Publication Types: Report


Fostering psychiatry in Ghana: the impact of a short review course through an international collaboration.
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OBJECTIVE: The aim of the current study was to evaluate a short review course in psychiatry conducted at the Kwame Nkrumah University of Science and Technology medical school and any change in student interest in a career in psychiatry. METHOD: Students were asked to complete a general psychiatric knowledge questionnaire before and immediately after the course. They were also asked to rate their attitude toward psychiatry as a career. The same questionnaire was readministered 1 month later. RESULTS: The average results on the knowledge test pre-course was 52% (N=129) and post-course was 78% (N=122), constituting a 50% increase in knowledge for the average student. The proportion of students showing considerable interest in a psychiatric career increased from 19% pre-course to 32% post-course. At 1-month follow-up, the average result for the knowledge test was 76%, and considerable interest in psychiatry as a career was noted at 21%. CONCLUSION: Results indicate that the course significantly improved core psychiatric knowledge and that this improvement was retained after 1 month. An initial increase in interest in psychiatry as a career decreased almost to baseline at 1-month follow-up. Study limitations include the use of the same questionnaire at each stage knowledge was tested and the absence of a control group.
PMID:22193734


Randomised clinical trial: Certolizumab pegol for fistulas in Crohn's disease - Subgroup results from a placebo-controlled study.
Schreiber S, Lawrance IC, et al.
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Background: Treatment options for fistulizing Crohn's disease (CD) are limited. Aim: To examine whether fistula closure is maintained at week 26 following treatment with certolizumab pegol. Methods: Patients with draining fistulas at baseline from PRECiSE 2 (n = 108) received open-label induction with certolizumab pegol 400 mg at weeks 0 (baseline), 2 and 4. Response was defined as >=100-point decrease from baseline in the Crohn's Disease Activity Index. Nonresponders (50/108) were excluded. At week 6, responders with draining fistulas (N = 58) were randomized to certolizumab pegol 400 mg (n = 28) or placebo (n = 30) every 4 weeks across weeks 8-24. Fistula closure was evaluated throughout the study, with a final assessment at week 26. Results: The majority of patients (55/58) had perianal fistula. At week 26, 36% of patients in the certolizumab pegol group had 100% fistula closure compared with 17% of patients receiving placebo (P = 0.038). Protocol-defined fistula closure (>=50% closure at two consecutive post-baseline visits >=3 weeks apart) was not statistically significant (P = 0.069) with 54% and 43% of patients treated with certolizumab pegol and placebo achieving this end point, respectively. Conclusion: Continuous treatment with certolizumab pegol improves the likelihood of sustained perianal fistula closure compared with placebo. 2010 Blackwell Publishing Ltd.


Androgen intervention therapy in a patient with familial Alzheimer's disease.

Martins R, Gupta VB, et al.

Background: Mutation in the presenilin-1 (PS-1), presenilin-2 (PS-2), or amyloid precursor protein (APP) genes results in autosomal dominant Familial Alzheimer's disease (FAD), in which the onset of the disease occurs at an unusually early age (onset under the age of 60). Previously, androgen modulating therapy for AD has been proposed by our group based on published animal and clinical studies. We present a case report on a symptomatic FAD mutation carrier (PS-1) prior to and following testosterone intervention therapy. Methods: We investigated clinical and blood biomarker correlates in this female aged 32 years. She underwent comprehensive neuropsychological and blood biomarker testing. We monitored blood plasma levels of amyloid beta 1-42, amyloid beta 1-40, clusterin, total apoE and TNF-alpha during the course of this treatment. Results: Neuropsychological testing revealed a Mini-Mental State Examination (MMSE) of 17 and severely impaired working and episodic memory, as examined by Rey Auditory Verbal Learning test (RAVLT). Analysis of a panel of biomarkers before treating with testosterone implant at two different time points (3 weeks apart) showed amyloid beta 42 (97.52 pg/ml; 115.43 pg/ml), amyloid beta 40 (148.87 pg/ml; 136.17 pg/ml), total apoE (18.5 mg/dl; 11.5 mg/dl), clusterin (450.21 mg/ml; 453.10 mg/ml), and TNF-alpha (28.6 pg/ml; 38.08 pg/ml). A repeated analysis of the same panel of biomarkers was then carried out one month after treatment with 200 mg of testosterone pellet implant. Testing revealed a MMSE score of 18 and constant memory performance. Plasma biomarkers showed amyloid beta 42 (87.13 pg/ml), amyloid beta 40 (155.46 pg/ml), total apoE (12.5 mg/dl), clusterin (420.34 mg/ml), and TNF-alpha (10.86 pg/ml). Conclusions: From our results it appears that amyloid beta 42/40 ratio, clusterin and TNF-alpha levels have significantly decreased after one month of testosterone treatment (P < 0.01). Total apoE levels showed an increase (p < 0.05) in response to treatment. These promising preliminary findings require longer follow up and investigation in additional patients before a definite decision can be reached on the clinical significance of this therapeutic approach.

