Specificity of symptoms of depression in Alzheimer disease: a longitudinal analysis.  
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OBJECTIVE: Authors examined the temporal stability of symptoms of major and minor depression and apathy in dementia. METHODS: A consecutive sample of 65 patients with Alzheimer disease (AD) and depression at baseline evaluation received a follow-up psychiatric assessment that included the Structured Clinical Interview for DSM-IV and the Hamilton Rating Scale for Depression an average of 17 months later. RESULTS: Half of the sample had no depression at follow-up, and showed a significant improvement in sadness, guilt, suicidal ideation, disruption in sleep, loss of interest, loss of energy, thoughts of death, social withdrawal, psychomotor changes, changes in appetite/weight, and symptoms of anxiety. No significant changes were found on scores of irritability or apathy. CONCLUSIONS: The study demonstrates the specificity of depressive symptoms in AD and suggests that apathy and depression are different behavioral domains.  
PMID:16166410

The construct of minor and major depression in Alzheimer's disease.  
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Objective: This study examined the frequency of major and minor depression in Alzheimer's disease and determined whether these types of depression have a different functional and psychopathological impact and whether there is a change in the prevalence of major and minor depression throughout the stages of Alzheimer's disease. Method: A consecutive series of 670 patients with probable Alzheimer's disease were assessed with the Structured Clinical Interview for DSM-IV; specific instruments to rate the presence and severity of depression, anxiety, apathy, irritability, delusions, pathological affective crying, performance of activities of daily living, and social functioning; and a standardized neuropsychological evaluation. Diagnoses of major and minor depression were generated from DSM-IV criteria. Results: Twenty-six percent of the patients had major depression, 26% had minor depression, and 48% were not depressed. Major depression was significantly associated with sad mood in all three stages of the illness, although this association dropped significantly for minor depression in severe Alzheimer's disease. Both major and minor depression were significantly associated with more severe psychopathology, functional impairments, and social dysfunction. Depressive symptoms that most strongly discriminated between Alzheimer's disease patients with and without sad mood were guilty ideation, suicidal ideation, loss of energy, insomnia, weight loss, psychomotor retardation/agitation, poor concentration, and loss of interest. Conclusions: Our study demonstrates that DSM-IV criteria for major and minor depression identify clinically relevant syndromes of depression in Alzheimer's disease, mild levels of depression can produce significant functional impairment, and the severity of psychopathological and neurological impairments increases with increasing severity of depression.  
PMID:2005508255
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Alcohol-associated severe hyperhomocysteinaemia.
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Publication Types: Case Reports

Radioimmunotherapy with iodine-131 anti-CD20 chimeric monoclonal antibody (rituximab) for relapsed or refractory indolent non-Hodgkin’s Lymphoma: results of an Australian phase II trial.
Leahy MF, Seymour JF, et al.
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Publication Types: Abstract

Effects of a high-fat meal on the relative oral bioavailability of piperaquine.
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Piperaquine (PQ) is an antimalarial drug whose high lipid solubility suggests that its absorption
can be increased by a high-fat meal. We examined the pharmacokinetics of PQ phosphate (500 mg given orally) in the fasting state and after a high-fat meal in eight healthy Caucasian volunteers (randomized crossover). Plasma PQ concentration-time profiles were analyzed by using noncompartmental pharmacokinetic analysis. In the fed state, the geometric mean C(max) increased by 213%, from 21.0 to 65.8 mug/liter (P < 0.001). The time of C(max) was not significantly different between the fasting and fed states. The geometric mean area under the concentration-time curve from zero onward (AUC(0-infinity)) increased by 98%, from 3,724 to 7,362 mug h/liter (P = 0.006). The oral bioavailability of PQ relative to the fasting state was 121% greater after the high-fat meal (95% confidence interval, 26 to 216% increase; P = 0.020).

The side effects, postural blood pressure changes, electrocardiographic corrected QT interval, serum glucose, and other biochemical and hematological indices were similar in the fasting and fed states over 28 days of follow-up.

Performing a colonoscopy 12 months after surgery for colorectal neoplasia.
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BACKGROUND: There appears to be acceptance that following up patients after surgery for colorectal neoplasia is of value. However, specific issues relating to which investigations to perform and how often remain unresolved. The aim of this project was to evaluate the clinical utility of performing a colonoscopy 12 months after curative surgery for colorectal neoplasia.

METHODS: Patients were selected if they had undergone a curative resection for colorectal neoplasia, and if they had had a completed colonoscopy prior to surgery. Study endpoints included: (i) compliance with follow up; (ii) the prevalence, total number, size, and histology of polyps; and (iii) identification of recurrent or metachronous cancer. RESULTS: The study group included 253 patients of mean age 69.7 years (SD 11.6) and a male : female ratio of 1.4:1.0. Colonoscopies were completed on 90% of patients at a mean of 1.1 years following surgery. A total of 149 polyps were identified in 30% of patients. On histology, 42% were tubular adenomas, 6% tubulo-villous adenomas, 7% were villous adenomas, and 37% were hyperplastic. Advanced adenomas were identified in 7.9% of patients (95% CI 4.8-12.1%). No recurrent or metachronous cancers were identified. CONCLUSION: We have observed a high prevalence of advanced adenomas in patients undergoing a 12-month, follow-up colonoscopy after curative surgery for colorectal neoplasia. The significance of these observations requires further evaluation.
PMID:15932437

Colorectal cancer surgical care and survival: do private health insurance, socioeconomic and locational status make a difference?
Hall SE, Holman CDAJ, et al.
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Background: The purpose of the present paper was to examine patterns of surgical care and the likelihood of death within 5 years after a diagnosis of colorectal cancer, including the effects of demographic, locational and socioeconomic disadvantage and the possession of private health insurance.
Methods: The Western Australian Data Linkage System was used to extract all hospital morbidity, cancer and death records for people with a diagnosis of colorectal cancer from 1982 to 2001. Demographic, hospital and private health insurance information was available for all years and measures of socioeconomic and locational disadvantage from 1991. A logistic regression model estimated the probability of receiving colorectal surgery. A Cox regression model estimated the likelihood of death from any cause within 5 years of diagnosis.

Results: People were more likely to undergo colorectal surgery if they were younger, had less comorbidity and were married/defacto or divorced. People with a first admission to a private hospital (odds ratio (OR) 1.31, 95% confidence interval (CI): 1.16-1.48) or with private health insurance (OR 1.27, 95% CI: 1.14-1.42) were more likely to undergo surgery. Living in a rural or remote area made little difference, but a first admission to a rural hospital reduced the likelihood of surgery (OR 0.76, 95% CI: 0.66-0.87). Residency in lower socioeconomic areas also made no difference to the likelihood of having surgical treatment. The likelihood of death from any cause was lower in those who were younger, had less comorbidity, were elective admissions and underwent surgery. Residency in lower socioeconomic status and rural areas, admission to a rural hospital or a private hospital and possession of private health insurance had no effect on the likelihood of death.

Conclusions: The present study demonstrates that socioeconomic and locational status and access to private health care had no significant effects on surgical patterns of care in people with colorectal cancer. However, despite the higher rates of surgery in the private hospitals and among those with private health insurance, their survival was no better.

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Publication Types: Article


Clinical utility of a de-functioning loop ileostomy.
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BACKGROUND: The de-functioning loop ileostomy was introduced as a technique to create a manageable stoma that would divert the faecal stream from a more distal anastomosis in order to reduce the consequences of any anastomotic leakage. The value of de-functioning stomas is currently being challenged. The purpose of the present study was to review the clinical utility of performing a de-functioning loop ileostomy in patients undergoing colorectal surgery.

METHODS: A review was undertaken of a prospective colorectal database maintained at Fremantle Hospital. All end-points were defined prior to the collection of data. The study reviewed the indications and type of surgery performed. The main end-points included (i) the prevalence and management of anastomotic leaks at the primary surgery; (ii) unplanned readmissions prior to stoma closure; and (iii) the mortality, reoperation rate, and morbidity associated with closure of the stoma.

RESULTS: The study involved 233 patients of mean age 58 years (range 15-89 years) and a male:female ratio of 1.1:1. The majority of patients were undergoing elective surgery (82%) for colorectal neoplasia (71%). The commonest surgical procedure was an ultra-low anterior resection (62%). At the initial surgery, 16 patients (7.0%) developed anastomotic leaks, but only two (0.9%) required reoperation. Eleven patients (4.8%) required 12 unplanned readmissions prior to stoma closure. At closure (n = 230), there were no postoperative deaths, one patient developed an ileal anastomotic leak that was managed with antibiotics, and five patients (2.2%) required reoperation within 30 days of surgery.

CONCLUSION: De-functioning loop ileostomy was found to be associated with a relatively low morbidity and no mortality.

PMID:15777395
Coronary artery bypass grafting with valvular heart surgery after pneumonectomy.
Shanker VR, Yadav S, et al.
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PMID:2005134601

Serum elastase in the diagnosis of acute pancreatitis: a prospective study.
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rwilson52@hotmail.com
BACKGROUND: The aim of the present study was to evaluate the usefulness of the elastase 1 (E1) enzyme-linked immunosorbent assay (ELISA) in the diagnosis of acute pancreatitis. This is the first Australian evaluation of the E1 ELISA. METHODS: Three groups of patients were prospectively assessed: control patients, patients with acute pancreatitis, and patients with acute non-pancreatic abdominal pain. Serum was collected on all patients on admission and the sensitivity, specificity and diagnostic accuracy of serum elastase, amylase and lipase was determined. RESULTS: Twenty-nine patients with 30 episodes of pancreatitis, 38 patients with acute non-pancreatic abdominal pain and 121 control patients were studied. For all patient episodes E1 ELISA at a cut-off of 3.5 ng/mL had a sensitivity of 80%, specificity of 96% and an efficiency of 94% in the diagnosis of acute pancreatitis. For episodes more than 48 h after onset of symptoms, sensitivity was 100%, specificity was 96% and diagnostic efficiency was 96%. This performance was equivalent to amylase but inferior to lipase. CONCLUSION: Of the biochemical markers for pancreatitis currently available, lipase is the most useful. The relatively inferior sensitivity and problematic reference range for the ELISA E1, together with its limitations in measuring total elastase, currently prevent its widespread use.
PMID:15777396

Alcohol misuse and mood disorders following traumatic brain injury.
Jorge RE, Starkstein SE, et al.
Department of Psychiatry, The University of Iowa, Iowa City (Drs Jorge, Arndt, Moser, Crespo-Facorro, and Robinson); and School of Psychiatry and Clinical Neurosciences, The University of Western Australia, Perth (Dr Starkstein)
CONTEXT: Alcohol abuse and/or dependence (AA/D) and mood disturbance are co-occurring conditions among patients who have had a traumatic brain injury (TBI). However, the relationship between these disorders has not been extensively studied. OBJECTIVE: To examine the relationship of AA/D and post-TBI mood disorders and the effect of these conditions on psychosocial outcome. DESIGN: Prospective, case-control surveillance study conducted during the first year following trauma. Settings University hospital level I trauma centers and specialized rehabilitation units. Patients One hundred fifty-eight TBI patients with closed head injury with and without a history of AA/D. METHODS: We prospectively compared psychiatric, neuropsychological, and psychosocial outcomes among the patients, who were evaluated at baseline and at 3, 6, and 12 months after trauma. Psychiatric diagnosis was made using a structured clinical interview and DSM-IV criteria. Neuropsychological testing results and quantitative magnetic resonance images were obtained at the 3-month follow-up. RESULTS: A history of AA/D was significantly more frequent among patients who developed mood disorders during the first year following TBI. There was also a significantly higher frequency of mood
disorders among patients with alcohol abuse relapse. Patients with a history of AA/D had significantly reduced frontal gray matter volumes than did patients without a history of alcohol abuse. In addition, patients who resumed alcohol abuse had decreased medial frontal gray matter volumes and impaired performance in executive tasks. Both AA/D and mood disorders following TBI were associated with a poor vocational outcome. CONCLUSIONS: Previous alcohol abuse increases the risk of developing mood disorders after TBI, and emotional disturbance, in turn, increases the risk of alcohol abuse relapse. Alcohol's neurotoxic effects and TBI likely interact to produce greater disruption of the neural circuits that modulate reward, mood, and executive function. Patients with a history of AA/D who also developed mood disorders following TBI had major difficulties resuming a productive life.

**Vitamin D, shedding light on the development of disease in peripheral arteries.**
Norman PE, Powell JT.
School of Surgery and Pathology, The University of Western Australia, Fremantle Hospital, Fremantle, Western Australia.
Vitamin D is generally associated with calcium metabolism, especially in the context of uptake in the intestine and the formation and maintenance of bone. However, vitamin D influences a wide range of metabolic systems through both genomic and nongenomic pathways that have an impact on the properties of peripheral arteries. The genomic effects have wide importance for angiogenesis, elastogenesis, and immunomodulation; the nongenomic effects have mainly been observed in the presence of hypertension. Although some vitamin D is essential for cardiovascular health, excess may have detrimental effects, particularly on elastogenesis and inflammation of the arterial wall. Vitamin D is likely to have a role in the paradoxical association between arterial calcification and osteoporosis. This review explores the relationship between vitamin D and a range of physiological and pathological processes relevant to peripheral arteries.
PMID:15499037

Arthritis and Rheumatism. 2005; 52(9): S75-S76.
**Primary osteoarthritis in the ankle joint is strongly associated with HFE gene mutations.**
Carroll GJ.
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PMID:ISI:000232207800126

**Severe tachycardia following low-dose clozapine treatment.**
Stampfer H, Swanepoel P.
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2Head, Mental Health Service, Alma Street Centre, Fremantle Hospital, WA, Australia.
OBJECTIVE: To report a case of severe and sustained tachycardia that developed asymptotically on a low dose of clozapine (150 mg daily). METHOD: Case report. RESULTS: Serially monitored 24 h heart rate after the introduction of clozapine showed an increase in the 24 h mean from 87 to 126 bpm, a reduction of pulse variability and anomalies in sleep-wake regulation. Cessation of clozapine was followed by a rapid return to preclozapine activity. Application of the Naranjo Adverse Drug Reaction Probability Scale indicated a probable relationship between clozapine and the sustained tachycardia. CONCLUSIONS: Severe and
sustained tachycardia can develop asymptotically with a relatively low dose of clozapine and a slow titration rate. The severity of the tachycardia may not be revealed in isolated pulse measurements and may escape clinical detection without closer monitoring of heart rate.

PMID:15777419

**Copper-induced cutaneous sarcoidosis.**
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A 52-year-old woman presented with gradual painless enlargement of both earlobes. Indurated plaques were also present elsewhere. There was no evidence of a systemic granulomatous disorder. Histopathology showed foreign material associated with granulomatous inflammation. Scanning electron microscopy and energy-dispersive analysis of X-rays demonstrated foreign material composed primarily of copper. Deposition is likely to have been related to corrosion of copper-containing earrings, or from deposition at the time of ear piercing. The presence of clinically similar granulomatous lesions remote from the earlobes and not containing copper suggest the presence of underlying cutaneous sarcoidosis. The earlobe lesions are more likely to be caused by foreign matter acting non-specifically as a nidus for cutaneous sarcoidosis, rather than by a specific pro-inflammatory effect of dermal copper. After 3 months, the lesions have partially responded to oral hydroxychloroquine 200 mg/day.

PMID:15670177

**Quality project to prevent delirium after hip fracture.**
Wong DM, Niam T, et al.
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Objectives: It has been demonstrated that a series of strategies supervised by a geriatrician can reduce the incidence of delirium in elderly hip fracture patients. The aims of this project were to determine if a geriatric registrar could introduce these strategies and alter the incidence of delirium in our orthopaedic unit. Methods: The program used quality improvement methods and included staff education and the use of a checklist to facilitate the use of the strategies. We counted the number of recommendations made, the subsequent adherence to the recommendations and the before and after monthly incidence of delirium. Results: The geriatric registrars made 424 recommendations (average six per patient) during a 3-month intervention period, of which 89.9% were adhered to. Baseline data indicated an incidence of delirium of 10/28 cases (35.7%). Following introduction of the strategies, subsequent monthly incidences of delirium were 4/28 cases (14.3%), 3/22 cases (13.6%) and 2/21 cases (9.5%) (P < 0.035 compared with baseline). Conclusions: We conclude from this short program that methods proven to prevent delirium can be introduced into routine clinical practice and that this appears to prevent cases of delirium. (PsyclINFO Database Record (c) 2006 APA, all rights reserved) (journal abstract).
Publication Types: Peer Reviewed Journal
PMID:Peer Reviewed Journal: 2006-03914-009

**Quality, risk management and governance in mental health: an overview.**
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OBJECTIVE: To consider the origin, current emphasis and relevance of the concepts of quality, risk management and clinical governance in mental health. CONCLUSIONS: Increasingly, health service boards and management teams are required to give attention to clinical governance rather than corporate governance alone. Clinical governance is a unifying quality concept that aims to produce a structure and systems to assure and improve the quality of clinical services by promoting an integrated and organization-wide approach towards continuous quality improvement. Many psychiatrists will find the reduction in clinical autonomy, the need to consider the welfare of the whole population as well as the individual patient for whom they are responsible, and the requirement that they play a part in a complex systems approach to quality improvement to be a challenge. Avoiding or ignoring this challenge will potentially lead to conflict with modern management approaches and increased loss of influence on future developments in mental health services.

PMID:15777407


Jekyll and Hyde: evolving perspectives on the function and potential of the adult liver progenitor (oval) cell.
Knight B, Matthews VB, et al.
School of Medicine and Pharmacology, University of Western Australia.
The liver progenitor cell (LPC) has enormous potential for use in cell therapy to treat liver disease. Since liver regenerates readily from pre-existing hepatocytes, a role for LPCs and, indeed, their existence have been questioned. Research during the last decade has established that LPCs are an important alternative source of cells for liver regeneration. Their utility for cell therapy lies in their ability to generate both hepatocytes and cholangiocytes. However, they are observed in liver diseases that often lead to cancer and there is experimental evidence that implicates LPCs as the source of tumours. This article provides a brief history of the studies that established the functional importance of LPCs in liver disease. It focuses on mouse models that have led to the identification of factors that regulate LPC growth and differentiation and discusses LPCs derived from different sources. Recent promising results from both in vitro and vivo studies suggest that LPCs could be useful for cell therapy. In the context of liver disease, LPCs may indeed be the cell of the future and understandably "our favourite cell".

