopy, and waiting time for colonoscopy were obtained. Patients were coded as having cancer if it was diagnosed by colonoscopy or if colonoscopy identified a lesion subsequently diagnosed as cancer. MAIN OUTCOME MEASURES: Colorectal carcinoma detected by outpatient colonoscopy and length of waiting time to colonoscopy. RESULTS: 1632 outpatient colonoscopies were recorded. Category I patients received a colonoscopy within the recommended 30 days from referral. Median waiting times for Category II and Category III patients exceeded recommendations (observed, 113 days and 258 days; recommended, within 90 days and 180 days, respectively), although the number of cancers detected was low (2.4% and 0.6% of referrals, respectively in each category). Early- and late-stage cancers had similar median waiting times from referral to diagnosis. Age over 65 years and the blood-loss indications - a positive faecal occult blood test or iron deficiency/anaemia - were predictors of an increased risk of carcinoma at colonoscopy. CONCLUSIONS: Waiting time for colonoscopy was not associated with an increase in the proportion of late-stage cancers diagnosed. Age over 65 years and evidence of blood loss increased the likelihood of a cancer diagnosis.

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Waiting times for colonoscopy and colorectal cancer diagnosis.
Viiala CH, Tang KW, et al.
Endoscopy Unit, Fremantle Hospital, Fremantle, WA. charliev@iinet.net.au.
OBJECTIVE: To evaluate whether prolonged waiting times for colonoscopy in public hospitals could result in delayed diagnosis of colorectal carcinoma. DESIGN, SETTING AND PATIENTS: Analysis of all outpatient colonoscopies performed at a Western Australian tertiary teaching hospital, 1 November 2003 - 31 October 2005. Colonoscopy data, corresponding pathological findings, category of urgency at referral for colonoscopy, and waiting time for colonoscopy were obtained. Patients were coded as having cancer if it was diagnosed by colonoscopy or if colonoscopy identified a lesion subsequently diagnosed as cancer. MAIN OUTCOME MEASURES: Colorectal carcinoma detected by outpatient colonoscopy and length of waiting time to colonoscopy. RESULTS: 1632 outpatient colonoscopies were recorded. Category I patients received a colonoscopy within the recommended 30 days from referral. Median waiting times for Category II and Category III patients exceeded recommendations (observed, 113 days and 258 days; recommended, within 90 days and 180 days, respectively), although the number of cancers detected was low (2.4% and 0.6% of referrals, respectively in each category). Early- and late-stage cancers had similar median waiting times from referral to diagnosis. Age over 65 years and the blood-loss indications - a positive faecal occult blood test or iron deficiency/anaemia - were predictors of an increased risk of carcinoma at colonoscopy. CONCLUSIONS: Waiting time for colonoscopy was not associated with an increase in the proportion of late-stage cancers diagnosed. Age over 65 years and evidence of blood loss increased the likelihood of a cancer diagnosis.
PMID:17371207

Movement Disorders. 2007; 22(15): 2156-2161.

The unified Parkinson's disease rating scale: Validation study of the mentation, behavior, and mood section.
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The objective of this study was to examine the validity of the mentation, behavior, and mood items included in Part I of the Unified Parkinson's Disease Rating Scale (UPDRS) and to assess its usefulness to screen for dementia, psychosis, depression, and apathy. A consecutive series of 168 patients with PD were assessed by neurologists with the UPDRS, and by psychiatrists using a comprehensive neuropsychiatric evaluation blind to each other's ratings. ROC analysis demonstrated that a score of 2 or greater on the intellectual impairment item of the UPDRS had 60% sensitivity and 92% specificity to detect dementia, as diagnosed with DSM-IV criteria. When a score of 23 or lower on the MMSE was included as an additional classification variable, the sensitivity increased to 85%. A score of 2 or greater on the thought disorder item had 43% sensitivity and 92% specificity to detect psychotic symptoms (delusions or hallucinations). A score of 2 or greater on the depression item had 77% sensitivity and 82% specificity to detect major depression as diagnosed with DSM-IV criteria. Finally, a score of 2 or greater on the motivation/initiative item had 73% sensitivity and 65% specificity to detect apathy, as diagnosed with a standardized criteria. When the sample was divided into mild (i.e. Hohen-Yahr stages I and II) versus moderate-severe PD (i.e. Hohen-Yahr stages III-V), findings remained unchanged, except that the UPDRS show unacceptably low accuracy to detect psychosis in mild PD. The mentation, behavior, and mood section of the UPDRS is an adequate screen for
depression and apathy, and has adequate sensitivity to detect dementia when combined with the Mini-Mental State Exam, but has low sensitivity to detect psychosis. copyright 2007 Movement Disorder Society.

