Outcome of primary resurfacing hip replacement: evaluation of risk factors for early revision.
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BACKGROUND AND PURPOSE: The outcome of modern resurfacing remains to be determined. The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) started collection of data on hip resurfacing at a time when modern resurfacing was started in Australia. The rate of resurfacing has been higher in Australia than in many other countries. As a result, the AOANJRR has one of the largest series of resurfacing procedures. This study was undertaken to determine the results of this series and the risk factors associated with revision. PATIENTS AND METHODS: Data from the AOANJRR were used to analyze the survivorship of 12,093 primary resurfacing hip replacements reported to the Joint Replacement Registry between September 1999 and December 2008. This was compared to the results of primary conventional total hip replacement reported during the same period. The Kaplan-Meier method and proportional hazards models were used to determine risk factors such as age, sex, femoral component size, primary diagnosis, and implant design. RESULTS: Female patients had a higher revision rate than males; however, after adjusting for head size, the revision rates were similar. Prostheses with head sizes of less than 50 mm had a higher revision rate than those with head sizes of 50 mm or more. At 8 years, the cumulative percent revision of hip resurfacing was 5.3 (4.6-6.2), as compared to 4.0 (3.8-4.2) for total hip replacement. However, in osteoarthritis patients aged less than 55 years with head sizes of 50 mm or more, the 7-year cumulative percent revision for hip resurfacing was 3.0 (2.2-4.2). Also, hips with dysplasia and some implant designs had an increased risk of revision. INTERPRETATION: Risk factors for revision of resurfacing were older patients, smaller femoral head size, patients with developmental dysplasia, and certain implant designs. These results highlight the importance of patient and prosthesis selection in optimizing the outcome of hip resurfacing.
PMID:20180719

Differences in metal ion release following cobalt-chromium and oxidized zirconium total knee arthroplasty.
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Ions are released from all metals after implantation in the body through processes of corrosive and mechanical wear. The aim of this study was to investigate whether serum metal ion levels are raised in patients following total knee arthroplasty. Serum levels of chromium, cobalt, aluminium, molybdenum and zirconium were measured in two groups of patients at a minimum of 3 years after knee arthroplasty. Twenty three patients had a cobalt-chromium femoral component and 14 patients had an oxidized zirconium femoral component, acting as a control group as this femoral component is free from cobalt and chromium. All patients had the same titanium tibial base plates, and no patellae were resurfaced. Despite the lack of cobalt and chromium in the prostheses used in the control group, no statistically significant differences in serum cobalt and chromium ion levels were found between the groups. On the basis of these results there does not appear to be any significant rise in serum metal ion levels following total knee arthroplasty several years after implantation. 2010, Acta Orthopaedica Belgica.
PMID:20973359

**Clinical effectiveness of a critical care nursing outreach service in facilitating discharge from the intensive care unit.**

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Background: Improved discharge planning and extension of care to the general care unit for patients transferring from intensive care may prevent readmission to the intensive care unit and prolonged hospital stays. Morbidity, mortality, and costs increase in readmitted intensive care patients.

Objectives: To evaluate the clinical effectiveness of a critical care nursing outreach service in facilitating discharge from the intensive care unit and providing follow-up in general care areas.

Methods: A before-and-after study design (with historical controls and a 6-month prospective intervention) was used to ascertain differences in clinical outcomes, length of stay, and cost/benefit. Patients admitted to intensive care units in 3 adult teaching hospitals were recruited. The service centered on follow-up visits by specialist intensive care nurses who reviewed and assessed patients who were to be or had been discharged to general care areas from the intensive care unit. Those nurses also provided education and clinical support to staff in general care areas. Results In total, 1435 patients were discharged during the 6-month prospective period. Length of stay from the time of admission to the intensive care unit to hospital discharge (P = .85), readmissions during the same hospital admission (5.6% vs 5.4%, P = .83), and hospital survival (P = .80) did not differ from before to after the intervention. Conclusions: Although other studies have shown beneficial outcomes in Australia and the United Kingdom, we found no improvement in length of stay after admission to the intensive care unit, readmission rate, or hospital mortality after a critical care nursing outreach service was implemented. 2010 American Association of Critical-Care Nurses.

PMID:20810409


**Patients' knowledge of the role of the anaesthetist - How can we improve our profile?**

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Introduction: Anaesthetists appear to lack identity in the public consciousness. Even within a short perioperative admission, patients may rarely see the same anaesthetist more than once. It remains unclear whether perioperative factors influence patients’ subsequent understanding of the role of anaesthetists. We designed a large survey of postoperative patients focusing on their knowledge of the duties and qualifications of anaesthetists to provide novel insight into which perioperative factors may influence patient knowledge of anaesthesia. Method: Postoperative patients were recruited.
consecutively from a single university teaching hospital. Important characteristics of anaesthesia, surgery, anaesthesia staff and postoperative pain management were recorded. A structured interview was conducted the day after surgery by a small team of independent interviewers. Results: Eight hundred and sixty-five patients completed the study questionnaire. The majority of patients were middle aged (mean 50 years), male (55%), ASA I or II (74%) and undergoing only minor procedures (69%). Forty-three percent of patients interacted primarily with the trainee, while 43% interacted with both the trainee and consultant. Only 15% of patients interacted primarily with a consultant anaesthetist. The most important predictors of correct identification of anaesthetists as medical specialists were number of prior anaesthetics ($P=0.003$), larger operation size ($P=0.007$) and consultant involvement prior to induction ($P=0.017$). Correct identification of anaesthetists' role in monitoring of vital signs was best predicted by number of prior anaesthetics ($P=0.000$) and increasing ASA ($P=0.003$). For correct identification of anaesthetists' role in emergency situations, only patient gender ($P=0.001$) and prior anaesthetics ($P=0.006$) appeared to influence patient response. Conclusion: The major modifiable factor found in our study was consultant involvement in patient interactions. Patients who had interaction with both the trainee and the consultant were significantly more likely to correctly identify the qualifications of anaesthetists, as well as their role in postoperative analgesia. As only a minority of patients interacted primarily with the consultant, we are unable to confidently state whether it was primarily the involvement of a more senior physician, or the patients' observation of professional interaction between teacher and trainee that accounted for more accurate patient responses.

Publication Types: Conference Abstract
PMID: 70314093

Prevalence of sexual activity and associated factors in men aged 75 to 95 years: a cohort study.
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BACKGROUND: Knowledge about sexuality in elderly persons is limited, and normative data are lacking. OBJECTIVE: To determine the proportion of older men who are sexually active and to explore factors predictive of sexual activity. DESIGN: Population-based cohort study. SETTING: Community-dwelling men from Perth, Western Australia, Australia. PARTICIPANTS: 3274 men aged 75 to 95 years. MEASUREMENTS: Questionnaires from 1996 to 1999, 2001 to 2004, and 2008 to 2009 assessed social and medical factors. Sex hormones were measured from 2001 to 2004. Sexual activity was assessed by questionnaire from 2008 to 2009. RESULTS: A total of 2783 men (85.0%) provided data on sexual activity. Sex was considered at least somewhat important by 48.8% (95% CI, 47.0% to 50.6%), and 30.8% (CI, 29.1% to 32.5%) had had at least 1 sexual encounter in the past 12 months. Of the latter, 56.5% were satisfied with the frequency of activity, whereas 43.0% had sex less often than preferred. In cross-sectional analyses, increasing age, partner's lack of interest, partner's physical limitations, osteoporosis, prostate cancer, diabetes, antidepressant use, and -blocker use were independently associated with reduced odds of sexual activity. Living with a partner and having a non-English-speaking background were associated with increased odds. In longitudinal analyses, higher testosterone levels were associated with increased odds of being sexually active. Other factors were similar to the cross-sectional model. LIMITATIONS: Response bias may have influenced findings because sexuality can be a sensitive topic. Attrition may have resulted in a healthier-than-average sample of older men. CONCLUSION: One half of elderly men consider sex important, and one third report being sexually active. Men's health problems were associated with lack of sexual activity. Key modifiable risk factors include diabetes, depression, and medication use. Endogenous testosterone levels predict sexual activity, but the role of testosterone therapy remains uncertain. PRIMARY

**B-vitamins reduce the long-term risk of depression after stroke: The VITATOPS-DEP trial.**
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Objective The consumption of certain B-vitamins through diet or supplementation decreases the total plasma concentration of homocysteine (tHcy) and may enhance response to standard antidepressant treatment. It is unclear if treatment with B-vitamins can reduce the long-term prevalence of depression in people at risk, such as stroke survivors. The purpose of this research was to determine if treatment with B-vitamins reduces the hazard of poststroke depression compared with placebo.

Methods Randomized, double-blind, placebo-controlled trial of tHcy-lowering treatment with daily folic acid (2 mg), vitamin B6 (25 mg), and vitamin B12 (0.5 mg) for 1 to 10.5 years in survivors of stroke. The primary endpoint was the onset of Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) major depression after randomization. Secondary outcomes were the prevalence of DSM-IV major or minor depression at the end of treatment. Other measured factors included age, gender, poststroke handicap associated with stroke, recurrence of strokes, cognitive impairment, and use of antidepressants.

Results Among 273 people who completed the final assessment after 7.1 +/- 2.1 years (mean +/- standard deviation) of follow up, random assignment to B-vitamins was associated with a lower hazard of major depression compared with placebo (18.4% vs 23.3%, adjusted hazard ratio [HR] = 0.48; 95% confidence interval [CI] = 0.31-0.76) and a trend toward a lower odds of major or minor depression at the end of the trial compared with placebo (19.1% vs 27.7%; adjusted odds ratio [OR] = 0.58; 95%CI = 0.31-1.09).

Interpretation Long-term treatment of poststroke survivors with folic acid, B6, and B12 was associated with a reduction in the hazard of major depression in our patient population. If these findings can be validated externally, B-vitamin supplementation offers hope as an effective, safe, and affordable intervention to reduce the burden of poststroke depression. 2010 American Neurological Association.

PMID:2010621224


**Intern pharmacists as change agents to improve the practice of nonprescription medication supply: Provision of salbutamol to patients with asthma.**

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BACKGROUND: Earlier work established an evidence practice gap during provision of nonprescription salbutamol (albuterol). Pharmacist interns are hypothesized to be in a position to improve professional practice in the community pharmacy setting. OBJECTIVE: To explore the potential of intern pharmacists to improve the professional practice of community pharmacy staff in the provision of nonprescription salbutamol. METHODS: Intern pharmacists (n = 157) delivered an asthma intervention in 136 pharmacies consisting of an educational activity to pharmacy staff and a health promotion campaign to consumers. Post-intervention, simulated patients presented to 100 intervention and 100 control community pharmacies with a request for salbutamol. The appropriate outcome was medical referral for poor asthma control and correction of poor inhaler technique. Incidence and quantity of patient assessment and counseling provided during the visit were also assessed. Logistic regression was used to determine the predictors of medical referral. RESULTS: A doubling in the rate of medical referral was seen in the intervention group (19% vs 40%; p = 0.001). Assessment of reliever use frequency was the main predictor of medical referral (OR = 22.7; 95% CI 9.06 to 56.9). Correction of poor inhaler technique did not improve; however, a reduction in salbutamol supplied without patient assessment (23% vs 8%; p = 0.009) or counseling (75% vs 48%; p < 0.001) was noted. CONCLUSIONS: A doubling in the rate of medical referral showed a clear improvement in professional practice during the provision of nonprescription salbutamol. The improved patient outcome in the intervention group was due to increased assessment of reliever use frequency. Identification of poor inhaler technique remained near zero in both groups, which suggests that intern pharmacists were able to improve the current practice of community pharmacies yet were unable to establish a new practice behavior. This study provides evidence that intern pharmacists can act as change agents to improve pharmacy practice.

PMID:2010388850


Pharmacokinetics of chloroquine and monodesethylchloroquine in pregnancy.
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In order to determine the pharmacokinetic disposition of chloroquine (CQ) and its active metabolite, desethylchloroquine (DECQ), when administered as intermittent presumptive treatment in pregnancy (IPTp) for malaria, 30 Papua New Guinean women in the second or third trimester of pregnancy and 30 age-matched nonpregnant women were administered three daily doses of 450 mg CQ (8.5 mg/kg of body weight/day) in addition to a single dose of sulfadoxine-pyrimethamine. For all women, blood was taken at baseline; at 1, 2, 4, 6, 12, 18, 24, 30, 48, and 72 h posttreatment; and at 7, 10, 14, 28, and 42 days posttreatment. Plasma was subsequently assayed for CQ and DECQ by high-performance liquid chromatography, and population pharmacokinetic modeling was performed. Pregnant subjects had significantly lower area under the plasma concentration-time curve for both CQ (35,750 versus 47,892 microg.h/liter, P < 0.001) and DECQ (23,073 versus 41,584 microg.h/liter, P < 0.001), reflecting significant differences in elimination half-lives and in volumes of distribution and clearances relative to bioavailability. Reduced plasma concentrations of both CQ and DECQ could compromise both curative efficacy and posttreatment prophylactic properties in pregnant patients. Higher IPTp CQ doses may be desirable but could increase the risk of adverse hemodynamic effects. Publication Types: Research Support, Non-U.S. Gov't
PMID:20086162


Pharmacokinetic properties of azithromycin in pregnancy.
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Azithromycin (AZI) is an azalide antibiotic with antimalarial activity that is considered safe in pregnancy. To assess its pharmacokinetic properties when administered as intermittent preventive treatment in pregnancy (IPTp), two 2-g doses were given 24 h apart to 31 pregnant and 29 age-matched nonpregnant Papua New Guinean women. All subjects also received single-dose sulfadoxine-pyrimethamine (SP) (1,500 mg or 75 mg) or chloroquine (450-mg base daily for 3 days). Blood samples were taken at 0, 1, 2, 3, 6, 12, 24, 32, 40, 48, and 72 h and on days 4, 5, 7, 10, and 14 for AZI assay by ultra-high-performance liquid chromatography-tandem mass spectrometry. The treatments were well tolerated. Using population pharmacokinetic modeling, a three-compartment model with zero-order followed by first-order absorption and no lag time provided the best fit. The areas under the plasma concentration-time curve (AUC(0-infinity)) (28.7 and 31.8 mg.h liter(-1) for pregnant and nonpregnant subjects, respectively) were consistent with the results of previous studies, but the estimated terminal elimination half-lives (78 and 77 h, respectively) were generally longer. The only significant relationship for a range of potential covariates, including malarial parasitemia, was with pregnancy, which accounted for an 86% increase in the volume of distribution of the central compartment relative to bioavailability without a significant change in the AUC(0-infinity). These data suggest that AZI can be combined with compounds with longer half-lives, such as SP, in combination IPTp without the need for dose adjustment.
surgery. Juggling emergency patients around the surgeons' and staffs' elective commitments resulted in semi-emergency procedures routinely being delayed. In an era of increasing financial pressure and the recent introduction of 'safe work hours' practices, the need for a new system which optimized available resources became apparent. [copyright sign] 2010 The Authors. ANZ Journal of Surgery [copyright sign] 2010 Royal Australasian College of Surgeons. METHODS: At Fremantle Hospital we developed a new system in a concerted effort to minimize the waiting time for general surgical referrals in the Emergency Department, as well as to move semi-urgent operating from the afterhours to the daytime. To analyse the impact of the ASU, data were collected during February, March, and April 2009 and compared with data from the same period in 2008. [copyright sign] 2010 The Authors. ANZ Journal of Surgery [copyright sign] 2010 Royal Australasian College of Surgeons. RESULTS: Although most referrals were received afterhours, over 85% of operations were performed during working hours compared with 72% in the 2008 period. The time from referral to review decreased from an average of 3.2 h in 2008 to 2.1 h. The mean duration of stay in 2009 was 3 days, which was a reduction from 4.2 days in 2008. An increase in weekend discharge rates was seen after the introduction of the ASU. [copyright sign] 2010 The Authors. ANZ Journal of Surgery [copyright sign] 2010 Royal Australasian College of Surgeons. CONCLUSION: Despite an increased workload, more referrals were seen and more operations performed during working hours and the time from referral to review was reduced. Higher discharge rates and reduced length of stays increased the availability of beds. We have demonstrated a successful new model which continues to evolve. PMID:21114736

Roentgen stereophotogrammetric analysis and clinical assessment of unipolar versus bipolar hemiarthroplasty for subcapital femur fracture: a randomized prospective study.
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BACKGROUND: Hemiarthroplasty is a well-established treatment for displaced subcapital fracture, but controversy exists about the optimal implant type. Bipolar hemiarthroplasty has proposed advantages over unipolar hemiarthroplasty in terms of better clinical results and decreased wear of acetabular cartilage. METHODS: This study is a randomized prospective study of 51 patients (52 hips) receiving either bipolar or unipolar hemiarthroplasty for displaced subcapital fractures. The outcome measurements were clinical scores and Roentgen stereophotogrammetric analysis (RSA) analysis to determine the rate of acetabular wear. RESULTS: Twenty-three patients completed 2-year follow-up. The RSA data demonstrated that there was slightly less acetabular wear by bipolar prostheses than by unipolar. The combined mean three-dimensional wear of the bipolar prostheses was 0.6 mm compared with 1.5 mm for the unipolar prostheses (P= 0.04). The bipolar group generally achieved higher scores in terms of the Harris Hip Score, Western Ontario and McMaster University Index of Osteoarthritis (WOMAC) questionnaire and 6-min walk test. These results were statistically significant at 3 months but not at 12 and 24 months. CONCLUSION: This study suggests that while the bipolar prosthesis performs slightly better than the unipolar in terms of acetabular cartilage wear and clinical outcomes, it remains debatable whether the benefits are worth the increased cost of the prosthesis. PMID:20575949

Optimising peri-operative fluid balance: UG09.
Ward M.
Fremantle, Western Australia
Publication Types: The Royal Australasian College of Surgeons Annual Scientific Congress Perth, Western Australia: 4-7 May, 2010: Upper GI Program Abstracts
**Archives of Orthopaedic & Trauma Surgery.** 2010; 130(5): 627-32.

**The treatment of periprosthetic fractures with locking plates: effect of drill and screw type on cement mantles: a biomechanical analysis.**

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**INTRODUCTION:** Periprosthetic fractures after cemented hip replacement are a challenging problem to manage. Biomechanical studies have suggested the benefit of using locking screws for plate fixation, but there are concerns whether screws damage the cement mantle and promote crack propagation leading to construct failure. **METHOD:** In this biomechanical study, different screw types were implanted into the cement mantle after pre-drilling holes of different sizes, in unicortical and bicortical configuration. The presence of cracks and the pull-out resistance of these screws were then evaluated. **RESULTS:** No unicortical screw induced cracks. Screws with a shortened tip, smaller flutes and double threads were significantly better for pull-out resistance. Bicortical screws were associated with a risk of local cement mantle damage, but also with a significantly greater holding power. By increasing the drill diameter, the onset of cracks decreased, but so does the pull-out resistance.

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

PMID:19685062


**Atherosclerosis and abdominal aortic aneurysm: cause, response, or common risk factors?**

[Editorial].

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**Knowledge, attitude and practices of indian dental surgeons towards tobacco control: Advances towards prevention.**

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Aims and Methods: We assessed the knowledge, attitude and practices of dental surgeons in the city of Bangalore, Karnataka, concerning use of tobacco in their patients. A self-administered questionnaire was administered to all dental surgeons prior to a sensitization program on nicotine dependence. Results: The dental surgeons who responded (n=100) reported a need for increasing sensitization on the issue of tobacco especially among health professionals. Only 33% knew that nicotine is the most addictive drug and knowledge was poor about pharmacological as well as non pharmacological methods of treatment of nicotine dependence. Only 52% asked all their patients about tobacco use. However, almost all dental surgeons agreed that there should be a ban on public use of tobacco. Implications: The results of this study call for sensitizing health professionals on a larger scale on the issue of tobacco use and its treatment.

PMID:21133605


**Intravesical chemotherapy plus BCG in non-muscle invasive bladder cancer - A systematic**
review with meta-analysis.
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Aim: To determine if the combination of intravesical chemotherapy and bacillus Calmette-Guerin (BCG), used in sequence, is superior to BCG alone in the treatment of NMIBC. ANZUP Cancer Trials Group Ltd. is planning a trial in this area using the Di Stasi [1] regimen but without the electromotive component. This review was conducted to assess the current level of evidence. Methods: We searched biomedical literature databases for randomized controlled trials (RCT) that compared sequential, intravesical chemotherapy added to maintenance BCG versus maintenance BCG alone. Data was extracted by 2 independent reviewers. Trial validity was examined using a risk of bias assessment. Meta-analysis was performed using the fixed effects model. The main outcomes were recurrence rate, progression rate, time to recurrence, time to progression and toxicity. Results: Four trials were identified including 801 patients. Adding chemotherapy to maintenance BCG did not result in a statistically significant reduction in recurrence (relative risk [RR] 0.92; 95% CI 0.79 to 1.09; p = 0.32) or progression (RR 0.88; 95% CI 0.61 to 1.27; p = 0.5). Toxicity was similar for both groups. In the preplanned subgroup analysis for tumor stage, the risk of recurrence (RR 0.75; 95% CI 0.61 to 0.92; p = 0.006) and progression (RR 0.45; 95% CI 0.25 to 0.81; p = 0.007) were reduced when the single trial that included isolated Tcis was excluded. Interaction p value 0.09. Conclusion: Though no overall effect was demonstrated with the addition of chemotherapy to maintenance BCG in the treatment of NMIBC, subgroup analysis suggests that combination therapy may be effective for Ta/T1 but not Tcis bladder tumours. Further studies are required to assess this hypothesis.

Publication Types: Conference Abstract
PMID:70332008


**Association of an allele on chromosome 9 and abdominal aortic aneurysm.**
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Objective: Abdominal aortic aneurysm (AAA) has been recognized as a multi-factorial disease with both genetic and environmental risk factors. A locus residing within non-coding DNA on chromosome 9p21.3 has recently been associated with AAA. To further investigate the significance of this site for AAA, we performed an association study on a large group of 3371 men aged 65-83 years of whom 513 had an AAA. Methods: All men were assessed for other risk factors in a uniform way and an ultrasound of the abdominal aorta was performed. Results: Our findings validated the strong association of the chromosome 9p21.3 SNPs rs10757278 and rs1333049 with AAA and demonstrated the upregulation of LINE-1 elements at the site of AAA. Conclusion: This study confirms a reproducible association between risk alleles on chromosome 9p21.3 and AAA. We also provide preliminary evidence for an association of LINE-1 elements with AAA which will require further investigation. 2010 Elsevier Ireland Ltd.
PMID:2010559999
Genetic and epigenetic mechanisms and their possible role in abdominal aortic aneurysm.
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Abdominal aortic aneurysm (AAA) is a common disease associated with significant cardiovascular morbidity and mortality. The pathogenesis of AAA is poorly defined, making targeting of new therapies problematic. Current evidence favours an interaction of multiple environmental and genetic factors in the initiation and progression of AAA. Epigenetics is the term used to define the properties of the genome that are not explained by the primary sequence, but are due to the modifications of DNA and/or associated proteins. Previous research indicates the association of gene specific promoter DNA hyper-methylation and global DNA hypo-methylation with atherosclerosis. Evidence also suggests an important role for epigenetic processes such as histone acetylation in cardiovascular diseases including atherosclerosis and restenosis. Altered DNA methylation or histone acetylation occur in inflammation, cellular proliferation and remodelling processes and therefore maybe relevant to the pathology of AAA. Important risk factors for AAA, including cigarette smoking, older age, male gender and hypertension, have been linked with epigenetic effects and thus could act in this way to promote AAA. In this review, we discuss the potential role of epigenetic mechanisms in AAA. Since epigenetic alterations are to some extent reversible, further study of this area may identify new treatment targets for AAA. 2010 Elsevier Ireland Ltd.
Publication Types: Review
PMID:2010476270

Transfers from residential aged care facilities to the emergency department are reduced through improved primary care services: An intervention study.
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To assess the impact of an enhanced primary care service for residential aged care facilities (RACF) on the transfer of patients from RACF to a hospital emergency department (ED). Methods: A before-after study of an enhanced primary care service provided by experienced ED-based nurses under the governance of general practitioners. The intervention was analysed comparatively using standardised normal deviates and seasonal autoregressive integrated moving average models, complemented by qualitative assessment. Results: There was a statistically significant reduction (17%, P < 0.001) in the number of transfers during the intervention period. This finding held when adjusting for the seasonality of ED referrals over a 4-year period. The intervention was highly valued by clinicians in RACF and ED. Conclusion: Enhanced primary care services reduce the number of transfers to ED from RACF. 2010 The Authors; Journal compilation 2010 ACOTA.
PMID:21143359
Quantification of the proportion of transfers from residential aged care facilities to the emergency department that could be avoided through improved primary care services. Codde J, Frankel J, et al. South Metropolitan Area Health Service, Western Australia, Australia.