PMID:16237666


Swiss Hypertension and Risk Factor Program (SHARP): Cardiovascular risk factors management in patients with type 2 diabetes in Switzerland.
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The prevalence of hypertension in type 2 diabetics is high, though there is no published data for
Switzerland. This prospective cohort survey determined the frequency of type 2 diabetes mellitus associated with hypertension from medical practitioners in Switzerland, and collected data on the diagnostic and therapeutic work-up for cardiovascular risk patients. The Swiss Hypertension And Risk Factor Program (SHARP) is a two-part survey: The first part, I-SHARP, was a survey among 1040 Swiss physicians to assess what are the target blood pressure (BP) values and preferred treatment for their patients. The second part, SHARP, collected data from 20,956 patients treated on any of 5 consecutive days from 188 participating physicians. In I-SHARP, target BP <= 135/85 mmHg, as recommended by the Swiss Society of Hypertension, was the goal for 25% of physicians for hypertensives, and for 60% for hypertensive diabetics; values >140/90 mmHg were targeted by 19% for hypertensives, respectively 9% for hypertensive diabetics. In SHARP, 30% of the 20,956 patients enrolled were hypertensive (as defined by the doctors) and 10% were diabetic (67% of whom were also hypertensive). Six percent of known hypertensive patients and 4% of known hypertensive diabetics did not receive any antihypertensive treatment. Diabetes was not treated pharmaceutically in 20% of diabetics. Proteinuria was not screened for in 45% of known hypertensives and in 29% of known hypertensive diabetics. In Switzerland, most physicians set target BP levels higher than recommended in published guidelines. In this country with easy access to medical care, high medical density and few financial constraints, appropriate detection and treatment for cardiovascular risk factors remain highly problematic.

PMID: ISI:000234504700003


Photodynamic therapy with topical methyl aminolaevulinate for 'difficult-to-treat' basal cell carcinoma.

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BACKGROUND: Basal cell carcinoma (BCC) may be difficult to treat by conventional means, particularly if the lesions are large or located in the mid-face (H-zone). Photodynamic therapy (PDT) using topical methyl aminolaevulinate (MAL) may be a good noninvasive option for these patients. OBJECTIVES: To investigate the efficacy and safety of PDT using MAL for BCCs defined as 'difficult to treat', i.e. large lesions, in the H-zone, or in patients at high risk of surgical complications. METHODS: This was a prospective, multicentre, noncomparative study. Patients were assessed 3, 12 and 24 months after the last PDT treatment. One hundred and two patients with 'difficult-to-treat' BCC were treated with MAL PDT, using 160 mg g(-1) cream and 75 J cm(-2) red light (570-670 nm), after lesion preparation and 3 h of cream exposure. Results Ninety-five patients with 148 lesions were included in the per protocol analysis. The histologically confirmed lesion complete response rate at 3 months was 89% (131 of 148). At 12 months, 10 lesions had reappeared, and therefore the cumulative treatment failure rate was 18% (27 of 148). At 24 months, an additional nine lesions had reappeared, resulting in a cumulative treatment failure rate of 24% (36 of 148). The estimated sustained lesion complete response rate (assessed using a time-to-event approach) was 90% at 3 months, 84% at 12 months and 78% at 24 months. Overall cosmetic outcome was judged as excellent or good in 79% and 84% of the patients at 12 and 24 months, respectively. Follow-up is continuing for up to 5 years. CONCLUSIONS: MAL PDT is an attractive option for 'difficult-to-treat' BCC. Because of the excellent cosmetic results, the treatment is particularly well suited for lesions that would otherwise require extensive surgical procedures.

PMID:15840111
The role of pharmaceutical care in diabetes management.
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Pharmaceutical care (PC) is a process through which a pharmacist works with other healthcare professionals and the patient to optimise pharmacotherapy. Early studies, carried out before PC was established, provided limited evidence of the benefits of pharmacist involvement in diabetes management. More recent research has examined the role of PC in a range of diabetic subgroups. Although few of these studies were randomised, prospective and included clinically important end points such as HbA<sub>1c</sub>, some beneficial effects of PC were reported. In the most recent study, a 12-month randomised controlled trial of PC in community-based diabetic patients, regular face-to-face and telephone interviews with an experienced clinical pharmacist improved glycosylated haemoglobin while glycaemic control did not change in the controls. In addition, reductions in blood pressure, and in absolute vascular risk for patients with no history of coronary artery disease, were significantly greater in the PC group. Available evidence suggests that PC can prove a valuable component of community-based multidisciplinary diabetes care.

PMID:2006026720

Lack of meal intake compensation following nutritional supplements in hospitalised elderly women.
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Undernutrition contributes to poor clinical outcomes in hospitalised elderly patients but the potential impact of oral nutritional supplements may be reduced by suppressing subsequent food intake. We investigated this possibility in elderly female patients recovering mainly from hip fracture by studying the effect of oral supplements on subsequent food intake during an ad libitum buffet luncheon meal. We tested the effect in seven women by giving the supplement 90 min before the meal and compared energy and macronutrient intake with a control water preload condition. A similar study was carried out in another seven women with the supplement or water drink given 30 min beforehand. Both self-rated appetite and energy intake were low in these women. The nutritional supplement did not alter ratings of hunger, fullness or prospective consumption or subsequent energy and macronutrient consumption whether given 90 or 30 min before the meal. There were significant independent correlations between the lack of adequate compensation of energy intake at meals and chronic undernutrition (as assessed by skinfold thickness) and energy intake during the control meal. We conclude that elderly women during the recovery phase after major fractures have low appetites and energy intakes and markedly impaired adjustment of energy intake following liquid oral nutritional supplements. The reasons for this are unknown but are related to anorexia and undernutrition. The consumption of liquid oral supplements given up to 30 min before a meal does not suppress subsequent energy intake from meals.


Immunological effects of chimeric anti-GD3 monoclonal antibody KM871 in patients with
metastatic melanoma.
Ludwig Institute for Cancer Research, Melbourne Tumour Biology Branch, Austin Hospital,
Heidelberg, Victoria, 3084, Australia.
We conducted an open label dose-escalation phase I trial of chimeric anti-GD3 mAb KM871 in
patients with metastatic melanoma. Patients were entered into one of five dose levels (1, 5, 10,
20, and 40 mg/m²) and received three infusions of KM871 at 2-wk intervals. A metastatic
melanoma site was biopsied at day 7-10. Pharmacokinetics, immune function, and mechanism
of action of KM871 were analysed. A total of 17 patients were entered into the trial; 15 were
evaluable. KM871 had a serum half-life (T1/2-beta) based on ELISA of 10.39 +/- 1.12 d (mean
 +/- SD). Trough levels >1.0 microg/mL KM871 at 2 wk postinfusion were seen with the 10
mg/m² and higher dose levels. There were no significant changes in white blood cell subsets or
serum complement levels during KM871 treatment. KM871 was stable in vivo and maintained
binding affinity and complement-dependent cytotoxicity (CDC) function up to 2 wk postinfusion.
No significant trends in CDC or antibody-dependent cellular-cytotoxicity (ADCC) activity in
patients were observed during treatment. Analysis of tumour biopsies demonstrated a
significant increase in CD4+ T cell infiltrates compared to control patient tumours (P = 0.010),
and in patients with either stable disease (2 patients) or a clinical partial response (1 patient) at
restaging, a significant increase in CD3 and CD4 infiltrates in tumour over nonresponding
patients was observed. The favourable immune properties of KM871, combined with this
preliminary clinical data, indicate that KM871 has potential for the treatment of metastatic
melanoma.
PMID:15723450

Inhibition of adult liver progenitor (oval) cell growth and viability by an agonist of the
peroxisome proliferator activated receptor (PPAR) family member gamma, but not alpha
or delta.
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Association of osteoprotegerin with human abdominal aortic aneurysm progression.
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BACKGROUND: Abdominal aortic aneurysm (AAA) is characterized by destruction of the
arterial media associated with loss of vascular smooth muscle cells, infiltration of mononuclear
cells, and high concentration of metalloproteinases (MMPs) and cytokines. Osteoprotegerin
(OPG) has recently been identified in atherosclerosis. The presence and functional importance
of OPG in human AAA was investigated. METHODS AND RESULTS: In 146 men with small
AAA followed up by ultrasound for 3 years, serum OPG was weakly correlated with aneurysm
growth rate. Western analysis showed 3-, 8-, and 12-fold-greater OPG concentrations in human
AAA biopsies compared with biopsies of atherosclerotic narrowed aorta (1.4+/-0.1 versus 0.5+/-
0.1 ng/mg tissue; P=0.002), postmortem nondiseased abdominal aorta (1.4+/-0.1 versus 0.2+/-
0.1 ng/mg tissue; P<0.001), and nondiseased thoracic aorta (1.4+/-0.1 versus 0.1+/-0.06 ng/mg
tissue; P<0.001). Healthy human aortic vascular smooth muscle cells incubated with
recombinant human (rh)OPG (0 to 20 ng rhOPG/10(5) cells per 1 mL per 24 hours) developed
an aneurysmal phenotype defined by impaired cell proliferation (P<0.001), increased apoptosis
(P<0.01), and increased MMP-9 (92 kDa) expression (P<0.001). Incubation of monocylic THP-1 cells with 1 ng rhOPG/10(5) cells per 1 mL per 24 hours induced a 2-fold increase in MMP-9 expression (P<0.001), a 1.5-fold increase in MMP-2 activity (P=0.005), and a 2-fold stimulation of IL-6 production in these cells (P=0.02). Finally, secretion of OPG from human AAA explant was abrogated by treatment with the angiotensin II blocker irbesartan, with the reduction in secreted levels averaging 63.0+/−0.9 ng/mg tissue per 48-hour period. CONCLUSIONS: These findings support a role for OPG in the growth of human AAA and suggest a potential benefit for angiotensin II blockade in slowing aneurysm expansion.

PMID:2009340001

Association of osteoprotegerin with human abdominal aortic aneurysm progression.
Moran CSM, McCann MP, et al.
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Background-: Abdominal aortic aneurysm (AAA) is characterized by destruction of the arterial media associated with loss of vascular smooth muscle cells, infiltration of mononuclear cells, and high concentration of metalloproteinases (MMPs) and cytokines. Osteoprotegerin (OPG) has recently been identified in atherosclerosis. The presence and functional importance of OPG in human AAA was investigated..
Methods and Results:- In 146 men with small AAA followed up by ultrasound for 3 years, serum OPG was weakly correlated with aneurysm growth rate. Western analysis showed 3-, 8-, and 12-fold-greater OPG concentrations in human AAA biopsies compared with biopsies of atherosclerotic narrowed aorta (1.4+/−0.1 versus 0.5+/−0.1 ng/mg tissue; P=0.002), postmortem nondiseased abdominal aorta (1.4+/−0.1 versus 0.2+/−0.1 ng/mg tissue; P<0.001), and nondiseased thoracic aorta (1.4+/−0.1 versus 0.1+/−0.06 ng/mg tissue; P<0.001). Healthy human aortic vascular smooth muscle cells incubated with recombinant human (rh)OPG (0 to 20 ng rhOPG/105 cells per 1 mL per 24 hours) developed an aneurysmal phenotype defined by impaired cell proliferation (P<0.001), increased apoptosis (P<0.01), and increased MMP-9 (92 kDa) expression (P<0.001). Incubation of monocylic THP-1 cells with 1 ng rhOPG/105 cells per 1 mL per 24 hours induced a 2-fold increase in MMP-9 expression (P<0.001), a 1.5-fold increase in MMP-2 activity (P=0.005), and a 2-fold stimulation of IL-6 production in these cells (P=0.02). Finally, secretion of OPG from human AAA explant was abrogated by treatment with the angiotensin II blocker irbesartan, with the reduction in secreted levels averaging 63.0+/−0.9 ng/mg tissue per 48-hour period., Conclusions:- These findings support a role for OPG in the growth of human AAA and suggest a potential benefit for angiotensin II blockade in slowing aneurysm expansion., (C) 2005 American Heart Association, Inc.

Iron overload.
Siah CW, Trinder D, et al.
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Iron overload disorders represent a heterogenous group of conditions resulting from inherited and acquired causes. With the discovery of new proteins and genetic defects we have gained greater insight into their causation at the molecular level and the complex mechanisms of normal and disordered iron homeostasis. Here we review the normal mechanisms and regulation of gastrointestinal iron absorption and liver iron transport and their dysregulation in
iron overload states. Advances in the understanding of the natural history of iron overload disorders and new methods for clinical detection and management of hereditary hemochromatosis are also reviewed.

PMID:15885682

Clinica Chimica Acta. 2005; Sep 30 [Epub ahead of print].

**Nurse-based evaluation of point-of-care assays for glycated haemoglobin.**
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ARC Consulting, Perth, W Australia 6050, Australia.


**Hepascore: An Accurate Validated Predictor of Liver Fibrosis in Chronic Hepatitis C Infection.**
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Background: Staging hepatic fibrosis by liver biopsy guides prognosis and treatment of hepatitis C, but is invasive and expensive. We sought to create an algorithm of serum markers that accurately and reliably predict liver fibrosis stage among hepatitis C patients. Methods: Ten biochemical markers were measured at time of liver biopsy in 117 untreated hepatitis C patients (training set). Multivariate logistic regression and ROC curve analyses were used to create a predictive model for significant fibrosis (METAVIR F2, F3, and F4), advanced fibrosis (F3 and F4), and cirrhosis (F4). The model was validated in 104 patients from other institutions. Results: A model (Hepascore) of bilirubin, \( \gamma \)-glutamyltransferase, hyaluronic acid, \( \alpha \)-2-macroglobulin, age, and sex produced areas under the ROC curves (AUCs) of 0.85, 0.96, and 0.94 for significant fibrosis, advanced fibrosis, and cirrhosis, respectively. In the training set, a score \( \geq 0.5 \) (range, 0.0-1.0) was 92% specific and 67% sensitive for significant fibrosis, a score \(< 0.5 \) was 81% specific and 95% sensitive for advanced fibrosis, and a score \(< 0.84 \) was 84% specific and 71% sensitive for cirrhosis. Among the validation set, the AUC for significant fibrosis, advanced fibrosis, and cirrhosis were 0.82, 0.90, and 0.89, respectively. A score \( \geq 0.5 \) provided a specificity and sensitivity of 89% and 63% for significant fibrosis, whereas scores \(< 0.5 \) had 74% specificity and 88% sensitivity for advanced fibrosis. Conclusions: A model of 4 serum markers plus age and sex provides clinically useful information regarding different fibrosis stages among hepatitis C patients.


**Prevalence and progression of subclinical hypothyroidism in women with type 2 diabetes: The Fremantle Diabetes Study.**
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Objective: To assess the prevalence and progression of subclinical hypothyroidism in women with type 2 diabetes. Design and Patients: Cross-sectional and longitudinal observational assessment of thyroid function in 420 adult females with type 2 diabetes randomly selected from participants in the community-based Fremantle Diabetes Study. Measurements: Serum TSH, antibodies to thyroperoxidase (anti-TPO) and serum free T4 were measured at baseline and after 5 years. Baseline glycated haemoglobin (HbA<sub>1c</sub>), serum glucose, serum total and high density lipoprotein (HDL) cholesterol, serum triglycerides and antibodies to glutamic acid decarboxylase (anti-GAD) were also used in analyses. Results: After exclusion of patients with known thyroid disease or taking amiodarone or lithium at baseline, the prevalence of subclinical hypothyroidism (a raised serum TSH and normal serum free T4) was 8.6%. Subclinical hypothyroidism was associated with anti-TPO status and age, but there were no independent associations with serum cholesterol, history of coronary heart disease, HbA<sub>1c</sub> or hypoglycaemic therapy. In the subgroup of patients restudied after 5 years, none of those who had subclinical hypothyroidism at baseline had overt hypothyroidism regardless of anti-TPO status. Conclusions: In women with type 2 diabetes without known thyroid disease, subclinical hypothyroidism is a common but incidental finding. The routine screening of thyroid function in type 2 diabetes is questionable. (C) 2005 Blackwell Publishing Ltd.

PMID:2005168817


The bulge, booze, and the liver.
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PMID:2005573503


The role of mechanical bowel preparation in patients undergoing elective colorectal surgery.
Fremantle Hospital, Perth, Australia


Randomised controlled trial of general practitioner compared to surgeon follow-up of patients with colon cancer.
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A collaborative model of community health nursing practice.
Downie J, Ogilvie S, et al.
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Consultant, South Metropolitan Population Health Service, Perth, Western Australia. This paper discusses a strategic collaborative partnership between a Western Australian university and a community health service based on a Practice-Research Model. The partnership has involved a senior academic (0.2 FTE) working in the community health setting as a Nurse Research Consultant since 1998. The first section of the paper draws on the nursing literature on collaborative models and describes the broad background to the partnership and development of the Model. The second section presents in detail the results of a recent evaluation that involved a brief survey and follow-up interviews to determine community health nurses’ understanding and perceptions of the partnership Model. Three main themes emerged from the interviews: (1) Advancement of learning captured the extent to which the Nurse Research Consultant position helped to educate nurses and promote and develop research and best-practice; (2) Job satisfaction and self-confidence encompassed the extent to which participants felt nursing management were supportive of their professional education and pursuit of best-practice solutions, and (3) Situational opportunity, which reflected the more negative comments expressed by participants and related mostly to the restricted availability of Nurse Research Consultant and a focus on mainstream research priorities. The results suggest that the partnership Model provided the nurses with the opportunity to develop an increased understanding of the role of research in clinical practice and confidence in their own ability to reflect on current nursing practice. This allowed them to identify clinical problems in order to deliver and evaluate best-practice solutions, as evidenced by a change in attitude from the previous evaluation. However, it was also noted that the operational performance of the Model needs continual monitoring to ensure that all nurses have equitable access opportunities. PMID:16393100

Establishing best practice guidelines for administration of intra muscular injections in the adult: A systematic review of the literature.
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This article describes best practice guidelines for the administration of intramuscular injections developed after the identification of 300 abstracts and a review of 150 articles on the subject area. While the administration of medication via the intramuscular route is a daily occurrence for nurses working in both hospitals and community settings, several concerns and complications have been identified with the procedure. Routinely, nurses are required to make numerous decisions regarding factors such as needle size, length and the site to be used during the administration of medication into muscle tissue. Therefore, it is important that relevant up-to-date guidelines are available to assist nurses to make informed decisions about the technique to use. Techniques delivering medication to the correct site will facilitate efficacious outcomes for the client and ensure the delivery of quality nursing care in all health care settings. PMID:16393108

Critical care research and ethics.
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PMID:16548823
Supplemental jet ventilation in a case of ARDS complicated by bronchopleural fistulae.