Publication Types: Conference Abstract
PMID:70502430

Thyroid hormones and depression: The health in men study.
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Context: Current practice guidelines suggest that thyroid function tests should be an integral part of the assessment of adults presenting with a depressive episode, although there is a paucity of data available to support such a recommendation. Objective: To determine if biochemical markers of thyroid dysfunction are associated with prevalent and incident clinically significant depressive symptoms. Design: Cross-sectional and cohort studies. Patients: Community-dwelling sample of 3,932 men age 69 to 87 free of overt thyroid disease. Main Outcome Measures: We used the 15-item Geriatric Depression Scale to ascertain the presence of prevalent clinically significant depressive symptoms, and the Western Australia Data Linkage System to establish the onset of a depressive episode according to the International Classification of Diseases. Results: The serum concentration of thyroid-stimulating hormone and free thyroxine (fT4) did not affect the odds of prevalent or the hazard of incident depression. The odds of prevalent depression were 0.8 (95% CI: = 0.5-1.3) for men with subclinical hypothyroidism and 1.4 (95% CI: = 0.3-5.8) for those with subclinical hyperthyroidism. The hazard ratio of incident depression associated with subclinical hypothyroidism was 0.7 (95% CI: = 0.3-1.9). No men with subclinical hyperthyroidism developed depression during the follow-up period of 5.5 +/- 1.4 years. Conclusions: Subclinical thyroid disease is not associated with prevalent or incident depression in older men. These findings do not support the routine screening of subclinical thyroid dysfunction among older adults with depression. 2011 American Association for Geriatric Psychiatry. PMID:2011492300


Diagnostic criteria for depression in Alzheimer disease: a study of symptom patterns using latent class analysis.
Starkstein SE, Dragovic M, et al.
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CONTEXT: Although depression in Alzheimer disease (AD) has a negative emotional and functional impact on patients and caregivers, specific criteria to diagnose depression in AD are still to be validated. OBJECTIVE: To validate a set of diagnostic criteria for major depression in AD. DESIGN: Cross-sectional design using latent cluster analysis (LCA). SETTING: Participants were recruited from consecutive referrals to a Memory Clinic of a tertiary hospital. PARTICIPANTS: A consecutive series of 971 outpatients with probable AD. MAIN OUTCOME MEASURE: Clusters of patients with or without major depression as determined with LCA. RESULTS: A LCA demonstrated three clusters that were considered to represent major depression, minor depression, and no depression. All nine Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for major depression were significantly associated with the major depression cluster. Although a diagnosis of generalized anxiety disorder (GAD) and apathy were also associated with the major depression cluster, irritability was not. CONCLUSIONS: The DSM-IV criteria for major depression should be used unmodified to diagnose depression in AD. Future studies should determine whether GAD should be included as an additional diagnostic criterion.
Mesenchymal cell proliferation and programmed cell death: Key players in fibrogenesis and new targets for therapeutic intervention.
Luna J, Masamunt MC, et al.
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An exquisite equilibrium between cell proliferation and programmed cell death is required to maintain physiological homeostasis. In inflammatory bowel disease, and especially in Crohn's disease, enhanced proliferation along with defective apoptosis of immune cells are considered key elements of pathogenesis. Despite the relatively limited attention that has been given to research efforts devoted to intestinal fibrosis to date, there is evidence suggesting that enhanced proliferation along with defective programmed cell death of mesenchymal cells can significantly contribute to the development of excessive fibrogenesis in many different tissues. Moreover, some therapies have demonstrated potential antifibrogenic efficacy through the regulation of mesenchymal cell proliferation and programmed cell death. Further understanding of the pathways involved in the regulation of mesenchymal cell proliferation and apoptosis is, however, required.