AIM: To describe elderly patient transfers from residential aged care facilities (RACF) to hospital emergency departments (ED), and to estimate the proportion of transfers that may be avoidable with improved primary care service to RACF. METHODS: A descriptive study analysing data from a single tertiary hospital ED patient database, medical record reviews from a random sample of RACF patients presenting to ED and previously published reports. RESULTS: Thirty-one per cent of all transfers at our hospital were potentially avoidable. This sits within the range (7% to 48%) found internationally. A small number of simple interventions could potentially reduce unnecessary ED transfer from RACF. CONCLUSIONS: Evidence from multiple sources suggests that a meaningful proportion of transfers from RACF to ED may be avoided.

Can transfers from residential aged care facilities to the Emergency Department be avoided through improved primary care services? Data from qualitative interviews. Arendts G, Reibel T, et al. (Arendts) Centre for Clinical Research in Emergency Medicine, Western Australian Institute for Medical Research and University of Western Australia, Perth, WA, Australia (Arendts) Discipline of Emergency Medicine, Royal Perth Hospital, Perth, WA, Australia (Arendts) School of Primary, Aboriginal and Rural Health Care, University of Western Australia, Perth, WA, Australia (Reibel) School of Primary, Aboriginal and Rural Health Care, University of Western Australia, Perth, WA, Australia (Codde) South Metropolitan Area Health Service, Perth, WA, Australia (Frankel) Fremantle GP Network, Fremantle, WA, Australia

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Aim: To explore the factors that influence the transfer of patients from residential aged care facilities (RACF) to hospital emergency departments (ED), and describe features of improved primary care in RACF that could result in reduced transfer. Methods: a. Three focus groups conducted with family and carers of RACF residents, along with RACF, ED and general practice staff. b. Semistructured one-on-one interviews with nine residents of RACF. Results: Five main themes emerged - staffing and skill mix in RACF, treatment options in RACF, end of life decision-making, communication and bureaucratic requirements. Analysis of the semistructured interviews demonstrated parallel concerns with many of the focus groups indicators. There was a strong but not universal preference among residents to minimise RACF to ED transfer. Conclusions: The transfer of residents from RACF to ED is influenced by multiple interrelated factors, and strategies to reduce transfer should address these.


Through a grant received from the Australian Library and Information Association (ALIA), Health
Libraries Australia (HLA) is conducting a twelve-month research project with the goal of developing a system-wide approach to education for the future health librarianship workforce. The research has two main aims: to determine the future skills, knowledge, and competencies for the health librarian workforce in Australia; and to develop a structured, modular education framework for specialist post-graduate qualifications together with a structure for ongoing continuing professional development. The paper highlights some of the drivers for change for health librarianship as a profession, and particularly for educating the future workforce. The research methodology is outlined and the main results of the second stage of the project are described together with the findings and their implications for the development of a structured, competency-based education framework.

Hepatitis A and B vaccination: The rate of uptake and course completion in patients with hepatitis C.
Fredericks T, Kwan K, et al.
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Background: Western Australian general practitioners may order Department of Health funded hepatitis A and B vaccines for patients newly notified with hepatitis C to prevent complications associated with co-infections. The aim of this study was to determine vaccination uptake of hepatitis C patients through this program. Methods: We reviewed hepatitis C notifications and hepatitis A and B vaccine orders received in 2007 and 2008 to determine the rate of vaccine uptake and course completion. Results: Vaccination orders for initial doses were received for 37% (448/1209) of patients. Vaccination uptake was positively associated with age and non-Aboriginality. Final vaccination doses were ordered for 30% of patients for whom an initial order had been received. Discussion: Uptake of hepatitis A and B vaccination was higher than that of similar populations. However, vaccination course completion was low. General practitioners need to emphasise to their patients the importance of completing a vaccine course.

Less germs, less mucus, less snot: teachers’ and health workers’ perceptions of the benefits and barriers of ear health programs in lower primary school classes.
Doyle J, Ristevski E.
South Metropolitan Public Health Unit, PO Box 546, Fremantle, WA 6959, Australia.
This study explored health and education professionals' perceptions of the health benefits and barriers of different ear health programs used in lower primary school classes in two district education areas in the Goldfields South East Health Region, Western Australia. Health and education staff providing services to children in kindergarten to year three primary school classes were sent a questionnaire about ear health programs provided in their school. Sixty-one questionnaires were returned from 43 teachers, 14 community health nurses, three Aboriginal health workers and one teacher's assistant. Some schools implemented all the ear health programs examined at all year levels while others implemented only one of the programs. Teachers, community health nurses and Aboriginal health workers identified that all ear health programs were beneficial to students. Reported physical health benefits included reduced ear infections, early detection of ear infections and improved hearing. Behavioural benefits included improved concentration, alertness and attention in the classroom. Barriers to implementing the programs were obtaining consent from parents/carers, student transience and attendance, time to implement and conduct the programs and human and physical resources.
Evaluation methods used varied from no evaluation for the Breathe Blow Cough and tissue spearing programs to limited data collection for audiometry, otoscopy and ear toilet programs. Respondents perceived that ear health programs were effective in improving health and behavioural outcomes for children. A formal pre-post evaluation to provide objective data to confirm this is needed to inform policy around this important health issue.

PMID:21138704

Grandparental investment: past, present, and future.
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What motivates grandparents to their altruism? We review answers from evolutionary theory, sociology, and economics. Sometimes in direct conflict with each other, these accounts of grandparental investment exist side-by-side, with little or no theoretical integration. They all account for some of the data, and none account for all of it. We call for a more comprehensive theoretical framework of grandparental investment that addresses its proximate and ultimate causes, and its variability due to lineage, values, norms, institutions (e.g., inheritance laws), and social welfare regimes. This framework needs to take into account that the demographic shift to low fecundity and mortality in economically developed countries has profoundly altered basic parameters of grandparental investment. We then turn to the possible impact of grandparental acts of altruism, and examine whether benefits of grandparental care in industrialized societies may manifest in terms of less tangible dimensions, such as the grandchildren's cognitive and verbal ability, mental health, and well-being. Although grandparents in industrialized societies continue to invest substantial amounts of time and money in their grandchildren, we find a paucity of studies investigating the influence that this investment has on grandchildren in low-risk family contexts. Under circumstances of duress - for example, teenage pregnancy or maternal depression - there is converging evidence that grandparents can provide support that helps to safeguard their children and grandchildren against adverse risks. We conclude by discussing the role that grandparents could play in what has been referred to as Europe's demographic suicide.

PMID:20377929

Toward an integrative framework of grandparental investment.
Coall DA, Hertwig R.
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Coall, David A.: School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle, WAU, Australia Hertwig, Ralph: Department of Psychology, University of Basel, Basel, Switzerland

Reply by the current authors to the comments made by D. C. Broadfield (see record 2010-08500-002), D. Cox (see record 2010-08500-003), H. A. Euler (see record 2010-08500-004), E. Fantino and S. Stolarz-Fantino (see record 2010-08500-005), T. W. Fawcett et al. (see record 2010-08500-006), D. Friedman and M. Hechter (see record 2010-08500-007), M. Gurven and E. Schniter (see record 2010-08500-008), R. Hames (see record 2010-08500-009), C. A. Hoppmann and P. L. Klumb (see record 2010-08500-010), B. R. Huber (see record 2010-08500-011), R. Kaptijn and F. Thomese (see record 2010-08500-012), K. L. Kramer (see record 2010-08500-013), R. D. Lee (see record 2010-08500-014), R. L. Michalski (see record 2010-08500-015), A. Pashos (see record 2010-08500-016), R. Sear and T. E. Dickins (see record 2010-08500-017), B. I. Strassmann and N. T. Kurapati (see record 2010-08500-018) and M. Voracek et al. (see record 2010-08500-019) on the original article by Coall
and Hertwig (see record 2010-08500-001), who addressed the question of whether the help that grandparents provide, which may have benefited grandchildren in traditional and historical populations, still yields benefits for grandchildren in industrialized societies. The response by Coall and Hertwig outlines more reasons why the integrative framework of grandparental investments and intergenerational transfers advocated in the target article is needed. Obstacles are discussed—from misconceptions to poor measures—that stand in the way of such a framework and of a better understanding of the effects of grandparenting in the developed world. New research directions that have emerged from the commentaries are highlighted. Coall and Hertwig end by discussing some of the things in their target article about which they may have been wrong. (PsycINFO Database Record (c) 2010 APA, all rights reserved).

Publication Types: Comment/Reply
PMID:Peer Reviewed Journal: 2010-08500-020


Review of cognitive therapy for suicidal patients: Scientific and clinical applications.
Jeffery S.
Jeffery, Sian: Fremantle Hospital, Fremantle, Australia
Reviews the book, Cognitive therapy for suicidal patients: Scientific and clinical applications by Amy Wenzel, Gregory K. Brown, and Aaron T. Beck (see record 2008-18315-000). Suicide is a major public health problem' (p. 3). In 2004 alone, suicide accounted for over 2,000 deaths in Australia; however, this represents only a small part of the impact of suicidal acts on society. Clinicians at the front line of this impact often experience a great deal of anxiety surrounding the treatment of actively suicidal clients. This text presents a straightforward, through and easy to follow guide to apply cognitive therapy principles to the treatment of suicidal patients. The key component of this text that makes it a must for clinicians working across a range of settings is the final section, 'Applications to special populations'. In a series of chapters the authors address the application of the treatment protocol to working with suicidal adolescents, suicidal older adults and suicidal patients with substance disorders. These chapters are again succinctly written, with the strategies employed when treating each of these populations highlighted through case examples. Experienced and novice clinicians alike will take comfort in the ease in which Wenzel and colleagues review the science of treating suicidal patients and translate this into easy to follow clinical protocol. (PsycINFO Database Record (c) 2011 APA, all rights reserved).

Publication Types: Review-Book
PMID:Peer Reviewed Journal: 2011-03813-007


The role of 11 -hydroxysteroid dehydrogenase type 2 in human hypertension.
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Cortisol and aldosterone have the same in vitro affinity for the mineralocorticoid receptor (MR), although in vivo only aldosterone acts as a physiologic agonist of the MR, despite circulating levels of cortisol in humans and corticosterone in rodents being three orders of magnitude higher than aldosterone levels. In mineralocorticoid target organs the enzyme 11beta-hydroxysteroid dehydrogenase type 2 (11betaHSD2) inactivates 11-hydroxy steroids, to their inactive keto-forms, thus protecting the nonselective MR from activation by glucocorticoids. The gene is highly expressed in all sodium-transporting epithelia, particularly in the kidney and colon, but also in human placenta and vascular wall. Mutations in the HSD11B2 gene cause a rare monogenic juvenile hypertensive
syndrome called apparent mineralocorticoid excess (AME). In AME, compromised 11betaHSD2 enzyme activity results in activation of the MR by cortisol, causing sodium retention, hypokalaemia, and salt-dependent hypertension. Whereas mutations or inhibition of 11betaHSD2 by licorice have been clearly shown to produce a congenital or acquired syndrome of mineralocorticoid excess, the questions remaining are the extent to which subtle abnormalities in MR/11betaHSD2 mechanisms may contribute to essential hypertension. Studies in patients with essential hypertension showed a prolonged half-life of cortisol and an increased ratio of urinary cortisol to cortisone metabolites, suggesting a deficient 11betaHSD2 activity. These abnormalities may be genetically determined, as suggested by the association of a microsatellite flanking the HSD11B2 gene with hypertension in black patients with end-stage kidney disease and with salt sensitivity of blood pressure in healthy subjects. These findings indicate that variants of the HSD11B2 gene may contribute to the enhanced blood pressure response to salt and possibly to hypertension in humans. 2009 Elsevier B.V.

BMJ Case Reports. 2010; 2010.
Duodenal adenocarcinoma arising from a pyloric gland adenoma with a brief review of the literature.

Pyloric gland-type adenoma of the duodenum with documented malignant progression is rare. A case is presented of an 87-year-old man with bloating and nausea, who on investigation was found to have a polyp on the anteroinferior wall of the duodenal cap. Histologic examination of the polyp showed features of a pyloric gland adenoma (PGA) demonstrating the full spectrum of progression from low- to high-grade dysplasia and finally invasive adenocarcinoma. The carcinoma showed gastric-type differentiation highlighted by its mucin immunohistochemistry profile and was of advanced stage with lymph node metastasis. The literature on PGAs and the little documentations on progression to carcinoma in duodenal PGAs are reviewed.

The frequency, clinical correlates, and mechanism of anosognosia after stroke.
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OBJECTIVE: To review the frequency, clinical correlates, and mechanism of anosognosia after stroke. METHODS: We searched the most recent relevant literature on anosognosia after stroke and carried out a critical analysis of the main findings. RESULTS: Anosognosia is present in about 10% of acute stroke patients and its diagnosis is relatively simple. Nevertheless, a valid and reliable standardization of diagnostic instruments and criteria for research purposes is more difficult to achieve. This limitation may partially account for various instruments available to assess anosognosia and the different strategies used to diagnose this phenomenon. Anosognosia is a fleeting phenomenon and chronic cases are infrequent. There is a robust association between anosognosia and right-hemisphere lesions involving cortical (insular, temporal, and parietal lobes) and subcortical structures (thalamus and basal ganglia). The main clinical correlates of anosognosia are the presence of neglect, cognitive deficits, previous strokes, and older age. Anosognosia has a negative impact on the rehabilitation of stroke patients. The mechanism of anosognosia remains unknown but was explained as owing to psychological denial, disconnection between left and right hemispheres, and dysfunction of a system that monitors the intention to move and actual movements. CONCLUSION: Anosognosia is a relatively frequent complication of acute stroke and may become an excellent model to understand the mechanism of human awareness.

Publication Types: Research Support, Non-U.S. Gov't
PMID:20540830
Who needs early aphasia therapy?
Godecke E, Hird K, et al.
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E. Godecke, Edith Cowan University, Perth, Australia

Introduction: Evidence indicates early intensive aphasia therapy provides almost twice the recovery as compared to aphasia therapy initiated later in recovery. Limited available clinical resources make patient selection a vital component of effective service provision. Currently, inadequate levels of evidence guide patient selection for early aphasia intervention. Method: This prospective randomised, open labelled, single blinded study investigated dose dependent effects of early post stroke therapy (N=59). Participants were randomised to daily or weekly therapy during their acute hospital stay (mean = 22 days). Multiple and longitudinal regression models were used to predict improved aphasia severity scores at acute hospital discharge and six months. Results: Daily therapy, shorter length of stay, PACS stroke syndrome, less dysphagia assessment, lower admission MRS score and lower aphasia severity rating predicted better outcomes at acute discharge. Lower aphasia severity rating was the only significant predictor of improved aphasia severity at six months. Daily therapy in the acute hospital setting showed a non-significant trend toward improved aphasia severity at six months. Conclusion: This study showed people with moderate to severe post stroke aphasia who can interact for more than forty minutes at five days post stroke are appropriate for and benefit from early aphasia therapy.

Publication Types: Conference Abstract
PMID:70330374

Site specificity of aneurysmal disease.
Norman PE, Powell JT.
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Case of normal tension glaucoma induced or exacerbated by wearing swimming goggles.
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Is posterior scleral reinforcement sufficient for the treatment of myopic foveoschisis?
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Publication Types: Letter
PMID:2010391931
Association of PPAR[gamma] allelic variation, osteoprotegerin and abdominal aortic aneurysm.


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Objective: We have previously demonstrated high concentrations of the glycoprotein osteoprotegerin (OPG) in biopsies of abdominal aortic aneurysm (AAA), and demonstrated that ligation of the nuclear receptor peroxisome proliferator-activated receptor gamma (PPAR[gamma]) downregulates OPG in vitro and within a mouse model. The aims of this study were to assess the associations between circulating concentrations of OPG, polymorphisms of the gene encoding PPAR[gamma] (PPARG), AAA presence and growth.

Design, patients and measurements: Two genetic polymorphisms in PPARG were assessed in 4227 men, 699 of whom had an AAA. For 631 men, who had AAAs, maximum aortic diameter was monitored by yearly ultrasound for a median of 5 years. Plasma OPG was measured in 838 men, 318 of whom had an AAA.

Results: Plasma concentrations of OPG were independently associated with AAA (adjusted odds ratio 1.38, 95% CI 1.10-1.72). The PPARG c.1347C > T polymorphism was associated with plasma concentrations of OPG (beta 0.12, P < 0.01). The PPARG c.34G > C polymorphism was weakly associated with AAA (adjusted odds ratio 1.28, 95% CI 1.01-1.61). PPARG c.1347C > T was associated with increased AAA growth (recessive model, P = 0.03).

Conclusions: Circulating concentrations of osteoprotegerin are associated with abdominal aortic aneurysm and with one peroxisome proliferator-activated receptor gamma gene polymorphism. Peroxisome proliferator-activated receptor gamma gene polymorphisms are weakly associated with abdominal aortic aneurysm presence and growth. Confirmation of these findings is required in other cohorts.

Lumbar puncture in children from an area of malaria endemicity who present with a febrile seizure.

Laman M, Manning L, et al.

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BACKGROUND: Although routine lumbar puncture (LP) is often recommended as part of the assessment of fever-associated seizures in children, accumulating evidence questions its value and reveals a decrease in its frequency. Our primary hypothesis was that children who present with a single seizure but with no clinical signs of meningitis or coma do not require LP as part of initial diagnostic assessment.

METHODS: We prospectively followed up 377 children aged 2 months through 10 years who presented with at least 1 fever-associated seizure to Modilon Hospital, Madang, Papua New Guinea, from November 2007 through July 2009. Clinical management was performed by hospital staff according to national pediatric guidelines.

RESULTS: Of 188 children with a single seizure and 189 children with multiple seizures, 139 (73.9%) and 154 (81.5%), respectively, underwent a LP as part of their initial assessment. Of the 130 children with a single seizure but no evidence of meningism (ie, neck stiffness, positive Kernig's or Brudzinski's sign, and bulging fontanelle) or coma (Blantyre Coma Score 2), none (95% confidence interval, 0%-3.6%) had proven or probable acute bacterial meningitis, and only 1 patient had viral encephalitis (subacute sclerosing panencephalitis). Eighty-one of these children (62.3%) had a final diagnosis of a simple febrile seizure. Proven or probable acute bacterial meningitis was more common in children with a single seizure and meningism or coma (10; 17.2%) and in those with multiple seizures without or with meningism or coma (2 [2.0%] and 30 [33.7%], respectively).

CONCLUSIONS: Initial LP is unnecessary when careful clinical assessment indicates features of a simple febrile seizure.
Clinical Microbiology & Infection. 2010; 16 Sup(2): S287.
Unique and changing epidemiology of group A streptococcal infection in western Australia: P1048.
McLellan D, O'Reilly L, et al. (Fremantle, Perth, AU)

Fenofibrate improves endothelial function in the brachial artery and forearm resistance arterioles of statin-treated Type 2 diabetic patients.
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Dyslipidaemia contributes to endothelial dysfunction and CVD (cardiovascular disease) in Type 2 diabetes mellitus. While statin therapy reduces CVD in these patients, residual risk remains high. Fenofibrate corrects atherogenic dyslipidaemia, but it is unclear whether adding fenofibrate to statin therapy lowers CVD risk. We investigated whether fenofibrate improves endothelial dysfunction in statin-treated Type 2 diabetic patients. In a cross-over study, 15 statin-treated Type 2 diabetic patients, with LDL (low-density lipoprotein)-cholesterol <2.6 mmol/l and endothelial dysfunction [brachial artery FMD (flow-mediated dilatation) <6.0%] were randomized, double-blind, to fenofibrate 145 mg/day or matching placebo for 12 weeks, with 4 weeks washout between treatment periods. Brachial artery FMD and endothelium-independent NMD (nitrate-mediated dilatation) were measured by ultrasonography at the start and end of each treatment period. PIFBF (post-ischaemic forearm blood flow), a measure of microcirculatory endothelial function, and serum lipids, lipoproteins and apo (apolipoprotein) concentrations were also measured. Compared with placebo, fenofibrate increased FMD (mean absolute 2.1+/-0.6 compared with -0.3+/-0.6%, P=0.04), but did not alter NMD (P=0.75). Fenofibrate also increased maximal PIFBF (median 3.5 [IQR (interquartile range) 5.8] compared with 0.3 (2.1) ml/100 ml/min, P=0.001) and flow debt repayment [median 1.0 (IQR 3.5) compared with -1.5 (3.0) ml/100 ml, P=0.01]. Fenofibrate lowered serum cholesterol, triacylglycerols (triglycerides), LDL-cholesterol, apoB-100 and apoC-III (P<=0.03), but did not alter HDL (high-density lipoprotein)-cholesterol or apoA-I. Improvement in FMD was inversely associated with on-treatment LDL-cholesterol (r=-0.61, P=0.02) and apoB-100 (r=-0.54, P=0.04) concentrations. Fenofibrate improves endothelial dysfunction in statin-treated Type 2 diabetic patients. This may relate partly to enhanced reduction in LDL-cholesterol and apoB-100 concentrations. The Authors.
PMID:201040361

http://eprints.qut.edu.au/37958/

Phenotypic expression of hereditary hemochromatosis: what have we learned from the
population studies?
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School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, WA, Australia.
Profound advances in our knowledge of hereditary hemochromatosis (HH) during the past 150 years have resulted in two distinct "iron ages": the pre-HFE gene era and the post-HFE gene era. During these periods, family studies, HLA association studies, and ultimately HFE gene studies in various populations informed us of the genotypic prevalence as well as the clinical and biochemical penetrance of HH. We learned that HH has a highly variable clinical penetrance in susceptible individuals of Northern European ancestry. Further, we now recognize that the natural history of HH is not as discrete as previously believed, because genetic and environmental modifiers of disease penetrance are increasingly identified as influencing the clinical expression of HH.

Current Opinion in Endocrinology, Diabetes & Obesity. 2010; 17(3): 269-76.

Androgens and cardiovascular disease.
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PURPOSE OF REVIEW: There is increasing interest in age-related changes in sex hormone levels as a potentially treatable cause of ill-health in men. Relationships between androgens and cardiovascular disease will be discussed, with particular attention to more recently published research. RECENT FINDINGS: In middle-aged and older men, lower testosterone levels are associated with insulin resistance, metabolic syndrome and diabetes, interrelated conditions that predispose to cardiovascular disease. The relationship between androgens and preclinical atherosclerosis requires confirmation. Nevertheless, lower testosterone levels predict cardiovascular events, such as stroke and transient ischaemic attack, in older men and are associated with higher cardiovascular and overall mortality. Testosterone is aromatized to oestradiol, and both higher and lower oestradiol levels have been associated with cardiovascular risk. Randomized trials have shown that testosterone supplementation in men with existing coronary artery disease can be protective against myocardial ischaemia. However, additional interventional studies are needed with endpoints of cardiovascular events. SUMMARY: Observational studies continue to relate reduced circulating testosterone to cardiovascular risk, atherosclerosis and mortality in men. The role of oestradiol as a marker for cardiovascular disease requires clarification. Larger randomized trials are needed to establish whether hormonal therapy would reduce the burden of cardiovascular disease in ageing men.

Sustained clearance of superficial basal cell carcinomas treated with imiquimod cream 5%: Results of a prospective 5-year study.
Quirk C, Gebauer K, et al.
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We conducted a prospective, multicenter, phase 3, open-label study to assess long-term sustained clearance of superficial basal cell carcinomas (sBCCs) treated with imiquimod cream 5%. A biopsy-
confirmed tumor (area \(\geq 0.5 \text{ cm}^2\) and diameter \(\leq 2.0 \text{ cm}\)) was treated once daily 7 times per week for 6 weeks. Participants with initial clinical clearance at 12 weeks posttreatment were followed for 60 months. Tumor recurrence, serious adverse events (AEs), local skin reactions (LSRs), and skin quality assessments (SQAs) were measured. The initial clearance rate was 94.1% (159/169). Estimated sustained clearance (proportion of participants who achieved initial clearance at the 12-week posttreatment visit and remained clinically clear at each time point during the long-term follow-up period; \(N=157\)) was 85.4% at 60 months (life-table method: 95% confidence interval [CI], 79.3%-91.6%). The overall estimate of treatment success was 80.4% at 60 months (\(N=169\); 95% CI, 74.4%-86.4%). Of 20 recurrent tumors, 14 (70%) occurred within the first 24 months of follow-up. Local skin reactions and application site reactions, the AEs reported by the most participants, occurred predominantly during the treatment period and resolved posttreatment. Compared to baseline, investigator-assessed SQA scores for the target tumor site improved for skin surface abnormalities and hyperpigmentation, and worsened for hypopigmentation. For low-risk sBCCs, daily application of imiquimod for 6 weeks had high initial and 5-year sustained clearance rates. Cutis 2010.