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OBJECTIVE: To present a case of unusual ventilatory strategy in a 17 year old girl with the acute respiratory distress syndrome (ARDS) complicated by bilateral bronchopleural fistulae.

METHODS: The patient was ventilated with a combination of conventional pressure control ventilation (PCV) and high frequency jet ventilation (HFJV) for 133 and 110 days, respectively.

RESULTS: Despite prolonged hypoxia, extensive barotrauma and nosocomial infections, she survived without significant impairment of respiratory function. Two years later she was healthy and independent with only mildly reduced respiratory reserve. CONCLUSIONS: The combination of PCV and HFJV was beneficial in this case of ARDS complicated by bronchopleural fistulae. The case also highlights the utility of HFJV in the desperately hypoxic patient with extensive airway disruption.

PMID:16548803

Ethical intensive care research: development of an ethics handbook.

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Conduct of research involving humans in the intensive care unit (ICU) setting is complex and challenging. The vulnerable nature of critically ill patients raises issues of patient safety, and informed consent is difficult. With an increasing global interest in human research ethics, broadened government mandates have targeted improvements in research participant protection and research governance. A parallel rise in health consumerism and advocacy for privacy and protection of personal health information requires a clear understanding of the research participant role and importance of risk disclosure. In addition, the potential for conflicts of interest in a climate of increasingly competitive research funding, requires caution and transparency in related financial and contractual arrangements. The Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG) fosters collaborative ICU research activity. We have developed An Ethics Handbook for Researchers (EH) for the ANZICS CTG for intended use by researchers in Australian and New Zealand ICUs. The purpose of the EH is to act as a practical advisory guide/supplement; to add clarification regarding ethical issues specific to intensive care research, to assist in the expedition of ethics committee research submission and to summarise available useful resources. This article introduces a precis of key issues from the EH including specific ethical difficulties pertaining to ICU research, a summary of the process by which ethics committee decisions in Australia and New Zealand are informed, and the use of ethical checklists to assist researchers.

Cardiovascular aspects of anaphylaxis: implications for treatment and diagnosis.

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PURPOSE OF REVIEW: Anaphylactic cardiovascular collapse can be resistant to treatment with epinephrine (adrenaline) and, in some cases, diagnostic uncertainty compromises follow-up
care. The purpose of this review is to examine recent studies relevant to the management and diagnosis of this condition. RECENT FINDINGS: Nausea, vomiting, incontinence, diaphoresis, dyspnoea, hypoxia, dizziness and collapse are associated with hypotension. Relative bradycardia (falling heart rate despite hypotension) is a consistent feature of hypotensive insect sting anaphylaxis and may represent a non-specific physiological response to severe hypovolaemia in conscious individuals. Upright posture has been found to be associated with death from anaphylaxis. Animal studies have found the intramuscular route for epinephrine is ineffective, intravenous boluses temporarily effective, but intravenous infusions of epinephrine are able to reverse anaphylactic shock. In one animal model, antihistamines were found to be harmful. A prospective human study provides evidence for the efficacy of treatment with intravenous epinephrine infusion and fluid (volume) resuscitation. Case reports support the use of the vasoconstrictors metaraminol, methoxamine and vasopressin if adrenaline is ineffective. Repeated measurements of mast cell tryptase are more sensitive and specific than a single measurement for the diagnosis of anaphylaxis. SUMMARY: Current evidence supports use of the supine/Trendelenburg position, epinephrine by intravenous infusion and aggressive volume resuscitation. If these fail, atropine should be considered for severe bradycardia and potent vasoconstrictors may be useful. To confirm the diagnosis of anaphylaxis, serial measurements of mast cell tryptase may be preferable to a single measurement.

PMID:15985820


Recent concepts in non-alcoholic fatty liver disease.
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Non-alcoholic fatty liver disease (NAFLD) is present in up to one-third of the general population and in the majority of patients with metabolic risk factors such as obesity and diabetes. Insulin resistance is a key pathogenic factor resulting in hepatic fat accumulation. Recent evidence demonstrates NAFLD in turn exacerbates hepatic insulin resistance and often precedes glucose intolerance. Once hepatic steatosis is established, other factors, including oxidative stress, mitochondrial dysfunction, gut-derived lipopolysaccharide and adipocytokines, may promote hepatocellular damage, inflammation and progressive liver disease. Confirmation of the diagnosis of NAFLD can usually be achieved by imaging studies, however, staging the disease requires a liver biopsy. NAFLD is associated with an increased risk of all-cause death, probably because of complications of insulin resistance such as vascular disease, as well as cirrhosis and hepatocellular carcinoma, which occur in a minority of patients. NAFLD is also now recognized to account for a substantial proportion of patients previously diagnosed with ‘cryptogenic cirrhosis’. Diabetes, obesity and the necroinflammatory form of NAFLD known as non-alcoholic steatohepatitis, are risk factors for progressive liver disease. Current treatment relies on weight loss and exercise, although various insulin-sensitizing medications appear promising. Further research is needed to identify which patients will achieve the most benefit from therapy.

PMID:16108837


Glycemic determinants of therapeutic progression in type 2 diabetes in a community-based cohort: The Fremantle Diabetes Study.
Davis TME, Davis WA, et al.
Longitudinal predictors of reduced mobility and physical disability in patients with type 2 diabetes: the Fremantle Diabetes Study.

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Effect of a pharmaceutical care program on vascular risk factors in type 2 diabetes: The Fremantle Diabetes Study.

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OBJECTIVE - To examine the effect of a 12-month pharmaceutical care (PC) program on vascular risk in type 2 diabetes. RESEARCH DESIGN AND METHODS - We recruited 198 community-based patients randomized to PC or usual care. PC patients had face-to-face goal-directed medication and lifestyle counseling at baseline and at 6 and 12 months plus 6-weekly telephone assessments and provision of other educational material. Clinical, biochemical, and medication-related data were sent regularly to each patient's physician(s). The main outcome measure was change in HbA1c. A diabetes-specific risk engine was used to estimate changes in 10-year coronary heart disease (CHD) and stroke risk in patients without a history of cardiovascular disease. RESULTS - At total of 180 patients (91%) completed the study. Mean (95% CI) reductions were greater in PC case subjects (n = 92) than control subjects (n = 88) for HbA1c (-0.5% [95% CI -0.7 to -0.3] vs. 0 [-0.2 to 0.2]) and systolic (-14 mmHg [-19 to -9] vs. -7 [-11 to -2]) and diastolic (-5 mmHg [-8 to -3] vs. -2 [-4 to 1]) blood pressure (P <= 0.043). The improvement in HbA1c persisted after adjustment for baseline value and demographic and treatment-specific variables. The median, (interquartile range) 10-year estimated risk of a first CHD event decreased in the PC case subjects (25.1% [15.6-36.2] to 20.3 [14.6-30.2]; n = 42, P = 0.002) but not in the control subjects (26.1% [17.2-39.4] vs. 26.4 [16.7-38.0]; n = 52, P = 0.17). CONCLUSIONS - A 12-month PC program in type 2 diabetes reduced glycemia and blood pressure. Pharmacist involvement contributed to improvement in HbA1c independently of pharmacotherapeutic changes. PC could prove a valuable component of community-based multidisciplinary diabetes care. (C) 2005 by the American Diabetes Association.

Determinants of diabetes-attributable non-blood glucose-lowering medication costs in type 2 diabetes: The Fremantle Diabetes Study.

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OBJECTIVE - To prospectively examine the magnitude and predictors of diabetes-attributable non-blood glucose-lowering (non-BGL) medication costs in type 2 diabetes. RESEARCH DESIGN AND METHODS - Detailed data from 593 community-dwelling patients were available over 4.3 +/- 0.4 years. Diabetes-attributable costs (in year 2000 Australian dollars [A$]) were calculated by applying a range of attributable proportions for each complication for which medication was prescribed. RESULTS - Non-BGL medications accounted for 75% of all prescription medication costs over the study period, and one-third were attributable to diabetes.
The median annual cost (in A$) of non-BGL medications per patient increased from A$220 to A$429 over 4 years (P < 0.001), whereas the diabetes-attributable contribution increased from A$31 (range 15-40) to A$159 (range 95-219) per patient (P < 0.001). Diabetes-attributable hospital costs remained stable during the study. Diabetes-attributable non-BGL costs were skewed and, therefore, square root transformed before regression analysis. Independent baseline determinants of [square root]cost/year were coronary heart disease, systolic blood pressure, total serum cholesterol, ln(serum triglycerides), ln(albumin-to-creatinine ratio), serum creatinine, education, and, negatively, male sex and fasting plasma glucose (P <= 0.043; \( R^2 = 29\% \)). Projected to the Australian population, diabetes-attributable non-BGL medication costs for patients with type 2 diabetes totaled A$79 million/year. CONCLUSIONS - The median annual cost of diabetes-attributable non-BGL medications increased fivefold over 4 years. This increase was predicted by vascular risk factors and complications at baseline. Better-educated patients had higher costs, probably reflecting improved health care access. Men and patients with higher fasting plasma glucose levels had lower costs, suggesting barriers to health care and/or poor self-care. The contemporaneous containment of hospital costs may be due to the beneficial effect of increased medication use. PMID:2005055830


Predictors of first stroke in Type 1 diabetes: The Fremantle Diabetes Study.
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AIMS: To examine prospectively the relationship between vascular risk factors and stroke in Type 1 diabetes. METHODS: A community-based sample of 126 adult Type 1 patients was recruited between 1993 and 1996 and followed annually for a mean+/-sd of 7.2 +/- 1.6 years. Cerebrovascular events before and after recruitment were identified from history and examination findings, hospital morbidity data and death notifications. RESULTS: Six patients suffered a first stroke during follow-up, of which five were ischaemic and one a subarachnoid haemorrhage on cranial computed tomography. Patients were subdivided into those with no history of stroke/transient ischaemic attack (TIA) at baseline and no subsequent ischaemic stroke (Group 1, n=114), those with a history of stroke/TIA at baseline (Group 2, n=7), and those with no history of stroke/TIA at baseline but who suffered a first ischaemic stroke during follow-up (Group 3, n=5). Group 1 patients were the youngest, had the shortest diabetes duration and were the least likely to be taking antihypertensive medication or aspirin. Amongst a range of potential baseline predictors of first stroke including glycated haemoglobin, only serum HDL-cholesterol differentiated Group 3 patients (0.69 +/- 0.17 mmol/l) from those in the other groups (1.26 +/- 0.42 and 1.28 +/- 0.45 mmol/l for Groups 1 and 2 respectively, P<0.05). CONCLUSIONS: The present association between low serum HDL-cholesterol and ischaemic stroke patients suggests that aggressive management of dyslipidaemia may protect against cerebrovascular disease in Type 1 diabetes. PMID:15842508


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Asymptomatic bacteriuria as a predictor of subsequent hospitalisation with urinary tract infection in diabetic adults: The Fremantle Diabetes Study.
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AIMS/HYPOTHESIS: We examined the prognosis of well-characterised community-based diabetic patients with asymptomatic bacteriuria (ASB). METHODS: We studied 496 adults with type 1 or 2 diabetes participating in a prospective observational study. In addition to detailed clinical and laboratory data, a single mid-stream urine sample was taken for aerobic culture and antibiotic-sensitivity testing. ASB was defined as >=10^5 colony-forming units/ml of one or two organisms without symptoms of urinary infection. Patients were followed for 2.9+-0.6 years for hospital admission for/with urosepsis or death. RESULTS: Thirty-six patients (7.3%) had ASB, comprising 33 females (14.4% of all females) and three males (1.1% of all males). Only female sex predicted ASB amongst a range of variables including indices of metabolic control. Twenty-nine patients (5.8%) were subsequently hospitalised with urosepsis. Of these, urosepsis was the principal diagnosis in 12 (41%). In a Cox proportional hazards model, ASB was associated with an increased risk of hospitalisation for urosepsis as principal diagnosis (hazard ratio [95% CI] 4.4 [1.2-16.5]; p=0.004). ASB did not predict the combined endpoint of hospitalisation with urosepsis as principal or secondary diagnosis (2.3 [0.8-6.7]; p=0.12), or of non-urinary sepsis as principal (n=12) or principal/secondary (n=28) diagnosis (p>0.3).
CONCLUSIONS/INTERPRETATION: ASB identifies diabetic patients who are at significantly increased risk of subsequent urosepsis requiring hospitalisation. Further large-scale studies are needed to establish the cost-effectiveness of screening for, and pre-emptive treatment of ASB, especially in females.
PMID:15918016

Islet autoantibodies in clinically diagnosed type 2 diabetes: prevalence and relationship with metabolic control (UKPDS 70).
Davis TME, Wright AD, et al.
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AIMS/HYPOTHESIS: We examined the prevalence of islet autoantibodies and their relationship to glycaemic control over 10 years in patients diagnosed clinically with new-onset type 2 diabetes. METHODS: Patient clinical characteristics and autoantibody status were determined at entry to the UK Prospective Diabetes Study (UKPDS) before randomisation to different glucose control policies. Patients were followed for 10 years. RESULTS: Data available on 4,545 of the 5,102 UKPDS patients showed that 11.6% had antibodies to at least one of three antigens: islet cell cytoplasm, glutamic acid decarboxylase and islet autoantibody 2A (IA-2A). Autoantibody-positive patients were younger, more often Caucasian and leaner, with lower beta cell function and higher insulin sensitivity than autoantibody-negative patients. They also had higher HbA1c, and HDL-cholesterol levels, and lower blood pressure, total cholesterol and plasma triglyceride levels. Despite relative hyperglycaemia, autoantibody-positive patients were less likely to have the metabolic syndrome (as defined by the National Cholesterol Education Program Adult Treatment Program III), reflecting a more beneficial overall risk factor profile. Of 3,867 patients with post-dietary run-in fasting plasma glucose (FPG) values between 6.0 and 14.9 mmol/l and no hyperglycaemic symptoms, 9.4% were autoantibody-positive, compared with 25.1% of 678 patients with FPG values of 15.0 mmol/l or higher, or hyperglycaemic symptoms. In both groups, no differences were seen between those with and without
autoantibodies in changes to HbA(1)c over time, but autoantibody-positive patients required insulin treatment earlier, irrespective of the allocated therapy (p<0.0001).

CONCLUSIONS/INTERPRETATION: Autoantibody-positive patients can be treated initially with sulphonylurea, but are likely to require insulin earlier than autoantibody-negative patients.

PMID:15729570

Lavage enhances the production of proinflammatory mediators by peritoneal mesothelial cells in an experimental model.
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PURPOSE: There is a lack of clinical evidence supporting the use of lavage in patients with peritonitis. It is known that fluids such as normal saline cause temporary damage to the peritoneum and that increased production of proinflammatory mediators is associated with a poor outcome. This study used an experimental model to evaluate the effect of lavage on the peritoneal mesothelium and the ability of peritoneal mesothelial cells to produce a battery of proinflammatory mediators (TNFalpha, IL-1beta, GROalpha, and ICAM-I.).

METHODS: Wistar rats were allocated into four groups (control, peritonitis, lavage, peritonitis plus lavage).

Peritonitis was induced by exposure to zymosan and saline was used for lavage. After 18, 24, and 43 hours, mesothelial imprints were taken from the peritoneum for histology, semiquantitative reverse transcription-polymerase chain reaction, Western blot analyses, and immunocytochemistry.

RESULTS: Both peritonitis and lavage caused peritoneal damage at 18 and 24 hours, and this effect was additive. At varying times, peritoneal mesothelial cells from animals undergoing lavage had greater up-regulation (P < 0.05) of mRNA expression for TNFalpha, IL-1beta, GROalpha, and ICAM-I and greater production (P < 0.05) of TNFalpha, IL-1RII, GROalpha, and ICAM-I. The latter was heavily concentrated at the cell membrane.

CONCLUSIONS: Lavage causes self-limiting peritoneal damage and this is associated with an up-regulation of proinflammatory mediators in animals with peritonitis.

PMID:15875296

Emergency department-based intervention with adolescent substance users: 12-month outcomes.
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We evaluated the 12-month outcomes of a brief intervention, enhanced by a consistent support person, which aimed to facilitate referral attendance for substance use treatment following a hospital alcohol or other drug (AOD) presentation. Outcomes were assessed as: attendance for substance use treatment; the number of hospital AOD ED presentations; change in AOD consumption and psychological wellbeing (GHQ-12). We recruited 127 adolescents, with 60 randomised to the intervention and 67 receiving usual care. At 12 months, 87 (69%) were re-interviewed. Significantly more of the intervention than the usual care group (12 versus 4) had attended a treatment agency. Excluding the index presentations, there were 66 AOD hospital presentations post intervention, with the proportion of AOD events falling for the intervention group, whilst no change occurred for the usual care group. Irrespective of randomisation, those who attended for substance use treatment had a greater decline in total self-reported drug use
than the remainder. Both intervention and usual care groups had improved GHQ-12 scores by 12 months, with reduction in GHQ scores correlated with reduced drug use. In conclusion, while brief intervention in ED only has limited success in facilitating adolescents to attend for subsequent AOD treatment, it can significantly reduce the number of AOD related ED presentations. (PsycINFO Database Record (c) 2005 APA, all rights reserved) (journal abstract).