Virtual crossmatch approach to maximize matching in paired kidney donation.
Ferrari P, Fidler S, et al.
Department of Nephrology, Fremantle Hospital, Perth, Western Australia.

We developed and tested a new computer program to match maximal sets of incompatible live donor/recipient pairs from a national paired kidney donation (PKD) registry. Data of 32 incompatible pairs included ABO and 4 digit-high-resolution donor and recipient HLA antigens and recipient's HLA antibodies. Three test runs were compared, in which donors were excluded from matching to recipients with either donor-specific antibodies (DSA) >8000MFI (mean fluorescent intensity) at low-resolution (Run 1) or >8000MFI at high-resolution (Run 2) or >2000MFI and high-resolution (Run 3). Run 1 identified 22,703 possible combinations, with 20 pairs in the top ranked, Run 2 identified 24,113 combinations, with 19 pairs in the top ranked and Run 3 identified 8843 combinations, with 17 pairs in the top ranked. Review of DSA in Run 1 revealed that six recipients had DSA 2000-8000MFI causing a possible positive crossmatch resulting in breakdown of two 3-way and three 2-way chains. In Run 2, four recipients had DSA 2000-8000MFI, also potentially causing breakdown of three 2-way chains. The more prudent approach of excluding from matching recipients with DSA with >2000MFI reduces the probability of matched pairs having a positive crossmatch without significantly decreasing the number of possible transplants.

Nuclear magnetic resonance: a tool for malaria diagnosis?

Nuclear magnetic resonance: a tool for malaria diagnosis?
Malaria control can be improved by rapid, sensitive, low-cost detection of infection. Several such strategies are being pursued. Rapid diagnostic tests can detect infections at parasite densities above 200 μL⁻¹. Polymerase chain reaction methods can detect low parasite densities, but are slow and prone to contamination under field conditions. Methods that detect hemozoin presence in blood have been proposed as alternatives for rapid detection of infection. In this study, we used a benchtop nuclear magnetic resonance (NMR) device to detect hemozoin. This device could be deployed in malaria-endemic settings. We measured synthetic hemozoin in phosphate-buffered saline and malaria parasites in human blood. The NMR detected hemozoin in suspensions of 4 ng μL⁻¹ and parasites at densities of 8,000-10,000 μL⁻¹ (0.2% parasitemia). Thus, our preliminary NMR approach, although providing very rapid measurements, is unlikely to achieve the required sensitivity and specificity for malaria diagnosis, unless a preliminary concentration step is performed.

PMID:22049032

Reference intervals for common laboratory tests in melanesian children.
Manning L, Laman M, et al.
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Abstract. Pediatric reference intervals for biochemical tests are often derived from studies in Western countries and may not be applicable to the developing world. No such intervals exist for Melanesian populations. The aim of this study was to provide specific reference intervals for children from Papua New Guinea (PNG). We assayed plasma from 327 healthy Melanesian children living in Madang Province for common biochemical and hematological analytes. We used well-validated commercially available assay methodology. Compared with reference intervals from children from Western countries and/or African children, there were substantial differences in hemoglobin, soluble transferrin receptor, ferritin, calcium, phosphate, and C-reactive protein. Differences in the upper limits of reference intervals for bilirubin and alanine aminotransferase were also observed. Available reference intervals from Western and African countries may be inappropriate in PNG and other Melanesian countries. This has implications for clinical care and safety monitoring in pharmaceutical intervention trials and vaccine studies.

PMID:21734123

Quantification of *Plasmodium falciparum* gametocytes by magnetic fractionation.
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Abstract. A method of gametocyte quantitation in human blood was developed based on magnetic fractionation using commercially available magnetic fractionation columns (MFCs) and exploiting the magnetic susceptibility of mature *Plasmodium falciparum* gametocytes. The technique uses magnetic microspheres as a calibration standard. Microspheres are added to each blood sample to a known concentration. When exposed to a magnetic field, gametocytes and magnetic microspheres are preferentially captured inside MFCs. After removal of the magnetizing field, the magnetically captured
material can be eluted, placed on a microscope slide that is stained, and counted by using conventional methods. The limits of quantitation for P. falciparum gametocytes were determined from serial dilutions of blood samples with known gametocyte density. The upper limit was 1,000 gametocytes/L. Quantitative analysis above this threshold is difficult because of an over-abundance of gametocytes. The lower limit was 0.1 gametocytes/L, and there is a significant probability of a false-negative result below this level.