PMID:20666194

Developmental Medicine & Child Neurology. 2010; 52(2 Suppl): 32-33. **Botulinum Toxin A treatment is safe in children with cerebral palsy in GMFCS levels IV and V [Concurrent Free Papers Session 2: Stream 2B: Spasticity Management].** Langdon K, Davidson S, et al. (1)Department of Paediatric Rehabilitation, Princess Margaret Hospital for Children, Perth, WA, Australia; (2)Department of Paediatrics, Fremantle Hospital, Perth, WA, Australia; (3)Department of Paediatric Rehabilitation, Princess Margaret Hospital for Children, Perth, WA, Australia; (4)Department of Paediatric Rehabilitation, Princess Margaret Hospital for Children, Perth, WA, Australia

Diabetes Research & Clinical Practice. 2010; 90(3): e75-8. **Cardiovascular risk prediction in adults with type 1 diabetes: the Fremantle Diabetes Study.** Davis WA, Davis TME. University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, Australia. wdavis@meddent.uwa.edu.au

The performance of the Fremantle Diabetes Study cardiovascular risk equation, derived in 1240 individuals with type 2 diabetes, was assessed in a parallel cohort of 117 adults with type 1 diabetes. Despite significantly different phenotypic characteristics, the equation successfully identified adults with type 1 diabetes at increased cardiovascular risk. Copyright [copyright sign] 2010 Elsevier Ireland Ltd. All rights reserved.

Publication Types: Research Support, Non-U.S. Gov't
PMID:20950885

Diabetologia. 2010; 53(Suppl): S392. **A matched case-control study of depressive symptoms in type 2 diabetes.** Davis WA, Hunter M, et al. (Davis, Peters, Davis) School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia (Hunter) Busselton Health Study, University of Western Australia, Busselton, Australia

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Background and aims: Diabetes and depression are important co-morbid conditions. Patients with diabetes are 1.5-2 times more likely to have depression compared with people without diabetes, although this risk is attenuated after adjustment for age, sex and cardiovascular disease (CVD). Risk
factors for depression include both clinical and personal factors, and there is some evidence that psychiatric conditions including depression are more common in rural vs. urban environments. We conducted an age- and sex-matched case-control study to elucidate the relationship between type 2 diabetes and depression in a rural setting. Materials and methods: In 2009, residents of Busselton Shire in the southwest of Western Australia who had been diagnosed with diabetes and randomly selected age- and sex-matched normoglycaemic residents were invited for a comprehensive assessment. In addition to medical history, examination and biochemical testing, participants completed the Personal Health Questionnaire Depression Scale (PHQ-9). Paired tests were used to compare potential associates of depression between cases and controls. Multiple logistic regression was used to determine independent associates of prevalent depression. Results: We assessed 172 adults with type 2 diabetes and 172 controls. Half (51.2%) were male. Cases and controls did not differ significantly in age (70.7+-10.4 vs. 71.0+-10.0, P=0.80), but cases had significantly higher mean body mass index (BMI) than controls (30.4+-5.3 vs. 27.0+-4.0, P<0.001) and higher prevalence of self-reported CVD, exertional chest pain, and current smoking habit. Those with diabetes had median duration of 8.9 [5.0-14.3] years; 35.7% were diet-treated, 46.8% were on oral treatment and 17.5% were using insulin. Those with type 2 diabetes were significantly more likely to have a current major or any depressive syndrome compared with those with normoglycaemia (5.9% vs. 0.6%, P=0.012, and 11.8% vs. 4.1%, P=0.019, respectively), but were no more likely to have been prescribed antidepressant therapy (11.6% vs. 12.6%, P=0.86). The majority (22/25 or 88.0%) of normoglycaemic subjects with any depressive syndrome and/or taking antidepressants were being treated for depression compared with less than two-thirds (20/35 or 57.1%) of those with type 2 diabetes. BMI, current smoking habit and exertional chest pain but not diabetes status were independently associated with the presence of a) any depressive syndrome, and b) any depressive syndrome and/or antidepressant medication use. Age, sex, income, marital status, born overseas, education, alcohol intake, and self-reported CVD were also not associated with depression. Conclusion: Depressive syndromes, especially major depression, were significantly more prevalent in rural-dwelling Australian adults with type 2 diabetes compared with age- and sex-matched normoglycaemic controls, but those with diabetes were less likely to be treated for depression. The higher prevalence of depressive syndrome in adults with type 2 diabetes compared with normoglycaemic adults may be explained largely by their significantly higher BMI.


Serum uric acid does not predict cardiovascular or all-cause mortality in type 2 diabetes: the Fremantle Diabetes Study.

Ong G, Davis WA, et al.

School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia, P.O. Box 480, Fremantle, WA, 6959, Australia.

AIMS/HYPOTHESIS: To determine whether serum uric acid: (1) is associated with cardiovascular disease (CVD) death and/or all-cause mortality in type 2 diabetes; and (2) consistent with published data, predicts these outcomes in older patients and those of southern European ethnicity. METHODS: We studied those 1,268 (98%) of 1,294 type 2 participants in the observational Fremantle Diabetes Study who had a fasting serum uric acid measured at baseline. Mortality data were collected over a mean (+/-SD) 10.3 +/- 3.9 years. Cox proportional hazards modelling was used to determine independent baseline predictors of CVD and all-cause death including fasting serum uric acid as a continuous variable and quartiles. RESULTS: During follow up, 525 deaths occurred (41.4% of the cohort) of which 271 (51.6%) were attributed to CVD. In univariate analyses, patients in the highest uric acid quartile had the greatest CVD and all-cause mortality (p = 0.007 and p = 0.001). After adjustment for significant variables in the most parsimonious model, baseline serum uric acid was not an independent associate of CVD or all-cause mortality whether entered as a continuous variable (HR 1.11 [95% CI 0.96-1.27] and 1.10 [95% CI 0.98-1.22] for a 0.1 mmol/l increase, respectively) or as
quartiles (p > 0.10). Analyses of 638 patients >65 years of age and 231 of southern European ethnicity produced similar results. CONCLUSIONS/INTERPRETATION: Serum uric acid was not an independent predictor of CVD or all-cause mortality in our community-based type 2 patients. Fasting serum uric acid concentrations do not appear to be prognostically useful in type 2 diabetes.

PMID:20349345


International emergency medicine: Building on a strong information-sharing foundation.
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Publication Types: Editorial
PMID:2010697732


Credentialing a new skill: what should the standard be for emergency department ultrasound in Australasia?
Goudie AM.
Publication Types: Comment
Editorial
PMID:20796006


Long-term clinical outcomes with the next-generation Resolute Stent System: A report of the two-year follow-up from the RESOLUTE clinical trial.
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I. T. Meredith, MonashHEART and Monash University, Monash Medical Centre, 246 Clayton Road, Melbourne, VIC, Australia. E-mail: ian.meredith@med.monash.edu.au
Aims: The 12-month results of RESOLUTE were favourable for the new Resolute stent. Two-year safety and efficacy results from RESOLUTE have been evaluated and are now reported. Methods and results: RESOLUTE was a prospective, multicentre, non-randomised, single-arm, controlled trial of the
Resolute stent in 139 participants with symptomatic ischaemic heart disease due to single de novo lesions in a native coronary artery. The 2-year rates of MACE (all-cause death, myocardial infarction, emergent cardiac bypass surgery, and target lesion revascularisation [TLR]), death, late stent thrombosis, target vessel revascularisation (TVR), and target vessel failure (TVF) were assessed. Clinical events included two MACE (one TLR; one non-cardiac death) occurring between year one and two resulting in cumulative 2-year TLR, TVR, and TVF rates of 1.4%, 1.4%, and 7.9%, respectively. One possible stent thrombosis event occurred in the first year after stent implantation however no late or very late ARC-defined definite and probable stent thromboses occurred through two years. Conclusions: The 2-year data from RESOLUTE demonstrated no safety concerns including no late stent thrombosis or loss of effectiveness with the Resolute stent. The finding that few events occurred in year two is encouraging, yet requires verification in a larger population. Europa Edition. All rights reserved.

PMID: 2011206422


Incidence and predictors of silent myocardial infarction in type 2 diabetes and the effect of fenofibrate: an analysis from the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study.

Burgess DC, Hunt D, et al.
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Aims: To determine the incidence and predictors of, and effects of fenofibrate on silent myocardial infarction (MI) in a large contemporary cohort of patients with type 2 diabetes in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study.

Methods and results: Routine electrocardiograms taken throughout the study were assessed by Minnesota-code criteria for the presence of new Q-waves without clinical presentation and analysed with blinding to treatment allocation and clinical outcome. Of all MIs, 36.8% were silent. Being male, older age, longer diabetes duration, prior cardiovascular disease (CVD), neuropathy, higher HbA1c, albuminuria, high serum creatinine, and insulin use all significantly predicted risk of clinical or silent MI. Fenofibrate reduced MI (clinical or silent) by 19% [hazard ratio (HR) 0.81, 95% confidence interval (CI) 0.69-0.94; P = 0.006], non-fatal clinical MI by 24% (P = 0.01), and silent MI by 16% (P = 0.16). Among those having silent MI, fenofibrate reduced subsequent clinical CVD events by 78% (HR 0.22, 95% CI 0.08-0.65; P = 0.003).

Conclusion: Silent and clinical MI have similar risk factors and increase the risk of future CVD events. Fenofibrate reduces the risk of a first MI and substantially reduces the risk of further clinical CVD events after silent MI, supporting its use in type 2 diabetes.

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Reduced serum total osteocalcin is associated with metabolic syndrome in older men via waist circumference, hyperglycemia, and triglyceride levels.

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Objective: Bone-derived undercarboxylated osteocalcin regulates insulin secretion and sensitivity in mice, and reduced serum total osteocalcin (TOC) is associated with diabetes in humans. However, the relationship between TOC levels and other cardiovascular risk factors is uncertain. We sought to determine whether serum TOC is associated with metabolic syndrome and its components in older men. Design: Cross-sectional analysis from a population-based cohort of men aged >=70 years. Methods: Early morning sera were assayed for TOC. Insulin resistance was estimated using a homeostatic model (HOMA2-IR). Metabolic syndrome was defined according to NCEP-ATPIII criteria. Results: TOC was assayed in 4047 men. Men who were not fasting and reported having bone fractures, Paget's disease, or bisphosphonate, glucocorticoid, or warfarin use were excluded, leaving 2765 men with metabolic syndrome present in 797 (28.8%). TOC was inversely associated with waist circumference, glucose, and triglyceride levels and HOMA2-IR (all P<0.001), and was lower in men with metabolic syndrome (mean+/-S.E.M.: 20.1+/-0.4 vs 21.4+/-0.2 mug/l, P=0.002). In multivariate analysis, men with TOC of 13.25-16.55 and <13.25 mug/l had 1.5- to 2-fold increased risk of metabolic syndrome compared with men with levels >=30 mug/l. TOC remained associated with metabolic syndrome after adjustment for individual components, but not after adjusting for both waist circumference and glucose. Conclusions: Increased waist circumference, reduced TOC, elevated glucose, and triglyceride levels are inter-related in aging men. Osteocalcin may lie in the causal pathway between central adiposity and insulin resistance. Further research is required to evaluate whether interventions which raise osteocalcin levels might decrease cardiovascular risk. 2010 European Society of Endocrinology.

Therapies for the medical management of persistent hypoglycaemia in two cases of inoperable malignant insulinoma.
Ong GSY, Henley DE, et al.
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OBJECTIVE: Hypoglycaemia poses a significant management challenge in patients with unresectable functional malignant insulinoma. Novel agents such as mammalian target of rapamycin (mTOR) inhibitors and radiolabelled peptides may be effective where there is failure of conventional therapy. DESIGN: We present the cases of two men diagnosed with inoperable malignant insulinoma and hepatic metastases who developed severe symptomatic hypoglycaemia, and review potential therapies for glycaemic support. METHOD: Despite treatment with diazoxide, frequent oral carbohydrate, prednisolone and somatostatin analogue therapy, both men required hospital admission for treatment with continuous i.v. dextrose. Both were treated with Lutetium-177 octreotate. One man was also treated with everolimus, a mTOR inhibitor. RESULT: Use of Lutetium-177 octreotate, and in one case everolimus, successfully achieved normoglycaemia, facilitating safe discharge from hospital. Both men also had regression in the size and number of hepatic metastases. CONCLUSION: Lutetium-177 octreotate and everolimus are options for managing hypoglycaemia due to unresectable malignant insulinoma when refractory to conventional supportive therapies.
Publication Types: Case Reports
PMID:20164213

Apolipoprotein genotype and mortality in Southern European and Anglo-Celt patients with type 2 diabetes: The fremantle diabetes study.
Davis WA, Chin E, et al.

Objective: To determine whether cardiac and all-cause mortality are lower in Southern European (SE) patients than in Anglo-Celt (AC) patients with type 2 diabetes in an urban Australian setting, and, if so, whether ethnicity-specific differences in apolipoprotein E (APOE) genotypes are contributory.

Design: Longitudinal observational cohort study. Methods: We analysed detailed data from 1057 patients from the community-based Fremantle Diabetes Study, 238 were of an SE migrant background and 819 of AC ethnicity. Cox proportional hazards modelling was used to identify independent predictors of cardiac and all-cause mortality.

Results: During 9.8±3.5 years of follow-up, 411 (38.9%) participants died, 161 (39.2%) from cardiac causes. Significant positive baseline independent predictors of cardiac death were age, male gender, coronary heart disease, cerebrovascular disease, peripheral arterial disease, retinopathy and peripheral neuropathy (P≤0.004), while maternal history of diabetes was protective (P=0.014). After adjusting for these variables, APOE4 carriage was predictive (hazard ratio (95% confidence interval) 1.61 (1.01-2.58) P=0.048). SE ethnicity did not add significantly to the model either as a single variable or as an interaction term with APOE4 carriage (P>=0.86). Significant independent predictors of all-cause mortality were age, male gender, smoking, coronary heart disease, cerebrovascular disease, peripheral arterial disease, retinopathy, peripheral neuropathy and microalbuminuria (P≤0.047), while overweight/obesity, lipid-lowering therapy and recent exercise were protective (P≤0.008). APOE4 carriage, SE ethnicity and their interaction did not add to the model (P≥0.32). Conclusions: SE ethnicity does not confer an independent survival advantage in community-based Australian type 2 diabetic patients, but APOE4 carriers are at higher risk of cardiac death.

2010 European Society of Endocrinology.


Therapies for the medical management of persistent hypoglycaemia in two cases of inoperable malignant insulinoma.

Ong GSY, Henley DE, et al.

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Objective: Hypoglycaemia poses a significant management challenge in patients with unresectable functional malignant insulinoma. Novel agents such as mammalian target of rapamycin (mTOR) inhibitors and radiolabelled peptides may be effective where there is failure of conventional therapy.

Design: We present the cases of two men diagnosed with inoperable malignant insulinoma and hepatic metastases who developed severe symptomatic hypoglycaemia, and review potential therapies for glycaemic support.

Method: Despite treatment with diazoxide, frequent oral carbohydrate, prednisolone and somatostatin analogue therapy, both men required hospital admission for treatment with continuous i.v. dextrose. Both were treated with Lutetium-177 octreotate. One man was also treated with everolimus, a mTOR inhibitor.

Result: Use of Lutetium-177 octreotate, and in one case everolimus, successfully achieved normoglycaemia, facilitating safe discharge from hospital. Both men
also had regression in the size and number of hepatic metastases. Conclusion: Lutetium-177 octreotate and everolimus are options for managing hypoglycaemia due to unresectable malignant insulinoma when refractory to conventional supportive therapies. 2010 European Society of Endocrinology.
PMID:2010589047

IGF1 and its binding proteins 3 and 1 are differentially associated with metabolic syndrome in older men.
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Objective: Circulating IGF1 declines with age, and reduced circulating IGF1 is associated with increased cardiovascular mortality in some but not all studies. The relationship between IGF-binding proteins 3 and 1 (IGFBP3 and IGFBP1) with risk of cardiovascular disease remains unclear. We sought to examine associations between IGF1, IGFBP3 and IGFBP1 with metabolic syndrome in older men. Design: Cross-sectional analysis of 3980 community-dwelling men aged >=70 years. Methods: Morning plasma levels of IGF1, IGFBP3 and IGFBP1 were assayed. Metabolic syndrome was defined according to National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII) criteria. Results: For IGF1 and IGFBP3, there was a U-shaped relationship, with middle quintiles possessing the lowest odds ratios (OR) for metabolic syndrome (reference Q1, Q3 IGF1: OR 0.74, 95% confidence intervals 0.57-0.96, Q3 IGFBP3:OR 0.67, 0.51-0.87). Increasing IGFBP1 was associated with reduced risk of metabolic syndrome with a dose-response gradient (reference Q1, OR for Q2 to Q5 IGFBP1: 0.56, 0.33,0.22 and 0.12 respectively, P< 0.001). IGF1 was associated with two, IGFBP1 with four and IGFBP3 with all five components of the metabolic syndrome. The ratio of IGF1/IGFBP3 was not associated with metabolic syndrome. Conclusions: In older men, both lower and higher IGF1 and IGFBP3 levels may be metabolically unfavourable. IGFBP1, as a marker of insulin sensitivity, is relevant in the assessment of metabolic syndrome, while the IGF1/IGFBP3 ratio is less informative. Longitudinal follow-up of this cohort would be needed to determine whether these distributions of IGF1, IGFBP3 and IGFBP1 predict incidence of cardiovascular events during male ageing. 2010 European Society of Endocrinology.
PMID:2010585726

Cost-effectiveness analysis: Compared with glyburide, sitagliptin associated with incremental cost-effectiveness ratio of $169,572 per QALY and exenatide with $278,935 per QALY as second-line treatment in adult diabetics in the USA.
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Publication Types: Comment
PMID:20436114
Prevention and treatment of malaria in pregnancy.
Davis TME, Mueller I, et al.
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Malaria in pregnancy is a substantial public health issue in many tropical countries. However, its prevention and treatment have been hindered because of fears of adverse drug effects in pregnant women recruited to intervention studies. This article details the pharmacological agents and management strategies currently or potentially available for use in pregnant women with or at risk of malaria. There are deficiencies in pharmacokinetic, tolerability, safety and efficacy data for even well-established drugs and combinations. This can have serious implications for the design of rational dose regimens. Approaches such as intermittent preventive treatment are increasingly employed in endemic areas with proven benefits, but the emergence of parasite drug resistance means that new strategies and drug regimens should be continually evaluated. 2010 Future Medicine Ltd.
Publication Types: Review
PMID:2010630976

HFE Cys282Tyr homozygotes with serum ferritin concentrations below 1000 mug/L are at low risk of hemochromatosis.
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Hemochromatosis gene (HFE)-associated hereditary hemochromatosis (HH) is a genetic predisposition to iron overload and subsequent signs and symptoms of disease that potentially affects approximately 80,000 persons in Australia and almost 1 million persons in the United States. Most clinical cases are homozygous for the Cys282Tyr (C282Y) mutation in the HFE gene, with serum ferritin (SF) concentration >1000 mug/L as the strongest predictor of cirrhosis. The optimal treatment regimen for those with SF concentrations above the normal range but <1000 mug/L is unknown. We assessed HFE mutations in a prospective cohort of 31,192 participants of northern European descent, aged 40-69 years. An HFE-stratified random sample of 1438 participants including all C282Y homozygotes with iron studies 12 years apart were examined by physicians blinded to participants'
HFE genotype. All previously undiagnosed C282Y homozygotes (35 male, 67 female) and all HFE wild-types (131 male, 160 female) with baseline and follow-up SF concentrations <1000 mug/L were assessed for HH-associated signs and symptoms including abnormal second/third metacarpophalangeal joints (MCP2/3), raised liver enzymes, hepatomegaly, and self-reported liver disease, fatigue, diabetes mellitus, and use of arthritis medication. The prevalence of HH-associated signs and symptoms was similar for C282Y homozygotes and HFE wild-types for both normal and moderately elevated SF concentrations. The maximum prevalence difference between HFE genotype groups with moderately elevated SF was 11% (MCP2/3, 95% confidence interval = -6%, 29%; P = 0.22) and for normal SF was 6% (arthritis medicine use, 95% confidence interval = -3%, 16%; P = 0.11). Conclusion: Previously undiagnosed C282Y homozygotes with SF concentrations that remain below 1000 mug/L are at low risk of developing HH-associated signs and symptoms at an age when disease would be expected to have developed. These observations have implications for the management of C282Y homozygotes. Copyright 2010 by the American Association for the Study of Liver Diseases. PMID:2010501849

Hepatology. 2010; 52: 415A-416A. Disruption of both HFE and TFR2 causes ironinduced liver injury.
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R. Delima, School of Medicine and Pharmacology, University of Western Australia, Nedlands, WA, Australia

Hereditary haemochromatosis (HH) is a common iron overload disorder caused by mutations in HFE or TFR2, which impair the liver iron regulatory hormone, hepcidin (Hamp). This study aimed to examine the effects of disruption of Hfe and Tfr2 on liver iron loading and injury in mouse models of HH. Methods: Iron status was determined in single mutant (Hfe<sub>-/-</sub> and Tfr2<sub>Y245X</sub>) and double mutant (Hfe<sub>-/-</sub>xTfr2<sub>Y245X</sub>) mice (10-14 weeks of age) by measuring plasma and liver iron concentration. Hamp expression was measured by real-time PCR. Liver injury was evaluated by measuring serum alanine transaminase (ALT) activity, hepatic histology, collagen deposition (Sirius red) and iron levels (Perls). Hepatic oxidative stress was determined by measuring F2-isoprostane, a marker of lipid peroxidation, by gas chromatography-mass spectrometry and anti-oxidant enzyme, superoxide dismutase (SOD). Results: Hfe<sub>-/-</sub>xTfr2<sub>Y245X</sub> mice had significantly elevated hepatic iron levels (1.5-fold; P<0.01) with a periportal iron distribution, increased plasma iron (1.7-fold; P<0.01) and transferrin saturation (1.3-fold; P<0.01) compared with Hfe<sub>-/-</sub> and Tfr2<sub>Y245X</sub> mice, which in turn, were increased compared with wild-type mice. Hamp was significantly reduced in Hfe<sub>-/-</sub> and Tfr2<sub>Y245X</sub> mice to 30% (P<0.01) and in Hfe<sub>-/-</sub>xTfr2<sub>Y245X</sub> mice to 1% (P<0.01) compared with wild-type mice. Hfe<sub>-/-</sub>xTfr2<sub>Y245X</sub> mice had elevated serum ALT activity (2 fold; P<0.001) compared with the other types of mice. Hfe<sub>-/-</sub>xTfr2<sub>Y245X</sub> mice had scattered lobular aggregates of mononuclear inflammatory cells, steatosis and increased portal tract collagen deposition. By contrast, Hfe<sub>-/-</sub> and Tfr2<sub>Y245X</sub> mice showed minimal hepatic inflammation, with no increased collagen deposition in Tfr2<sub>Y245X</sub> mice. F2-isoprostane levels were significantly elevated in Hfe<sub>-/-</sub>xTfr2<sub>Y245X</sub> mice (4.2-fold; P<0.001), Tfr2<sub>Y245X</sub> mice (3.2-fold; P<0.001) and Hfe<sub>-/-</sub>xTfr2<sub>Y245X</sub> mice (2.0-fold; P<0.01) and SOD was increased in Hfe<sub>-/-</sub>xTfr2<sub>Y245X</sub> (1.5-fold; P<0.05) compared with wild-type mice. Conclusion: The disruption of Hfe or Tfr2 causes hepatic iron loading and lipid peroxidation. However, the disruption of both Hfe and Tfr2 produces more severe hepatic iron overload and lipid peroxidation, with
Iron and cholesterol are both essential metabolites in mammalian systems, and too much or too little of either can have serious clinical consequences. In addition, both have been associated with steatosis and its progression, contributing, inter alia, to an increase in hepatic oxidative stress. The interaction between iron and cholesterol is unclear, with no consistent evidence emerging with respect to changes in plasma cholesterol on the basis of iron status. We sought to clarify the role of iron in lipid metabolism by studying the effects of iron status on hepatic cholesterol synthesis in mice with differing iron status. Transcripts of seven enzymes in the cholesterol biosynthesis pathway were significantly upregulated with increasing hepatic iron ($R^2$ between 0.602 and 0.164), including those of the rate-limiting enzyme, 3-hydroxy-3-methylglutarate-coenzyme A reductase (Hmgcr; $R^2 = 0.362$, $P < 0.002$). Hepatic cholesterol content correlated positively with hepatic iron ($R^2 = 0.255$, $P < 0.007$). There was no significant relationship between plasma cholesterol and either hepatic cholesterol or iron ($R^2 = 0.101$ and 0.014, respectively). Hepatic iron did not correlate with a number of known regulators of cholesterol synthesis, including sterol-regulatory element binding factor 2 ($Srebfa2$; $R^2 = 0.015$), suggesting that the increases seen in the cholesterol biosynthesis pathway are independent of $Srebfa2$. Transcripts of genes involved in bile acid synthesis, transport, or regulation did not increase with increasing hepatic iron. Conclusion: This study suggests that hepatic iron loading increases liver cholesterol synthesis and provides a new and potentially important additional mechanism by which iron could contribute to the development of fatty liver disease or lipotoxicity. Copyright 2010 by the American Association for the Study of Liver Diseases.