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**Piperaquine: a resurgent antimalarial drug.**
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Piperaquine is a bisquinoline antimalarial drug that was first synthesised in the 1960s, and used extensively in China and Indochina as prophylaxis and treatment during the next 20 years. A number of Chinese research groups documented that it was at least as effective as, and better tolerated than, chloroquine against falciparum and vivax malaria, but no pharmacokinetic characterisation was undertaken. With the development of piperaquine-resistant strains of Plasmodium falciparum and the emergence of the artemisinin derivatives, its use declined during the 1980s. However, during the next decade, piperaquine was rediscovered by Chinese scientists as one of a number of compounds suitable for combination with an artemisinin derivative. The rationale for such artemisinin combination therapies (ACTs) was to provide an inexpensive, short-course treatment regimen with a high cure rate and good tolerability that would reduce transmission and protect against the development of parasite resistance. This approach has now been endorsed by the WHO, Piperaquine-based ACT began as China-Vietnam 4 (CV4(R): dihydroartemisinin [DHA], trimethoprim, piperaquine phosphate and primaquine phosphate), which was followed by CV8(R) (the same components as CV4 but in increased quantities), Artecom(R) (in which primaquine was omitted) and Artekin(R) or Duo-Cotecxin(R) (DHA and piperaquine phosphate only). Recent Indochinese studies have confirmed the excellent clinical efficacy of piperaquine-DHA combinations (28-day cure rates >95%), and have demonstrated that currently recommended regimens are not associated with significant cardiotoxicity or other adverse effects. The pharmacokinetic properties of piperaquine have also been characterised recently, revealing that it is a highly lipid-soluble drug with a large volume of distribution at steady state/bioavailability, long elimination half-life and a clearance that is markedly higher in children than in adults. The tolerability, efficacy, pharmacokinetic profile and low cost of piperaquine make it a promising partner drug for use as part of an ACT. Copyright 2005 Adis Data Information BV
characterisation was undertaken. With the development of piperaquine-resistant strains of Plasmodium falciparum and the emergence of the artemisinin derivatives, its use declined during the 1980s. However, during the next decade, piperaquine was rediscovered by Chinese scientists as one of a number of compounds suitable for combination with an artemisinin derivative. The rationale for such artemisinin combination therapies (ACTs) was to provide an inexpensive, short-course treatment regimen with a high cure rate and good tolerability that would reduce transmission and protect against the development of parasite resistance. This approach has now been endorsed by the WHO. Piperaquine-based ACT began as China-Vietnam 4 (CV4): dihydroartemisinin [DHA], trimethoprim, piperaquine phosphate and primaquine phosphate), which was followed by CV8 (the same components as CV4 but in increased quantities), Artecom (in which primaquine was omitted) and Artekin or Duo-Cotecxin (DHA and piperaquine phosphate only). Recent Indochinese studies have confirmed the excellent clinical efficacy of piperaquine-DHA combinations (28-day cure rates >95%), and have demonstrated that currently recommended regimens are not associated with significant cardiotoxicity or other adverse effects. The pharmacokinetic properties of piperaquine have also been characterised recently, revealing that it is a highly lipid-soluble drug with a large volume of distribution at steady state/bioavailability, long elimination half-life and a clearance that is markedly higher in children than in adults. The tolerability, efficacy, pharmacokinetic profile and low cost of piperaquine make it a promising partner drug for use as part of an ACT.


HIV antibody seroprevalence in the emergency department at Port Moresby General Hospital, Papua New Guinea.
Curry C, Bunungam P, et al.
Fremantle Hospital, Fremantle, Western Australia, Australia. chriscurry1@compuserve.com
OBJECTIVE: To determine the prevalence of HIV antibody in patients presenting to the ED at Port Moresby General Hospital in Papua New Guinea. METHOD: Three hundred patients in whom blood samples were taken for investigation of illness or injury between April and July 2003 were surveyed for HIV antibodies. Sex, age and presenting illness were recorded. RESULTS: Fifty-four tests (18%, 95% confidence interval [CI] 14-23%) were positive. Forty-seven per cent were men and 53% were women. The most common presenting illnesses were respiratory tract infections (37%) and gastrointestinal tract infections (26%). Because of resource constraints results were not linked to patients and there was no follow up. CONCLUSION: These limited data support the prediction that the developing HIV/AIDS epidemic in Papua New Guinea will be serious.


A double-blind, randomized trial of intravenous versus intramuscular antivenom for red-back spider envenoming.
Ellis RM, Sprivulis PC, et al.
Department of Emergency Medicine, Fremantle Hospital.
OBJECTIVE: To compare the efficacy of intravenous versus intramuscular antivenom (AV) in the treatment of Red-back spider (RBS) envenoming. METHODS: Randomized, double-dummy, double-blind, multicentre trial of patients with red-back spider envenoming requiring AV treatment recruited from five hospital EDs in Western Australia. RESULTS: Thirty-five patients were recruited; two were excluded; 33 were available for initial analysis, but two who were unblinded after one ampoule of trial AV and given i.v. AV had limited data; 31 remained in the
study and had more complete data. After AV, pain scores for both i.m. and i.v. groups improved rapidly. At 24 h, the i.v. group was better with a 55% absolute difference (76% vs. 21%; 95% CI 25-85% difference) in the proportion pain-free. There were no safety issues. CONCLUSIONS: Red-back spider antivenom was initially effective by both i.m. and i.v. routes. The study generates the hypothesis that at 24 h, significantly more patients are pain-free with i.v. administration. Definitive recommendations on the optimal route of administration of RBS AV await the results of further studies.

PMID:15796730


Triage nurses validly and reliably estimate emergency department patient complexity. Vance J, Sprivulis P.
Emergency Department, Fremantle Hospital, Fremantle, Western Australia, Australia.

OBJECTIVE: To access the validity and reliability of triage nurse estimates of ED patient complexity. METHODS: Prospective, single-blinded evaluation of triage nurse estimates of patient complexity, where a high-complexity patient is defined as a patient requiring two or more procedures or investigations or consultations. Validity of complexity estimates was assessed by comparison with the number of actual procedures, investigations and consultations requested. Reliability of triage nurse estimates of complexity was assessed by comparison with assessment nurse estimates of complexity. RESULTS: The specific proportion of agreement and spearman correlation coefficient of triage nurse estimates of complexity with actual procedure, investigations and consultation use were 0.83 (95% confidence interval [CI] 0.79-0.88) and 0.59 (95% CI 0.51-0.66), respectively. The specific proportion of agreement and kappa of triage nurse estimates of complexity with assessment nurse estimates were 0.80 (95% CI 0.73-0.87) and 0.59 (95% CI 0.47-0.71), respectively. CONCLUSIONS: Triage nurses make valid and reliable estimates of patient complexity. This information might be used to guide ED work flow and ED casemix system analysis.

PMID:16091102


Emergency physicians can reliably assess emergency department patient cardiac output using the USCOM continuous wave Doppler cardiac output monitor. Dey I, Sprivulis P.
Department of Emergency Medicine, Fremantle Hospital, Fremantle, Western Australia, Australia.

Abstract Objectives: 1 To develop a training package for ultrasonic cardiac output monitor (USCOM) cardiac output assessments and determine the number of proctored studies necessary for skill acquisition. 2 To develop criteria for acceptance of cardiac output results obtained with the USCOM. 3 To evaluate the reliability of USCOM cardiac output assessments in the ED. Methods: The authors developed an audiovisual training package. Four emergency physicians and one geriatrician subsequently underwent hands-on training, and skill acquisition was assessed at the fifth, 10th, 15th and 20th examinations. Six image-scoring criteria were developed to assess acoustic image quality. Upon completion of training a protocol was developed to optimize interassessor reliability. Two trained emergency physicians then performed blinded examinations on ED patients using the protocol and interassessor reliability was evaluated. Results: During training average image score improved between the fifth and 20th assessed patient from 4.6 (95% CI 4.0-5.3) to 5.5 (95% CI 5.0-6.0, P(t-test) = 0.02) out of 6 and average intra-assessor cardiac output difference improved from 17% (95% CI 4-25) to 5% (95% CI 0-11, P(t-test) = 0.02). Analysis of 52 cardiac output assessments in 21 ED patients
demonstrated excellent interassessor correlation \( r = 0.96, 95\% \text{ CI } 0.90-0.98, P < 0.001 \). The average interassessor difference in cardiac output and index was 0.2 L/min (4\%, 95\% CI 3-6) and 0.1 L/min/m\(^2\) (4\%, 95\% CI 2-6), respectively. Conclusion: Emergency physicians with no prior ultrasonographic experience can be trained to obtain reliable cardiac output estimations upon conscious ED patients with the USCOM over the course of 20 patient assessments.


Thyrotoxic, hypokalaemic periodic paralysis.
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Publication Types: Case Reports


The ACEM training programme: Flexibility and diversity are important.
Curry C.
C. Curry, Fremantle Hospital, Fremantle, WA; Australia.
PMID:2005074938


Ambulance diversion is not associated with low acuity patients attending Perth metropolitan emergency departments.
Sprivilus P, Grainger S, et al.
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OBJECTIVE: To examine the relationship between ambulance diversion and low acuity patient (LAP) attendances to EDs. METHODS: Comparison of LAP attendance rates at inner metropolitan EDs and outer metropolitan EDs using a previously validated methodology. RESULTS: The percentage of LAP attendances was lower at inner metropolitan EDs (11.4\%, 95\% CI 11.3-11.6) compared to outer metropolitan hospitals (22.9\%, 95\% CI 22.6-23.2, \( P < 0.001 \)). The proportion of LAP attendances was slightly higher at both inner and outer metropolitan hospitals after-hours compared to working hours. Average daily LAP attendances per inner metropolitan hospital (13.4 attendances, 95\% CI 13.2-13.6) which averaged 89.2 min of diversion daily (95\% CI 88.7-89.7) were lower than at outer metropolitan hospitals (19.3 attendances, 95\% CI 19.0-19.6, \( P < 0.001 \)), which averaged 12.4 min of diversion daily (95\% CI 12.1-12.5, \( P < 0.001 \)). CONCLUSIONS: Inner metropolitan hospitals experience low LAP attendance rates. Attempts to further reduce LAP attendance rates at Perth inner metropolitan hospitals have limited scope to reduce ambulance diversion.
PMID:15675899


Access block causes emergency department overcrowding and ambulance diversion in Perth, Western Australia.
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<fls@health.wa.gov.au>
OBJECTIVE: Access block refers to the situation where patients in the emergency department
(ED) requiring inpatient care are unable to gain access to appropriate hospital beds within a reasonable time frame. We systematically evaluated the relationship between access block, ED overcrowding, ambulance diversion, and ED activity. METHODS: This was a retrospective analysis of data from the Emergency Department Information System for the three major central metropolitan EDs in Perth, Western Australia, for the calendar years 2001-2. Bivariate analyses were performed in order to study the relationship between a range of emergency department workload variables, including access block (>8 hour total ED stay for admitted patients), ambulance diversion, ED overcrowding, and ED waiting times. RESULTS: We studied 259,580 ED attendances. Total diversion hours increased 74% from 3.39 hours/day in 2001 to 5.90 hours/day in 2002. ED overcrowding (r = 0.96; 95% confidence interval (CI) 0.91 to 0.98), ambulance diversion (r = 0.75; 95% CI 0.49 to 0.88), and ED waiting times for care (r = 0.83; 95% CI 0.65 to 0.93) were strongly correlated with high levels of ED occupancy by access blocked patients. Total attendances, admissions, discharges, and low acuity patient attendances were not associated with ambulance diversion. CONCLUSION: Reducing access block should be the highest priority in allocating resources to reduce ED overcrowding. This would result in reduced overcrowding, reduced ambulance diversion, and improved ED waiting times. Improving hospital inpatient flow, which would directly reduce access block, is most likely to achieve this.

PMID:15843704


Activity of 11 beta-hydroxysteroid dehydrogenase type 2 in normotensive blacks and whites.


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Background: Salt-sensitive hypertension occurs more commonly in Blacks than in Whites. A decrease in activity of the enzyme 11 beta HSD2 that results in overstimulation of the mineralocorticoid receptor by cortisol could contribute to greater retention of sodium in Blacks. We tested the hypothesis that less activity of the enzyme 11 beta-hydroxysteroid dehydrogenase type 2 (11 beta HSD2) is present in Blacks than in Whites.

Methods: Eighty-nine subjects (42 Whites and 47 Blacks), ages 12 to 24 years were recruited from a young cohort that was followed longitudinally in a study of blood pressure regulation. For purposes of study, they were admitted to the General Clinical Research Center. Excretion of tetrahydrocortisol (THF), 5 alpha-THF, and tetrahydrocortisone (THE) was measured in 12-hour overnight urine collections. In vivo 11 beta HSD2 activity was estimated from the urinary (THF + 5 alpha-THF)/THE ratio.

Results: Blacks appeared to retain more sodium as evidenced by a lower level of 2-hour upright plasma aldosterone (P <.001) and marginally lower plasma renin activity (P=.06). The (THF + 5a-THF)/THE ratio in Blacks and Whites was similar: 0.91 +/- 0.41 (standard deviation), 0.86 +/- 0.52, 1.13 +/- 0.36, and 0.66 +/- 0.26, in White males, White females, Black males, and Black females, respectively; P= .35 for an overall effect of race.

Conclusion: 11 beta HSD2 activity appears to be similar in Blacks and Whites and probably contributes minimally, if at all, to race differences in sodium retention.

PMID:ISI:000231199700007
Validation of prospective whole-body bone marrow dosimetry by SPECT/CT multimodality imaging in (131)I-anti-CD20 rituximab radioimmunotherapy of non-Hodgkin's lymphoma.

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PURPOSE: Radioimmunotherapy (RIT) for relapsed non-Hodgkin's lymphoma is emerging as a promising treatment strategy. Myelosuppression is the dose-limiting toxicity and may be particularly problematic in patients heavily pretreated with chemotherapy. Reliable dosimetry is likely to minimise toxicity and improve treatment efficacy, and the aim of this study was to elucidate the complex problems of dosimetry of RIT by using an integrated SPECT/CT system.

METHODS: As a part of a clinical trial of (131)I-anti-CD20 rituximab RIT of non-Hodgkin's lymphoma, we employed a patient-specific prospective dosimetry method utilising the whole-body effective half-life of antibody and the patient's ideal weight to calculate the administered activity for RIT corresponding to a prescribed radiation absorbed dose of 0.75 Gy to the whole body. A novel technique of quantitation of bone marrow uptake with hybrid SPECT/CT imaging was developed to validate this methodology by using post-RIT extended imaging and data collection. RESULTS: A strong, statistically significant correlation (p=0.001) between whole-body effective half-life of antibody and the patient's ideal weight was demonstrated. Furthermore, it was found that bone marrow activity concentration was proportional to administered activity per unit weight, height or body surface area (p<0.001). CONCLUSION: The results of this study show the proposed whole-body dosimetry method to be valid and clinically applicable for safe, effective RIT.

PMID:15821965

Tension pneumopericardium relieved by pigtail catheter.

Yadav S, Sadasivan D, et al.
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PMID:15691694

Oncostatin M induces an acute phase response but does not modulate the growth or maturation-status of liver progenitor (oval) cells in culture.

Matthews VB, Knight B, et al.
UWA Centre for Medical Research, Western Australian Institute for Medical Research, University of Western Australia, Crawley 6009, Australia; School of Biomedical and Chemical Sciences, University of Western Australia, Crawley 6009, Australia.

Following acute injury, the liver regenerates through hepatocyte division. If this pathway is impaired, liver repair depends on the recruitment of adult liver progenitor (oval) cells. Mice fed a choline deficient, ethionine supplemented (CDE) diet possess substantial numbers of oval cells, which can be isolated, or examined in vivo. Oncostatin M (OSM) has been shown to induce maturation of murine fetal hepatoblasts into hepatocytes. We recently confirmed this in human fetal liver cultures. Here, we show that liver OSM expression increases in mice fed a CDE diet and CDE-derived oval cell isolates express OSM and its receptor (OSMR). Oval cell lines (PIL cells), as well as primary oval cell cultures, displayed STAT-3 phosphorylation following OSM stimulation. OSM had no effect on the growth of primary oval cells, but it was pro-apoptotic to
PIL cells, suggesting that the two cell models are not directly comparable. Expression of PCNA and cyclin D1 was not affected by OSM treatment. No evidence was obtained to suggest an effect on oval cell maturation with OSM treatment. However, decreased albumin production, accompanied by increased expression of haptoglobin and fibrinogen, suggests that OSM induced an acute phase reaction in cultured oval cells.