PMID:21212220

Nonoperative management of intra-abdominal hypertension and abdominal compartment syndrome: evolving concepts.
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Intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) are associated with significant morbidity and mortality. Nonoperative medical management strategies play an important role in the current treatment of IAH and ACS. There are five medical treatment options to be considered to reduce elevated intra-abdominal pressure (IAP): 1) improvement of abdominal wall compliance; 2) evacuation of intralumarinal contents; 3) evacuation of abdominal fluid collections; 4) optimization of systemic and regional perfusion; and 5) correction of positive fluid balance. Nonsurgical management is an important treatment option in critically ill patients with raised IAP.
PMID:21944450

Intra-abdominal measurement techniques: is there anything new?
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Intra-abdominal pressure (IAP) measurements are essential to the diagnosis and management of intra-abdominal hypertension (IAH) and abdominal compartment syndrome. A variety of IAP measurement techniques have been described. The intravesicular or "bladder" technique remains the gold standard. This commentary reviews each of the different techniques for IAP measurement and discusses their clinical application. It also explores how IAP is affected by changes in body position, body mass index, and positive end-expiratory pressure (PEEP). IAP should be measured every 4 to 6 hours in patients with risk factors for IAH. Putting patients in the semirecumbent position changes the IAP measurement significantly. The role of prone positioning in unstable patients with IAH remains unclear. PEEP has a small effect on IAP.
PMID:21944447

Retrospective audit of blood transfusion and comparison with haemoglobin concentration in patients undergoing elective primary and revision lower limb arthroplasty.
Evans S, O'Loughlin E, et al.
Department of Anaesthesia, Fremantle Hospital, Fremantle, Western Australia, Australia.
We retrospectively audited the incidence of blood transfusion and related this to preoperative haemoglobin levels in 181 patients undergoing lower limb arthroplasty over a six-month period. This included 102 primary total knee replacements, 52 primary total hip replacements, 11 revision total knee replacements and 16 revision total hip replacements. The overall incidence of transfusion was 16.0%. The incidence in primary arthroplasty was 11% (9.8% for total knee replacements and 13.5% for total hip replacements), and in revision surgery was 44.4% (27.3% for total knee replacements and
56.3% for total hip replacements). Combining data for primary total knee replacements and primary total hip replacements, a preoperative haemoglobin threshold of 120 g/l divided patients into high and low risk groups for transfusion. Below or equal to this threshold the incidence of transfusion was 47.7%; above this threshold the incidence was 7.2%. We suggest that patients having primary lower limb arthroplasty with a preoperative haemoglobin of 120 g/l or less should undergo investigation of their anaemia and optimisation of erythropoiesis.

Publication Types: Comparative Study
PMID:21675071

A double-blinded randomised evaluation of alfentanil and morphine versus fentanyl: Analgesia and sleep trial (‘DREAMFAST’).
Lee A, O'Loughlin E, et al.
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A. Lee, Sir Charles Gairdner Hospital, Fremantle Hospital, Perth, WA, Australia

Introduction: Although patient-controlled analgesia (PCA) is a safe and effective technique, some patients complain of poor sleep, particularly with shorter duration opioids such as fentanyl. The combination of alfentanil and morphine provides analgesia of rapid onset and prolonged duration1,2. The aim of this study was to compare PCA fentanyl with alfentanil/morphine, to determine whether the latter resulted in less sleep disruption in the early postoperative period. Methods: Following institutional ethics committee approval and informed consent, ASA I to III adults undergoing major surgery at two major metropolitan hospitals were randomised in a double-blind fashion to postoperative PCA with a bolus dose of either fentanyl 20 mug (Group F) or alfentanil 75 mug/morphine 1 mg (Group AM). The primary outcome measure was self-reported number of pain-related awakenings on the second postoperative night. Secondary measures included other sleep measures, verbal rating pain scores (VRS), side-effect incidence/treatment, and requirement for analgesia rescue including bolus dose escalation and ketamine infusion. Results: Two hundred and twelve patients were randomised with data analysed for 206 (104 Group F, 102 Group AM), following exclusion of six patients where PCA was not commenced or who met exclusion criteria. Demographic characteristics and usual sleep quality did not differ between groups. Both groups reported sleep disturbance, with over 90% of patients waking three or more times and more than 40% rating their sleep on the second postoperative night as ‘poor’ or ‘very poor’. No significant difference in pain-related awakenings was found (53% Group F, 40% Group AM; P=0.086). The most common reason for sleep disturbance was ‘activity in the room’. Group AM had lower pain scores in the first 24 hours (median VRS 2 vs 3; P=0.002), and were less likely to require the addition of ketamine (2 vs 14%; P=0.001). Nausea and vomiting was less frequent in Group AM (18 vs 35%; P=0.015) but pruritus was more common (35 vs 19%; P=0.017). Conclusions: The PCA alfentanil/morphine, when compared with PCA fentanyl, did not reduce the number of pain-related awakenings. Postoperative sleep disturbance was common and is likely to be of multifactorial aetiology, with the choice of opioid only one influence. The improvement in early postoperative analgesia with the combination of alfentanil and morphine may be due to the requirement for patients using PCA fentanyl to load themselves with the drug due to its rapid redistribution.
Publication Types: Conference Abstract
PMID:70504500