PMID:2010449168
Adolescents are spending increasing amounts of their leisure time engaged in non-exercise activity. Nonalcoholic fatty liver disease (NAFLD) is being diagnosed at alarming rates amongst adolescents. This project aims to determine if physical activity, sedentary behaviour and aerobic fitness are important risk factors for the development of NAFLD in adolescents.

Methods: 1170 individuals in the Western Australia Pregnancy Cohort (Raine) Study underwent assessment at 17 years of age including liver ultrasound, anthropometry, biochemistry as well as questionnaires regarding diet, alcohol intake, sedentary behaviour (total daily hours spent sitting, watching television or computer screens) and physical activity (the international physical activity questionnaire). Aerobic fitness was quantified using a bicycle ergometer test (PWC170). The association between physical activity, sedentary behaviour and aerobic fitness with NAFLD was examined by multivariable logistic regression.

Results: NAFLD was diagnosed in 12.8% of the cohort (10.1% male, 15.6% female, p=0.004). Adolescents with NAFLD had greater waist circumference and BMI than those without NAFLD (p<0.005). Females but not males with NAFLD compared to those without, were more likely to watch more hours of television on weekdays (p=0.06) and weekends (p=0.048), however, this relationship was lost after adjustment for waist circumference (OR 1.04, 95% CI 0.84-1.29 and OR 1.06, 95% CI 0.87-1.30). The mean (SD) daily level of physical activity was not different in subjects with NAFLD compared to those without [661 (704) vs. 701 (730) METs, p=0.6] nor was the mean daily time spent doing physical activity different between NAFLD and non-NAFLD subjects (154 (146) vs 153 (148) minutes, p=0.9). Furthermore, there was no association between walking, moderate or vigorous activity and NAFLD (p>0.1 for all). However, subjects with NAFLD had a lower aerobic fitness capacity than those without NAFLD [1.47 (0.47) vs. 1.97 (0.56) W/kg, p<0.001]. After adjustment for gender, waist circumference and caloric intake, a higher aerobic fitness capacity remained associated with a significantly reduced risk of NAFLD (OR=0.35, 95%CI 0.18-0.66, p=0.001). Aerobic fitness was also inversely associated with alanine aminotransaminase levels after adjustment for gender (beta=-0.18, p<0.001). Conclusion: The relationships between sedentary behaviour, levels of physical activity and aerobic fitness and adolescent NAFLD differ. Aerobic fitness is independently associated with a lower risk of NAFLD in adolescents. Preventative and treatment interventions should be aimed at increasing aerobic fitness.

Publication Types: Conference Abstract
PMID:70388210

Hepatology. 2010; 52: 1133A-1134A.

**CO-regulation of fibrogenic and liver progenitor cell responses in both pre-and postliver transplant recurrent chronic hepatitis C infection.**

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BACKGROUND: There is co-regulation of fibrogenic and liver progenitor cell (LPC) responses in a range of human chronic liver diseases including chronic hepatitis C virus (HCV) infection, which is the commonest indication for orthotopic liver transplantation (OLT) in western countries. Recurrent and accelerated hepatitis C infection in grafted livers is a frequent cause of graft loss. LPC numbers increase significantly with progression of fibrosis severity in pre-transplant chronic HCV disease, however it is not known whether LPCs proliferate following recurrent HCV infection post-OLT and contribute to accelerated fibrosis in this setting. The aim of this study was to determine whether LPCs are detected and associated with inflammation and fibrosis in recurrent HCV disease following OLT.

METHODS: Liver biopsies were available from 16 pre-OLT and 16 post-OLT subjects with chronic
HCV. De-identified specimens underwent blind evaluation following haematoxylin/eosin (histology) and Masson's trichrome staining (fibrosis) as well as pan cytokeratin (LPCs) and CD45 (inflammation) immunohistochemistry. Fibrosis was scored according to the Metavir system and digital whole slide scanning was conducted to evaluate numbers of positively stained cells. Results were expressed semiquantitatively using a 0-4+ scoring system and confirmed by algorithm-based positive pixel count per area. Statistical analyses were conducted using SPSS version 17. RESULTS: In pre-OLT biopsies, the number of LPCs increased with advancing fibrosis and inflammation. Seven of 16 pre-OLT subjects had severe F3 or F4 fibrosis and these had a median score of 4+ for numbers of CKpan+ LPCs. This was significantly higher (p = 0.012) than for subjects with only mild F0-F2 fibrosis, who showed a median score of only 2.5+ for LPC numbers. Increasing numbers of CD45+ cells were also associated with increasing LPC proliferation and fibrosis severity in pre-OLT livers. Similarly, in post-OLT subjects, increasing levels of inflammation and fibrosis were associated with increased numbers of LPCs. Five of 16 post-OLT subjects had severe F3 or F4 fibrosis and these had a median score of 3.5+ for CKpan+ LPCs. In contrast, post-OLT subjects with mild F0-F2 fibrosis had a significantly lower median score of 2.5+ for LPC proliferation (p = 0.019). CONCLUSION: Hepatic fibrosis occurring in chronic HCV disease either before or after OLT is associated with increasing numbers of LPCs suggesting co-regulation of the fibrogenic and LPC responses. Thus, targeting of the LPC compartment after OLT might be a novel treatment strategy to prevent accelerated fibrosis progression to cirrhosis and hepatocellular carcinoma.

Publication Types: Conference Abstract
PMID:70389281


**Tumor necrosis factor-like weak inducer of apoptosis is a mitogen for liver progenitor cells.**

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Liver progenitor cells (LPCs) represent the cell compartment facilitating hepatic regeneration during chronic injury while hepatocyte-mediated repair mechanisms are compromised. LPC proliferation is frequently observed in human chronic liver diseases such as hereditary hemochromatosis, fatty liver disease, and chronic hepatitis. In vivo studies have suggested that a tumor necrosis factor family member, tumor necrosis factor-like weak inducer of apoptosis (TWEAK), is promitotic for LPCs; whether it acts directly is not known. In our murine choline-deficient, ethionine-supplemented (CDE) model of chronic liver injury, TWEAK receptor [fibroblast growth factor-inducible 14 (Fn14)] expression in the whole liver is massively upregulated. We therefore set out to investigate whether TWEAK/Fn14 signaling promotes the regenerative response in CDE-induced chronic liver injury by mitotic stimulation of LPCs. Fn14 knockout (KO) mice showed significantly reduced LPC numbers and attenuated inflammation and cytokine production after 2 weeks of CDE feeding. The close association between LPC proliferation and activation of hepatic stellate cells in chronic liver injury prompted us to investigate whether fibrogenesis was also modulated in Fn14 KO animals. Collagen deposition and expression of key fibrogenesis mediators were reduced after 2 weeks of injury, and this correlated with LPC numbers. Furthermore, the injection of 2-week-CDE-treated wildtype animals with TWEAK led to increased proliferation of nonparenchymal pan cytokeratin-positive cells. Stimulation of an Fn14-positive LPC line with TWEAK led to nuclear factor kappa light chain enhancer of activated B cells (NFkappaB) activation and dose-dependent proliferation, which was diminished after targeting of the p50 NFkappaB subunit by RNA interference. CONCLUSION: TWEAK acts directly and stimulates LPC mitosis in an Fn14-dependent and NFkappaB-dependent fashion, and signaling via this pathway mediates the LPC response to CDE-induced injury and regeneration.

PMID:20578156
Donor specific anti-HLA antibody (DSA) at the time of transplant associates with increased rejection and impaired graft function.

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Background: The development of de novo donor-specific antibodies (DSA) post-renal transplant is strongly associated with rejection and graft failure. However, the importance of pre-transplant DSA upon graft outcomes remains unclear. The aims of this study were to determine the prevalence of DSA in renal transplant recipients (RTR) at transplant and their effect upon graft outcomes. Methods: 257 RTR (64% cadaveric) were prospectively studied with a median follow-up of 4 years. All patients had negative CDC T-cell crossmatches. Patients with positive antibody Class I and II screening (Luminex platform One Lambda) underwent Single Antigen Bead testing to determine specificity. We defined a donor specific antibody (DSA) as any donor specific bead with MFI $\geq 500$. Outcomes included BPAR, eGFR, proteinuria and graft failure. Results: Of 257 recipients, 35 (13%) had DSA pre-transplant, 30 (11%) had non-DSA and 192 (76%) no antibody (Ab-). BPAR occurred in 59% of DSA vs 33% nonDSA and 32% Ab- (P=0.01). C4d+ve rejection occurred in 21% of DSA vs 4% nonDSA and 6% Ab- (P=0.007). KM Graft survival was 83% DSA, 100% nonDSA and 89% Ab- (P=0.21) at 4 years. After 2 years follow-up, the mean eGFR in DSA showed a progressive and significant decline with higher proteinuria (protein/creatinine ratio 109+/-154mg/mmol vs 51.7+/-93mg/mmol; P<=$0.05$) compared with RTR with non-DSA and Ab-where eGFR is stable over time. Conclusions: Presence of DSA, but not nonDSA pre-transplant, increases the absolute risk of rejection and the severity. Although early graft survival is acceptable, there is a progressive deterioration in graft function evident as early as 2 years post transplant in patients with DSA.

Publication Types: Conference Abstract
PMID:70313627

The effect of third-party red-cell transfusion in the first 30 days after renal transplantation in patients with and without anti-HLA antibody.

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Aim: We hypothesised that third party transfusion at the time of renal transplant may induce an immune response and that this could be influenced by the presence of preformed donor specific anti-HLA antibody (DSA). Methods: We examined post-operative transfusion and biopsy proven graft rejection (BPAR) in a cohort of 257 patients with donor specific anti-HLA antibody (DSA defined as MFI$\geq 500$ by Luminex SAB) and those without DSA (nonDSA group). Results: 79/222 nonDSA (36%) and 22/35 DSA (63%) P=0.005 were transfused a mean of 3.2U nonDSA and 3.6U DSA (P=0.6)
within the first 30 days after transplant, mostly in the first 2 days (90% nonDSA, 75% DSA P=0.9). There was no difference in patients with delayed graft function (nonDSA 30.4 vs DSA 31.8% P=0.9), proportion of cadaveric donors (66% nonDSA vs 77% DSA P=0.3) but 77% DSA vs 38%nonDSA had BPAR (P=0.001). The median (IQR) time to rejection from transfusion for nonDSA was 58 (12-274) and DSA 38 (14-250) days (P=0.9). In Patients who were not transfused post operatively, 29% of nonDSA and 31% of DSA had BPAR (P=0.9). Transfusion did not significantly boost post transplant DSA(Table presented) Conclusions: Patients with DSA who receive transfusion have significantly higher BPAR than transfused nonDSA. There is no difference in BPAR between DSA and nonDSA patients who are not transfused. Early post-operative 3rd party transfusion in patients with pre-formed DSA maybe harmful, perhaps by additional allo-antigen stimulation.

Publication Types: Conference Abstract
PMID:70313635


The peak and Sum MFI of the single antigen beads (SAB) of donor specific anti-HLA antibodies (DSA) at the time of transplantation in renal transplant recipients (RTR) associate with the risk of C4d+ rejection.
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Introduction: We have shown that any DSA at the time of transplant was associated with increased severity and risk of rejection in RTR. We examined whether the class or amount of antibody, as indicated by the highest donor specific mean fluorescence intensity (MFI) (Peak) and the sum of all SAB MFI (Sum), better defines the risk of rejection. Methods: Using the Luminex platform we defined a DSA as any donor specific bead with MFI >=500. All patients had a negative T-cell CDC crossmatch. Results: Any BPAR and in particular C4d+ rejection, was associated with the presence of DSA, with C4d+ rejection occurring in 12/222 (5%) without DSA and 8/35 (23%) with DSA (P=0.002). The association was particularly evident in those with class II DSA (with or without class I) as shown below. (Table presented) Higher MFI was associated with more C4d+ rejection, median Peak MFI in DSA patients was 9600 (IQR 1100-12000) in those with C4d+ rejection vs 2800 (IQR 870-5698) in those without (P=0.06) and median Sum MFI was 13212 (5541-22541) vs 3697 (1055-9011) respectively (P=0.01). The association of higher MFI was also evident when the rejection rate (%) by categories of the Sum of MFI was examined as shown above. Conclusion: DSA are associated with an increased risk of BPAR (especially C4d+ rejection). The risk is better defined by the presence of class II antibody (with or without class I antibody) and by higher peak or sum of the MFI of the donor specific antibodies.

Publication Types: Conference Abstract
PMID:70313636

A case of legionella longbeachae pneumonia complicated by rhabdomyolysis and acute renal failure requiring hemodialysis.
Clark BM, Boan P, et al.
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We describe a case of pneumonia due to Legionella longbeachae complicated by rhabdomyolysis and acute renal failure requiring hemodialysis. The infection occurred in a 61-year-old man from Fremantle, Western Australia after exposure to potting mix while gardening. Whereas Legionella pneumophila is a rare but well-described cause of rhabdomyolysis and renal failure, we believe this to be the first case reported in the English language literature caused by L. longbeachae. The case illustrates the ongoing dangers to gardeners in Australia if advised precautions against Legionella infection are not followed. Copyright 2010 by Lippincott Williams & Wilkins.

PMID:2010631043

The effect of diazepam on myocardial function and coronary vascular tone after endotoxemia in the isolated rat heart model.
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OBJECTIVE AND DESIGN: Tumor necrosis factor alpha (TNF-α) has been implicated in the pathogenesis of cardiovascular disease and sepsis-associated cardiac dysfunction. Although initially described solely as a lipopolysaccharide (LPS)-induced macrophage product, evidence exists that cardiac myocytes themselves produce substantial amounts of TNF-α in response to ischemia as well as LPS. The use of phosphodiesterase inhibitors has been shown to decrease LPS-induced TNF-α elaboration. The aim of the present study was to determine the effect of diazepam (Type IV phosphodiesterase inhibitor) on (1) myocardial function and (2) coronary vascular flow after LPS-induced endotoxic shock in an isolated rat heart model. MATERIALS AND METHODS: Endotoxemia was induced by intraperitoneal LPS administration in adult male Wistar rats. Hearts were isolated after 6 h and perfused in a working mode with oxygenated Krebs-Henseleit buffer at 37°C. Diazepam was mixed with Krebs-Henseleit buffer and administered (3.0 μg/ml) for 20 min. RESULTS: LPS-treated hearts showed depressed cardiac function and reduced coronary flow. Myocardial functional parameters (LVDP, +dP/dt, -dP/dt, RPP) and coronary flow (ml/min) were significantly (p < 0.01) improved by diazepam administration. CONCLUSIONS: These findings suggest that diazepam can salvage myocardial function and undo coronary vascular constriction in the endotoxemic rat heart. These findings are clinically relevant to the treatment of cardiovascular depression caused by endotoxic shock.
PMID:20694572

Late extrusion of pulmonary plombage outside the thoracic cavity.
Yadav S, Sharma H, et al.
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Plombage, a variant of collapse therapy for patients with pulmonary tuberculosis that uses a variety of foreign materials, was undertaken until the 1950s before the invention of effective antimicrobial therapy. Complications related to previous plombage procedures are not uncommon. Management of these complications can be challenging. We report a patient presenting with extrusion of plombage 59 years later and managed successfully with removal of the plomb and pectoral muscle flap transposition. 2010 Published by European Association for Cardio-Thoracic Surgery.
PMID:2010391289
A case of IGG4 related systemic sclerosing disease: An important mimic of malignancy.

Brusch A, Mallon D.

We present the case of a 55 year old man who presented with features that were initially suspicious for a malignant process but following biopsy and serum IGG4 testing was found to have IGG4 related systemic sclerosing disease. The patient presented with a month long history of fatigue, malaise, anorexia, weight loss and abdominal pain. In the few days preceding his admission he became mildly jaundiced. Initial testing showed a cholestatic pattern of liver function tests and elevated lipase. Imaging revealed upper abdominal lymphadenopathy. The concern was therefore of an abdominal malignancy such as lymphoma. Biopsy was performed which did not show any malignant cells. Rather, there were areas of obliterative phlebitis and collections of IGG4 positive plasma cells. Subsequent testing for serum IGG4 confirmed a markedly high antibody level and thus a diagnosis of IGG4 related systemic sclerosing disease was made. The patient was commenced on oral steroids with swift improvement of his symptoms. This was accompanied by falling liver function tests and IGG4 level within the first two weeks of treatment. The most well characterised IGG4 related disorder is autoimmune pancreatitis. However, in the past few years, clinicopathologically related conditions of other tissues and organs have been reported. These include IGG4 associated cholangitis, retroperitoneal fibrosis, lymphadenopathy and hypophysitis. Interestingly, this patient developed unexplained hypopituitarism twelve years earlier. In retrospect this may have been another manifestation of IGG4 related disease. As this case highlights, this unusual disorder has a range of presentations and is important to recognise, as it can present like a malignancy yet is very treatable with steroids.

PMID:70264396

The epidemiology and characteristics of type 2 diabetes in urban, community-based young people.

Sillars BA, Davis WA, et al.

As little is known about the impact of type 2 diabetes amongst Australian youth despite international increases in childhood obesity, we aimed to identify and characterize people aged <25 years with type 2 diabetes in an urban community with 60000 people aged 10-24 years. The estimated maximum prevalence (59/100000 persons) was lower than US estimates but higher than in Asia and Europe. In eight patients assessed in detail, obesity and related comorbidities were common, and quality of life was low.

PMID:21199223

Hereditary haemochromatosis (HH) is characterized by a clinically definable arthropathy that correlates with iron load: ARP13.

Carroll GJ, Breidahl WH, et al.

PMID:25520592

An Australian cardiovascular risk equation for type 2 diabetes: the Fremantle Diabetes Study.
BACKGROUND: There is no valid cardiovascular disease (CVD) risk prediction equation for Australians with diabetes. The aim of this study is to develop and validate a multivariate risk function for 5-year cardiovascular risk prediction in Australian type 2 diabetes patients. METHODS: The Fremantle Diabetes Study is a community-based longitudinal observational study. A total of 1240 type 2 diabetic patients (95.8% of the baseline cohort) with all required risk factor data were followed from baseline (1993-1996) for 5 years or until they experienced a cardiovascular event or died, whichever came first. CVD during follow up was defined as hospitalization for/with myocardial infarction or stroke, and death from cardiac or cerebrovascular causes or sudden death. Validation of the algorithm was performed on an independent diabetic cohort from the Busselton Health Study. RESULTS: During 5570 patient-years of follow up, 185 (14.9%) had at least one CVD event and 175 (14.1%) died (57.7% from CVD). Variables in the final model comprised age, sex, prior CVD, ln(urinary albumin : creatinine ratio), lnHbA(1c), ln(high density lipoprotein-cholesterol), Southern European ethnic background and Aboriginality. The mean 5-year predicted risk of a CVD event was 15.5%. Applied to the Busselton cohort, discrimination of the model was good (AUC = 0.84, P < 0.001) as was the goodness-of-fit (Hosmer-Lemeshow C-test, P= 0.85) and accuracy (mean squared error (95% confidence interval) = 0.09 (0-0.76)). The positive and negative predictive values for a 10% 5-year CVD risk cut-off were 23.4% and 97.7% respectively. CONCLUSION: This simple diabetes-specific 5-year CVD risk equation is the first validated, population-based Australian model. It should have a role in diabetes management in primary and specialist care.

Preliminary outcomes of cholesteatoma screening in children using non-echo-planar diffusion-weighted magnetic resonance imaging.

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OBJECTIVE: Diffusion-weighted (DW) MRI imaging is evolving into an alternative to second look surgery in detection of cholesteatoma recurrence. Insights into the DW MRI appearances of postoperative or inflammatory mucosal changes have recently described using non-echo-planar, turbo spin-echo (TSE) DW MRI which reliably distinguishes between postoperative changes and cholesteatoma. We investigated the use of TSE DW MRI in our pediatric population in order to validate a rapid and cost-effective MRI sequence that can be used to screen for cholesteatoma.

METHODS: Prospective comparative study with adult and pediatric patients at a tertiary referral centre. Patients in the study underwent TSE DW MRI prior to second look or revision surgery for cholesteatoma. A Siemens 1.5 T scanner was employed, using the HASTE sequence (EPI DW MRI) as well as standard echo-planar DWI, T1 and T2 sequences. The MRI findings were then correlated with the intraoperative findings at surgery 9-15 months after primary surgery, or of revision surgery in the cases that were referred from other centres. Detection and localisation of cholesteatoma on TSE DW MRI were compared with the findings at second surgery, long considered the gold standard for detection of residual or recurrent disease. Scanning time between the TSE sequence and the standard planar DW MR were also compared. RESULTS: In a cohort of 92 patients, 21 pediatric patients were identified. 15 patients have had their 15 second look or revision procedures and DW MRI prior to their surgery. TSE DW MRI detected cholesteatoma and reliably identified the location of the cholesteatoma in 2 patients whom all had disease confirmed at surgery. The 13 cases with negative preoperative DW MRI for cholesteatoma were all confirmed to be disease free at surgery. Scanning time of the TSE sequence takes 100 s as opposed to 20 min using standard echo-planar DW MRI techniques without the requirement of a contrast agent and without the need for a general anaesthetic for any of the children. CONCLUSION: TSE (HASTE) DW MRI is emerging as a cost-effective alternative to standard DW MRI for detection of residual or recurrent cholesteatoma in children.
Intracranial arteriopathy in biopsy proven giant cell arteritis (GCA).
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Background: Giant cell arteritis is a chronic, idiopathic inflammatory condition associated with polymyalgia rheumatica. It affects mostly patients over the age of 50 and involves medium to large arteries, especially the external carotid system. Intracranial arteries are rarely involved in GCA.

Aims: To illustrate two unusual cases of stroke.

Methods: Case records of two patients admitted to the Fremantle Hospital Stroke Unit were reviewed.

Results: Case 1: A 72 year old lady presented with acute onset right sided weakness and speech difficulty. She had polymyalgia rheumatica and 10 days previously had acute loss of vision in her right eye which prompted biopsy of her temporal artery, confirming GCA. Magnetic resonance imaging/angiography (MRI/MRA) showed left sided watershed infarction with occlusion of the intracranial left internal carotid artery (ICA). Case 2: An 82 year old lady with biopsy proven GCA and on steroid therapy presented with sudden onset of left sided weakness and facial droop and speech difficulties. MRI/MRA showed bilateral high grade supraclinoid ICA stenoses and small vessel parenchymal changes suggestive of vasculitis.

Conclusion: GCA is an uncommon cause of stroke. It is important to recognise giant cell arteritis in association with stroke as this condition is amenable to treatment with steroids.

Publication Types: Conference Abstract
PMID:70334750

The prevalence of atrial fibrillation-related strokes and use of anticoagulation in patients admitted to a tertiary hospital stroke unit-audit.
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Background: Atrial fibrillation (AF) is a common cause of stroke. AF-related strokes are of greater severity with worse outcome when compared with non-AF-related strokes. Anticoagulation with warfarin with International Normalised Ratio (INR) in the target therapeutic range reduces the overall risk for stroke.

Aim: To determine the prevalence of AF-related stroke and appropriate use of anticoagulation in AF patients admitted with stroke, and identify reasons for sub-therapeutic anticoagulation in patients admitted to the stroke unit.

Methods: Data from files of patients admitted to the stroke unit, including demographic and clinical data (AF classification, type and territory of stroke, CHADS2 Score, medications, INR and reasons for no anticoagulation) will be collected.

Results: Data collection is currently underway. Discussion: Results will be presented at the Conference. Current evidence supports the use of anticoagulation in AF patients to prevent severe embolic strokes. Audit outcomes will reveal the degree of congruence with current guidelines with respect to anticoagulation at time of admission in patients admitted to the stroke unit with AF-related stroke, and assist in the identification of reasons for sub-therapeutic or no anticoagulation in our stroke unit population.