The natural history of nonalcoholic fatty liver disease: a population-based cohort study.
Adams LA, Lymp JF, et al.
BACKGROUND & AIM: The natural history of nonalcoholic fatty liver disease (NAFLD) in the community remains unknown. We sought to determine survival and liver-related morbidity among community-based NAFLD patients. METHODS: Four hundred twenty patients diagnosed with NAFLD in Olmsted County, Minnesota, between 1980 and 2000 were identified using the resources of the Rochester Epidemiology Project. Medical records were reviewed to confirm diagnosis and determine outcomes up to 2003. Overall survival was compared with the general Minnesota population of the same age and sex. RESULTS: Mean (SD) age at diagnosis was 49 (15) years; 231 (49%) were male. Mean follow-up was 7.6 (4.0) years (range, 0.1-23.5) culminating in 3192 person-years follow-up. Overall, 53 of 420 (12.6%) patients died. Survival was lower than the expected survival for the general population (standardized mortality ratio, 1.34; 95% CI, 1.003-1.76; P = .03). Higher mortality was associated with age (hazard ratio per decade, 2.2; 95% CI, 1.7-2.7), impaired fasting glucose (hazard ratio, 2.6; 95% CI, 1.3-5.2), and cirrhosis (hazard ratio, 3.1, 95% CI, 1.2-7.8). Liver disease was the third leading cause of death (as compared with the thirteenth leading cause of death in the general Minnesota population), occurring in 7 (1.7%) subjects. Twenty-one (5%) patients were diagnosed with cirrhosis, and 13 (3.1%) developed liver-related complications, including 1 requiring transplantation and 2 developing hepatocellular carcinoma. CONCLUSIONS: Mortality among community-diagnosed NAFLD patients is higher than the general population and is associated with older age, impaired fasting glucose, and cirrhosis. Liver-related death is a leading cause of mortality, although the absolute risk is low.

Geriact. 2005; 23(2): 5-11.
Carer training project for the management of behavioural and psychological symptoms of dementia (BPSD) by home-based carers: phase 2.
Dicker BS, Chawla S, et al.
Behavioural and psychological symptoms of dementia (BPSD) have been identified in several studies as the single greatest contributor to caregiver stress. Research has also shown that training carers of persons with dementia reduces carer stress, can delay residential placement and improves the quality of life of carer and care recipient. An evidence-based training package that focuses specifically on BPSD management was developed and trialed with 50 home-based carers. The package utilises a one-to-one, customised (modular) approach and can be delivered in the carer's home. Pre- and post-tests administered to carers demonstrated statistically significant learning gains. Evaluation questionnaires completed by carers following delivery of the training indicated that statistically significant gains were made in self-perceived knowledge of dementia and BPSD, management of BPSD, care-giving ability and stress reduction. With the exception of stress reduction, these gains were maintained six and 12 months post-training. Twelve months post-training, however, carer stress had returned to near pre-intervention levels. A customised, evidence-based approach to training home-based carers increased carer competence and confidence in the management of BPSD and had an
immediate effect on reducing carer stress.
Publication Types: Journal Article
PMID:2009035991

 Challenges in coding and classification.
 Kolednik N.
 Clinical Coder, South Metropolitan Area Health Service, Alma Street, Fremantle, WA 6962, Australia
 Publication Types: Journal article
 PMID:2009078924

 Eight methods for improving coding quality and efficiency.
 Haggarty C, Ives J.
 Senior Clinical Information Coder, Fremantle Hospital & Health Service, Fremantle, WA 6160, Australia; Carolyn.Haggarty@health.wa.gov.au
 Publication Types: Journal article
 PMID:2009078926

 Return to work after coronary artery bypass surgery in a population of long-term survivors.
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dDepartment of Cardiothoracic Surgery, Fremantle Hospital, Australia
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BACKGROUND: Return to paid employment may be facilitated by coronary artery bypass graft (CABG) surgery. We assessed work status in a population-based study of long-term outcomes of CABG. AIM: To determine the association between returning to work after CABG and clinical and socio-demographic factors. METHODS: A postal survey of 2,500 randomly selected patients 6-20 years post-CABG. The outcomes assessed were work status in the year before and after CABG and health-related quality of life (HRQOL) measured with SF-36. RESULTS: Response was 82% (n = 2,061). Employment fell from 56% in the year prior to CABG to 42% in the year after. Workers in 'blue-collar' occupations were more likely to reduce their work status than those in 'white collar' occupations (46% versus 29%, p < 0.001). Independent predictors of reducing employment were increasing age (9% per year, 99% CI: 1.06-1.11, p < 0.001), 'blue-collar' versus 'white collar' occupation (OR: 2.1, 99% CI: 1.4-3.1) and female sex (OR: 2.1, 99% CI: 1.1-3.6). HRQOL among participants under 60 years of age at follow-up was better for those who returned to work after CABG surgery. CONCLUSION: CABG surgery is followed by a net loss to paid employment of working age patients which increases with age, and is more likely for
those in blue-collar occupations and women.
PMID:16352276

Boucher E, Turner HJ, et al.
Boucher E (reprint author), Ctr E Marquis, Dept Med Oncol, Rennes, France
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Ctr E Marquis, Dept Nucl Med, Rennes, France
PMID:ISI:000229517300026

Lack of increase in iron release despite increased uptake by hepatocytes contributes to hepatic iron loading in the HFE knockout mouse.
Chua A, Olynyk J, et al.
Univ Western Australia, Fremantle, Australia
PMID:ISI:000232480300153

Iron absorption and hepatic uptake is increased in a TFR2 (Y245X) mutant mouse model of hemochromatosis type 3.
Chua A, Olynyk J, et al.
Univ Western Australia, Fremantle, Australia
PMID:ISI:000232480300151

Peroxisome proliferator activated receptors (PPARs) and hepatocarcinogenesis.
Knight B, Yeap BB, et al.
Univ Western Australia, Fremantle, WA Australia
Univ Western Australia, Nedlands, WA 6009 Australia
PMID:ISI:000232480300277

Hepatology. 2005; 42(4): 711A-711A.
Intermediate hepatobiliary cells are resistant to infection with hepatitis B virus and proliferate as a result of mediators secreted by inflammatory cells.
Tian YW, Knight B, et al.
Univ Western Australia, Fremantle, WA 6009 Australia
PMID:ISI:000232480302358

Is HFE involved in increased hepcidin expression and hypoferremia in inflammation and anemia of chronic disease?
Milward EA, Trinder D, et al.
A novel mutation in the steroidogenic acute regulatory (star) protein gene promoter leading to reduced promoter activity.
(1) University Hospital, Geneva, Switzerland, (2) Fremantle Hospital, Perth

Tesaglitazar (AstraZeneca).
Kamber N, Davis TME.
N. Kamber, University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, PO Box 480, Fremantle, WA 6959; Australia. E-Mail: nkamber@meddent.uwa.au
AstraZeneca plc is developing tesaglitazar, an oral dual peroxisome proliferator-activated receptor a/gamma agonist, for the potential improvement of dyslipidemia and glycemic control in type 2 diabetic patients. copyright The Thomson Corporation.

Liver inflammation and cytokine production, but not acute phase protein synthesis, accompany the adult liver progenitor (oval) cell response to chronic liver injury.
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Oval cells are facultative liver progenitor cells, which are invoked during chronic liver injury in order to replenish damaged hepatocytes and bile duct cells. Previous studies have observed inflammation and cytokine production in the liver during chronic injury. Further, it has been proposed that inflammatory growth factors may mediate the proliferation of oval cells during disease progression. We have undertaken a detailed examination of inflammation and cytokine production during a time course of liver injury and repair, invoked by feeding mice a choline-deficient, ethionine-supplemented (CDE) diet. We show that immediately following initial liver injury, B220-expressing leucocytes transiently infiltrate the liver. This inflammatory response occurred immediately before oval cell numbers began to expand in the liver, suggesting that the two events may be linked. Two waves of liver cytokine production were observed during the CDE time course. The first occurred shortly following commencement of the diet, suggesting that it may represent a hepatic acute phase response. However, examination of acute phase marker expression in CDE-fed mice did not support this hypothesis. The second wave of cytokine expression correlated with the expansion of oval cell numbers in the liver, suggesting that these factors may mediate oval cell proliferation. No inflammatory signalling was detected following withdrawal of the injury stimulus. In summary, our results document a close correlation between inflammation, cytokine production and the expansion of oval cells in the liver during experimental chronic injury.
PMID:16033531
Proteomics: an overview.
Lawrance IC, Klopcic B, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle.
ilawranc@cyllene.uwa.edu.au
Publication Types: Review
PMID:16189423

Inflammatory Bowel Diseases. 2005; 11(10): 927-36.

A comparative study of goblet cell and pancreatic exocrine autoantibodies combined with ASCA and pANCA in Chinese and Caucasian Patients with IBD.
Lawrance IC, Hall A, et al.
Dr. I.C. Lawrance, School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Alma Street, Fremantle, WA 6059; Australia. E-Mail: ilawranc@cyllene.uwa.edu.au
Background: The incidence of Crohn's disease (CD) and ulcerative colitis (UC) is increasing, but differentiating between them is often extremely difficult. Pancreatic (PAB) and goblet cell autoantibodies (GAB) are specific for CD and UC, respectively, but with low sensitivity. In combination with anti-Saccharomyces cerevisiae (ASCA) and anti-neutrophil cytoplasmic antibodies (pANCA) testing, these antibodies may improve differentiation between the diseases. This study determined the sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of PAB and GAB +/- ASCA and pANCA testing in Chinese and Caucasian IBD populations. Results: Patients were recruited from Caucasian and Chinese populations (CD, n = 100; UC, n = 99; controls, n = 100). PAB was highly specific for CD, and detection was greater in patients less than 35 years old and in Chinese compared with Caucasian patients with CD (CD, 46% versus 22%, P = 0.018; UC, 2% versus 6%; controls, 0% versus 2%). GAB detection was poor in all groups (<2%). PAB showed a PPV of 93% to differentiate all patients with CD from patients with UC, but only 62% for those with isolated colonic disease. The PPV of PAB increased to 100%, specificity was 100%, and sensitivity was 21% for isolated colonie disease when combined with pANCA and ASCA. PAB expression was not associated with stricturing or perforating CD. Conclusions: This study identified that GAB was not useful in our patients with IBD. PAB expression was highly specific for CD and more sensitive in Chinese than Caucasian patients with CD. The combination of PAB, pANCA, and ASCA testing improved the differentiation between UC and CD, particularly in isolated colonie disease, compared with pANCA and ASCA testing alone. Copyright copyright 2005 by Lippincott Williams & Wilkins. PMID:2005456624

Metachronous' adenocarcinoma of the small intestine.
Varghese R, Weedon R.
Department of General Surgery, Fremantle Hospital, Fremantle, Western Australia 6160, Australia. vargheseraphael@hotmail.com
Adenocarcinoma of the small intestine accounts for less than 1% of primary gastrointestinal malignancies (1). Small intestine contains 75% of the length of the gastrointestinal tract with 90% of the surface mucosal area, and yet carcinoma is rare. Symptoms of small bowel adenocarcinoma are vague and non-specific, and this region is relatively inaccessible which together contributes to their late diagnosis and poor prognosis. The authors report a case of two primary adenocarcinomas of the small intestine in the same patient. PMID:15875642
Risperidone for psychosis of Alzheimer's disease and mixed dementia: results of a double-blind, placebo-controlled trial.
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7Janssen-Cilag Belgium, Beerse, Belgium
8Janssen Psychiatry Inc., LLC, Titusville, New Jersey, USA

OBJECTIVE: To evaluate the efficacy and safety of low-dose risperidone in treating psychosis of Alzheimer's disease (AD) and mixed dementia (MD) in a subset of nursing-home residents who had dementia and aggression and who were participating in a randomized placebo-controlled trial of risperidone for aggression.

METHOD: This post-hoc analysis included only patients diagnosed with AD or MD with psychosis, defined by a score of $\geq 2$ on any item of the Behavioral Pathology of Alzheimer's Disease (BEHAVE-AD) psychosis subscale at both screening and baseline. Co-primary efficacy endpoints were changes in scores on BEHAVE-AD psychosis subscale and Clinical Global Impression of Change (CGI-C).

RESULTS: Overall, 93 patients (46 risperidone and 47 placebo) fulfilled the psychosis of AD criteria. Mean change at endpoint in BEHAVE-AD psychosis subscale with risperidone was superior to placebo (-5.2 vs -3.3; $p = 0.039$). Distribution of CGI-C at endpoint also favoured risperidone ($p < 0.001$). The superior improvement with risperidone compared with placebo occurred as early as the first two weeks and persisted to the end of the treatment period. At endpoint, 59% of risperidone-treated patients were responders (i.e. were 'very much' or 'much' improved) compared with 26% of patients receiving placebo. The mean risperidone dose was 1.03 +/- 0.61 mg/day. Twelve weeks of treatment were completed by 37 patients treated with risperidone (80%) and 35 with placebo (74%). A total of 46 (98%) placebo- and 44 (96%) risperidone-treated patients experienced at least one adverse event, with only somnolence occurring more frequently in the risperidone group.

CONCLUSION: Risperidone effectively reduces psychosis and improves global functioning in elderly patients with moderate-to-severe psychosis of AD and MD.

PMID:16315159

Effects of a multidisciplinary, post-discharge continuance of care intervention on quality of life, discharge satisfaction, and hospital length of stay: a randomized controlled trial.
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PMID:16315159
OBJECTIVE: To determine the impact of a hospital-coordinated discharge care plan, involving a multidisciplinary team of primary health care providers, on hospital length of stay, quality of life, and both patient and general practitioner inclusion in, and satisfaction with, discharge procedures. DESIGN: This investigation comprised a prospective, randomized, controlled, clinical trial. SETTING: This multicentre and cross-jurisdictional study focused on areas of tertiary and primary health care as well as community allied health in Western Australia. PARTICIPANTS: Patients (n = 189) with chronic cardiorespiratory diagnoses were recruited from respiratory, cardiovascular, and general medical wards at two tertiary hospitals. INTERVENTION: Subjects were randomly assigned to one of two groups. Intervention group patients received a discharge care plan in accordance with that outlined in the Australian Enhanced Primary Care Package, completed before discharge and sent to the patient's general practitioner and other community service providers for review. Control patients were discharged under existing hospital processes. Outcome measures. Patients and general practitioners were surveyed pre-discharge and 7 days post-discharge for quality of life and opinion of discharge procedures. Hospital length of stay was also determined. RESULTS: Significant improvements in discharge planning involvement, health service access, confidence with discharge procedures, and opinion of discharge based on previous experience were seen for patients who received the discharge care plan. Further, improved perceptions of mental quality of life were observed within the first week post-discharge for intervention patients. Length of stay showed no difference between groups. Extent and speed of hospital-general practitioner communication were significantly improved via the intervention. CONCLUSIONS: Our results indicate that a multidisciplinary discharge care plan, initiated before separation, improves quality of life, involvement, and satisfaction with discharge care, and hospital-general practitioner integration. As such, it possesses benefits over current Western Australian hospital discharge procedures for the care of chronically ill populations.

Enzyme replacement therapy for Gaucher disease in Australia.

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AIM: To study the effectiveness of a specific national programme of enzyme replacement therapy (ERT) for patients with severe forms of Gaucher disease, a disorder of sphingolipid metabolism resulting from an inherited deficiency of the lysosomal enzyme beta-Glucocerebrosidase. METHODS: Prospective analysis of data submitted at entry and every 6 months on therapy. The responses of haemoglobin (Hb) and platelet (plt) concentrations, liver and spleen volumes were assessed. PATIENTS: Forty-eight patients were treated with ERT for a minimum of 6 months. Forty patients had Type 1 disease and eight had Type 3B. The age range was 1-70 years (median 24 years). Duration of therapy at the time of analysis was 6-114 months. RESULTS: Thirty-six per cent of patients started with a normal Hb increasing to 76% after 6 months. The mean improvement in Hb from baseline to the end of study period was 20 g/L, when the Hb was normal in 85% (41 patients). Thirty per cent of patients had a normal plt count at the start of therapy, with a more gradual increase in the count at 6 monthly intervals of
50, 91, 108 and 142% of starting value. Seventy-five per cent of patients had a normal plt count at the end of study. Spleen volumes reduced by a mean of 56% in 33 evaluable patients, and the liver by 27% in 30 of 38 evaluable patients. Eight patients had an increase in liver volume of 28%. CONCLUSION: Enzyme replacement therapy produced a spectrum of beneficial responses in patients with Gaucher disease, but all had some evidence of reversal of haematological complications and/or reduction in visceromegaly. Future analyses will examine the effect of therapy on bone disease, prepubertal growth and quality of life.

PMID:15737135


Nursing and midwifery management of hypoglycaemia in healthy term neonates.

Curtin University of Technology and The Western Australian Centre for Evidence-based Nursing and Midwifery (a collaborating centre of the Joanna Briggs Institute), Perth, Western Australia, Australia

The objective of this systematic review was to determine the best available evidence for maintenance of euglycaemia in healthy full-term neonates, and the management of asymptomatic hypoglycaemia in otherwise healthy full-term neonates. This review updates the World Health Organization's 1997 literature review which comprehensively addressed aspects such as the glucose homeostasis and metabolic adaptation at birth, effects of hypoglycaemia on the central nervous system, definition of hypoglycaemia, screening, prevention and treatment. In identifying areas of primary research that need to be undertaken, the World Health Organization (1997) noted that only a few studies of breast-fed babies had been undertaken up to that time. At birth the newborn infant must make significant adaptations from the in utero environment to the outside world. Failures of metabolic adaptation are most commonly manifested as hypoglycaemia. If unrecognised severe hypoglycaemia can lead to death, and the effects on long term mental and neurodevelopmental outcomes are not clear. “Normal ranges” of blood glucose values have yet to be decisively defined, aspects of management remain controversial and a number of related research questions are still to be addressed.

The availability of point-of-care and micro-sampling techniques to detect “low” blood glucose levels and an increasingly litigious society have resulted in a definition for hypoglycaemia that is considerably higher than that postulated by Hartmann & Jaudon in 1937. Concern has been expressed that setting an unnecessarily high blood glucose level may result in needless trauma and cost. The administration of intravenous glucose to otherwise healthy newborn infants in the NICU may result in unnecessary pain to the neonate, emotional trauma to parents, increased cost to the hospital, and separation of the newborn infant at a crucial time in the bonding/breastfeeding process.


Factors that influence Asian communities' access to mental health care.