Venlafaxine to treat severe hypotension.
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Pre-transplant pharmacokinetics as a predictor of dose requirement post renal transplantation: 1103.
Campbell S, Hawley C, et al.
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Prescribing angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in chronic kidney disease.
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In Australia the number of patients developing end-stage kidney disease is growing. Almost 70% of new cases of treated end-stage kidney disease are due to diabetes, hypertension or glomerulonephritis. The majority of these patients have a chronic decline of renal function over many years before dialysis is required, even when the initial insult is no longer present. Hypertension and the degree of proteinuria are the most important determinants for this progression and ample evidence suggests that angiotensin II is the key player in sustaining both hypertension and proteinuria. Angiotensin II mediates not only haemodynamic changes but also profibrotic and pro-inflammatory processes. Blockade of the renin-angiotensin system decreases proteinuria and slows the progression of both diabetic and non-diabetic proteinuric renal disease. Angiotensin-converting enzyme (ACE) inhibitors are first-line therapy in patients with type 1 diabetes mellitus and nephropathy, whereas angiotensin receptor blockers (ARB) are first-line therapy in patients with type 2 diabetes mellitus and microalbuminuria or overt nephropathy. Finally, treatment with ACE inhibitors delays the progression of proteinuric nephropathy in non-diabetic patients. Combination therapy with ACE inhibitors and ARB may allow a more complete blockade of the renin-angiotensin system and clinical trials show that ACE inhibitor-ARB combinations have an additive antiproteinuric effect of up to 40% compared with ACE inhibitor or ARB alone, without additional blood pressure-lowering effect. Finally, it is important to emphasize that progressive lowering of blood pressure to 120 mmHg is associated with improved renal outcome and that this effect is independent of baseline renal function.

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PMID:17295666
Antibody-mediated acquired pure red cell aplasia (PRCA) after treatment with darbepoetin.
Howman R, Kulkarni H.
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PMID:17314208