Publication Types: Conference Abstract
PMID:70334759

A cross-sectional community study of serum iron measures and cognitive status in older
The relationship of iron status with cognition and dementia risk in older people is contentious. We have examined the longitudinal relationship between serum ferritin and cognition in 800 community-dwelling Australians 60 years or older. Iron studies (serum iron, transferrin saturation, serum ferritin) were performed in 1994/5 and 2003/4 and clinical and cognitive assessments were conducted in 2003/4 for 800 participants of the Busselton Health Study. All participants completed the Cambridge Cognitive test (CAMCOG). Those with CAMCOG scores < 84 underwent expert clinical review for cognitive disorders, including the Clinical Dementia Rating scale. Mean serum iron (18.3 mu mol/l) and transferrin saturation (28.5%) in 2003/4 did not differ significantly from 1994/5 whereas mean serum ferritin decreased from 162 mu g/l in 1994/5 to 123 mu g/l in 2003/4, possibly reflecting aging or dietary changes. No relationships were observed between serum iron or transferrin saturation and presence or absence of dementia (p > 0.05). In participants without dementia (n = 749), neither serum ferritin in 1994/5 or 2003/4 nor change in serum ferritin between these times was related to total CAMCOG or executive function scores, with or without adjustment for gender, age, National Adult reading test, or stroke history (all p > 0.05). No relationships were observed between ferritin and cognition for participants with possible or probable dementia (n = 51). All participants identified as HFE C282Y homozygous or with serum ferritin > 1,000 ng/ml had normal CAMCOG scores. We conclude abnormal body iron stores (low or high) are unlikely to have clinically significant effects on cognition or dementia risk in community-dwelling older people. (PsycINFO Database Record (c) 2010 APA, all rights reserved) (journal abstract).


Lateral subvastus approach with osteotomy of the tibial tubercle for total knee replacement: A two-year prospective, randomised, blinded controlled trial.

Hay GC, Kampshoff J, et al.

From the Fremantle Hospital, Fremantle, Australia: The lateral subvastus approach combined with an osteotomy of the tibial tubercle is a recognised, but rarely used approach for total knee replacement (TKR). A total of 32 patients undergoing primary TKR was randomised into two groups, in one of which the lateral subvastus approach combined with a tibial tubercle osteotomy and in the other the medial parapatellar approach were used. The patients were assessed radiologically and clinically using measurement of the range of movement, a visual analogue patient satisfaction score, the Western Ontario McMasters University Osteoarthritis Index and the American Knee Society score. Four patients were lost to the complete follow-up at two years. At two years there were no significant differences between the groups in any of the parameters for clinical outcome. In the lateral approach group there was one complication due to displacement of the tibial tubercle osteotomy and two
osteotomies took more than six months to unite. In the medial approach group, one patient had a partial tear of the quadriceps. There was a significantly greater incidence of lateral patellar subluxation in the medial approach group (3 of 12) compared with the lateral approach group (0 of 16) (p = 0.034), but without any apparent clinical detriment. We conclude that the lateral approach with tibial tubercle osteotomy is a safe technique with an outcome comparable with that of the medial parapatellar approach for TKR, but the increased surgical time and its specific complications do not support its routine use. It would seem to be more appropriate to reserve this technique for patients in whom problems with patellar tracking are anticipated. (C) 2010 British Editorial Society of Bone and Joint Surgery

Determinants of severe hypoglycemia complicating type 2 diabetes: the Fremantle diabetes study.
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CONTEXT: There are limited published data characterizing severe hypoglycemia complicating type 2 diabetes. OBJECTIVE: The objective of the study was to determine the incidence and predictors of severe hypoglycemia in community-dwelling type 2 patients. DESIGN: This was a longitudinal observational cohort study. SETTING: This was a community-based study. PATIENTS: There were 616 patients (mean age 67.0 yr, 52.3% males, median diabetes duration 7.7 yr) assessed in 1998 and followed up to the end of June 2006. MAIN OUTCOME MEASURES: Severe hypoglycemia defined as that requiring ambulance attendance, emergency department services, and/or hospitalization. Cox proportional hazards modeling was used to determine predictors of first episode, and Poisson, negative binomial, zero-inflated Poisson, and zero-inflated negative binomial regression models identified predictors of frequency. RESULTS: Fifty-two (8.4%) experienced 66 episodes during 3953 patient-years (incidence 1.7 per 100 patient-years). Those experiencing severe hypoglycemia had one to four episodes. Significant independent predictors of time to first episode were duration of insulin treatment, estimated glomerular filtration rate less than 60 ml/min per 1.73 m(2), peripheral neuropathy, education beyond primary level, and past severe hypoglycemia. The zero-inflated negative binomial provided the best model of severe hypoglycemia frequency. Lower fasting serum glucose and higher glycosylated hemoglobin were significantly associated with frequency, whereas patients at minimal risk of repeated severe hypoglycemia were unlikely to use insulin or to have short-duration insulin treatment, to have renal impairment or peripheral neuropathy, or to be educated beyond primary level. CONCLUSIONS: Duration of insulin treatment was confirmed as an independent risk factor for severe hypoglycemia. The novel association with educational attainment suggests knowledge-driven intensive glycemic self-management. The positive relationship between frequency and glycosylated hemoglobin may identify patients with unstable glycemic control.
Publication Types: Research Support, Non-U.S. Gov't
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Associations of total testosterone, sex hormone-binding globulin, calculated free testosterone, and luteinizing hormone with prevalence of abdominal aortic aneurysm in older men.
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Context: Abdominal aortic aneurysm (AAA) is associated with mortality in older adults, and increasing aortic diameter predicts incident cardiovascular events. Although AAA occurs predominantly in men, its association with male sex hormones is unclear. Objective: The objective of the study was to examine whether male sex hormones are independently associated with AAA or increased abdominal
aortic diameter. Design: This was a cross-sectional analysis. Setting and Participants: Participants included 3620 community-dwelling men aged 70-88 yr. Main Outcome Measures: Abdominal aortic diameter was measured with ultrasound. Early morning sera were assayed for total testosterone, SHBG, and LH. Free testosterone was calculated using mass action equations. Results: AAA (aortic diameter > or =30 mm) was present in 262 men (7.2%). Men with AAA had lower serum total and free testosterone (mean +/- sd 14.5 +/- 6.0 vs. 15.5 +/- 5.6 nmol/liter, P = 0.005 and 256 +/- 87 vs. 280 +/- 97 pmol/liter, P < 0.001, respectively) compared with men without. LH was higher in men with AAA (median, interquartile range: 4.9, 3.1-7.9 vs. 4.3, 3.0-6.4 IU/liter, P = 0.013). In multivariate analysis adjusting for potential confounders, free testosterone was negatively associated with AAA (odds ratio per 1 sd increase: 0.84, 95% confidence interval 0.72-0.98, P = 0.026). LH was positively associated (odds ratio 1.14, 95% confidence interval 1.03-1.25, P = 0.008). Comparable results were seen with aortic diameter analyzed as a continuous variable. Conclusions: Lower free testosterone and higher LH levels are independently associated with AAA in older men. Impaired gonadal function may be involved in arterial dilatation as well as occlusive vascular disease in older men. Additional studies are needed to clarify direction of causality and determine possible scope for preventive intervention.


Structural decay of bone microarchitecture in men with prostate cancer treated with androgen deprivation therapy.

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Context: Androgen deprivation therapy (ADT) used in the treatment of prostate cancer reduces bone mineral density (BMD) and predisposes to fractures. The structural basis of the BMD deficit and bone fragility is uncertain. Objective and Patients: We investigated changes in bone microarchitecture in 26 men (70.6 +/- 6.8 yr) with nonmetastatic prostate cancer during the first year of ADT using the new technique of high-resolution peripheral quantitative computed tomography. Design and Setting: We conducted a 12-month prospective observational study in the setting of a tertiary referral center. Results: After 12 months of ADT, total volumetric density decreased by 5.2 +/- 5.4% at the distal radius and 4.2 +/- 2.7% at the distal tibia (both P < 0.001). This was due to a decrease in cortical volumetric BMD (by 11.3 +/- 8.6% for radius and 6.0 +/- 4.2% for tibia, all P < 0.001) and trabecular density (by 3.5 +/- 6.0% for radius and 1.5 +/- 2.3% for tibia, all P < 0.01), after correcting for trabecularization of cortical bone. Trabecular density decreased due to a decrease in trabecular number at both sites (P < 0.05). Total testosterone, but not estradiol, levels were independently associated with total and corrected cortical volumetric BMD at the tibia. Conclusions: Sex steroid deficiency induced by ADT for prostate cancer results in microarchitectural decay. Bone fragility in these men may be more closely linked to testosterone than estradiol deficiency. Copyright 2010 by The Endocrine Society.

PMID:2010681629


Low free testosterone predicts frailty in older men: The health in men study.

Hyde Z, Flicker L, et al.
Context: The prevalence of frailty increases, whereas testosterone decreases, as men age. Low testosterone may be a risk factor for development of this syndrome. Objective: Our objective was to determine whether testosterone levels are associated with frailty. Design: We conducted a prospective cohort study. Setting and Participants: Between 2001 and 2004, frailty was assessed in 3616 community-dwelling men aged 70-88 yr. Frailty was reassessed in 1586 men aged 76-93 yr in 2008-2009. Main Outcome Measures: Frailty was assessed with the FRAIL scale, comprising five domains: fatigue, difficulty climbing a flight of stairs, difficulty walking more than 100 m, more than five illnesses present, or weight loss greater than 5%. Testosterone, SHBG, and LH were assayed at baseline. Free testosterone was calculated using mass action equations. Results: At baseline, 15.2% of men (n=548) were frail (at least three deficits), increasing to 23.0% (n = 364) at follow-up. At baseline, each 1 SD decrease in total or free testosterone level was associated with increased odds of frailty [odds ratio (OR) = 1.23; 95% confidence interval (CI) = 1.11-1.38, and OR = 1.29; 95% CI = 1.15-1.44 for total and free testosterone, respectively]. Lower LH was associated with reduced odds of frailty (OR = 0.88; 95% CI = 0.81-0.95). Adjustments were made for age, body mass index, smoking, diabetes, social support, and other covariates. At follow-up, only lower free testosterone levels (OR = 1.22; 95% CI = 1.05-1.42) predicted frailty. Conclusions: Lower free testosterone was independently associated with frailty at baseline and follow-up. Randomized trials should explore whether testosterone therapy can prevent the development of frailty. Copyright 2010 by The Endocrine Society.

The C282Y polymorphism of the hereditary hemochromatosis gene is associated with increased sex hormone-binding globulin and normal testosterone levels in men.

Yeap BB, Beilin J, et al.

Background: Hereditary hemochromatosis resulting either from homozygosity for the C282Y polymorphism of the HFE gene, or compound heterozygosity for C282Y and H63D, manifests with liver disease and hypogonadism. However, it is unclear whether men who are heterozygotes for C282Y or H63D exhibit subtle abnormalities of sex hormone status. Aims: To evaluate whether heterozygosity for either of the HFE gene polymorphisms C282Y or H63D is associated with circulating testosterone and SHBG in men. Subjects and methods: We performed a cross-sectional analysis of 388 community-dwelling men. Men were genotyped for C282Y and H63D. Sera were
analysed for testosterone and SHBG, and insulin resistance was estimated using a homeostatic model (HOMA2-IR). Results: Mean age of men in the cohort was 56.9 yr. Men who were heterozygous for the C282Y polymorphism in the HFE gene had higher SHBG levels than men who did not carry this polymorphism (mean+/-SE, 38.2+/1.64 vs 32.8+/0.71 nmol/l, p=0.006). Total and free testosterone levels did not differ in the two groups. In multivariate analysis adjusting for potential confounders including age, waist circumference, testosterone, and HOMA2-IR, C282Y heterozygosity remained associated with SHBG levels (p<0.001). Conclusion: The C282Y polymorphism is associated with SHBG levels in men who do not manifest iron overload. Further studies are needed to clarify potential mechanisms and determine the clinical relevance of this finding. 2010, Editrice Kurtis.

PMID:2010601508

Ecabet sodium: a potential new agent in the management of distal colitis.
Lawrance IC.
Publication Types: Comment
PMID:20594242

Serious infections in patients with inflammatory bowel disease receiving anti-tumor-necrosis-factor-alpha therapy: an Australian and New Zealand experience.
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BACKGROUND AND AIM: Anti-tumor-necrosis-factor-alpha (anti-TNF-) medications are effective in inflammatory bowel disease (IBD), but have an increased risk of tuberculosis (TB) and serious infections. The aim of this study was to examine the Australian/New Zealand experience of serious infections and TB in IBD patients receiving anti-TNF- therapy from 1999-2009. METHODS: Serious infections, defined as 'requiring hospital admission' and TB cases in patients receiving, or within 3 months following, anti-TNF- therapy were analyzed across Australia and New Zealand. Patient demographics, IBD medications, duration of anti-TNF- therapy, and infection details were collected. RESULTS: A total of 5562 IBD patients were managed across the centers. Of these, 489 (16.8%) Crohn's disease and 137 (5.2%) ulcerative colitis patients received anti-TNF- therapy. There were three cases of latent TB that received prophylaxis prior to anti-TNF- therapy. No cases of active TB were reported. Fourteen (2.2%) serious infections occurred. Seven occurred in patients receiving anti-TNF- therapy for less than 6 months, including two cases of primary Varicella zoster (VZV), two cases of Pneumocystis jiroveci pneumonia, two cases of Staphylococcus aureus bacteremia, and one severe flu-like illness. Six patients were taking additional immunosuppressive medications. The other seven infections occurred after 6 months (mean 32.6 +/- 24.3 months) and included one case of primary VZV, one flu-like illness, and five bacterial infections. All infections resolved with treatment. CONCLUSION: TB is a very rare complication of anti-TNF- therapy in Australia and New Zealand. Serious infections are uncommon but early opportunistic infections with Pneumocystis jiroveci pneumonia suggest a need for vigilance in patients on multiple immunosuppressive medications. VZV vaccination prior to immunosuppressive therapy should be considered in VZV-naive patients.
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PMID:21039834

PAHA model: an alternative non-invasive predictor of liver cirrhosis in patients with chronic hepatitis B infection.
Genetic susceptibility in IBD: Overlap between ulcerative colitis and Crohn's disease.

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Background: The aetiology of Ulcerative colitis (UC) and Crohn's disease (CD) involves both genetic and environmental components. Multiple UC and CD susceptibility genes have been identified through genome-wide association studies and subsequent meta-analyses. These studies have also highlighted the presence of susceptibility genes common to both disorders, and shared with several other autoimmune disorders. The aim of this study was to determine whether any SNPs recently identified by the International IBD Genetics Consortium (IIBDGC) as demonstrating highly significant associations with CD could also confer genetic susceptibility to UC.

Methods: Statistical modelling using Random Forest (RF) and stepwise Generalized Linear Models (sGLM) was performed on 29 CD-associated SNPs from the IIBDGC study in 1652 UC cases (ANZIBDC) and 2363 Australian population-based controls. Odds ratio's (95% Confidence Interval) were calculated. UC cases were phenotyped according to the Montreal classification. Genotyping was done using Sequenom technology. Results: One SNP from the 29, rs3024505, was identified from both RF and sGLM models as significantly associated with UC (P = 0.001). Independent Chi Square analyses identified odds ratio's of 2.22 (1.48- 3.37) for the rare homozygous genotype, and 1.20 (1.06-1.35) for the minor allele. Five other SNPs demonstrated moderate to weak associations with UC.

Conclusions: Of the 29 SNPs conferring high genetic susceptibility to CD, one SNP, rs3024505 (Chr 1q32.1, upstream of IL10), was identified as conferring genetic susceptibility to UC, thus indicating that for this SNP set, there is a low level of overlap between the two major forms of IBD. The identification of this SNP replicates a finding from Franke et al. (2008), where the rs3024505 SNP was strongly associated with UC across multiple European populations.

The risk of skin cancer development in IBD patients on azathioprine/6 mercaptopurine.

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Azathioprine (AZA) or 6 mercaptopurine (6MP) are frequently used to treat IBD. Non-melanoma skin cancer (NMSC) is the most common form of cancer in Australia. AZA may increase the risk of NMSC but there are no studies focusing on the risk of NMSC with AZA/6MP use in IBD. This study aimed to investigate the effect of AZA/6MP use in IBD patients and the development of NMSC. 200 patients are to be recruited from each of 4 specialist IBD centers in Brisbane (Bris) (latitude 27°25'S, with the highest UV index and the highest rate of NMSC in the world), Perth (latitude 31°57'S) and Adelaide (Ade) (latitude 34°52'S) with differing sunshine hours and UV indices, and Christchurch (CC), New Zealand (latitude 43°39'S) with the lowest UV index and sunshine hours. A validated questionnaire was completed by patients at each site. Patients were divided into 3 groups, 1. never taken or taken AZA/6MP for <3 months; 2. AZA/6MP for 3 months to 3 years and; 3. AZA/6MP for >3 years. Demographic data and data on ethnicity, occupation, risk factors for skin cancer, AZA/6MP dosage and metabolite levels, and number and type of skin cancers/lesions also obtained. To date 665 patients have returned the questionnaire. 58% were female, age 46.5 years +/- 15.4 years. 53% of patients in Bris, 46% in Ade, 31% in CC and 28% in Perth had skin lesions removed. Patients in Bris were significantly more likely to have lesions removed than patients in CC or Perth. No statistical differences were identified in the rate of melanomas, melanotic naevi, dysplastic naevi or solar keratoses. The rate of squamous cell carcinomas (SCC) was statistically greater in group 3 (5.4%) than group 1 (2.0%, p = 0.0001) or group 2 (2.1%, p = 0.001). Basal cell carcinomas were more common in group 3 than group 1 or 2, but did not reach significance. On this interim analysis, the risk for melanoma, dysplastic naevi, solar keratoses, melanotic naevi, and the percentage of patients with lesions removed is not increased with AZA/6MP use. The risk of SCCs is, however, increased in IBD patients taking AZA/6MP for >3 years.

Publication Types: Conference Abstract
PMID: 70440510


Inter-observer agreement for Crohn's disease sub-phenotypes using the Montreal classification: How good are we? A multi-centre Australasian study.
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Crohn's Disease (CD) exhibits significant clinical heterogeneity. Classification systems attempt to describe this; however, their utility and reliability is dependent on Inter-Observer Agreement (IOA). We therefore formally sought to evaluate IOA using the Montreal Classification (MC). Methods Data from 35 CD patients, diagnosed from January 2004 onwards, were randomly contributed from 6 Australian IBD centres (5-7 cases per site). De-identified records were presented to a panel of 13 expert practitioners from 8 member centres of the Australia and New Zealand Inflammatory Bowel Disease Consortium (ANZIBDC). The practitioners (clinicians and nurses) classified the cases using the MC and forwarded their data for central blinded analysis. Data on smoking, surgery, medications and a prediction for future disease outcome was also tested. IOA was evaluated using Kappa statistics, with pre-specified outcomes of > 0.8 excellent; 0.61-0.8 good; 0.41-0.6 moderate and <0.4 poor. Results: Of the 35 cases, 22(63%) were male, average age was 33 years (19-69) and 7 had resections, with average disease duration of 3.5 years (1-6). With regard to IOA at diagnosis: 10 complete rating sets are available on 27-35 subjects (missing data on some). Agreement was excellent for age (A1-A3), = 0.84; good for disease location (L1-L3), = 0.73; only moderate for disease behaviour (B1-B3), = 0.54; and good for the presence of perianal disease (p), = 0.6. At last follow-up, 9 complete rating sets are
IOA was good for disease location, \( = 0.68 \); and only moderate for disease behaviour, \( = 0.46 \); but excellent for the presence of perianal disease, \( = 0.88 \). IOA for the use of Immunosuppression ever during follow-up and for the presence of stricture were both good (\( = 0.79 \) and 0.64 respectively). Conclusion IOA is generally robust amongst this panel of experts; however some areas are less consistent than others. The reasons for this deserve further attention to ensure a uniform approach to classification or perhaps better initial recording of clinical data. Omissions and inaccuracies reduce the value of clinical data when comparing cohorts across different centres, and potentially impact on the ability to translate recent genetic discoveries into novel tools that aim to improve clinical practice.

Publication Types: Conference Abstract
PMID:70440548


**Genotype markers predict time to first resection in Crohn's disease patients.**
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Background: With the identification of many CD-associated SNPs from recent IBD genome-wide association studies, the most promising role for these genetic markers exists in prediction of disease course. Our aim in this study was to establish whether any CD-associated SNPs identified in recent IBD genome-wide association studies could predict time to first resection in a group of well-characterised CD patients from the Australian and New Zealand IBD Consortium (ANZIBDC).

Methods Molecular prediction of disease severity via time to first resection was assessed in a primary dataset of 320 CD cases from North Brisbane. We conducted variable selection of 104 SNPs using Random Survival Forest (RSF) and standard Random Forest (RF). We conducted Cox Proportional Hazards (CPH) models to survey time to first resection adjusting for age at diagnosis, sex and disease location. Further survival analyses using the ATG16L SNP rs2214880 was conducted on two replication datasets from the ANZIBDC. CD cases were phenotyped according to the Montreal classification. Genotyping was done using Sequenom technology and high resolution melt analysis (HRM). Results RF and RSF analyses identified four SNPs (rs2241880 [ATG16L1], rs9268877 [HLA-DRB1], rs9268480 [BTNL2], rs2542151 [PTPN2]) in common from the top 10 SNPs to predict resection. After adjustment for age, sex, and location, three SNPs remained significantly associated with time to resection (rare homozygous genotype rs2241880, \( P = 0.00036 \), rare homozygous genotype rs9268877, \( P = 0.05 \) and heterozygous genotype rs9268480, \( P = 0.05 \)). There was no additive effect from an individual having risk alleles from combinations of SNPs. Survival analysis of rs2241880 in replication datasets (Christchurch, Fremantle) did not reach significance. Conclusions: Three SNPs were associated with time to early CD surgery in a North Brisbane dataset. Lack of replication was due to cohort differences in genotype frequencies, possibly due to founder effects, and median time to surgery.

Publication Types: Conference Abstract
PMID:70440505


**An Australian single centre study evaluating the role of smoking in the phenotype and clinical course of Crohn's disease.**
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Of environmental factors, tobacco smoking is the most strongly implicated in the aetiology of Crohn's
disease (CD). Studies from the 1990s observed that smokers with CD experienced more clinical
relapses, increased complications and a greater need for surgery. Patient categorisation by the
Montreal classification, however, has suggested that smoking does not directly influence behavior of
CD or the need for surgery. The study aimed to further investigate the role of smoking in CD with
respect to Montreal disease classification at diagnosis, complications, medication use and need for
surgery. Methods: CD patients were assessed from a single specialist IBD centre. Demographic data
including Montreal classification at diagnosis and at last follow-up, medication use (steroids,
immunomodulators, anti-TNF alpha), surgical history and family history were recorded. A detailed
smoking history was collected including starting and stopping date. 'Ever smokers' was defined as
patients who have smoked >100 cigarettes in their life. Data were analysed using the statistical
software package SPSS for windows, version 15. Results: 194 smokers and 204 ever-smokers with
CD were included. Older age was found to be significantly associated with smoking status (p < 0.05).
In comparison to smokers, non smokers were statistically more likely to be on immunomodulators and
anti-TNF alpha but not on steroids. The need for initial surgery was not different between the
nonsmokers, exsmokers and current smokers. Current smokers were significantly more likely to have
stricturing (B2) disease compared to nonsmokers and exsmokers at last follow-up (p < 0.05). In
comparison to nonsmokers, significantly fewer people, who had ceased smoking more than 1 year
prior to CD diagnosis or within 1-year post diagnosis, had complicated disease (p < 0.05). Conclusions
Smoking impacts on progression to complicated disease. However with cessation of smoking even
within 1-year post diagnosis, fewer had complicated disease in comparison to non smokers.
Measuring tobacco exposure prior to diagnosis and afterward is essential to understanding disease
evolution with implications for counselling.
Publication Types: Conference Abstract
PMID:70440554

Co-regulation of fibrogenic and liver progenitor cell responses in pre- and post-liver transplant recurrent chronic hepatitis C infection.
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J.E.E. Tirnitz-Parker, Curtin University of Technology, Perth, WA, Australia

Background: There is co-regulation of fibrogenic and liver progenitor cell (LPC) responses in a range
of human chronic liver diseases including chronic hepatitis C virus (HCV) infection, which is the
commonest indication for orthotopic liver transplantation (OLT) in western countries. The aim of this
study was to determine whether LPCs are detected and associated with inflammation and accelerated
fibrosis progression in recurrent HCV disease following OLT. Methods: Liver biopsies were available
from 16 pre-OLT and 16 post-OLT subjects with chronic HCV. De-identified specimens underwent
blind evaluation following haematoxylin/eosin (histology) and Masson's trichrome staining (fibrosis) as
well as pan cytokeratin (LPCs) and CD45 (inflammation) immunohistochemistry. Fibrosis was scored
according to the Metavir system and digital whole slide scanning was conducted to evaluate numbers
of positively stained cells. Results: were expressed semiquantitatively using a 0-4+ scoring system
and confirmed by algorithmbased positive pixel count per area. Statistical analyses were conducted
using SPSS version 17. Results: In pre-OLT biopsies, the number of LPCs increased with advancing
fibrosis and inflammation. Seven of 16 pre-OLT subjects had severe F3 or F4 fibrosis and these had a median score of 4+ for numbers of CKpan+ LPCs. This was significantly higher (p = 0.012) than for subjects with only mild F0-F2 fibrosis, who showed a median score of only 2.5+ for LPC numbers. Increasing numbers of CD45+ cells were also associated with increasing LPC proliferation and fibrosis severity in pre-OLT livers. Similarly, in post-OLT subjects, increasing levels of inflammation and fibrosis were associated with increased numbers of LPCs. Five of 16 post-OLT subjects had severe F3 or F4 fibrosis and these had a median score of 3.5+ for CKpan+ LPCs. In contrast, post-OLT subjects with mild F0-F2 fibrosis had a significantly lower median score of 2.5+ for LPC proliferation (p = 0.019). Conclusion Hepatic fibrosis occurring in chronic HCV disease either before or after OLT is associated with increasing numbers of LPCs suggesting co-regulation of the fibrogenic and LPC responses. Thus, targeting of the LPC compartment after OLT might be a novel treatment strategy to prevent accelerated fibrosis progression to cirrhosis and hepatocellular carcinoma.