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This paper presents the findings of a qualitative study to identify factors that influence Asian communities' access to mental health care and how mental health care is delivered to them. Semistructured interviews were completed with Asian community members/leaders and health-care professionals. Content analysis identified major themes. Participants also completed a demographic data sheet. The research aimed to provide health professionals with an increased understanding of the values and beliefs held by people from Asian communities regarding the cause and treatment of mental illness. Data analysis identified six main themes that influenced
Asian communities’ access to mental health care and how mental health care is delivered to them. They were: shame and stigma; causes of mental illness; family reputation; hiding up; seeking help; and lack of collaboration. The findings highlighted that people from Asian communities are unwilling to access help from mainstream services because of their beliefs, and that stigma and shame are key factors that influence this reluctance. The findings also highlight that the mental health needs of refugee women are significant, and that they comprise a vulnerable group within Australian society.

PMID:15896255

Impact of patient confidentiality on carers of people who have a mental disorder.

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This paper discusses how patient confidentiality issues impact on carers of people with mental disorders. Data obtained from interviews with 27 primary carers were analysed using the grounded theory method. Despite the emphasis that Australian mental health policy documents place on collaboration with carers, the findings of this Western Australian study showed that carers were expected to undertake the caring role with little support, education or understanding. The lack of collaboration with health professionals increased carers’ level of distress and left them feeling frustrated and resentful. Carers have identified that patient confidentiality was one reason why health professionals were unwilling to collaborate with them. To ensure carers’ continued commitment to caring, negotiation about patient confidentiality issues must occur at the onset of the caregiving process. Carers have the right to certain information in order to maintain their level of well-being and their personal safety. Moreover, in certain circumstances, patient confidentiality may need to be breached if the life of the ill family member or others is in danger. A greater carer involvement in and understanding of the ill family member's illness will facilitate better treatment outcomes in the community for the ill family member., Copyright (C) 2005 Blackwell Publishing Ltd.

Dementia after traumatic brain injury.

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Early retrospective studies suggested that individuals with a history of a traumatic brain injury (TBI) had a higher risk for dementia than those without a history of TBI. Two meta-analyses demonstrated that the risk for dementia is higher among men, but not women, with a history of TBI. More recent prospective studies, however, are providing discrepant findings, probably due to important methodological differences. TBI is usually associated with significant neuropsychological deficits, primarily in the domains of attention, executive functioning and memory. These deficits may not improve with time. TBI may also lower the threshold for the clinical expression of dementia among predisposed individuals, and the onset of Alzheimer's disease (AD)-like neuropathological and biochemical changes immediately after severe TBI may play an important role in this mechanism.

PMID:16240486
Uncommon causes of cerebrovascular dementia.

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BACKGROUND: The concept of Binswanger's disease (BD) remains unclear and may not constitute a useful diagnostic category. However, cognitive decline may be present in a proportion of patients with subarachnoid hemorrhages (SAH) or subdural hematomas (SH).

METHOD: We provide a critical review of the concept of BD and summarize the main findings on the association between SAH, SH and cognitive decline.

RESULTS AND CONCLUSIONS: BD was originally identified as a type of dementia different from neurosyphilis and with characteristic white matter atrophy. The phenomenology of BD is currently construed around the concept of frontosubcortical dementia, but the validity of this construct is unclear. Patients with SAH frequently develop a variety of cognitive and behavioral problems that usually result in poor psychosocial adjustment and poor quality of life. SH is a rare cause of progressive cognitive impairment. A proportion of patients (particularly functionally impaired old individuals) are at a high risk for cognitive deficits after surgical drainage of the hematoma.

PMID:16240483

A clinicopathologic review of lethal nonmelanoma skin cancers in Western Australia.

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BACKGROUND: Nonmelanoma skin cancer (NMSC) comprises a heterogeneous group of cancers. A comprehensive review of NMSC mortality has not been performed previously in this region.

OBJECTIVE: We sought to document the population affected by lethal NMSC, the types of tumors involved, and their histopathologic features.

METHODS: Death certificates of all patients who died from NMSC were examined. Histology of the primary lesion was reviewed in cases when the primary lesion was identified and sections were available.

RESULTS: A total of 120 NMSC deaths occurred, including 89 caused by squamous cell carcinoma, 22 by Merkel cell carcinoma, and 9 others. The median age at death was 79 years, unless the patients were immune deficient (68 years). When the primary lesion was identified (n = 45), the median survival after diagnosis was 17 months; 75% of patients died within 3 years. Lethal neoplasms were deeply invasive and infiltrated into the reticular dermis and beyond. Three squamous cell carcinomas were reclassified as adenosquamous carcinoma.

CONCLUSION: Lethal NMSC occurs in the elderly and consists mainly of 3 types of deeply invasive cancers.

PMID:15627087

Lymphotoxin-beta production following bile duct ligation: possible role for Kupffer cells.

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BACKGROUND AND AIMS: Lymphotoxin-beta (LT-beta) may play a role in the pathogenesis of chronic liver injury. The aim of this study was to determine in an animal model of bile duct ligation liver injury whether LT-beta expression is induced and whether Kupffer cells are an intrahepatic source of LT-beta.

METHODS: Sprague-Dawley rats were divided into two groups: one group received a single dose of GdCl (a Kupffer cell-blocking agent, 10 mg/kg i.v.), whereas the other group received saline. One day later, the groups underwent bile duct ligation or a
sham operation. Liver tissue was obtained on days 1, 3, 5, and 8 for assessment of Kupffer cell numbers, early fibrogenic events and LT-beta gene expression. Kupffer cells were isolated using pronase/collagenase perfusion and centrifugal elutriation. RESULTS: Hepatic LT-beta mRNA expression increased early following bile duct ligation. Pretreatment of bile duct-ligated animals with GdCl significantly reduced the number of Kupffer cells, delayed the rise in LT-beta expression, but had no effect on fibrogenesis. Recovery of the Kupffer cell population in these animals was accompanied by increased hepatic LT-beta expression. The LT-beta ligand and receptor were expressed by isolated normal Kupffer cells. CONCLUSIONS: Hepatic LT-beta expression is induced early following bile duct ligation. Kupffer cells may be an intrahepatic source of LT-beta.

PMID: 16246198


Effects of HFE gene mutations and alcohol on iron status, liver biochemistry and morbidity.
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BACKGROUND AND AIMS: The aims of the present study were to determine: (i) whether alcohol consumption is greater in individuals with HFE mutations; and (ii) whether common HFE mutations modify the effects of alcohol on serum iron and liver biochemistry or morbidity.

METHODS: The residents of the town of Busselton in Western Australia were subject to cross-sectional health surveys between 1966 and 1983. In 1994/1995 all surviving participants of the earlier surveys were invited to take part in a follow-up survey. Logistic, linear and Poisson log-linear regression analyses were performed in 1490 men and 1452 women from the 1994/1995 survey to assess the relationships between HFE mutations, alcohol, iron levels, liver biochemistry and morbidity.

RESULTS: Heavy or moderate alcohol consumption was present in 7% or 36% of men and 0.5% or 12% of women, respectively. Alcohol consumption strongly influenced levels of serum ferritin and gamma glutamyl transpeptidase (GGT) and mean cell volume (MCV) in men and women but only alanine aminotransferase (ALT) levels in women. These effects were independent of HFE gene mutations. Hospital admission rates for respiratory disorders were higher in men with the C282Y mutation.

CONCLUSIONS: Alcohol consumption strongly influences serum ferritin and GGT levels and MCV in men and women but only ALT levels in women, and these effects are independent of HFE mutations. HFE gene mutations do not predispose to moderate or heavy alcohol consumption. The C282Y mutation is associated with increased respiratory admission rates in men.

PMID: 16105133


A two-year follow-up study of remote memory in Alzheimer's disease.
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The authors assessed long-term changes in autobiographical and public remote memory in a series of 21 patients with Alzheimer's disease (AD) and 10 age-comparable healthy comparison subjects who underwent two evaluations, with an interval ranging from 24 to 36 months. The assessment consisted of the Remote and Autobiographical Memory Scales and the Buschke Selective Reminding Test. The AD group showed a significantly greater decline on both types of remote memory than the comparison group. Alzheimer's disease patients performed
significantly better on recognition than on free-recall, suggesting more severe retrieval than encoding/storage deficits. The decline in anterograde verbal memory correlated significantly with the decline in autobiographical memory, suggesting a common final pathway for both deficits.

PMID:16179655


Efficacy of ant venom immunotherapy and whole body extracts.
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Neurological soft signs are associated with APOE genotype, age and cognitive performance.
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Kangaroo versus freestyle stentless bioprostheses in a juvenile sheep model: Hemodynamic performance and calcification behavior.
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Background: Glutaraldehyde-preserved bioprosthetic heart valve substitutes have limited performance and longevity due to tissue degeneration and calcification. The Freestyle valve (Medtronic Heart Valves, Inc, Minneapolis, MN) combines zero fixation pressure and [proportional to]-amino oleic acid (AOA) as antidegeneration and antimineralization measures. The aim of this study was to compare the calcification behavior of glutaraldehyde-preserved kangaroo aortic valves with Freestyle stentless bioprostheses in a juvenile sheep model.
Methods: Pulmonary artery and valve replacements were performed in juvenile sheep with Freestyle stentless aortic valves (n = 4) or glutaraldehyde-preserved kangaroo stentless aortic valves with no antimineralization measures (n = 6), and explanted at 200 postoperative days.
Results: Freestyle stentless valves and stentless kangaroo aortic valves showed normal valve function immediately postoperatively and up to 120 days. Valve leaflets of all valves were macroscopically free of visible calcification with normal histology. Valve leaflet calcification ([mu]g Ca/mg tissue) was less in kangaroo than Freestyle (1.27 +/- 0.43 versus 2.38 +/- 1.37, p = 0.856). Aortic wall tissue calcification was severe in kangaroo and Freestyle (127.93 +/- 12.22 versus 122.19 +/- 11.99, p = 0.596). Conclusions: We conclude that glutaraldehyde-preserved kangaroo aortic valve leaflets are equal to AOA-treated Freestyle stentless valve leaflets with regard to calcification in juvenile sheep. Both bioprostheses are prone to aortic wall calcification. The low calcification features of the kangaroo aortic valve leaflets without antimineralization treatment may benefit the longevity of the valve.
PMID:2005057341
Interaction between testosterone and APOE (epsilon)4 status on cognition in healthy older men.
Burkhardt MS, Foster JK, et al.
School of Psychology, Murdoch University, Murdoch, Western Australia; Sir James McCusker Alzheimer's Disease Research Unit, School of Exercise, Biomedical & Health Sciences, Edith Cowan University, and School of Psychiatry & Clinical Neurosciences, University of Western Australia, c/o Hollywood Private Hospital, Nedlands, Western Australia; Neurosciences Unit, Health Department of Western Australia; Department of Geriatric Medicine, Fremantle Hospital, Fremantle, Western Australia; Department of Biochemistry, Fremantle Hospital, Fremantle, Western Australia; School of Medicine & Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia; Department of Endocrinology & Diabetes, Fremantle Hospital, Fremantle, Western Australia.

CYP11B2-CYP11B1 haplotypes associated with decreased 11beta-hydroxylase activity.
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Reduced adrenal 11[beta]-hydroxylation has been associated with an aldosterone synthase (CYP11B2) polymorphism. The 11[beta]-hydroxylase gene (CYP11B1) lies close to CYP11B2. We hypothesize that a molecular variant in CYP11B2 is in linkage disequilibrium (LD) with a key quantitative trait in CYP11B1 determining this phenotype. Polymorphisms and inferred haplotypes at CYP11B loci were studied in two independent populations from Europe (n = 100) and South America (n = 99). The latter underwent detailed hormonal studies. LD was estimated by alternative Bayesian methods for inferring the extent of LD when haplotypes at different loci are inferred. Population differences in single nucleotide polymorphisms were modest, indicating the stability of both genes across populations. Using five of nine potentially informative loci at CYP11B sites with allele frequency greater than 0.1, two major contrasting haplotypes, CwtCG and TconvGTA, were found. In both populations the CwtCG haplotype accounted for 44% and the TconvGTA for 32% of subjects. Haplotype distribution did not differ between Europeans and South Americans ([chi<sup>2</sup>] = 2.81; P = 0.09). In vivo 11[beta]-hydroxylase activity, estimated from urinary steroid profiling, was lower in subjects with an increased aldosterone to renin ratio or with the TconvGTA haplotype. These findings indicate that genotypes at the CYP11B locus are in strong LD and that identified haplotypes predict 11[beta]-hydroxylase activity.
PMID:2005092074

Interactions among thyroid function, insulin sensitivity, and serum lipid concentrations: the Fremantle diabetes study.
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Combination assay detecting both human immunodeficiency virus (HIV) p24 antigen and anti-HIV antibodies opens a second diagnostic window.

Fourth-generation human immunodeficiency virus (HIV) screening immunoassays reduce the diagnostic window between infection and diagnosis by the inclusion of HIV p24 antigen detection together with HIV antibody detection in the same test. We compared third- and fourth-generation HIV immunoassays and a dedicated HIV p24 antigen test for detection of a case of HIV seroconversion. This demonstrated a second diagnostic window using the fourth-generation assay due to a decline of HIV p24 antigen prior to the detection of HIV antibody. However, HIV p24 antigen was detected in the same sample by the dedicated HIV p24 antigen test, as was HIV proviral DNA. Although it is likely to be rare, this phenomenon has also been reported for other fourth-generation HIV immunoassays and has implications for the reported diagnostic windows of these assays.

PMID: ISI:000232762500087
techniques may be required to identify the infecting organism. Prophylactic antibiotics against skin organisms should be considered for all implantations and arterial diagnostic and therapeutic procedures traversing a stent-graft. 
PMID:ISI:000234188800005
cognitive complaints, and hyperactive and disinhibited behavior. It is reasonable to assume that these symptomatic clusters have specific underlying mechanisms that need to be integrated in a comprehensive pathophysiologic model., (C) 2005 Lippincott Williams & Wilkins, Inc.

**Hereditary haemochromatosis: to screen or not to screen?**
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**Prorenin cryoactivation as a possible cause of normal renin levels in patients with primary aldosteronism.**
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PMID:15662238

**Predicting intradialytic hypotension from experience, statistical models and artificial neural networks.**
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Background: Symptomatic intradialytic hypotension (IDH) associated with increased mortality in hemodialysis patients is difficult to predict and hence prevent. Artificial Neural Networks (ANNs) are promising tools to solve multidimensional non-linear problems. The aim of the study was to verify in which way mathematical models, statistics or knowledge of patients influence the ability of the nephrologists to predict IDH.
Methods: The performance of ANNs was compared with that of independent nephrologists supported by a logistic regression giving odds ratio for each studied variable (NEPHiS) or of nephrologists in charge of the patients without (NEPHc) or with statistical support as for NEPHiS (NEPHcS). Data from 98 hemodialysis patients were analysed in order to select patients with frequent IDH (< 10% of the dialysis sessions). Complete data on 1979 dialysis sessions from 7 patients were retrieved. The ability to predict the occurrence of hypotension episodes was compared (ROC curves) between ANNs, NEPHcS (N = 7) in Switzerland and NEPHiS from independent dialysis centers in Western Australia (N = 10).
Results: ANN gave the most accurate correlation between estimated and observed IHD episodes compared to NEPHc (p < 0.001), but a similar performance was attained by NEPHcS (p < 0.001). NEPHiS were superior to NEPHc (P < 0.05), but inferior to ANN (P < 0.01). For a sensitivity of 80%, specificity was 44% for ANNs, 33% for NEPHcS and 20% for NEPHc.
Conclusions: ANNs are superior to nephrologists in predicting IDH episodes; however when supported by a statistical analysis, nephrologists reach ANNs in their prediction ability. IDH still remains difficult to predict even with mathematical models.
PMID:ISI:000232848400010
On the overlap between apathy and depression in dementia.  
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Background: Whereas apathy is increasingly recognised as a frequent abnormal behaviour in dementia, its overlap with depression remains poorly understood. Aims: To assess the psychometric characteristics of a structured interview for apathy, and to examine the overlap between apathy and depression in dementia. Methods: A total of 150 patients with Alzheimer's disease (AD) underwent a comprehensive psychiatric and cognitive assessment. Results: Twelve per cent of the sample met criteria for both apathy and depression, 7% met criteria for apathy only, and 31% met criteria for depression only. Apathy (but not depression) was significantly associated with more severe cognitive deficits. Apathy and anxiety scores accounted for 65% of the variance of depression scores in dementia, and the diagnosis of apathy had a minor impact on the rating of severity of depression. Conclusions: The Structured Interview for Apathy demonstrated adequate psychometric characteristics. Using a novel structured interview for apathy in AD we demonstrated that whereas the construct of depression primarily consists of symptom clusters of apathy and anxiety, apathy is a behavioural dimension independent of depression.

Physical disability contributes to caregiver stress in dementia caregivers.  
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BACKGROUND: Previous findings of studies on the impact of physical illness on caregiver health have been inconsistent. The authors wanted to determine whether physical disability, as determined by the SF-12 survey that provides information on both physical and mental health problems, contributes to caregiver stress. METHODS: The authors interviewed 91 primary caregivers (aged 38-85 years) of persons with dementia who had been referred by their family physicians for the first time for formal support services or memory evaluation. Caregivers completed the SF-12 version of the Medical Outcomes Study Short Form Health Survey that generates Mental Component Summary (MCS) and Physical Component Summary (PCS) scores and reported on caregiver stress and concurrent medical conditions and medications. RESULTS: Most caregivers reported stress (76.9%), having medical conditions (72.4%), or taking medications (67%). The MCS but not the PCS scores were significantly lower than community norms, indicating an excess of disability due to mental health problems. Nevertheless, 40.7% had PCS scores indicating some degree of physical disability. Using multiple logistic regression analysis, PCS scores but not the presence of medical problems were independently associated with caregiver stress. CONCLUSIONS: Chronic disability as assessed by SF-12 PCS scores is independently associated with caregiver stress. These data suggest that caregivers of persons with dementia should be assessed for disabling physical conditions and mental health problems. In addition, reducing the impact of physical disability could ameliorate caregiver stress.
Patella intraosseous blood flow disturbance during a medial or lateral arthrotomy in total knee arthroplasty: a laser Doppler flowmetry study.