Maintenance therapy with Certolizumab Pegol for Crohn's Disease.
For the PRECISE 2 Study Investigators*, From the Hospital for General Internal Medicine, Christian Albrechts University, Kiel, Germany (S.S.); Dalhousie University, Halifax, NS, Canada (M.K.-K.); School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Australia (I.C.L.); Department of Gastroenterology, Herlev Hospital, University of Copenhagen, Herlev, Denmark (O.O.T.), Section of Gastroenterology and Nutrition, University of Chicago Medical Center, Chicago (S.B.H.); UCB Pharma, Slough, Berkshire, United Kingdom (J.M., R.B.); and Division of Gastroenterology, Mayo Clinic, Rochester, MN (W.J.S.). Address reprint requests to Dr. Schreiber at the Klinik fur Allgemeine Innere Medizin, Universitatsklinikum Schleswig-Holstein, Schittenhelmstr. 12, Kiel 24105, Germany, or at s.schreiber@mucosa.de., *The Pegylated Antibody Fragment Evaluation in Crohn's Disease: Safety and Efficacy 2 (PRECISE 2) investigators are listed in the Appendix. Background: Certolizumab pegol is a pegylated humanized Fab' fragment with a high binding affinity for tumor necrosis factor (alpha) that does not induce apoptosis of T cells or monocytes., Methods: In our randomized, double-blind, placebo-controlled trial, we evaluated the efficacy of certolizumab pegol maintenance therapy in adults with moderate-to-severe Crohn's disease. As induction therapy, 400 mg of certolizumab pegol was administered subcutaneously at weeks 0, 2, and 4. Patients with a clinical response (defined as reduction of at least 100 from the baseline score on the Crohn's Disease Activity Index [CDAI]) at week 6 were stratified according to their baseline C-reactive protein level and were randomly assigned to receive 400 mg of certolizumab pegol or placebo every 4 weeks through week 24, with follow-up through week 26., Results: Among patients with a response to induction therapy at week 6 (428 of 668 [64%]), the response was maintained through week 26 in 62% of patients with a baseline C-reactive protein level of at least 10 mg per liter (the primary end point) who were receiving certolizumab pegol (vs. 34% of those receiving placebo, P<0.001) and in 63% of patients in the intention-to-treat population who were receiving certolizumab pegol (vs. 36% receiving placebo, P<0.001). Among patients with a response to induction therapy at week 6, remission (defined by a CDAI score of less than/equal to 150) at week 26 was achieved in 48% of patients in the certolizumab group and 29% of those in the placebo group (P<0.001). The efficacy of certolizumab pegol was also shown in patients taking and those not taking glucocorticoids or immunosuppressants and in patients who had and those who had not previously taken infliximab. Infectious serious adverse events (including one case of pulmonary tuberculosis) occurred in 3% of patients receiving certolizumab pegol and in less than 1% of patients receiving placebo. Antinuclear antibodies developed in 8% of the patients in the certolizumab group; antibodies against certolizumab pegol developed in 9% of all patients who entered the induction phase., Conclusions: Patients with moderate-to-severe Crohn's disease who had a response to induction therapy with 400 mg of certolizumab pegol were more likely to have a maintained response and a remission at 26 weeks with continued certolizumab pegol treatment than with a switch to placebo. (ClinicalTrials.gov number, NCT00152425.), N Engl J Med 2007;357: 239-50., Copyright (C) 2007 Massachusetts Medical Society. All rights reserved.
Pre-clinical evaluation of 2,3-dimercaptosuccinic acid as a radiation nephrotoxicity protective agent during radiopeptide therapy of neuroendocrine malignancy.
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AIM: To determine if dimercaptosuccinic acid (DMSA), an agent originally developed as a safe non-toxic antidote for heavy metal poisoning, would be useful as a kidney radiation dose reduction agent in patients undergoing radiopeptide therapy for cancer. METHODS: Thirty-six adult male Wistar rats were injected via the penile vein with 10 MBq of Lu-DOTA-tyr(3)-octreotate. At 30 min after the radiopeptide injection, 18 of the animals (intervention group) were injected with 0.15 mg.g of DMSA (i.p.). Samples were collected for gamma counting at 24 (n=12), 48 (n=12) and 72 h (n=12) after administration of the radiopeptide. At each time point, the percentage injected dose per gram of tissue in each sample of the six control animals was compared with that of the six animals from the DMSA injection regimen. RESULTS: The i.p. injection of 0.15 mg.g of DMSA 30 min following the administration of the Lu-DOTATATE reduced the mean (95% CI) kidney retention of radiopeptide by 15.6% (2.6-24.6) at 72 h while not significantly affecting uptake in other organs. Statistical testing of the difference between the two groups of animals (DMSA versus controls) at 72 h post-administration of the radiopeptide indicated only a 3% chance that the magnitude of the reduction in kidney radiopeptide retention observed would be expected due to natural variation (i.e., if there was no difference between the groups). CONCLUSION: This study has indicated that DMSA has the potential to selectively reduce radiopeptide kidney retention. Further work is necessary to determine the most effective dose of DMSA and the most effective timing regimen, and to examine the clinical efficacy of several other chelating agents.
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Neck dissection for squamous cell carcinoma of the head and neck.
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OBJECTIVES: To investigate the successes and failures of 172 patients receiving neck dissections for squamous cell carcinoma (SCC) managed through a multidisciplinary head and neck clinic and to observe factors in predicting failure (death with head and neck cancer or local regional recurrence) or local regional recurrence alone. STUDY DESIGN: A retrospective, 14-year surgical audit. METHODS: The information from patient medical records was correlated with that of a database. Multivariate analysis was performed with the use of a logistic regression model. RESULTS: The most common site for head and neck SCC was the oral cavity (42%), with 17% of patients having tumors of unknown primary site. The disease-free survival probability was 76.7% at five years. Patients who were older at neck dissection, were nonsmokers, or who did not have radiotherapy to the primary site were more likely to die with head and neck cancer or to have local regional recurrence (P < 0.1). Patients with more radical neck dissections did not have better survival or recurrence outcomes. Lymphatic invasion appears to be the only important factor in predicting local regional recurrence alone (P = 0.1), of which 67% occurred within the first postoperative year. CONCLUSIONS: Patients with smoking-related SCC are likely to have a less aggressive disease. Adjuvant radiotherapy plays an
important role in the treatment of patients with head and neck SCC. Follow-up, especially within the first postoperative year, is essential in managing head and neck SCC. Head and neck surgeons can confidently continue their practice away from more radical neck dissections.