Publication Types: Conference Abstract
PMID:70440639

Mitigation of calcification and cytotoxicity of a glutaraldehyde-preserved bovine pericardial matrix: improved biocompatibility after extended implantation in the subcutaneous rat model.
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BACKGROUND AND AIMS OF THE STUDY: Implanted non-crosslinked tissues suffer rapid degeneration, shrinkage and absorption, whereas standard crosslinked tissues cause local cytotoxicity and calcification. Both approaches diminish implant capacity for long-term function. The study aim was to examine the tissue-engineered characteristics (cytotoxicity, calcification potential, biocompatibility) of bovine pericardium, crosslinked with a low concentration of glutaraldehyde (GA) followed by ADAPT anti-mineralization, following prolonged implantation in a subcutaneous rat model. METHODS: Bovine pericardium was decellularized with Triton X-100, deoxycholate, IgePal CA-630, and nucleases. The resulting matrices were allocated to: group I (control, n=10), crosslinked in 0.2% polymeric GA; and group II (treatment, n=10), crosslinked in 0.05% monomeric GA + ADAPT. Cytotoxicity was determined by in vitro cell seeding with human fibroblasts, and quantified using an Alamar Blue assay. The matrices were then implanted in a subcutaneous rat model and retrieved after extended implantation times (26 and 52 weeks). This was followed by further histology, immunohistochemical staining, and measurement of calcium deposition. RESULTS: Complete acellularity and biostability were significantly (p < 0.01) achieved in group II. Inflammatory responses were reduced and beneficial host cell infiltration with neocapillary formation was limited to group II. Fibroblast infiltration was significantly increased from six to 12 months’ implantation time. Only group II tested positive for Factor VIII and vimentin. After 52 weeks, extractable calcium levels were significantly (p < 0.001) reduced in group II (2.56 +/- 0.22 microg Ca/mg tissue) compared to group I (136.02 +/- 0.39 microg Ca/mg tissue). CONCLUSION: Acellular bovine pericardium, when crosslinked with a low concentration of GA and treated with ADAPT, retains and improves its integrity with a low immunoreactivity over a prolonged period. Host cell infiltration is also optimized over time. The maintenance of reduced calcification levels in group II suggests that such a biomaterial might have an advanced long-term in vivo potential.
PMID:21214104

Invading macrophages play a major role in the liver progenitor cell response to chronic liver injury.
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Background & Aims: Although a strong association between liver progenitor cells (LPCs) and inflammation exists in many chronic liver diseases, the exact role of the immune system in LPC-mediated hepatic regeneration remains unclear. A number of pro-inflammatory factors were identified in cytokine knockout mice in which the LPC response was attenuated but neither the mechanism nor the producing cells are known. Methods: To identify the critical immune cells and cytokines required in the LPC response, we compared two diet-induced models of liver injury with two recently established transgenic models of immune-mediated hepatitis. Results: Despite severe inflammation being observed in all models, the generation of LPCs was highly dependent on the cause and kinetics of liver damage. The LPC response was associated with an increase of macrophages and CD8<sup>+</sup> T cells but not natural killer cells. T cell-deficient mice were able to mount a LPC response, albeit delayed, suggesting that T cells are not essential. Mice mounting an LPC response showed elevated numbers of Kupffer cells and invading CX<sub>3</sub>CR1<sup>high</sup>CCR2<sup>high</sup> macrophages secreting persistent high levels of tumour necrosis factor alpha (TNFalpha), a major cytokine involved in the LPC response. Conclusions: Liver macrophages are an important determinant of LPC expansion during liver regeneration in models of diet- and immune-mediated liver injury. Invading macrophages in particular provide pro-mitogenic cytokines such as TNFalpha that underpin the process. LPC themselves are a source of chemokines (CCL2, CX<sub>3</sub>CL1) that attract infiltrating macrophages. 2010 European Association for the Study of the Liver. Published by Elsevier B.V. All rights reserved.

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Iron uptake from plasma transferrin by a transferrin receptor 2 mutant mouse model of haemochromatosis.

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BACKGROUND & AIMS: Hereditary haemochromatosis type 3 is caused by mutations in transferrin receptor (TFR) 2. TFR2 has been shown to mediate iron transport in vitro and regulate iron homeostasis. The aim of this study was to determine the role of Tfr2 in iron transport in vivo using a Tfr2 mutant mouse. METHODS: Tfr2 mutant and wild-type mice were injected intravenously with (59)Fe-transferrin and tissue (59)Fe uptake was measured. Tfr1, Tfr2 and ferroportin expression was measured by real-time PCR and Western blot. Cellular localisation of ferroportin was determined by immunohistochemistry. RESULTS: Transferrin-bound iron uptake by the liver and spleen in Tfr2 mutant mice was reduced by 20% and 65%, respectively, whilst duodenal and renal uptake was unchanged compared with iron-loaded wild-type mice. In Tfr2 mutant mice, liver Tfr2 protein was absent, whilst ferroportin protein was increased in non-parenchymal cells and there was a low level of expression in hepatocytes. Tfr1 expression was unchanged compared with iron-loaded wild-type mice. Splenic Tfr2 protein expression was absent whilst Tfr1 and ferroportin protein expression was increased in Tfr2 mutant mice compared with iron-loaded wild-type mice. CONCLUSIONS: A small reduction in hepatic transferrin-bound iron uptake in Tfr2 mutant mice suggests that Tfr2 plays a minor role in liver iron transport and its primary role is to regulate iron metabolism. Increased ferroportin expression due to decreased hepcidin mRNA levels is likely to be responsible for impaired splenic iron uptake in Tfr2 mutant mice. Copyright (c) 2009 European Association for the Study of the Liver. Published by Elsevier B.V. All rights reserved.
Teaching hand hygiene to medical students using a hands-on approach.
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Mediators of innate and adaptive immune responses differentially affect immune restoration disease associated with Mycobacterium tuberculosis in HIV patients beginning antiretroviral therapy.
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Background. Initiation of antiretroviral therapy (ART) in human immunodeficiency virus patients with treated or unrecognized Mycobacterium tuberculosis infection may result in tuberculosis-associated immune reconstitution inflammatory syndrome (TB-IRIS) or ART-associated tuberculosis (ART-TB), respectively. Both conditions appear to be immune restoration disease but their immunopathogenesis is not completely understood. Methods. Chemokines and cytokines produced by the innate immune system (CCL2, CXCL8, CXCL9, CXCL10, and interleukin 18 [IL-18]) were assayed in plasma from unstimulated whole blood cultures obtained from 15 TB-IRIS case patients, 11 ART-TB case patients, and matched control participants over 24 weeks of ART. Results. When compared with control participants, levels of IL-18 and CXCL10 were higher in TB-IRIS case patients (P = .002 and .006, respectively), whereas CCL2 was lower (P = .006). IL-18 level was higher in ART-TB case patients (P = .002), but CXCL10 was only marginally higher (P = .06). When TB-IRIS case patients were compared with ART-TB case patients, IL-18 was higher in ART-TB (P = .03), whereas CXCL10 was higher in TB-IRIS (P = .001). Using receiver operating characteristic curves, pre-ART levels of CCL2, CXCL10, and IL-18 were predictive of TB-IRIS and additive to IFN- responses. Conclusions. Perturbations of the innate immune response to M. tuberculosis before and during ART may contribute to the immunopathology of TB-IRIS, whereas elevated IL-18 alone suggests adaptive immune responses predominate in ART-TB. These findings may have implications for therapy in TB-IRIS. 2010 by the Infectious Diseases Society of America. All rights reserved.
Targeting the glycoprotein 130 receptor subunit to control pain and inflammation.


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The glycoprotein 130 (gp130) is a shared signal-transducing-membrane-associated receptor for several hematopoietic cytokines. Its activation is implicated in pain and in a variety of diseases via signaling of proinflammatory cytokines. These include interleukin-6 (IL-6) subfamily cytokines, many of which play important roles in the pathogenesis of diseases such as rheumatoid arthritis, Castleman's disease, and Kaposi's sarcoma. Several strategies have been developed to block gp130-receptor-mediated signaling. These include the application of monoclonal antibodies, the creation of mutant form(s) of the gp130 with increased binding affinity for such ligands as IL-6/sIL-6R complex, and the generation of antagonists by selective mutagenesis of the specific cytokine/gp130 receptor binding site(s). Other strategies include targeting gp130-mediated signaling pathways such as that involving signal transducer and activator of transcription-3. This review provides a summary of the latest research pertaining to the role of gp130 in the pathogenesis of inflammatory and other diseases in which the gp130 receptor is implicated. An overview of antagonists targeting the gp130 receptor is included with particular emphasis on their mechanism of action and their limitations and potential for therapeutic application.

Publication Types: Review
PMID:2010678531

Traps and pitfalls in cardiac CT.

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Cardiac computerised tomography has now become established as an essential part of the diagnostic armamentarium in the investigation of ischaemic and other heart disease. However, as with any investigation there are limitations with currently available technologies that can result in misdiagnosis. Angiographic pitfalls can be largely grouped into artefacts related to cardiac or respiratory motion, beam hardening and phasic changes in the coronary circulation. Pitfalls in functional assessment can result from irregular cardiac rhythm. The risk that these potential errors result in misdiagnosis can be minimised by recognition of the causes and careful performance of the study to avoid them. This review will highlight the significant potential traps and provide strategies to reduce the risk of such misdiagnosis.

Publication Types: Conference Abstract
PMID:70305682

Right paratracheal air cysts: Cases and literature review.

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Publication Types: Review
PMID:2010678531
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Learning objectives: To illustrate the CT signs of right paratracheal air cysts and review their pathology and clinical significance. Background: A right paratracheal air collection has been reported to be observed in 2% of CT scans. We do not infrequently observe these in our clinical practice. They are almost always an incidental finding. The literature and general knowledge concerning this entity is sparse. There are a few reports of histological examination of surgically resected cases, which have shown that they are lined by ciliated columnar epithelia and communicate with the tracheal lumen. Right paratracheal air cysts are located at the thoracic inlet. They are clinically associated with chronic cough, radiologically associated with emphysema and sabre trachea, and, pathologically associated with chronic tracheitis, which is a feature of chronic obstructive pulmonary disease (COPD). These associations suggest that raised intra-tracheal pressure is involved in their pathogenesis. The differential diagnosis of right paratracheal air cysts includes other air-filled paratracheal pathologies, such as pneumomediastinum, pneumothorax, laryngocoele, pharyngocoele, Zenker's diverticulum, apical hernia of lung, and apical paraseptal blebs or bullae. These can usually be readily distinguished from right paratracheal air cysts with CT. Rarely, they can become complicated by pooling of secretions, infection, compression of the recurrent laryngeal nerve and inadvertent endotracheal tube placement and perforation. Imaging findings: CT scans of the chest or neck demonstrate a small right posterolateral paratracheal air collection at the T1 - T3 level. This is best visualised on the lung window. Sub-millimetre sections may demonstrate a communication with the tracheal lumen. Dynamic CT scan shows expansion during expiration and contraction during inspiration. Associated radiologic findings include emphysema and sabre trachea. Conclusion: A small right paratracheal air collection at the level of the thoracic inlet is not infrequently observed on CT scans, and this poster shows cases and reviews the literature.

Publication Types: Conference Abstract
PMID:70305806

The CT anatomy of internal hernias.
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Learning objectives: To learn the CT anatomy of the peritoneum and mesentery. To understand the anatomical basis and CT signs of internal hernias. Background: An internal hernia is the pathological protrusion of a viscus through a congenital or acquired peritoneal or mesenteric opening into an intra-abdominal compartment. The most common internal hernia is a paraduodenal hernia, followed by periceacal, Foramen of Winslow, and transmesenteric hernia. Other types of internal hernia are rare. Clinically, they may be silent, or present with abdominal pain and intestinal obstruction. A delay in diagnosis may result in strangulation and infarction. Historically, pre-operative investigation has been with radiographs and endoluminal contrast studies. CT scan can provide a preoperative diagnosis, or suggest the diagnosis. CT interpretation requires knowledge of the anatomy of the peritoneum, the characteristic locations of internal hernias, and the CT signs. Imaging findings: The CT findings of internal hernias include small bowel obstruction, the gathering of dilated bowel loops in an abnormal location, and abnormalities of the vascular pedicle. The CT findings will be illustrated on CT reformations as well as axial images. Conclusion: This poster illustrates and explains the anatomical basis of internal hernias as demonstrated on CT scan.
Publication Types: Conference Abstract
PMID:70305816

Transperineal ultrasound in evaluation of urethral diverticulae.
Learning objectives: To compare MRI with transperineal ultrasound in the evaluation of suspected urethral diverticulae. Background: Urethral diverticulae are estimated to occur in 1-6% of women. These are usually diagnosed between the 3rd and the 5th decade. Urethral diverticulae can be asymptomatic, but symptoms usually include: urinary frequency, urgency, dysuria, post-void dribbling and dyspareunia. Presentation may also occur following the finding of a palpable mass. It is thought that urethral diverticulae develop secondary to repeated infections and obstruction of the periurethral and urethral glands. The infection results in cyst or abscess formation. These eventually rupture into the urethral lumen and remain as an outpouching which epithelialises to become a true diverticulum. Rare congenital cases are thought to be the remnants of Gartner duct cysts. 90% of urethral diverticulae open into the distal 2/3 of the urethra, most commonly at the posterolateral wall of the mid urethra. Diagnosis can be difficult, particularly in view of the relatively non-specific symptoms. Investigations include voiding cystourethrography (VCUG) and MRI. VCUG is an invasive procedure and MRI is not always easily accessible and can be expensive. Transperineal ultrasound is a further technique which can be used to identify urethral diverticulae. This is a non-invasive and cheap investigation and is well tolerated by the patients. As with MRI, transperineal ultrasound has the added benefit of further evaluating peri-urethral masses shown not to be diverticulae. The differential for a peri-urethral mass would include: vaginal wall cyst, Skene's gland abscess, ectopic ureterocele or peri-urethral fibrosis. We have reviewed cases of suspected urethral diverticulae and performed both MRI and transperineal ultrasound for comparative purposes. Imaging findings or procedure details: Transperineal ultrasound, in the cases reviewed, showed good correlation with MRI in evaluating for urethral diverticulae, and for evaluation of peri-urethral masses. A selection of the cases will be presented and the images compared. Conclusion: Transperineal ultrasound showed good correlation with the findings at MRI with regards to peri-urethral imaging. It is suggested that initial investigation of suspected urethral diverticulae or peri-urethral abnormality be performed with transperineal ultrasound. This technique is non-invasive and acceptable to the patients and less costly than MRI.

Publication Types: Conference Abstract
PMID:70305842

The role of delayed-enhancement MRI (DE-MRI) in the assessment of myocardial viability.
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A. Gupta, Fremantle Hospital, Fremantle, WA, Australia
Learning objectives: To understand the physics, technical factors, physiology, image interpretation, and clinical utility of DE-MRI in the assessment of myocardial viability prior to coronary artery revascularisation. Background: Historically, improvement in left ventricular function following coronary artery revascularisation has been a measure of myocardial viability. DE-MRI demonstrates viable myocardium corresponding to areas of contractile dysfunction pre-operatively, and these patients receive the greatest benefit from coronary artery revascularisation. DE-MRI images are acquired ten minutes following the injection of gadolinium, using an ECG-gated segmented gradient-recalled echo sequence with an inversion recovery pre-pulse. Imaging findings: The DE-MRI sequence is T1 weighted. The inversion time is set so that signal from normal myocardium is nulled. Acute and old myocardial infarction both demonstrate high signal. The exception to this rule is 'no reflow', which is infarcted myocardium that has microvascular occlusion; matched first-pass perfusion images show a corresponding perfusion defect. Delayed enhancement that involves the subendocardium and conforms to a vascular territory allows differentiation from non-ischaemic causes of myocardial damage. DE-MRI images are acquired as a stack of short axis views, as well as long axis views, and these are interpreted alongside matched CINE images. CINE images show left ventricular function. Stunned myocardium and hibernating myocardium have impaired function and are viable. Stunned
myocardium has normal perfusion and is the result of a recent brief ischaemic episode. Hibernating myocardium has chronic hypoperfusion and ischaemia with sufficient blood flow to maintain viability. Stunned myocardium and hibernating myocardium appear viable on DE-MRI. In patients with infarcted myocardium, DE-MRI shows the transmural extent of infarction, which has an inverse correlation with recovery of contractile function following revascularization. Conclusion: DE-MRI provides pre-operative assessment of myocardial viability, and identifies patients who would benefit from revascularization.

Publication Types: Conference Abstract
PMID:70305849

Case report - Aberrant postero-inferior middle turbinate.
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Learning objectives: To describe a rare case of variant turbinate anatomy. Background: Many variations of the turbinates have been described. These can contribute to chronic or recurrent rhinosinusitis, apparent masses, or epistaxis. Nasoseptal and sinus embryology is complex. Common variations will be discussed. Imaging findings: Non contrast CT examination of the sinuses revealed a left middle turbinate without the normal lateral nasal wall attachment, and therefore lack of a left middle meatus. The aberrant middle turbinate had an abnormal posterior lateral nasal wall attachment, curving postero-inferiorly to extend into the left nasopharynx. The turbinate was covered in thick, nodular mucosa, and may have caused intermittent obstruction to nasopharyngeal drainage. The patient had presented with recurrent epistaxis, presumably from the thickened aberrant turbinate mucosa. Conclusion: Naso-septal variations are common, but we present a rare variation, with only one previous case in the literature. Appreciation for variant anatomy is important to identify potential causes of obstruction, identify possible surgical approaches, and to differentiate variant anatomy from true neoplastic lesions.

Publication Types: Conference Abstract
PMID:70305852

A new view of lobar collapse.
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Learning objectives: To understand the radiographic signs of lobar collapse and its causes by illustration and description of multidetector CT (MDCT) reformations. Background: The radiographic signs of lobar collapse are fundamental to interpretation of the chest radiograph. A CT scan is a powerful teacher of anatomy and radiographic signs. An image that looks like a chest radiograph can be generated from a MDCT scan of the chest using post-processing software. The generated radiograph looks identical to a conventional radiograph, except for minor differences related to supine position and absence of magnification effects. Imaging findings: PA and lateral chest radiographs have been generated from MDCT scans of lobar collapse using post-processing software. The PA radiograph has been compared with coronal CT sections, and the lateral radiograph has been compared with sagittal CT sections to illustrate radiographic signs. The CT sections have been presented with lung windows to show radiopacity of the collapsed lobe(s), hyperexpansion of uninvolved lobes, fissural displacement and reorientation, and the direction of collapse; mediastinal windows or maximum intensity projection (MIP) images to show mediastinal shift, hiliar displacement and ipsilateral elevation of the diaphragm; MIP images to show crowding or paucity of vascular markings and the silhouette sign; minimum intensity projection (MinIP) images to show tracheal
deviation, crowding of bronchi and bronchial reorientation; and, volume rendered images to show ipsilateral reduction in size of the rib cage. Multiplanar reformations (MPRs) have also been used. Conclusion: A MDCT scan of lobar collapse can be viewed with postprocessing software to generate an image that resembles a PA chest radiograph and lateral chest radiograph. The post-processing software also allows coronal and sagittal CT sections to be viewed with different techniques to illustrate and explain radiographic signs. This poster also discusses the causes of collapse, and radiographic and clinical nuances.

Publication Types: Conference Abstract
PMID:70305860

CT knee arthrography: A pictorial review of pathology, pitfalls and correlation with MRI.
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Learning Objectives: 1. Learn the technique of CT knee arthrography. 2. Know the strengths and weaknesses of CT knee arthrography compared with MRI. 3. Be able to recognise normal variants that can mimic pathology. 4. Be able to recognise common pathology of cartilage, menisci, ligaments and bone. Background: CT knee arthrography remains a common imaging technique used in Australia. Although this is partly because of limited access to MRI scans, it is also a useful imaging modality in its own right and even has advantages over MRI in some instances. It is commonly reported by both the general and musculoskeletal radiologist and is therefore an important skill to master. Details: 1. The technique of CT knee arthrography will be outlined. 2. Normal variants that can mimic pathology. 3. Examples of pathology involving cartilage, menisci, ligaments and bone. 4. Common pitfalls. 5. The post operative knee. 6. Strengths and weaknesses when compared with MRI. Cases with MRI correlation will be shown. Conclusion: CT knee arthrography is a commonly used imaging technique. This exhibit will enable the reader to improve the quality of their scan, quality of their report and know its strengths and weaknesses when compared with MRI.

Publication Types: Conference Abstract
PMID:70305748

Junior doctors' perceptions regarding patient consent for common medical imaging investigations.
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Purpose: To review pre-vocational (junior) doctors' perceptions regarding patient consent to commonly requested medical imaging investigations. Further, to seek recommendations for further postgraduate education initiatives regarding radiation dose and consent with a structured questionnaire. Methods and materials: An anonymous questionnaire was distributed to junior medical doctors working at two metropolitan hospitals in Western Australia. Participants were asked to comment on the practice of informed consent, barriers to gaining consent and perceptions of the amount of radiation associated with commonly requested imaging investigations. International Commission for Radiological Protection1 estimations were used for radiation dose reference. Qualitative and quantitative data were analysed utilising SPSS software. Results: A response rate of 32% (n = 51) from 160 distributed questionnaires was achieved, of which 2 were excluded. 29% (n = 14) of respondents estimated the approximate dose associated with each investigation, 39% (n = 19) significantly underestimated the dose and 15% (n = 7) overestimated the dose significantly. Of note 18% (n = 9) of respondents incorrectly reported radiation dose associated with MRI and/or ultrasound. Only 12% (n = 6) of participants 'usually' or 'always' consented patients in regards to radiation risks associated with
39% (n = 19) of participants noted barriers to informed consent including that 'I don'\textquoteleft{}t understand the risks', 'the patient is too unwell to comprehend' and that the 'radiographer/radiologist should explain the risk'. 77% (n = 38) favoured further postgraduate education and 47% (n = 23) made specific recommendations, the most popular of which was a tutorial in regards to radiation dose from medical imaging. Conclusion: Results indicate that junior doctors are unfamiliar with the radiation dosage associated with imaging investigations, a conclusion supported by current literature\(^2,3,4,5,6\), and that they welcome further educational interventions. Additionally the need for discussion regarding the appropriateness of, and barriers to, informed consent of patients is also highlighted.

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**Complex EVARS where are we.**

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The EVAR I trial confirmed the efficacy of endoluminal repair of Abdominal Aortic Aneurysms (AAA). However approximately only 50 % of AAA are suitable for standard endoluminal repair mainly due to unsuitable infrarenal neck anatomy. In the late 1990s the development of fenestrated endoluminal grafts allowed treatment of AAAs with short infrarenal necks by extending the landing zone above the renal arteries. Major advances have taken place in the interim 10 years with gradual progression and sophistication of endoluminal techniques to allow total endoluminal repair of thoraco abdominal aneurysms with branched and/or fenestrated grafts incorporating all 4 major visceral vessels. The final frontier for endoluminal repair is the arch of the aorta and early experience in this area will also be discussed.

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**Interventional radiology in abdominal trauma.**

Van Schie G.

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Interventional Radiology plays an important role in the multidisciplinary management of abdominal trauma. In the management of arterial bleeding from unstable pelvic fractures the role is now reasonably established. Embolisation is also having an increasing role in the management of haemorrhage from Hepatic, Splenic and Renal lacerations, extending the range of conservative management of such patients and reducing the frequency of emergency laparotomies. The role of Interventional Radiology in each of these areas will be reviewed, with emphasis on indications and technique, illustrated by case examples, along with a review of relevant literature.

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**Non-variceal G.I. bleeding: Role of intervention.**

Van Schie G.