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Patella complications are recognized sequelae of total knee arthroplasty (TKA). Disruption of blood flow to the patella and adjacent soft tissues during surgery may contribute to reduced viability of the bone and patella ligament tissue. The effect on genicular blood flow to the medial and lateral patella was compared for a medial (MA) and lateral arthrotomy (LA) during TKA. Laser Doppler flowmetry was used to measure both baseline and postarthrotomy flow in vivo for 16 primary TKA patients. Flow in the lateral patella was reduced approximately 20% for both MA and LA. Conversely, the use of MA resulted in substantial reduction in flow to the medial patella (53%) compared to the lateral approach (27%). A large standard deviation of scores was evident in all cases. Although there was a tendency for LA to disturb the patellar blood flow less, the difference was not significant. It was concluded that neither approach is superior regarding the blood flow preservation to the patella. Hence, a lateral approach might only have an advantage in knee joints that are likely to need a lateral release in combination with an MA-e.g., a valgus deformity or preoperative patella maltracking.

PMID:ISI:EFIRST040271561

A phase II study of dexamethasone, ifosfamide, cisplatin and etoposide (DICE) as salvage chemotherapy for patients with relapsed and refractory lymphoma.

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The 4-day combination of dexamethasone, ifosfamide, cisplatin, and etoposide (DICE) is a salvage regimen for lymphoma. We report a prospective phase II multi-center trial of a modified DICE regimen in relapsed or refractory Hodgkin (HL) or non-Hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL), constituting a single day of intravenous administration followed by 3 days of oral administration, aimed at reducing inpatient days without losing efficacy. Forty patients (median age 56, range 25 - 79) were included: 28 (70%) NHL, 9 (23%) HL and 3 (8%) CLL. Fifty-three per cent had received 2 prior treatment regimens. International Prognostic Index (IPI) was 2 in 75% of NHL patients. Patients aged 55 and those with previous autologous stem cell transplantation (ASCT) started on a lower-dose regimen, with dose escalation possible in 2 patients. Overall response rate was 41%. Thirty-eight per cent of patients had stable disease. With a median of 3.1 years of follow-up, estimated progression-free survival (PFS) and overall survival (OS) rates at 3 years were 15% and 43% respectively. OS was longer in the < 55 compared to the 55 age cohort (P = 0.0091), longer for HL than NHL (P =
0.59 and 0.039 respectively) and longer for Low/Low-Int IPI than High/High-Int IPI (P = 0.0074 and 0.0009 respectively). Median duration of inpatient stay was 3 days. There were no treatment-related deaths. In conclusion, this modification of DICE is an effective and well tolerated salvage regimen, even in this poor prognosis group of patients. Further clinical studies of DICE in first relapse and in older patients, possibly with the addition of rituximab, are warranted.

PMID:15621802

Prognostic features for response and survival in elderly patients with de novo acute myeloid leukemia treated with mitoxantrone and intermediate dose cytarabine.
Grigg AP, Reynolds J, et al.
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Forty-three fit elderly patients with de novo acute myeloid leukemia (AML) received chemotherapy with mitoxantrone and intermediate dose cytarabine (MIDAC) in a phase II clinical trial conducted by the Australasian Leukaemia and Lymphoma Group. The main aim of the study was to evaluate the tolerability and efficacy of MIDAC in inducing durable remissions. While the chemotherapy was generally well tolerated, less than half the patients achieved complete remission (CR) after induction and many of those in CR could not receive planned consolidation cycles. The median overall survival for all patients was 6.5 months and the median disease-free survival for those achieving CR was 8.3 months. Only 2 patients survived beyond 4 years. Factors significantly associated with shorter survival were adverse cytogenetics, marrow dysplasia and increasing age. These results suggest that only selected elderly patients with AML are likely to benefit from aggressive chemotherapy and that novel therapies are required to improve the poor prognosis of this group.

PMID:15621826

Hepatic expression of the tumor necrosis factor family member lymphotoxin-beta is regulated by interleukin (IL)-6 and IL-1beta: transcriptional control mechanisms in oval cells and hepatoma cell lines.
Subrata LS, Lowes KN, et al.
Biochemistry and Molecular Biology, School of Biomedical and Chemical Sciences, The University of Western Australia, Crawley, Western Australia, Australia.

Who has the con?
Pearn-Rowe BS.

**A new focus of Rickettsia honei spotted fever in South Australia.**
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We recently diagnosed rickettsial spotted fever in four patients from the south-eastern coastal region of South Australia near Adelaide, an area not known to be endemic for this infection. All infections were acquired within the geographic range of Aponomma hydrosauri, the tick vector of Rickettsia honei. Infection by R. honei was confirmed in two patients. This extension of the known geographic range of R. honei infection may be explained, in part, by alterations in host-parasite ecology.

PMID:ISI:000231692300009


**Notifications of imported malaria in Western Australia, 1990-2001: incidence, associated factors and chemoprophylaxis.**
School of Medicine and Pharmacology, University of Western Australia, Fremantle, WA, Australia.
OBJECTIVE: To assess changes in and factors associated with recent malaria notifications in Western Australia (WA). DESIGN: Retrospective analysis of the WA Notifiable Infectious Diseases Database and enhanced surveillance questionnaires completed by attending medical practitioners. PATIENTS: Cases of malaria notified between January 1990 and December 2001. MAIN OUTCOME MEASURES: Annual notifications by demographic variables (including age, sex, occupation and place of residence), region/country of acquisition, chemoprophylaxis used, Plasmodium species and outcome. RESULTS: 482 patients were notified (mean age, 31 years; 80% male); 57% lived in Perth, 31% in country areas and 12% in an immigration detention centre. Comparison between the 6-year periods 1990-1995 and 1996-2001 showed that Plasmodium falciparum cases increased from 29 (14%) to 108 (44%; P < 0.001), while Plasmodium vivax cases decreased from 157 (77%) to 122 (50%; P < 0.001); immigrants in detention, defence force personnel and cases from Africa were increasingly represented (P < 0.05 in each case). Only 31% of patients took regular chemoprophylaxis and, among these, the regimen was appropriate in only a quarter. There was a median period of 3 days between symptom onset and diagnosis. One patient died. CONCLUSIONS: There has been an increase in P. falciparum cases in WA since 1990. This reflects the influx of immigrants in detention, deployment of military personnel to East Timor and increasing numbers of cases from Africa. A significant number of Australian travellers who developed malaria had not taken chemoprophylaxis either regularly or at all, and, of those who had, the regimen was inadequate in most.

PMID:15720171


**Artemisinin-based combination therapies for uncomplicated malaria.**
Davis TME, Karunajeewa HA, et al.
University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, PO Box 480, Fremantle, WA 6959, Australia. tdavis@cyllene.uwa.edu.au.
There has been a relentless increase in resistance of malaria parasites to conventional antimalarial drugs, including chloroquine, sulfadoxine-pyrimethamine and mefloquine. In response to this situation, short-course artemisinin-based combination therapies (ACTs) have been developed. The World Health Organization has endorsed ACT as first-line treatment where the potentially life-threatening parasite Plasmodium falciparum is the predominant infecting species. ACTs combine the rapid schizontocidal activity of an artemisinin derivative (artesunate, artemether or dihydroartemisinin) with a longer-half-life partner drug. Although the use of chloroquine and sulfadoxine-pyrimethamine as partners in ACT improves their efficacy, this may only have value as a short-term measure in patients with a degree of immunity to malaria. Alternative currently available partner drugs include mefloquine, lumefantrine and piperaquine. Artesunate-mefloquine is highly effective but is expensive and side effects (mainly neurotoxicity) can be problematic. Artemether-lumefantrine, the only ACT available in Australia, appears less effective than artesunate-mefloquine and needs to be administered with food to ensure adequate bioavailability. Dihydroartemisinin-piperaquine is highly effective, well tolerated and relatively inexpensive. The goal of potent, safe, easy-to-administer and inexpensive ACTs may see trioxolanes in place of artemisinin derivatives, as well as novel partner drugs such as pyronaridine or naphthoquine, in the future.  
PMID:15720175


**A new focus of Rickettsia honei spotted fever in South Australia.**
J.R. Dyer, Department of Infectious Diseases, Fremantle Hospital, PO Box 480, Fremantle, WA 6959; Australia. E-Mail: John.Dyer@health.wa.gov.au.
We recently diagnosed rickettsial spotted fever in four patients from the south-eastern coastal region of South Australia near Adelaide, an area not known to be endemic for this infection. All infections were acquired within the geographic range of Aponomma hydrosauri, the tick vector of Rickettsia honei. Infection by R. honei was confirmed in two patients. This extension of the known geographic range of R. honei infection may be explained, in part, by alterations in host-parasite ecology.
PMID:2005119400


**Allergic rhinitis an unrecognised disability.**
Nolan RC, Mallon DF.
Department of Clinical Immunology and Allergy, Fremantle and Princess Margaret Hospitals, Perth, WA
* Allergic rhinitis can substantially reduce affected patient's quality of life through influence on sleep, work and leisure activities. * Investigation relies heavily on history and targeted testing for confirmation of specific allergic triggers. * Allergen avoidance measures are worthwhile but have only a moderate effect. * Intranasal corticosteroids are effective at controlling symptoms in almost all patients with allergic rhinitis if used correctly. * Immunotherapy (desensitisation) is the most effective treatment in selected patients. The GP's role in ongoing immunotherapy is substantial but the therapy should be initiated by an allergist.
PMID:2005547676
The childbirth expectations of a self-selected cohort of Western Australian women.

Fenwick J, Hauck Y, et al.

Edith Cowan University, School of Nursing and Public Health, Churchlands, Western Australia.

OBJECTIVES: to explore and describe the labour and birth expectations of a cohort of Western Australian women, and to identify the factors that influence these expectations.

DESIGN: a qualitative study using an explorative descriptive design and techniques associated with constant comparison. Data were collected from tape-recorded telephone interviews.

SETTING: Perth, Western Australia.

PARTICIPANTS: two hundred and two women who were pregnant or who had birthed within the last 12 months.

FINDINGS: five major themes were identified. Three of the five themes reflected a positive outlook on birth. These were labelled, 'owning and believing in birth as a natural event', 'satisfaction with the birth process and outcome' and 'involvement and participation in the birthing experience'. The remaining two themes 'birth is a negative event' and 'birth is a medical event' encapsulated the women's statements that described childbirth as a potential negative and unaffirming experience. Particularly influential on the formation of childbirth expectations were the public and private discourses of childbirth, especially those related to books and magazines, and the stories of mothers and sisters.

Professional discourses, women's own history, and factors such as age and life-style choices also influenced decisions and contributed to how women perceived their experiences.

IMPLICATIONS FOR PRACTICE: the findings of the study challenge the anecdotal evidence that many contemporary western women willingly and knowingly choose or expect birth to be a medicalised event. Although midwives and other maternity healthcare providers need to help women develop realistic expectations, there is also a need to examine the influence of healthcare professionals in perpetuating a technical approach to birth. The findings do, however, confirm that some women are anxious, scared and frightened of the childbirth experience. It is essential that research continues to focus on developing strategies to assist women confront and deal with these fears.

PMID:15740814

Apparent Addison's disease following ileostomy.

Yeap BB, Platell CF, et al.

Department of Endocrinology, Fremantle Hospital and School of Medicine and Pharmacology; Department of Surgery, Fremantle Hospital and School of Surgery and Pathology; Department of Nephrology, Fremantle Hospital and School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia

Publication Types: Case Reports
Letter

Effects of smoking on renal function in patients with type 1 and type 2 diabetes mellitus.

Orth SR, Schroeder T, et al.

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Background. Smoking increases the risk of end-stage renal failure in patients with primary renal disease. Whether and to what extent smoking affects the kidneys in diabetic patients with normal renal function and variable degrees of proteinuria has not been fully studied. Methods. We followed 185 patients with type 1 or 2 diabetes mellitus and with or without signs of overt renal disease for at least 3 years, median 5.1 (3/6.8) years. Each patient had a baseline visit
and at least four follow-up visits (average 4.8 +/- 0.3). Cases were patients who were smoking (n= 44) at the time the survey was started. Controls were patients who had never smoked (n= 141). Glomerular filtration rate (GFR) was estimated using the MDRD formula. Multiple logistic regression was used to correct for confounding factors. Results. At baseline, smokers were younger (47 +/- 14 vs 54 +/- 16 years, P<0.01), and had a lower GFR (95 +/- 26 ml/min) than non-smokers (107 +/- 33 ml/min, P<0.05). Mean GFR remained constant during follow-up in non-smokers (106 +/- 31 ml/min), but decreased significantly in smokers (83 +/- 22 ml/min, P<0.0001), and this relationship persisted when adjusted for retinopathy, glycaemic control, age, body habitus, ACE-inhibitor treatment, blood pressure control or severity of proteinuria. The effect of smoking on GFR decline was stronger in patients with type 1 diabetes or male gender. Conclusions. Cigarette smoking causes a decrease in GFR in diabetic patients with normal or near-normal renal function, independent of confounding factors including severity of proteinuria. The latter finding suggests a mechanism independent of glomerular damage. copyright The Author [2005]. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved. PMID:2005491829


Natalizumab induction and maintenance therapy for Crohn's disease.


For the International Efficacy of Natalizumab as Active Crohn’s Therapy (ENACT-1) and the Evaluation of Natalizumab as Continuous Therapy (ENACT-2) Trial Groups., From the Mayo Clinic, Rochester, Minn. (W.J.S.); Hopital Huriez, Centre Hospitalier Regional Universitaire de Lille, Lille, France (J.F.C.); St. Paul's Hospital, University of British Columbia, Vancouver, Canada (R.E.); Robarts Research Institute, University of Western Ontario, London, Canada (B.G.F.); the University of Chicago, Chicago (S.B.H.); the School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Australia (I.C.L.); the University of Calgary, Calgary, Alta., Canada (R.P.); ProPharma International Ventures, Hillsborough, Calif. (M.S.); University Hospital Schleswig-Holstein, Christian Albrechts University, Kiel, Germany (S.S.); Cedars-Sinai Medical Center, Los Angeles (S.T.); Academic Medical Center, Amsterdam (S.D.); Elan Pharmaceuticals, San Diego, Calif. (R.G., D.D., G.S.H.); and Universitaire Ziekenhuizen Leuven, Leuven, Belgium (P.R.). Address reprint requests for the ENACT-1 trial to Dr. Rutgeerts at Universitaire Ziekenhuizen Leuven, Inwendige Geneeskunde, UZ Gasthuisberg, Herestraat 49-B-3000, Leuven, Belgium, or at paul.rutgeerts@uz.kuleuven.ac.be. Address reprint requests for the ENACT-2 trial to Dr. Sandborn at the Mayo Clinic, 200 First St. SW, Rochester, MN 55905, or at sandborn.william@mayo.edu.

Background: Natalizumab, a humanized monoclonal antibody against (alpha)(4)) integrin, inhibits leukocyte adhesion and migration into inflamed tissue., Methods: We conducted two controlled trials to evaluate natalizumab as induction and maintenance therapy in patients with active Crohn’s disease. In the first trial, 905 patients were randomly assigned to receive 300 mg of natalizumab or placebo at weeks 0, 4, and 8. The primary outcome was response, defined by a decrease in the Crohn’s Disease Activity Index (CDAI) score of at least 70 points, at week 10. In the second trial, 339 patients who had a response to natalizumab in the first trial were randomly reassigned to receive 300 mg of natalizumab or placebo every four weeks through week 56. The primary outcome was a sustained response through week 36. A secondary outcome in both trials was disease remission (a CDAI score of less than 150),. Results: In the first trial, the natalizumab and placebo groups had similar rates of response (56 percent and 49 percent, respectively; P=0.05) and remission (37 percent and 30 percent, respectively; P=0.12) at 10 weeks. Continuing natalizumab in the second trial resulted in higher rates of sustained
response (61 percent vs. 28 percent, P<0.001) and remission (44 percent vs. 26 percent, P=0.003) through week 36 than did switching to placebo. Serious adverse events occurred in 7 percent of each group in the first trial and in 10 percent of the placebo group and 8 percent of the natalizumab group in the second trial. In an open-label extension study, a patient treated with natalizumab died from progressive multifocal leukoencephalopathy, associated with the JC virus, a human polyomavirus.

Conclusions: Induction therapy with natalizumab for Crohn’s disease resulted in small, nonsignificant improvements in response and remission rates. Patients who had a response had significantly increased rates of sustained response and remission if natalizumab was continued every four weeks. The benefit of natalizumab will need to be weighed against the risk of serious adverse events, including progressive multifocal leukoencephalopathy. (ClinicalTrials.gov numbers, NCT00032786 and NCT00032799.), N Engl J Med 2005;353: 1912-25., Copyright (C) 2005 Massachusetts Medical Society. All rights reserved.


Management and outcomes of postoperative endophthalmitis since the endophthalmitis vitrectomy study - The endophthalmitis population study of western Australia (EPSWA)’s fifth report.
Ng JQ, Morlet N, et al.
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Purpose: To examine if changes in the diagnosis and management of postoperative endophthalmitis have occurred since 1995, and to identify factors that might predict final visual outcome.

Design: Retrospective, population-based, noncomparative, consecutive case series.

Participants: Patients with clinically diagnosed endophthalmitis after cataract surgery and lens-related surgery in Western Australia from 1980 to 2000.

Methods: Endophthalmitis cases were identified using record linkage and cross-referencing with the surgical logbooks of vitreoretinal surgeons before validation by medical record review.

Main Outcome Measures: Microbiological data (microorganisms isolated and antibiotic susceptibilities), diagnostic interventions, surgical procedures, therapeutic interventions, and visual acuity (VA).