Buprenorphine added to low dose interscalene brachial plexus block for ambulatory shoulder surgery - A dose finding study (BLISS study).
(Tan, Kwei, Hennessy, Watts, Hocking, Edgecombe) Sir Charles Gairdner Hospital, Perth and Fremantle Hospital, Fremantle, WA, Australia (Tan, Kwei, Hennessy, Watts, Hocking, Edgecombe)
Introduction: Buprenorphine is one of many adjuvants that have been added to local anaesthetics in peripheral nerve blocks to improve and prolong the duration of analgesia while minimising side-effects. However, there is little supporting evidence for its use and no evidence on any dose response. The aim of the study was to assess the effectiveness and duration of action of buprenorphine when added with ropivacaine and to define the optimal dose of buprenorphine. Methods: A multicentre, single-blinded, stratified, randomised controlled trial was performed in patients undergoing ambulatory shoulder surgery. Patients were randomised into four groups depending on the dose of buprenorphine added to 15 ml 0.25% ropivacaine: 0 μg, 75 μg, 150 μg, 300 μg. Blocks were performed using the anaesthetist's standard technique. Power calculation suggested 25 patients in each group.

Results: The study was stopped after 18 months due to recruitment difficulty as the casemix in the institution had changed. At the point of stopping the study, 41 patients had been recruited. Ten received no buprenorphine, 12 received 75 μg, 10 received 150 μg and nine received 300 μg. There was no significant difference in duration of block, intraoperative or postoperative opioid requirement, and side-effects profile between the four groups. Conclusion: We were unable to show an analgesic effect of buprenorphine when added to ropivacaine in interscalene blocks. We acknowledge these results conflict with other evidence suggesting an effect when added to bupivacaine. These results may be underpowered due to a lack of appropriate patient recruitment. However, we failed to see even a trend towards an effect or dose response. We suggest that a larger study is required to assess whether there is any analgesic benefit from adding buprenorphine to ropivacaine and to determine the dose response.

Publication Types: Conference Abstract
PMID:70504529
community pharmacies provided appropriate primary care by recommending medical referral advice to patients with chronic cough. The majority of pharmacy staff members acquired information from the patient that suggested a need for medical referral, yet did not provide referral advice. CONCLUSIONS: Appropriate medical referral is more likely when adequate assessment is undertaken and when a pharmacist is directly involved in the consultation. This highlights the need for pharmacies to ensure that processes are in place for patients to access the pharmacist.

PMID:2011150304

Manning L, Laman M, et al.
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In Papua New Guinean (PNG) children with acute bacterial meningitis (ABM), all Haemophilus influenzae isolates were resistant to chloramphenicol. Although Streptococcus pneumoniae isolates had a median chloramphenicol MIC of 3 μg/ml, it was >=4 μg/ml in 42.8%, and the likelihood of an area under the 24-hour concentration-time curve/MIC ratio of >100 h at a MIC of >=4 μg/ml was approximately 50%. All isolates were ceftriaxone sensitive. These data support ceftriaxone rather than conventional chloramphenicol for all PNG children with suspected ABM.
PMID:21709079