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Angiography with embolisation where possible and appropriate is an important and accepted part of the multidisciplinary management of non-variceal gastrointestinal bleeding. There is however little in the way of consensus or evidence based guidelines as to the use and timing of interventions, with practice varying according to local expertise and equipment. Even within an institution the algorithm can vary according to whether the patient comes to the Interventional Radiologist via a surgical or gastrointestinal route. Differences also exist between the upper and lower gastrointestinal tract, and between acute and chronic (obscure) bleeding. The presentation will attempt to review literature and guidelines to suggest a practical approach to the interventional management of gastrointestinal haemorrhage, illustrated by relevant case examples.

Publication Types: Conference Abstract
PMID:70305774


The tail end: Rectal cancer imaging.

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Rectal cancer is staged locally using a combination of clinical examination, endorectal ultrasound (EUS) and pelvic MRI. Metastatic spread is assessed with CT. PET and liver MRI may provide problem solving. Staging is according to the TNM classification. For malignancy contained to the mesorectum, local recurrence is more likely when the tumour lies within 1 mm of the circumferential resection margin (CRM). This is the plane of surgical dissection along the mesorectal fascia. Patients with a potentially involved CRM need to be identified preoperatively, so that they can be treated with chemoradiotherapy in an attempt to downstage the tumour. Some centres modify both the type and duration of preoperative treatment, dependent on whether the tumours are staged as early (just penetrating through the muscularis propria layer) or late (involving the CRM) T3, and others do not. This may place greater reliance on imaging staging differentiating T2 versus T3 disease. Imaging has proven useful for preoperative staging, but there are a number of further difficulties encountered viz. tumours that are small, low or anterior and identification of tumour nodal involvement. The role of diffusion weighted imaging, restaging following preoperative chemoradiotherapy and assessment of suspected local recurrence has also not been established.

Publication Types: Conference Abstract
PMID:70305782


Immune restoration disease associated with Leishmania donovani infection following antiretroviral therapy for HIV infection.

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Immune restoration disease following antiretroviral therapy for human immunodeficiency virus infection can cause significant morbidity and mortality. We describe the dramatic clinical course of an human immunodeficiency virus-infected patient who developed severe immune restoration disease associated with Leishmania donovani infection in a non-endemic area of the world. It highlights the need to consider previous travel history when screening for opportunistic infections before starting antiretroviral therapy, and demonstrates the effectiveness of corticosteroid therapy for life-threatening immune restoration disease.

PMID:20434127
Anticholinergic activity and cognitive decline in Parkinson's disease.
Starkstein SE.
Publication Types: Comment
PMID:20145024

Anosognosia is a significant predictor of apathy in Alzheimer's disease.
Starkstein SE, Brockman S, et al.
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Anosognosia and apathy are among the most common behavioral and psychological disorders of Alzheimer's disease and are significantly associated in cross-sectional studies. The aim for this study was to carry out for the first time a longitudinal assessment of this association with the aim of clarifying the predictive role between anosognosia and apathy in Alzheimer's disease. A consecutive series of 213 patients with probable Alzheimer's disease were assessed for the presence of apathy and anosognosia using a specific neuropsychiatry assessment. One hundred fifty four of the patients (72%) had a follow-up assessment between 1 and 4 years after the baseline evaluation. Patients with anosognosia at baseline had a significant increase in apathy scores during follow-up relative to patients without anosognosia at both assessments. Conversely, patients with or without apathy had an increase of similar magnitude in anosognosia scores. In conclusion, anosognosia is a significant predictor of apathy in Alzheimer's disease. This may be related to a specific pattern of progression of neuropathology and/or to poor adjustment of Alzheimer's disease patients with poor insight into their functional deficits.
PMID:21037121

Tardive oculogyric crisis associated with amisulpride monotherapy.
Mendhekar DN, Lohia D, et al.
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D. N. Mendhekar, Department of Neuropsychiatry, Headache Clinic, 10867 Pratap Nagar, New Delhi, India. E-mail: dnmendhekar@vsnl.net
Oculogyric crisis (OGC) is a dystonic and distressing side-effect which occurs immediately after the administration of high-potency antipsychotic drugs and is usually reported as a subtype of dystonia. We report a case of a young woman with schizophrenia who presented with tardive OGC related to amisulpride.
PMID:2010575338

Oculogyric crisis (OGC) is a dystonic and distressing side-effect which occurs immediately after the administration of high-potency antipsychotic drugs and is usually reported as a subtype of dystonia. We report a case of a young woman with schizophrenia who presented with tardive OGC related to amisulpride.
PMID:2010575338
Australia’s health libraries: A research-directed future.


Health Libraries Australia, a group from the Australian Library and Information Association, is currently undertaking a research project to determine the future requirements for the health librarian workforce in Australia. The study has yielded an in-depth literature review exploring the Australian health care system and health library sector and international trends in health libraries that may impact Australian health librarian education. It has also produced surveys of Australian health librarians and health library managers. This article reviews the first stage of the project. The data will provide a solid foundation for development of the next phase of the project—scoping a structured, modular education framework for postgraduate qualifications in health librarianship and an ongoing continuing professional development structure.

Clinical and parasitological response to oral chloroquine and primaquine in uncomplicated human Plasmodium knowlesi infections.

Daneshvar C, Davis TME, et al.

Background. Plasmodium knowlesi is a cause of symptomatic and potentially fatal infections in humans. There are no studies assessing the detailed parasitological response to treatment of knowlesi malaria infections in man and whether antimalarial resistance occurs. Methods. A prospective observational study of oral chloroquine and primaquine therapy was conducted in consecutive patients admitted to Kapit Hospital, Sarawak, Malaysian Borneo with PCR-confirmed single P. knowlesi infections. These patients were given oral chloroquine for three days, and at 24 hours oral primaquine was administered for two consecutive days, primarily as a gametocidal agent. Clinical and parasitological responses were recorded at 6-hourly intervals during the first 24 hours, daily until discharge and then weekly to day 28. Vivax malaria patients were studied as a comparator group. Results. Of 96 knowlesi malaria patients who met the study criteria, 73 were recruited to an assessment of the acute response to treatment and 60 completed follow-up over 28 days. On admission, the mean parasite stage distributions were 49.5%, 41.5%, 4.0% and 5.6% for early trophozoites, late trophozoites, schizonts and gametocytes respectively. The median fever clearance time was 26.5 [inter-quartile range 16-34] hours. The mean times to 50% (PCT<sub>50</sub>) and 90% (PCT <sub>90</sub>) parasite clearance were 3.1 (95% confidence intervals [CI] 2.8-3.4) hours and 10.3 (9.4-11.4) hours. These were more rapid than in a group of 23 patients with vivax malaria 6.3 (5.3-7.8) hours and 20.9 (17.6-25.9) hours; P = 0.02). It was difficult to assess the effect of primaquine on P. knowlesi parasites, due to the rapid anti-malarial properties of chloroquine and since primaquine
was administered 24 hours after chloroquine. No P. knowlesi recrudescences or re-infections were detected by PCR. Conclusions. Chloroquine plus primaquine is an inexpensive and highly effective treatment for uncomplicated knowlesi malaria infections in humans and there is no evidence of drug resistance. Further studies using alternative anti-malarial drugs, including artemisinin derivatives, would be desirable to define optimal management strategies for P. knowlesi. 2010 Daneshvar et al; licensee BioMed Central Ltd. PMID:2010486233

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**Parameterization of high magnetic field gradient fractionation columns for applications with Plasmodium falciparum infected human erythrocytes.**

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**Background:** Magnetic fractionation of erythrocytes infected with Plasmodium falciparum has several research uses including enrichment of infected cells from parasite cultures or enhanced detection of P. falciparum gametocytes. The aim of the present study was to quantitatively characterize the magnetic fractionation process and thus enable optimization of protocols developed for specific uses. **Methods.** Synchronized cultures of P. falciparum parasites incubated with human erythrocytes were magnetically fractionated with commercially available columns. The timing of the fractionation experiments was such that the parasites were in second half of their erythrocytic life cycle with parasite densities ranging from 1 to 9%. Fractionations were carried out in a single pass through the columns. Cells were enumerated and differentiated in the initial samples as well as in the positive and negative fractions. The capture of cells by the fractionation column was described by a saturation binding model. **Results:** The magnetic binding affinity to the column matrix was approximately 350 times greater for infected cells compared with uninfected cells. The purity of infected cells in the captured fraction was generally >80% but decreased rapidly (to less than 50%) when the number of infected cells that passed through the column was substantially decreased (to less than 9.5 x 10^5 cells). The distribution of captured parasite developmental stages shifted to mature stages as the number of infected cells in the initial samples and flow rate increased. The relationship between the yield of infected cells in the captured fraction and flow rate of cells conformed to a complementary cumulative log-normal equation with flow rates >1.6 x 10^5 cells per second resulting in yields <50%. **Conclusions:** A detailed quantitative analysis of a batchwise magnetic fractionation process for malaria infected erythrocytes using high gradient magnetic fractionation columns was performed. The models applied in this study allow the prediction of capture efficiency if the initial infected cell concentration and the flow rate are known. 2010 Karl et al; licensee BioMed Central Ltd. PMID:2011513872


**Precocious bilateral hip joint osteoarthritis is a "form-fruste" of the arthropathy of hereditary haemochromatosis.**

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Osteoarthritis (OA) of the hip joint is a common disorder, especially in aging peoples of Caucasian descent. Hip OA like OA in other joints is heterogeneous and may manifest in early or late adult life. The aetiology of early onset (precocious) bilateral hip OA is poorly understood, but the clinical and
radiological characteristics of this form of OA suggest that chondral resorption due to biochemical or metabolic factors is likely to be of pre-eminent importance. The hip arthropathy which occurs in Hereditary Haemochromatosis (HH) and the ostensibly idiopathic precocious bilateral concentric form of hip OA are virtually indistinguishable. Accordingly, the possibility exists that the causal factors for these conditions may be very similar. On the basis of this premise and in the light of the finding in a small observational study that HFE gene mutations are very common in precocious bilateral hip OA (100% amongst 8 sequentially collected patients), it is hypothesised that precocious bilateral hip OA is a "form-fruste" of the arthropathy of HH in which HFE gene mutation mediated articular iron deposition in hip joint tissues may be of pivotal pathogenetic importance. Confirmation of this hypothesis could have implications for the prevention and strategic medical management of this form of OA. (c) 2009 Elsevier Ltd. All rights reserved.


Rosiglitazone and cardiovascular disease revisited.
Davis TME, Prins JB.
Publication Types: Editorial
PMID:20678037

Straight from the crocodile's mouth.
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PMID:21143069

A multilevel analysis of three randomised controlled trials of the Australian Medical Sheepskin in the prevention of sacral pressure ulcers.
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Objective: To assess the effectiveness of the Australian Medical Sheepskin in preventing sacral pressure ulcers (PUs), based on combined data from existing published trials. Design and setting: Data from two randomised controlled trials (RCTs) among Australian hospital patients and one RCT among Dutch nursing home patients were pooled, comprising a total population of 1281 patients from 45 nursing wards in 11 institutions. These data were analysed in two ways: with conventional meta-analysis based on the published effect sizes; and with multilevel binary logistic regression based on the combined individual patient data. In the multilevel analysis, patient, nursing ward and institution were used as levels and we controlled for sex, age, PU risk and number of days of observation. Main outcome measure: Incidence of sacral PUs. Results: Overall, the incidence of sacral PUs was 12.2% in the control group versus 5.4% in the intervention group with an Australian Medical Sheepskin. Conventional metaanalysis showed significantly reduced odds of developing a PU while using the
sheepskin (odds ratio [OR], 0.37 [95% CI, 0.17-0.77]). Multilevel analysis gave an OR of 0.35 and narrowed the confidence interval by almost 50% (95% CI, 0.23-0.55). Conclusions: These analyses of pooled data confirm that the Australian Medical Sheepskin is effective in preventing sacral PUs. Multilevel analysis of individual patient data gives a more precise effect estimate than conventional meta-analysis.

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Diagnosis and management of iron deficiency anaemia: A clinical update.
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* Iron deficiency anaemia (IDA) remains prevalent in Australia and worldwide, especially among high-risk groups. * IDA may be effectively diagnosed in most cases by full blood examination and serum ferritin level. Serum iron levels should not be used to diagnose iron deficiency. * Although iron deficiency may be due to physiological demands in growing children, adolescents and pregnant women, the underlying cause(s) should be sought. * Patients without a clear physiological explanation for iron deficiency (especially men and postmenopausal women) should be evaluated by gastroscopy/colonoscopy to exclude a source of gastrointestinal bleeding, particularly a malignant lesion. * Patients with IDA should be assessed for coeliac disease. * Oral iron therapy, in appropriate doses and for a sufficient duration, is an effective first-line strategy for most patients. * In selected patients for whom intravenous (IV) iron therapy is indicated, current formulations can be safely administered in outpatient treatment centres and are relatively inexpensive. * Red cell transfusion is inappropriate therapy for IDA unless an immediate increase in oxygen delivery is required, such as when the patient is experiencing end-organ compromise (eg, angina pectoris or cardiac failure), or IDA is complicated by serious, acute ongoing bleeding. * Consensus methods for administration of available IV iron products are needed to improve the utilisation of these formulations in Australia and reduce inappropriate transfusion. * New-generation IV products, supported by high-quality evidence of safety and efficacy, may facilitate rapid administration of higher doses of iron, and may make it easier to integrate IV iron replacement into routine care.

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* Pancreatic exocrine insufficiency (PEI) occurs when the amounts of enzymes secreted into the duodenum in response to a meal are insufficient to maintain normal digestive processes. * The main clinical consequence of PEI is fat maldigestion and malabsorption, resulting in steatorrhoea. * Pancreatic exocrine function is commonly assessed by conducting a 3-day faecal fat test and by measuring levels of faecal elastase-1 and serum trypsinogen. * Pancreatic enzyme replacement therapy is the mainstay of treatment for PEI. * In adults, the initial recommended dose of pancreatic enzymes is 25 000 units of lipase per meal, titrating up to a maximum of 80 000 units of lipase per meal. * In infants and children, the initial recommended dose of pancreatic enzymes is 500 units of lipase per gram of dietary fat; the maximum daily dose should not exceed 10 000 units of lipase per kilogram of bodyweight. * Oral pancreatic enzymes should be taken with meals to ensure adequate mixing with the chyme. * Adjunct therapy with acid-suppressing agents may be useful in patients who continue to experience symptoms of PEI despite high-dose enzyme therapy. * A dietitian experienced in treating PEI should be involved in patient management. * Dietary fat restriction is not recommended for patients with PEI. * Patients with PEI should be encouraged to consume small, frequent meals and to abstain from alcohol. * Medium-chain triglycerides do not provide any clear nutritional advantage over long-chain triglycerides, but can be trialled in patients who fail to gain or to maintain adequate bodyweight in order to increase energy intake.

Population-based observational study of claudication in older men: the Health in Men Study.


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OBJECTIVES: To assess the prevalence of and risk factors for claudication and its association with subsequent cardiovascular events. DESIGN, SETTING AND PARTICIPANTS: Observational cohort study of 12 203 Western Australian men aged 65 years and over, recruited from 1996 to 1999, and followed up from 2001 to 2004. MAIN OUTCOME MEASURES: Prevalence of claudication and incidence of peripheral arterial disease (PAD); risk factors for claudication and its association with subsequent cardiovascular events. RESULTS: The prevalence of claudication was 5.3% (638 of 11 970 men). At follow-up, after exclusion of 148 men with claudication at baseline and 76 with missing data at follow-up, the crude average annual incidence of new PAD (claudication or procedure for PAD) was 0.85% (95% CI, 0.72%-0.96%). The risk factors for prevalent claudication and incident PAD were similar, with age, smoking, hypertension, diabetes and history of cardiovascular disease dominating. Of the men with claudication at baseline, nearly half (47.5%; 303 of 638) were not taking aspirin. At follow-up, 42.5% (82 of 193) of the men with incident PAD were not taking aspirin. Claudication at baseline was associated with twice the risk of cardiovascular death (hazard ratio, 2.00; 95% CI, 1.52-2.64). There was a J-shaped relationship between aortic diameter, and both prevalent claudication and subsequent cardiovascular events. CONCLUSIONS: Among older men, claudication is prevalent.
and is associated with factors that can still be modified in older age, including smoking, exercise and diet. Relatively few men with claudication or at risk of PAD use aspirin. Claudication is a significant predictor of cardiovascular outcome.

PMID:20528717

Effect of ankle taping on knee and ankle joint biomechanics in sporting tasks.
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INTRODUCTION: Prophylactic taping is commonly used to prevent ankle injuries during sports. However, unnatural constraint of the ankle joint may increase the risk of injury to proximal joints such as the knee. The association between ankle taping and knee joint loading during open sporting tasks has not been quantified. This research aimed to measure changes in knee and ankle kinetics and kinematics during dynamic athletic activities undertaken with and without ankle tape. METHODS: A kinematic and inverse dynamics model was used to determine ankle and knee joint motion and loading in 22 healthy male participants undertaking running and sidestepping tasks. Both tasks were randomized to planned and unplanned conditions and undertaken with and without the use of ankle tape. RESULTS: At the knee, peak internal rotation moments (P < 0.001) and peak varus moments (P < 0.05) were significantly reduced during all running and sidestepping trials (planned and unplanned) when undertaken with ankle tape. Internal rotation impulse (P < 0.001) was reduced for sidestepping tasks. Varus impulse during unplanned sidestepping maneuvers (P = 0.04) was reduced with the use of ankle tape. However, there was a trend toward increased valgus moments and impulse for planned sidestepping trials undertaken with ankle tape (P = 0.056). Taping reduced the range of motion at the ankle in all three planes (P < 0.05). Peak inversion (P < 0.001) was reduced for running trials only. Average eversion and peak dorsiflexion moments were significantly reduced in sidestepping tasks by use of taping. CONCLUSIONS: By limiting motion at the ankle, taping increased mechanical stability at this joint. Ankle taping also provided protective benefits to the knee via reduced internal rotation moments and varus impulses during both planned and unplanned maneuvers. Medial collateral and anterior cruciate ligament injuries may, however, occur through increased valgus impulse during sidestepping undertaken with ankle tape.

Publication Types: Research Support, Non-U.S. Gov't
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An approach to the patient with bloody diarrhoea.
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Publication Types: Short Survey
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Genome-wide meta-analysis increases to 71 the number of confirmed Crohn’s disease susceptibility loci.
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d'Investigacio Biomedica August Pi i Sunyer (IDIBAPS),
We undertook a meta-analysis of six Crohn's disease genome-wide association studies (GWAS) comprising 6,333 affected individuals (cases) and 15,056 controls and followed up the top association signals in 15,694 cases, 14,026 controls and 414 parent-offspring trios. We identified 30 new susceptibility loci meeting genome-wide significance (P < 5 x 10^-8). A series of in silico analyses highlighted particular genes within these loci and, together with manual curation, implicated functionally interesting candidate genes including SMAD3, ERAP2, IL10, IL2RA, TYK2, FUT2, DNMT3A, DENND1B, BACH2 and TAGAP. Combined with previously confirmed loci, these results identify 71 distinct loci with genome-wide significant evidence for association with Crohn's disease.

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Pre-transplant pharmacokinetic profiling and tacrolimus requirements post-transplant.
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Aim: To determine the proportion of patients achieving tacrolimus whole-blood concentrations of >=10 ng/mL within 3 days of kidney transplantation, after randomization either to standard dosing (control group) or post-transplantation dosing guided by a 2-hour (C(2)) level following a preoperative tacrolimus dose (T2 group). Methods: The first postoperative tacrolimus dose was given either according to standard care (control group) or 0.15 mg/kg b.d. if the pre-transplant C(2) level was <=20 ng/mL, 0.1 mg/kg b.d. if the C(2) level was 21-59 ng/mL or 0.05 mg/kg b.d. if the C(2) level was >=60 ng/mL (T2 group). Subsequent dosing in both groups was based upon tacrolimus trough level monitoring. Participants received concomitant mycophenolate mofetil and steroids. Results: Ninety patients were recruited, of which 84 were included in the analysis (control group n=43; T2 group n=41). There was no difference in the proportion of subjects achieving tacrolimus trough levels >=10 ng/mL (82.9% Control vs 93.0% T2; P=0.19) or between 10 and 15 ng/mL (41.5% Control vs 41.9%
T2; P=0.97) at day 3 post transplant. The T2 group achieved tacrolimus trough levels of >=10 ng/mL significantly faster than the control group (100% achievement in 14 days (Control) versus 4 days (T2); P=0.01). CONCLUSION: Performing a pre-transplant tacrolimus C(2) does not significantly increase the high proportion of subjects achieving 10 ng/mL tacrolimus concentrations by day 3 using routine protocols. However, compared with standard care, performing a pre-transplant tacrolimus C(2) does lead to patients achieving a whole-blood concentration of >=10 ng/mL sooner. [copyright sign] 2010 The Authors. Nephrology [copyright sign] 2010 Asian Pacific Society of Nephrology.

Cumulative iron dose, but not high serum ferritin predicts liver iron overload in ESKD patients on dialysis.
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Aim: To assess whether liver iron concentration (LIC) is best predicted by ferritin, transferrin saturation (TSAT) or cumulative iron dose (CID) in end-stage kidney disease (ESKD) patients with high serum ferritin. Background: Maintenance parenteral iron is frequently used in anaemia of ESKD and guidelines recommend withholding iron therapy when serum ferritin is >500 mug/l. However, the debate over the upper limit of a safe serum ferritin level remains unresolved. Methods: LIC was assessed non-invasively using magnetic resonance imaging (FerriScan) and compared to conventional serum iron-markers in 15 ESKD patients who were on chronic haemodialysis, were receiving maintenance parenteral iron and had serum ferritin levels of >500 mug/l. Results: Mean duration of dialysis was 940 +/- 417 days and the mean cumulative dose of intravenous iron 6560 +/- 3098 mg. Mean TSAT was 31 +/- 10%, serum ferritin 781 +/- 169 mug/l and LIC 81 +/- 58 mumol/g. LIC correlated with CID (R<sup>2</sup> = 0.44, P < 0.01) and duration of dialysis (R<sup>2</sup> = 0.39, P < 0.05), but not with current ferritin or TSAT. CID remained a significant independent predictor of LIC (R<sup>2</sup> = 0.73, P < 0.01) in a multiple regression model. Nine patients had LIC > 60 mumol/g, a threshold above which chelation therapy is usually recommended in secondary iron overload disorders. Only 2 of 8 subjects with CID < 6000 mg, but all subjects with >6000 mg CID had LIC > 60 mumol/g. In the latter group, 2 patients had LIC > 130 mumol/g, which are associated with increased risk of liver injury. Conclusions: FerriScan is suitable to non-invasively assess iron load in ESKD patients. TSAT and ferritin are poor indicators of body iron load in ESKD patients with high serum ferritin. Amounts of LIC that are found in patients with haemochromatosis are observed in some ESKD patients who received >=6000 mg of parenteral iron.

Match optimisation for paired kidney donation using the newly developed NOMS module.
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Aim: To assess the performance of the paired kidney exchange (PKE) module of the National Organ Matching System (NOMS) to match incompatible donor/recipient pairs using authorisation of strong
vs. moderate/strong antibody thresholds. Background: The NOMS PKE computer matching algorithm was developed to identify maximal sets of compatible donor/recipient pairs from a PKE registry of incompatible pairs. The algorithm matches recipients' HLA antibody against donors' HLA antigens using 2 main principles: maximisation of the number of suitable pairs using match probability and maximisation of the number of ABO identical pairs. Methods: Human Leucocyte Antigen (HLA) data of 32 incompatible pairs (because of ABO blood group or positive crossmatch) were submitted for computer analysis and matching in the NOMS PKE testing module. Data included ABO and high-resolution HLA antigens of donors and recipients and HLA antibody specificity (by One Lambda assay) of recipients. Donors were excluded from matching to recipients with donor specific antibodies at >8000 MFI (run 1) and >2000 MFI (run 2), respectively. These thresholds were chosen because MFI values of <8000 are unlikely to have a positive CDC crossmatch, and values of <2000 are unlikely to have a positive flow cross match. Results: Run 1 was completed in 3 hours, 58 minutes and identified 24113 possible combinations, with the highest ranking comprising 19 pairs in 5 x 3-way and 2 x 2-way exchanges. Run 2 was completed in 50 minutes and identified 8843 possible combinations, with the highest ranking comprising 17 pairs in 5 x 3-way and 1 x 2-way exchanges. Conclusions: The more prudent approach of excluding from matching recipients with antibody MFI-values >2000 does not result in a significantly lower number of possible transplants compared to exclusion of recipients with antibody MFI-values >8000 (X<sup>2</sup> =0.57). However, the latter may result in a higher number of matched pairs having a positive CDC or flow crossmatch.