Results: During the 21-year period, 213 episodes of endophthalmitis occurred after cataract surgery. Since 1995, both anterior chamber sampling and vitreous sampling have increased significantly. The overall use of vitrectomy has also increased, but we did not observe a difference according to presenting VA. Intravitreal antibiotic use increased significantly, whereas the use of both subconjunctival and IV antibiotics decreased. In one third of patients, the VA at least 6 months after admission for endophthalmitis was worse than 6/18. This was associated with treatment that did not include the use of oral antibiotics (odds ratio [OR], 3.86; 95% confidence interval [CI], 1.21-12.39; P=0.02), growth from intraocular samples of organisms other than coagulase-negative staphylococci (OR, 9.84; 95% CI, 2.84-34.09; P < 0.001), and a discharge VA worse than 6/18 (OR, 6.10; 95% CI, 1.63-22.89; P=0.01).

Conclusions: Although we observed noticeable changes in the diagnosis and management of endophthalmitis since 1995, visual outcomes have not improved and remain poor. Our finding
that treatment with oral antibiotics may be associated with a better visual outcome warrants further investigation. (c) 2005 by the American Academy of Ophthalmology. PMID:ISI:000230121100005

**Not only 'Flinders Island' spotted fever.**
Unsworth NB, Stenos J, et al.
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Department of Microbiology and Infectious Diseases, Royal Hobart Hospital, Tasmania. Infectious Diseases Department, Fremantle Hospital, Western Australia, Australia.
AIM: To demonstrate that Flinders Island spotted fever (FISF), a spotted fever group rickettsial infection caused by Rickettsia honei, is found not only on Flinders Island (Bass Strait), Tasmania, but elsewhere in south-east Australia. METHODS: Cases of FISF were identified by rickettsial serology, culture and the detection of rickettsial DNA via PCR. Isolates and PCR products were sequenced to identify the aetiological agent as R. honei. RESULTS: Three new cases of FISF were detected outside of Flinders Island. One on Schouten Island, south of the Freycinet Peninsula, Tasmania, and two in south-eastern South Australia (McLaren Vale and Goolwa). CONCLUSIONS: These cases show that FISF extends beyond Flinders Island and most likely has the same distribution across south-east Australia as its vector, the reptile tick Aponomma hydrosauri. FISF should be considered as a differential diagnosis in patients from south-eastern Australia presenting with fever, headache and rash following a tick bite. PMID:16175900

**Gastrointestinal stromal tumours (GISTs): a clinicopathological and molecular study of 66 cases.**
Department of Anatomical Pathology, PathCentre, Western Australia.
AIMS: Predicting the clinical behaviour of gastrointestinal stromal tumours (GISTs) is difficult and criteria delineating benign from malignant cases are not firmly established. The aims of this study were to define the clinicopathological and molecular features of 66 GISTs, and to determine whether any specific parameters were associated with patient outcome. METHODS: Archival cases of GIST from two major teaching hospitals in Western Australia were studied. Inclusion criteria for the study were: (1) appropriate morphology, (2) CD117 positivity, (3) adequacy of pathological material for study, and (4) exclusion of other tumour types on the basis of immunophenotypic and/or ultrastructural features. Expression of CD117, CD34, S100 protein, keratin (using broad spectrum MNF116), alpha-smooth muscle actin (SMA) was determined by immunohistochemistry. PCR and single strand conformation polymorphism (PCR-SSCP) analysis were used to screen for mutations in exons 11 and 9 of c-kit. RESULTS: There were equal numbers of males and females with a mean age at diagnosis of 60 years, followed up for a mean of 54 months. Thirteen patients (21%) had died of GIST by the end of the study. Tumours were mostly located in the stomach (67%) and small intestine (SI; 25%). The cell types were pure spindle (68%), pure epithelioid (12%) and mixed epithelioid/spindle (20%). c-kit mutations were found in 69% of GISTs, with the large majority (91%) occurring in exon 11. Size > or = 10 cm, tumour necrosis and pure epithelioid cell morphology each were the only factors significantly associated with adverse survival (p=0.038, and p=0.047 and p=0.028, respectively). Mitotic activity > or = 5/50 HPF showed a definite trend association with adverse
survival, but unlike some other studies, did not achieve statistical significance (p=0.067). c-kit mutations were more frequent in small intestinal GISTs (p=0.05) and in those with pure spindle cell morphology (p=0.023) but were not associated with patient outcome. CONCLUSION: In this study, size > or = 10cm, necrosis and/or pure epithelioid cell morphology correlated significantly with adverse survival. Mitotic activity showed a strong association with survival but this did not reach statistical significance. c-kit mutations occurred mainly in GISTs of the SI, and in purely spindle cell tumours. While the mutation status did not associate with patient outcome in this series, this remains a controversial issue, and further studies are needed to assess whether the type of mutation affects response to tyrosine kinase inhibitor therapy in metastatic GISTs. CD117 staining of any mesenchymal lesion of the gastrointestinal tract should be mandatory for accurate classification. PCR-SSCP analysis is a fast, sensitive and relatively inexpensive method of analysing c-kit mutations, which may be important prognostically and also of therapeutic relevance in the assessment of new tyrosine kinase inhibitor therapies.

PMID:15875730


Rajan GP, Fergie N, et al.
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BACKGROUND: The routine use of antibiotics in septorhinoplasty is widespread and recommended in many textbooks despite the lack of scientific evidence for their use. This practice has led to extensive discussions in the face of the emerging threat of antibiotic resistance and rising health care costs. The aim of our study was to investigate the role of antibiotic prophylaxis in septorhinoplasty. METHODS: The authors conducted a prospective, randomized, single-blind study at a tertiary referral center in a private practice setting, including 200 patients undergoing septorhinoplasty over a 4-year period. One hundred patients received preoperative single-shot antibiotics, and the other 100 received a combined regimen with preoperative single-shot antibiotics plus a postoperative 7-day course of oral antibiotics. RESULTS: Three patients (3 percent) developed postoperative local wound infections in the group with combined treatment; no infections occurred in the group treated with the preoperative single intravenous dose at induction alone, and the difference was not statistically significant. The rate of common antibiotic-induced side effects (e.g., nausea, diarrhea, skin rashes, pruritus) was significantly higher in the combined treatment group (29 percent versus 2 percent, p = 0.03). The cost for antibiotics and medication to treat the side effects per patient was significantly higher in the combined treatment group (93.45 AUD versus 14.50 AUD, p= 0.04). CONCLUSION: The authors' results would suggest that a single dose of antibiotics administered preoperatively in endonasal septorhinoplasty with autologous cartilage grafting is sufficient for prophylaxis of postoperative infections, thus eliminating the costs for postoperative antibiotics and the management of their side effects.

Publication Types: Randomized Controlled Trial


Identification of an agent suitable for disinfecting boots of visitors to the Antarctic.
Curry CH, McCarthy JS, et al.
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Studies of Antarctic fauna have led to tentative identification of a range of potential pathogens for both animals and humans. The rapid increase in visitors on tourist ships to the continent, now exceeding 10,000 per year, raises the concern that humans might transmit pathogens into...
and between wildlife colonies. The authors investigated the feasibility and efficacy of chemical disinfection of the microbial contamination on visitors' boots. During three voyages to penguin colonies in the Ross Sea, swabs were collected from the boots of visitors prior to landing, immediately on return to the ship, after a water wash, and after a chemical disinfectant wash using Virkon S. For the first two visits, abundant growth of bacteria was identified on boots at all three stages prior to disinfection. Following disinfection, the growth of bacteria was virtually eliminated. On the third visit, previously disinfected boots grew virtually no bacteria. After this landing the bacterial growth was substantially reduced by disinfection. These results indicate that consideration should be given to including disinfection in cleaning the boots of visitors to wildlife sites in the Antarctic to reduce the risk of translocation of microbial pathogens.

PMID:BACD200500197074


A simple lifestyle score predicts survival in healthy elderly men.
Spencer CA, Jamrozik K, et al.
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bSchool of Population Health, University of Queensland, Herston, Australia
cSchool of Surgery and Pathology, The University of Western Australia, Fremantle Hospital, Fremantle, Australia
dThe Mount Hospital, Perth, Australia

BACKGROUND: Although improvements in life expectancy have been attributed in part to the adoption of a more prudent lifestyle, few studies have examined the association of lifestyle with survival, using several lifestyle factors simultaneously, in a healthy elderly population.

METHODS: We investigated the association of health related behaviors with mortality in 7989 men aged 65 to 83 years participating in a population-based trial in Perth, Western Australia, by calculating a lifestyle score as a simple tally of how many of eight prudent behaviors each individual followed. RESULTS: Invitations to screening produced a corrected response of 70.5%. Out of a possible score of 8, 46% of men had a score of less than 5. Within 5 years, a total of 703 men (9%) had died from any cause. The hazard ratio in men with a low lifestyle score was 1.3 [95% confidence interval (CI): 1.1-1.5] compared with men with a score of 5 or more. CONCLUSIONS: Lifestyle remains an important predictor of mortality even in old age. Survival in older men without a history of cardiovascular disease can potentially be enhanced by promoting a healthy lifestyle.

PMID:15850869


Lifestyle still predicts mortality in older men with established vascular disease.
Spencer CA, Jamrozik K, et al.
School of Population Health, University of Western Australia

BACKGROUND: It is uncertain whether accepted associations between health behaviors and mortality are pertinent to elderly people. No previous studies have examined the patterns of lifestyle in elderly men with and without clinically evident vascular disease by using a lifestyle score to predict survival. METHODS: We measured prevalence of a healthy lifestyle (four or more healthy behaviors out of eight) and examined survival in 11,745 men aged 65-83 years participating in a randomized population-based trial of screening for abdominal aortic aneurysm in Perth, Western Australia. After stratifying participants into five groups according to history and
symptoms of vascular disease, we compared survival of men in each subgroup with that of 'healthy' men with no history or symptoms of vascular disease. RESULTS.: Invitations to screening produced a corrected response of 70.5%. After adjusting for age and place of birth, having an unhealthy lifestyle was associated with an increase of 20% in the likelihood of death from any cause within 5 years (95% CI: 10-30%). This pattern was consistently evident across subgroups defined by history of vascular disease, but was less evident for deaths from vascular disease. CONCLUSIONS.: Our results highlight the importance of maintaining a healthy lifestyle through to old age, regardless of history of vascular disease.

PMID:15917056


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Background. This study examines whether community treatment orders (CTOs) reduce psychiatric admission rates or bed-days for patients from Western Australia compared to control patients from a jurisdiction without this legislation (Nova Scotia). Method. A population-based record linkage analysis of an inception cohort using a two-stage design of matching and multivariate analyses to control for sociodemographics, clinical features and psychiatric history. All discharges from in-patient psychiatric services in Western Australia and Nova Scotia were included covering a population of 2.6 million people. Patients on CTOs in the first year of implementation in Western Australia were compared with controls from Nova Scotia matched on date of discharge from in-patient care, demographics, diagnosis and past in-patient psychiatric history. We analysed time to admission using Cox regression analyses and number of bed-days using logistic regression. Results. We matched 196 CTO cases with an equal number of controls. On survival analyses, CTO cases had a significantly greater readmission rate. Co-morbid personality disorder and previous psychiatric history were also associated with readmission. However, on logistic regression, patients on CTOs spent less time in hospital in the following year, with reduced in-patient stays of over 100 days. Conclusions. Although compulsory community treatment does not reduce hospital admission rates, increased surveillance of patients on CTOs may lead to earlier intervention such as admission, so reducing length of hospital stay. However, we do not know if it is the intensity of treatment, or its compulsory nature, that effects outcome. copyright 2005 Cambridge University Press.

PMID:2005405446


A two-year prospective study of the health-related quality of life of children with chronic illness—the parents’ perspective.

Sawyer MG, Reynolds KE, et al.

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The aim of this study was to assess prospectively changes in the health-related quality of life (HRQL) of children and adolescents with diabetes, asthma or cystic fibrosis (CF). One hundred and twenty-two parents of children aged 10-16 years with asthma, diabetes, or CF were recruited from specialist paediatric clinics. Parents described their children's HRQL using the Child Health Questionnaire (PF98) at baseline, 6, 12, 18 and 24 months post-baseline. They reported that the general health of children with CF was significantly worse than that of children
with asthma and diabetes at baseline. In other domains there were few differences between the HRQL of children in the three groups. In several domains, the HRQL of children with asthma or diabetes improved over the 2 years of the study. This improvement was less evident for children with CF.

PMID:15892428


**Misconceptions about the big bang.**
Lineweaver CH, Davis TM.
Mount Stromlo Observatory, Canberra, Australia.
PMID:15859210


**Screening for HFE and iron overload.**
Department of Gastroenterology, Fremantle Hospital, Fremantle, Western Australia, Australia.
Type 1 hereditary hemochromatosis is a common disorder of iron overload occurring in individuals homozygous for the C282Y HFE gene mutation. It can be a progressive and fatal condition. Early detection and phlebotomy prior to the onset of cirrhosis can reduce morbidity and normalize life expectancy. It is readily identified through biochemical testing for iron overload using serum transferrin saturation and genetic testing for C282Y homozygosity. General population screening has been waived in preference to targeting high-risk groups such as first-degree relatives of affected individuals and those with clinical features suggestive of iron loading. This screening strategy is likely to continue until uncertainties regarding the natural history of the disease, age-related penetrance, and management of asymptomatic individuals are clarified. Potential ethical, legal, and psychosocial issues arising through application of genetic screening programs also must be resolved prior to implementation of general population screening programs.
PMID:16315134


**An inflammatory role for the mammalian carboxypeptidase inhibitor latexin: relationship to cystatins and the tumor suppressor TIG1.**
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Latexin, the only known mammalian carboxypeptidase inhibitor, has no detectable sequence similarity with plant and parasite inhibitors, but it is related to a human putative tumor suppressor protein, TIG1. Latexin is expressed in the developing brain, and we find that it plays a role in inflammation, as it is expressed at high levels and is inducible in macrophages in concert with other protease inhibitors and potential protease targets. The crystal structure of mouse latexin, solved at 1.83 A resolution, shows no structural relationship with other carboxypeptidase inhibitors. Furthermore, despite a lack of detectable sequence duplication, the structure incorporates two topologically analogous domains related by pseudo two-fold symmetry. Surprisingly, these domains share a cystatin fold architecture found in proteins that inhibit cysteine proteases, suggesting an evolutionary and possibly functional relationship. The structure of the tumor suppressor protein TIG1 was modeled, revealing its putative membrane binding surface.
PMID:15698574
The current status and potential role of laboratory testing to prevent transfusion-transmitted malaria.
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Publication Types: Review

Quantifying the relationship between disease severity, utility and health care resource use in Crohn's disease.
Weston AR, Gibson PR, et al.
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The efficacy of a malarial antibody enzyme immunoassay for establishing the reinstatement status of blood donors potentially exposed to malaria.
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BACKGROUND AND OBJECTIVES: The two key objectives of the study were, first, to evaluate the sensitivity and specificity of a recombinant antigen-based malarial enzyme-linked immunoassay (EIA) and, second, to estimate the risk associated with implementing this test with a shortened cellular component restriction period (6 months rather than the standard 12-36 months) for blood donors with a malarial risk exposure. MATERIALS AND METHODS: Blood donors were recruited into four distinct groups [non-exposed (control), malarial area 'visitors', 'residents' and 'previous infection') and screened by using the Newmarket malarial antibody EIA. Assay specificity was evaluated in unexposed blood donors, and sensitivity was determined in acute clinical samples. RESULTS: No parasitaemic donors were detected amongst 337 malarial 'visitors' who had returned from a malaria-endemic area less than 6 months previously, or for 402 'visitors' or 'residents' who had returned from a malaria-endemic area more than 6 months previously. The incidence of malarial antibodies within the exposed blood donor groups was 1.33% (10/751). In acute clinical non-donor samples, the Newmarket EIA detected 106/108 (98.1; 93.5-99.5%) ‘film’ positive Plasmodium falciparum infections and 12/12 (100, 75.7-100.0%) P. vivax infections. The estimated additional risk exposure of the proposed new strategy was one infectious P. falciparum donation per 175 years or 1 per 4.2 years for P. vivax. CONCLUSIONS: The study findings support the efficacy and safety of a targeted screening strategy combining antibody screening with a 6-month cellular component restriction period for donors with a declared malarial risk.
PMID:15720607

Using the polymerase chain reaction coupled with denaturing gradient gel electrophoresis to investigate the association between bacterial translocation and systemic inflammatory response syndrome in predicted acute severe pancreatitis.
Pearce CB, Zinkevich V, et al.
AIM: To investigate the use of PCR and DGGE to investigate the association between bacterial translocation and systemic inflammatory response syndrome in predicted severe AP.

METHODS: Patients with biochemical and clinical evidence of acute pancreatitis and an APACHE II score $\geq 8$ were enrolled. PCR and DGGE were employed to detect bacterial translocation in blood samples collected on d 1, 3, and 8 after the admission. Standard microbial blood cultures were taken when there was clinical evidence of sepsis or when felt to be clinically indicated by the supervising team.

RESULTS: Six patients were included. Of all the patients investigated, only one developed septic complications; the others had uneventful illness. Bacteria were detected using PCR in 4 of the 17 collected blood samples. The patient with sepsis was PCR-positive in two samples (taken on d 1 and 3), despite three negative blood cultures. Using DGGE and specific primers, the bacteria in all blood specimens which tested positive for the presence of bacterial DNA were identified as E. coli.

CONCLUSION: Our study confirmed that unlike traditional microbiological techniques, PCR can detect the presence of bacteria in the blood of patients with severe AP. Therefore, this latter method in conjunction with DGGE is potentially an extremely useful tool in predicting septic morbidity and evaluating patients with the disease. Further research using increased numbers of patients, in particular those patients with necrosis and sepsis, is required to assess the reliability of PCR and DGGE in the rapid diagnosis of infection in AP.

PMID:16437661