Meningeal inflammation increases artemether concentrations in cerebrospinal fluid in Papua New Guinean children treated with intramuscular artemether.
Manning L, Laman M, et al.
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Although the artemisinin-associated neurotoxicity identified in vitro and in animal studies has not been confirmed clinically, only one adult study has measured cerebrospinal fluid (CSF) concentrations after administration of conventional doses. Potential artemisinin neurotoxicity could be serious in children, especially those with meningitis and, consequently, a compromised blood-brain barrier. We measured CSF/plasma artemether and dihydroartemisinin (DHA) concentrations in 32 Papua New Guinean children with a mean age of 39 months with suspected or proven severe falciparum malaria who underwent a single lumbar puncture after intramuscular artemether administration. CSF artemether concentrations were 0 to 43.5 μg/liter and CSF concentration/plasma concentration ratios were 0 to 38.1%. DHA was measurable in CSF in only two children. The seven children with meningeal inflammation (CSF white cell count > 20/mm(3)) had higher CSF artemether concentration/plasma artemether concentration ratios than those without (median, 6.7% [interquartile ratio, 2.5 to 27.8%] versus 0.0% [interquartile ratio, 0.0 to 2.5%]; P = 0.002). Meningeal inflammation was associated with a 4.6-fold increase in the CSF artemether concentration/plasma artemether concentration ratio in a population pharmacokinetic model. These data suggest that pharmacovigilance should be heightened when intramuscular artemether is given to severely ill children with evidence of meningeal inflammation.
PMID:21859936

There are sparse published data relating to the pharmacokinetic properties of artemether, lumefantrine, and their active metabolites in children, especially desbutyl-lumefantrine. We studied 13 Papua New Guinean children aged 5 to 10 years with uncomplicated malaria who received the six recommended doses of artemether (1.7 mg/kg of body weight) plus lumefantrine (10 mg/kg), given with fat over 3 days. Intensive blood sampling was carried out over 42 days. Plasma artemether, dihydroartemisinin, lumefantrine, and desbutyl-lumefantrine were assayed using liquid chromatography-mass spectrometry or high-performance liquid chromatography. Multicompartmental pharmacokinetic models for a drug plus its metabolite were developed using a population approach that included plasma artemether and dihydroartemisinin concentrations below the limit of quantitation. Although artemether bioavailability was variable and its clearance increased by 67.8% with each dose, the median areas under the plasma concentration-time curve from 0 h to infinity (AUC0-∞) for artemether and dihydroartemisinin (3,063 and 2,839 μg·h/liter, respectively) were similar to those reported previously in adults with malaria. For lumefantrine, the median AUC0–∞ (459,980 μg·h/liter) was also similar to that in adults with malaria. These data support the higher dose recommended for children weighing 15 to 35 kg (35% higher than that for a 50-kg adult) but question the recommendation for a lower dose in children weighing 12.5 to 15 kg. The median desbutyl-lumefantrine/lumefantrine ratio in the children in our study was 1.13%, within the range reported for adults and higher at later time points because of the longer desbutyl-lumefantrine terminal elimination half-life. A combined desbutyl-lumefantrine and lumefantrine AUC0–∞ weighted on in vitro antimalarial activity was inversely associated with recurrent parasitemia, suggesting that both the parent drug and the metabolite contribute to the treatment outcome of artemether-lumefantrine.

PMID:21876056

Pharmacokinetic properties of conventional and double-dose sulfadoxine-pyrimethamine given as intermittent preventive treatment in infancy.
Salman S, Griffin S, et al.
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Intermittent preventive treatment in infancy (IPTi) entails routine administration of antimalarial treatment doses at specified times in at-risk infants. Sulfadoxine-pyrimethamine (SDX/PYR) is a combination that has been used as first-line IPTi. Because of limited pharmacokinetic data and suggestions that higher milligram/kilogram pediatric doses than recommended should be considered, we assessed SDX/PYR disposition, randomized to conventional (25/1.25 mg/kg of body weight) or double (50/2.5 mg/kg) dose, in 70 Papua New Guinean children aged 2 to 13 months. Blood samples were drawn at baseline, 28 days, and three time points randomly selected for each infant at 4 to 8 h or 2, 5, 7, 14, or 21 days. Plasma SDX, PYR, and N(4)-acetylsulfadoxine (NSX, the principal metabolite of SDX) were assayed by high-performance liquid chromatography (HPLC). Using population modeling incorporating hepatic maturation and cystatin C-based renal function, two-compartment models provided best fits for PYR and SDX/NSX plasma concentration profiles. The area under the plasma concentration-time curve from 0 h to infinity (AUC(0-)) was greater with the double dose versus the conventional dose of PYR (4,915 versus 2,844 g/day/liter) and SDX (2,434 versus 1,460 mg/day/liter). There was a 32% reduction in SDX relative bioavailability with the double dose but no evidence of dose-dependent metabolism. Terminal elimination half-lives (15.6 days for PYR, 9.1 days for SDX) were longer than previously reported. Both doses were well tolerated without changes in hemoglobin or hepatorenal function. Five children in the conventional and three in the double-dose group developed malaria during follow-up. These data support the potential use of double-dose SDX/PYR in infancy, but further studies should examine the influence of hepatorenal maturation in very young infants.