**Impact of the SMAS on Frey's Syndrome after parotid surgery: a prospective, long-term study.**

Wille-Bischofberger AMD, Rajan GPMD, et al.
Zurich and Luzern, Switzerland; and Fremantle, Australia, From the Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Zurich; Otolaryngology, Head and Neck Surgery Unit, Ear Sciences Center, Lions Ear and Hearing Institute, University of Western Australia; and Department of Otorhinolaryngology, Head and Neck Surgery, Kantonsspital Luzern.

Background: Clinical observations indicate that creation of the superficial musculoaponeurotic system (SMAS) flap during parotid surgery decreases postoperative gustatory sweating (Frey's syndrome) and improves cosmesis after surgery., Methods: On the basis of their previous study with 23 patients where no SMAS flap was used, the authors performed a prospective, long-term study of 61/2 years in 25 patients, using the SMAS flap, and compared these results with the postoperative results of their initial study. Twenty-two patients of the SMAS flap group were available for reassessment of gustatory sweating and symptoms. The Minor starch test was used to document the extent and intensity of postoperative sweating. Satisfaction with postoperative cosmetic results was assessed through a semiquantitative questionnaire as used in the previous study., Results: The incidence of symptomatic Frey's syndrome was significantly higher in the no-SMAS flap group after 23 months (43 percent versus 0 percent; p = 0.003). The surface extent of Frey's syndrome after 23 months was significantly reduced in the SMAS flap group (p = 0.006). At final follow-up, the incidence and extent of symptomatic Frey's syndrome showed no significant differences between the two groups (41 percent versus 56 percent; p = 0.42). The rate of satisfactory cosmetic results was significantly higher in the SMAS flap group (96 percent versus 35 percent; p < 0.05)., Conclusions: Creation of the SMAS flap in parotid surgery for benign lesions delays the onset and reduces the intensity and extent, but does not prevent the occurrence, of Frey's syndrome. It reliably improves the cosmetic results by reducing the retromandibular depression after parotid surgery., (C)2007American Society of Plastic Surgeons


**The association between C-reactive protein concentration and depression in later life is due to poor physical health: results from the Health in Men Study (HIMS).**

Almeida OP, Norman P, et al.
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Background: C-reactive protein (CRP) is a non-specific marker of inflammation that has been associated with depression and vascular disease, particularly in men. This study aimed to investigate the association between high CRP concentration and depression while taking physical health into account., Method: A cross-sectional study of a community-dwelling sample
of 5438 men aged 70+. Participants with scores >=7 on the 15-item Geriatric Depression Scale (GDS-15) were considered to display clinically significant depressive symptoms. We measured the serum concentration of CRP with a high-sensitivity assay. The assessment of physical co-morbidity included three components: the Charlson weighted index, self-report of major health events on a standardized questionnaire, and the physical component of the 36-item Short-Form Health Survey (SF-36). Other measured factors included age, native language, education, a standardized socio-economic index, smoking, prior or current history of depression treatment, cognitive impairment (Mini-Mental State Examination score <24) and body mass index (BMI).

Results: Participants with depression (n= 340) were older than their controls without depression (age in years: 76.6 +/- 4.4 v. 75.4 +/- 4.1). Men with CRP concentration >3 mg/l had an increased odds ratio (OR) [1.59, 95% confidence interval (CI) 1.20-2.11] of being depressed compared to men with CRP <= 3 mg/l. This association became non-significant once we adjusted the analysis for the measures of physical co-morbidity and other confounding factors (OR 1.22, 95% CI 0.86-1.73).