Publication Types: Conference Abstract
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Incidence and significance of screening for de novo donor specific anti-HLA antibody (DSA) formation in patients without HLA antibody at the time of renal transplantation - A long-term prospective study.
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Aim: To prospectively determine the incidence and significance of de novo donor specific anti-HLA antibody (DSA) in renal transplant recipients (RTR) without antibody at the time of renal transplantation. Background: DSA in prevalent RTR is associated with subsequent graft loss. The factors associated with de novo DSA in incident patients and relevance of screening are uncertain. Methods: A prospective cohort of 272 RTR was screened at transplant and at regular time points for a median follow up of 46 (range 24-74) months by Luminex Mixed Screen assay. Demographic and relevant clinical outcome data was also collected. The appearance of a de novo DSA was defined as class 1 (C1) or class 2 (C2) antibody against donor HLA detected by Single Antigen beads at a MFI >500. Results: 185 patients who had no antibody at the time of transplant had follow up serum for testing. Nineteen (10%) formed any DSA (C1 n = 2, C2 n = 11, Both C1&2 n = 6). New DSA formation did not relate to transfusion history, CNI use, gender, delayed graft function, or IL2RAb induction use. As expected 100% of C2 DSA vs 72% without DSA were DR mismatched. Biopsy-proven acute rejection (BPAR) occurred in 60% with de novo DSA vs 29% without DSA and 23% of new DSA (all C2 based) vs 2% without DSA had C4d+ve rejection (P < 0.01). In all but 1 case DSA was first detected with or after BPAR. At last follow-up GFR for DSA was 38 vs 51 mls/min without DSA (P < 0.05). Conclusions: Over a median of 4 years, de novo predominantly C2 type DSA developed in 10% of RTR and adversely impacted upon graft function. This data suggests increasing DR matching in RTR rather than post transplant DSA screening may be a more effective strategy to improve long-term graft outcome.

Publication Types: Conference Abstract
PMID:70467092
Third party blood transfusion before and after renal transplantation: A powerful predictor of rejection and transplant outcome.

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Aim: To evaluate the relationship between blood transfusion and transplant outcome in renal transplant recipients (RTR). Background: Third party blood transfusion (BT) prior to transplant is immunomodulatory and associated with a lower risk of rejection in historic series but its contemporary significance and the effect of post-transplant BT is rarely studied. Methods: We determined the BT history of 256 renal transplant recipients (RTR) and examined the association with relevant clinical and demographic factors, and patient and graft outcomes. BT after transplant was defined as within the first 30 post-operative days. Results: 105 RTR (41%) never received a BT, 50 (19%) pre BT only, 44 (17%) post BT only and 57 (22%) both pre and post BT. Factors associated with transfusion included recipient gender (female), increasing donor and recipient age, retransplant, delayed graft function (DGF), CMV disease and cadaveric donation. Compared with those never transfused, the univariate HR for rejection was 0.74 (pre), 1.2 (Post) and 2.0 (both) P =0.012, and Graft loss 0.64 (pre), 1.5 (post) and 5.1 both (P =0.026). After adjusting for age, gender, donor type, DGF, DR match, CNI use, and re-transplant the HR for rejection were 0.95 (pre) 1.6 (post) and 2.2 (both) and graft loss 0.77 (pre) 2 (post) and 5.2 (both). eGFR at last follow up was 49 (never) 55 (pre) 49 (post) and 43 mls/min (both) P =0.03. Conclusions: BT pre and post transplant are clinically determined and associated with recipient gender, donor and recipient age and donor type. Compared with RTR never transfused and pre or post BT only, previously transfused RTR receiving BT within the first 30 days of surgery have significantly increased risk of rejection, graft loss and reduced long term eGFR.

Publication Types: Conference Abstract
PMID:70467053

Previous antigen mismatches without donor-specific antibodies are not a contraindication to transplantation in patients at high immunological risk.

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Aim: To assess the outcome of kidney transplant recipients with previous mismatched (PMM) antigens to their current donor in the absence of donor-specific antibody (DSA) matched to exchange donors in paired kidney exchange (PKE) program. Background: In deceased donor transplantation National Organ Matching System (NOMS) by default excludes all PMM from matching to a donor sharing any PMM. The NOMS PKD matching algorithm has the capacity to remove PMM antigens from the authorised panel when a specific antibody to the PMM is absent. Methods: HLA data of 13 PKE patients transplanted between 2007 and 2009 and their donors was reviewed. PMM, antibody specificity and strength and transplant outcomes in highly sensitised patients were analysed. Results: Four highly sensitised patients, all undergoing 2nd or 3rd transplantation, successfully received an allograft from a matched donor of the PKE pool. One patient (PRA 95%) received a 3rd kidney transplant after rejection of 2 previous allografts. The patient was matched to a donor sharing a PMM antigen A0101 with the 2nd donor. The allele was an acceptable mismatch by HLA-MatchMaker and there were no DSA to this allele (>300 MFI) in current and peak previous sera. The patient received a kidney from the exchange donor and has not developed DSA against the PMM antigen or any episodes of humoral rejection and has a serum creatinine of 106 mumol/l at 8 months post-transplant. Conclusions: The Ignore PMM (IPMM) antigen register in the newly developed NOMS PKD module
will result in a recipient not being excluded for a donor bearing the PMM-listed HLA antigen allele. This case suggests that this strategy is safe provided suitable historical sera are available and careful consideration by clinicians and immunologists is given.

Nephrology. 2010; 15: 45.

**Serum iron markers do not predict changes in liver iron content upon high-dose parenteral iron in pre-dialysis CKD patients.**

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Aim: To assess the relationship between conventional iron (Fe) markers and liver iron concentration (LIC) following high-dose parenteral Fe treatment in chronic kidney disease (CKD) patients.

Background: Parenteral Fe is frequently used prior to initiating therapy with erythropoietic-stimulating agents (ESA) in anaemia of CKD. Serum Fe markers do not accurately reflect the amount of Fe in the body and the debate over the safety of high-dose Fe therapy remains unresolved. Methods: LIC was assessed non-invasively using magnetic resonance imaging (MRI) (FerriScan) in 25 Fe-deficient pre-dialysis CKD patients before and after 2 and 12 weeks following a single high-dose intravenous Fe administration. Changes in LIC were compared to serum ferritin, transferrin saturation (TSAT) and administered Fe dose. Results: The average Fe dose was 14.9 +/- 2.8 mg/kg. At week 2 after parenteral Fe, TSAT averaged 31 +/- 12% and ferritin 563 +/- 282 μg/l (both P < 0.0001) and at week 12 mean TSAT was 25 +/- 9% (P < 0.0001) and ferritin 299 +/- 221 μg/l (P mu0.001). LIC increased from a baseline of 20.6 +/- 7.9 μmol/g to 46.1 +/- 15.6 μmol/g at week 2 (P < 0.0001) and 33.7 +/- 11.3 μmol/g at week 12 (P < 0.0001). The change in TSAT from baseline showed a dose-dependency at week 2 (P < 0.05), but not at week 12, whereas there was no dose dependency for changes in serum ferritin either at week 2 or 12. The increase in LIC showed a clear dependence on the administered Fe dose at both week 2 and 12 (P < 0.01 and P < 0.05, respectively). Conclusions: FerriScan is a non-invasive MRI-based method suitable to assess Fe load in CKD patients. In pre-dialysis CKD patients with Fe-deficiency intravenous Fe therapy is associated with increases in LIC that are not related to changes in conventional Fe markers.


**Current practice pattern for the management of blood borne viruses in Australia and New Zealand dialysis units.**

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Aim: To assess current practices to prevent transmission of blood borne viruses (BBV) in haemodialysis patients in Australia and New Zealand (ANZ). Background: In an environment where multiple patients receive haemodialysis concurrently, repeated opportunities exist for person-to-person transmission of BBV. It is unclear if a standardised approach to prevent BBV in ANZ haemodialysis units congruent with evidenced based practice and local epidemiology exists. Methods: A 30-questions survey was sent to 66 ANZ renal units to assess their practice of BBV screening, frequency, isolation, prevention strategies and acceptance of holiday haemodialysis patients. Results: Of the 28
centres (42%) that responded, all conducted baseline screening for HBVsAg, anti-HBVsAb, anti-HCVAb and anti-HIVAb. Subsequent screenings for any of the 4 tests were conducted by all centres at variable intervals and 6-monthly in 54%. Anti-HBcAb IgM was screened in all patients at baseline by 22% of centres, while 8% screened only at risk patients and the rest did not test it. Changes in infection control practice for patients testing positive for BBV are adopted by 75%. Isolation is undertaken in 86% of centres for hepatitis B, 38% for hepatitis C and 43% for HIV and 18% isolate for all 3 viruses. 21% of centres accept holiday patients in their units without knowledge of their BBV status. Centre's practice was based on personal choice in 21% and some type of guidelines in 50% of centres. Conclusions: Baseline screening for BBV in Australian haemodialysis units is uniform, but subsequent screening and infection control practices and acceptance of holiday dialysis are highly variable. There appears to be a lack of clear evidence and the need for clear and non-discriminating national guidelines.

**Mycobacterium haemophilum in renal transplant patients: Spread by direct contact?**


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A 34-year-old female, who had received a 3rd renal transplant 9 months earlier from her ABO-incompatible mother, presented in June 2009 with an erythematous plaque-like eruption on the nose extending onto adjacent malar region, which was unresponsive to conventional cellulitis treatment. She was diagnosed with rosacea and started on minocycline 50 mg once daily. Skin biopsy revealed dermal granulomata and micro-abscesses and grew Mycobacterium haemophilum after some weeks of incubation. She was subsequently treated with rifabutin, clarithromycin and ciprofloxacin, requiring significant modification of her tacrolimus dose. Four months later, a 42-year-old female who had received a renal transplant in August 2008 presented with a progressive erythematous papular eruption on the chin. Skin biopsy revealed non-necrotising granuloma, but was not submitted for culture. She was started by a dermatologist on minocycline 50 mg twice daily, and had improved when seen 4 weeks later. The patients had regular direct contact at clinic appointments, where they would greet one another with a kiss on the cheek. Mycobacterium haemophilum is an opportunistic pathogen with a global distribution, but its natural habitat and mode of acquisition in human infection are unknown. Cutaneous infection commonly affects extremities like the nose and chin, presumably due to the organism’s optimal growth at 30-32.8degreeC. Outbreaks among renal transplant patients have been reported and considered likely due to common environmental exposures. The cases described here suggest direct skin-to-skin contact as a possible route of transmission between immunocompromised individuals and highlight complexities in treating mycobacterial infection in transplant patients taking immunosuppressive drugs.

**Outcomes of renal light chain deposition disease: A single centre experience.**

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Aim: To determine the clinical outcomes of light chain deposition disease with predominant renal involvement. Background: Light chain deposition disease (LCDD) is associated with deposition of immunoglobulin light chains predominantly in the kidney. Methods: A single centre retrospective
review of all patients with renal biopsy proven LCDD since 1999 with renal and patient survival analyses. Results: 24 patients were included in the analysis of whom 15 patients (63%) were males with a mean age of 66 +/- 11.7. 14 of 22 patients (63.6%) had kappa light chain deposition with 72.2% confirmed having multiple myeloma. Mean serum creatinine at presentation was 371.9 +/- 223.0 mumol/L. 19 patients (79.2%) received chemotherapy +/- plasmapheresis. During follow-up, 7 patients (29.2%) reached dialysis dependence at a median duration of 609 days (25<sup>th</sup>-75<sup>th</sup> percentiles: 15, 1307) with 7 deaths (29.2%) reported at median duration of 558 days (25<sup>th</sup>-75<sup>th</sup> percentiles: 296-1425). The sole independent predictor of dialysis dependence was serum creatinine at presentation (beta = -0.55, p = 0.04). Factors independently associated with death were serum creatinine at presentation (beta = -0.79, p < 0.05) and history of hypertension (beta = -0.492, p < 0.05). Conclusions: LCDD is associated with significant renal impairment at presentation with risk of dialysis dependence and death.

Rapid pulsating ultrafiltration profile in haemodialysis: PO02-104.
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Anticoagulant free haemodialysis with blood transfusion: PO02-103.
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Pentoxifylline improves haemoglobin and interleukin-6 levels in chronic kidney disease.
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AIM: To assess whether pentoxifylline improves anaemia of chronic kidney disease (CKD) via suppression of interleukin-6 (IL-6) and improved iron mobilization. BACKGROUND: CKD patients may have elevated IL-6 and tumour necrosis factor alpha levels. These cytokines can increase hepcidin production, which in turn reduces iron release from macrophages resulting in reduced availability of iron for erythropoiesis. In experimental models, pentoxifylline was shown to reduce IL-6 expression. METHODS: We studied 14 patients with stages 4-5 CKD (glomerular filtration rate <30mL/min per 1.73 m(2)) due to non-inflammatory renal diseases. None of the patients had received immunosuppressive or erythropoietin-stimulating agents or parenteral iron. Patients had weekly blood tests for iron studies and cytokines during a control run-in period of 3 weeks and during 4 weeks of pentoxifylline treatment. RESULTS: Ten patients (eGFR 23 + or - 6 mL/min) completed the study. At the end of the run-in period average haemoglobin was 111 + or - 5 g/L, ferritin 92 + or - 26 microg/L, transferrin saturation 15 + or - 3% and circulating IL-6 10.6 + or - 3.8 pg/mL. Tumour necrosis factor alpha values were below threshold for detection. Treatment with pentoxifylline reduced circulating IL-6 (6.6 + or - 1.6 pg/mL, P < 0.01), increased transferrin saturation (20 + or - 5%, P < 0.003) and decreased serum ferritin (81 + or - 25 microg/L, P = NS). Haemoglobin increased after the second week of pentoxifylline, reaching 123 + or - 6 g/L by week 4 (P < 0.001). CONCLUSIONS: Pentoxifylline reduces circulating IL-6 and improves haemoglobin in non-inflammatory moderate to severe CKD. These changes are associated with changes in circulating transferrin saturation and ferritin, suggesting improved iron release. It is hypothesized that pentoxifylline improves iron disposition possibly through modulation of hepcidin.
Levin B, Kuthubutheen J, et al.
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Visser EJ, Davies S.

Building capacity for acute care in developing countries.
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The article provides a 'short journey' to neighbours in the Australasian region to highlight some innovation in health policy, rural health education, and professional teams, in developing countries. The innovations are described and challenges discussed.

Ferritin concentrations in synovial fluid are higher in osteoarthritis patients with HFE gene mutations (C282Y or H63D).
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OBJECTIVES: In view of the clinical similarities between polyarticular osteoarthritis (POA) with metacarpophalangeal (MCP) joint involvement and the arthropathy that occurs in hereditary haemochromatosis (HH), it was hypothesized that osteochondral damage in both disorders may be due to localized iron overload. Accordingly, it was predicted that the concentration of ferritin in synovial fluid (SF) would be higher in OA patients with HFE gene mutations than in HFE wild-type (wt) OA patients. The aim of this study was to test this proposition. METHODS: Sequential patients with physician-diagnosed OA and, for comparison, diverse inflammatory diseases of the joints, who required diagnostic or therapeutic arthrocentesis, were studied. Participants underwent HFE genotyping. SF samples were assayed for ferritin and also for selected cytokines and matrix metalloproteinases (MMPs). RESULTS: Seventy-three patients with diverse rheumatic disorders were recruited. Of the 29 patients who had knee OA, 15 were wt and 14 were heterozygous for HFE mutations (C282Y or H63D). Mean SF ferritin concentrations in the wt and heterozygous OA groups were 273 and 655 ng/mL, respectively (p = 0.0146). CONCLUSIONS: A predicted difference in SF ferritin concentrations in patients with knee OA was confirmed. Concentrations of ferritin in the SF...
were found to be two- to threefold higher in knee OA patients with HFE gene mutations compared to
wt patients. This finding is consistent with the possibility that, in OA patients with HFE gene mutations,
localized iron overload may contribute either directly or indirectly to osteochondral damage, possibly in
a similar way to that which occurs in the arthropathy that complicates HH.


Chlamydia at an inner metropolitan sexual health service in Sydney, NSW: Australian Collaboration for Chlamydia Enhanced Sentinel Surveillance (ACCESS) Project.

Franklin N, O'Connor CC, et al.

Background: Australia has a widely dispersed network of public sexual health services that test large
numbers of people from high prevalence populations for genital Chlamydia trachomatis infection.
These populations include young sexually active heterosexuals, men who have sex with men, sex
workers and Aboriginal and Torres Strait Islander people. The Australian Collaboration for Chlamydia
Enhanced Sentinel Surveillance (ACCESS) Project was established to monitor chlamydia testing rates
and positivity rates at a national level, which in turn will help interpret trends in chlamydia diagnoses
reported through passive surveillance. The ACCESS Project is the first time that chlamydia-related
data including priority population and testing denominators has been collated at a national level. The
present paper reports on chlamydia testing and positivity rates in a sexual health service in the inner
west of Sydney between 2004 and 2008 and compares these to published national data from the
ACCESS Project in sexual health services. Methods: Chlamydia positivity and testing rates at an inner
western Sydney sexual health service were compared with aggregate data from the ACCESS Project
obtained from 14 sexual health services across Australia. Using a standardised extraction program,
retrospective de-identified line-listed demographic and chlamydia testing data on all patients were
extracted from patient management systems. Results: Over the 5-year period, 5145 new patients
attended the inner-west sexual health service. Almost 66% had a chlamydia test at first visit and there
was no significant difference in this testing rate when compared with the ACCESS Project national
rate for sexual health services (67.0%; odds ratio [OR] 0.94, 95% confidence intervals 0.88-1.00). The
testing rate increased over time from 61% in 2004 to 70% in 2008. There were 281 chlamydia
diagnoses at this service, giving an overall chlamydia positivity rate of 9.3%, significantly higher than
the ACCESS Project national rate of 8.2% (OR 1.16, 95% confidence intervals 1.02-1.32). Discussion:
Testing rates were similar and positivity rates for Chlamydia trachomatis were higher in this sexual
health service in Sydney than national trends. CSIRO 2010.


Human liver progenitor cell lines are readily established from non-tumorous tissue adjacent to
hepatocellular carcinoma.

Non-tumorous liver tissue removed during surgery to resect hepatocellular carcinoma (HCC) is potentially a useful source of material from which cells, particularly liver progenitor/stem cells (LPCs), can be isolated to establish cell lines. The purpose of this study was to evaluate the applicability of the "plate-and-wait" method to derive LPCs from resections to remove HCC. Three independent non-tumorous liver samples from HCC resection and 3 samples from liver donors were used for LPC isolation. Staining for LPC markers, OV6, CK19, and EpCAM, in the above liver samples demonstrated staining in only 2 of the non-tumorous samples. We isolated 2 human liver epithelial cell lines (HLECs) from these 2 samples. These HLECs were positive for general stem cell markers CD133, EpCAM, and Oct4. They expressed the liver progenitor cell markers OV6, CK14, and M2PK but not CK19. They also expressed the hepatocellular markers albumin, CK8, CK18, HNF4-alpha, and the drug-metabolizing gene CYP3A4. These cells accumulated glycogen, indocyanine green, and synthesized urea. They produced colonies in soft agar that showed anchorage-independent growth and their tumorigenic status was confirmed when they produced tumors following transfer to athymic nude mice. In contrast, the third non-tumorous tissue and 3 normal liver samples did not produce cell lines. This study establishes a correlation between the presence of LPCs in the source liver tissue and the ability to derive cell lines from these tissues. The phenotypic similarities between the LPCs and the HLECs suggest that a precursor-product relationship may exist between the 2 cell types. Copyright 2010, Mary Ann Liebert, Inc. 2010.
Cryptococcal meningitis in immunocompetent Papua New Guinean children.
Laman M, Hwaihwanje I, et al.
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We report three cases of meningo-encephalitis caused by Cryptococcus neoformans var. gattii in apparently immunocompetent children presenting to a provincial hospital in Papua New Guinea (PNG) over a nine-month period. After a postmortem diagnosis was made in the first case, a further two were identified quickly using Indian ink staining of cerebrospinal fluid (CSF). The second case had a complicated course and recovered after relapse. The third made a full recovery with appropriate antifungal therapy. Despite the fact that an environmental reservoir has not been established, cryptococcal meningo-encephalitis occurs regularly in PNG. In developing countries such as PNG, a lack of laboratory resources and limited therapeutic options can complicate the management of severe infections such as cryptococcosis. Nevertheless, with inexpensive diagnostic tests (such as Indian ink staining of CSF), a high index of suspicion and a pragmatic approach to antifungal therapy, good therapeutic outcomes can be achieved.
PMID:20075429

In vitro sensitivity of Plasmodium falciparum to conventional and novel antimalarial drugs in Papua New Guinea.
Wong RPM, Lautu D, et al.
Fremantle Unit, School of Medicine and Pharmacology, University of Western Australia, Nedlands, WA, Australia.
OBJECTIVE: Recent clinical studies have shown high rates of malaria treatment failure in endemic areas of Papua New Guinea (PNG), necessitating a change of treatment from chloroquine (CQ) or amodiaquine (AQ) plus sulphadoxine-pyrimethamine to the artemisinin combination therapy (ACT) artemether plus lumefantrine (LM). To facilitate the monitoring of antimalarial drug resistance in this setting, we assessed the in vitro sensitivity of Plasmodium falciparum isolates from Madang Province.
METHODS: A validated colorimetric lactate dehydrogenase assay was used to assess growth inhibition of 64 P. falciparum isolates in the presence of nine conventional or novel antimalarial drugs [CQ, AQ, monodesethyl-amodiaquine (DAQ), piperaquine (PQ), naphthoquine (NQ), mefloquine (MQ), LM, dihydroartemisinin and azithromycin (AZ)]. RESULTS: The geometric mean (95% confidence interval) concentration required to inhibit parasite growth by 50% (IC(50)) was 167 (141-197) nM for CQ, and 82% of strains were resistant (threshold 100 nM), consistent with near-fixation of the CQ resistance-associated pfcrt allele in PNG. Except for AZ [8.351 (5.418-12.871) nM], the geometric mean IC(50) for the other drugs was <20 nM. There were strong associations between the IC(50)s of 4-aminoquinoline (CQ, AQ, DAQ and NQ), bisquinoline (PQ) and arylation alcohol (MQ) compounds suggesting cross-resistance, but LM IC(50) only correlated with that of MQ. Conclusions Most PNG isolates are resistant to CQ in vitro but not to other ACT partner drugs. The non-isotopic semi-automated high-throughput nature of the Plasmodium lactate dehydrogenase assay facilitates the convenient serial assessment of local parasite sensitivity, so that emerging resistance can be identified with relative confidence at an early stage.
PMID:20070627

Iron: an emerging factor in colorectal carcinogenesis.
Chua ACG, Klopcic B, et al.
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The carcinogenic potential of iron in colorectal cancer (CRC) is not fully understood. Iron is able to undergo reduction and oxidation, making it important in many physiological processes. This inherent redox property of iron, however, also renders it toxic when it is present in excess. Iron-mediated generation of reactive oxygen species via the Fenton reaction, if uncontrolled, may lead to cell damage as a result of lipid peroxidation and oxidative DNA and protein damage. This may promote carcinogenesis through increased genomic instability, chromosomal rearrangements as well as mutations of proto-oncogenes and tumour suppressor genes. Carcinogenesis is also affected by inflammation which is exacerbated by iron. Population studies indicate an association between high dietary iron intake and CRC risk. In this editorial, we examine the link between iron-induced oxidative stress and inflammation on the pathogenesis of CRC.

Publication Types: Editorial
PMID:20135713


**Novel topical therapies for distal colitis.**
Lawrance IC.
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Distal colitis (DC) can be effectively treated with topical 5ASA agents. Suppositories target the rectum while enemas can reliably reach the splenic flexure. Used in combination with oral 5ASAs, the control of the inflammation is even more effective. Unfortunately, resistant DC does occur and can be extremely challenging to manage. In these patients, the use of steroids, immunosuppressants and the anti-tumor necrosis factor agents are often required. These, however, can be associated with systemic side effects and are not always effective. The investigation of new topical therapeutic agents is thus required as they are rarely associated with significant blood drug levels and side effects are infrequent. Some of the agents that have been proposed for use in resistant distal colitis include butyrate, cyclosporine and nicotine enemas as well as tacrolimus suppositories and tacrolimus, ecabet sodium, arsenic, lidocaine, rebamipide and Ridogrel() enemas. Some of these agents have demonstrated impressive results but the majority of the agents have only been assessed in small open-labelled patient cohorts. Further work is thus required with the investigation of promising agents in the context of randomized double-blinded placebo controlled trials. This review aims to highlight those potentially effective therapies in the management of resistant distal colitis and to promote interest in furthering their investigation.

PMID:21577301


**Extracellular function of the actin-remodelling protein flightless I may be important in acute and chronic wound responses: 69.**
Ruzehaji N, Zola H, et al.
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**Impaired colonic collagen assembly and reduced intestinal fibrosis in the absence of SPARC: 6.**
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Bowel Diseases; ([S])Department of Histopathology Fremantle Hospital, Fremantle