Conclusions: The physiological mechanisms that lead to the onset and maintenance of depressive symptoms in older men remain to be determined, but CRP concentration is unlikely to play a significant role in that process.


Randomized and non-randomized evidence for the effect of compulsory community and involuntary out-patient treatment on health service use: Systematic review and meta-analysis.
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Background: There is limited randomized controlled trial (RCT) evidence for compulsory community treatment. Other study methods may clarify their effectiveness. We reviewed RCT and non-RCT evidence for the effect of compulsory community treatment on hospital admissions, bed-days, compliance and out-patient contacts. Method: A systematic review of RCTs, controlled before-and-after (CBA) studies, and interrupted time series (ITS) analyses. Meta-analysis of RCTs. Results: Eight papers covering five studies (two RCTs and three CBAs) met inclusion criteria (total n = 1108). There was no statistical difference in 12-month admission rates between subjects on involuntary out-patient treatment and controls. Survival analyses of time to admission were equivocal. All five studies reported decreases in the number of bed-days following involuntary out-patient treatment but this only reached statistical significance in one situation; patients receiving the intervention were less likely to have admissions of over 100 days. There was no difference in treatment adherence between the intervention and control groups in either RCT or two of the CBA studies. However, the third CBA study reported a statistically significant increase of nearly five visits in the mean number of overall contacts in the involuntary out-patient treatment group. Conclusions: The evidence for involuntary out-patient treatment in reducing either admissions or bed-days is very limited. It therefore cannot be seen as a less restrictive alternative to admission. Other effects are uncertain. Evaluation of a wide range of outcomes should be included if this type of legislation is introduced. (PsycINFO Database Record (c) 2007 APA, all rights reserved) (journal abstract).

PMID:Peer Reviewed Journal: 2007-01920-001

The effect of antipsychotic treatment on Theory of Mind.
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Background: Deficits in a patient's 'theory of mind' (TOM) have been proposed to lead to psychosis. However, it remains unclear whether TOM deficits constitute a trait- or a state-related deficit and whether they respond to antipsychotic treatment, and also whether the change in TOM and change in psychosis are associated.

Method: In the cross-sectional component of this study, 71 patients with psychotic disorders were included and TOM ability was measured using a hinting task in which subjects had to infer real intentions behind indirect speech. In the longitudinal study, a different cohort of 17 drug-free patients were included wherein they received antipsychotic treatment for 6 weeks and the effect on psychotic symptoms and TOM was measured every 2 weeks. Associations between TOM and psychopathology were assessed and a mixed effects model was used to investigate the rate of change over time.

Results: Positive and Negative Syndrome Scale (PANSS) total scores were significantly associated with TOM scores. The hinting task was not associated with positive symptoms but was significantly associated with negative and general symptoms. The longitudinal arm of the study showed that both PANSS positive scores and TOM improved after medication was started, particularly during the first 2 weeks of antipsychotic treatment, but these changes were not associated. The TOM response at 2 weeks of antipsychotic treatment reached similar values to those obtained in the cross-sectional sample.

Conclusions: Although TOM and psychotic symptoms are related to each other, antipsychotic treatment impacts each independently, suggesting a dissimilar cognitive or neurobiological substrate for the two.

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Jack jumper ant sting anaphylaxis in South Australia.
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Liver iron transport.
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The liver plays a central role in iron metabolism. It is the major storage site for iron and also expresses a complex range of molecules which are involved in iron transport and regulation of iron homeostasis. An increasing number of genes associated with hepatic iron transport or regulation have been identified. These include transferrin receptors (TFR1 and 2), a ferrireductase (STEAP3), the transporters divalent metal transporter-1 (DMT1) and ferroportin (FPN) as well as the haemochromatosis protein, HFE and haemojuvelin (HJV), which are signalling molecules. Many of these genes also participate in iron regulatory pathways which focus on the hepatic peptide hepcidin. However, we are still only beginning to understand the complex interactions between liver iron transport and iron homeostasis. This review outlines our current knowledge of molecules of iron metabolism and their roles in iron transport and regulation of iron homeostasis.
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