PMID:21282434
**Molecular assessment of Plasmodium falciparum resistance to antimalarial drugs in Papua New Guinea using an extended ligase detection reaction fluorescent microsphere assay.**
Wong RPM, Karunajeewa H, et al.
School of Medicine and Pharmacology, Fremantle Unit, University of Western Australia, Nedlands, Western Australia, Australia.
Surveillance for Plasmodium falciparum drug resistance mutations is becoming an established tool for assessing antimalarial treatment effectiveness. We used an extended version of a high-throughput post-PCR multiplexed ligase detection reaction fluorescent microsphere assay (LDR-FMA) to detect single-nucleotide P. falciparum drug resistance polymorphisms in 402 isolates from children in Papua New Guinea (PNG) participating in an antimalarial treatment trial. There was a fixation of P. falciparum crt (pfcrt) K76T, pfdhfr C59R and S108N, and pfmdr1 mutations (92%, 93%, 95%, and 91%, respectively). Multiple mutations were frequent. Eighty-eight percent of isolates possessed a quintuple mutation (underlined), SVMNT, NRNI, KAA, and YYSND, in codons 72 to 76 for pfcrt; 51, 59, 108, and 164 for pfdhfr; 540, 581, and 613 for pfdhps; and 86, 184, 1034, 1042, and 1246 for pfmdr1, and four of these carried the K540E pfdhps allele. The pfmdr1 D1246Y mutation was associated with PCR-corrected day 42 in vivo treatment failure in children allocated piperaquine-dihydroartemisinin (P = 0.004). Although the pfmdr1 NFSDD haplotype was found in only four isolates, it has been associated with artemether-lumefantrine treatment failure in Africa. LDR-FMA allows the large-scale assessment of resistance-associated single-nucleotide polymorphisms (SNPs). Our findings reflect previous heavy 4-aminoquinoline/sulfadoxine-pyrimethamine use in PNG. Since artemether-lumefantrine and piperaquine-dihydroartemisinin will become first- and second-line treatments, respectively, the monitoring of pfmdr1 SNPs appears to be a high priority.
PMID:21078925

**Desbutyl-lumefantrine is a metabolite of lumefantrine with potent in vitro antimalarial activity that may influence artemether-lumefantrine treatment outcome.**
Wong RPM, Salman S, et al.
University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, P.O. Box 480, Fremantle, Western Australia 6959, Australia. tdavis@cyllene.uwa.edu.au.
Desbutyl-lumefantrine (DBL) is a metabolite of lumefantrine. Preliminary data from Plasmodium falciparum field isolates show greater antimalarial potency than, and synergy with, the parent compound and synergy with artemisinin. In the present study, the in vitro activity and interactions of DBL were assessed from tritium-labeled hypoxanthine uptake in cultures of the laboratory-adapted strains 3D7 (chloroquine sensitive) and W2mef (chloroquine resistant). The geometric mean 50% inhibitory concentrations (IC(50)s) for DBL against 3D7 and W2mef were 9.0 nM (95% confidence interval, 5.7 to 14.4 nM) and 9.5 nM (95% confidence interval, 7.5 to 11.9 nM), respectively, and those for lumefantrine were 65.2 nM (95% confidence interval, 42.3 to 100.8 nM) and 55.5 nM (95% confidence interval, 40.6 to 75.7 nM), respectively. An isobolographic analysis of DBL and lumefantrine combinations showed no interaction in either laboratory-adapted strain but mild synergy between DBL and dihydroartemisinin (sums of the fractional inhibitory concentrations of 0.92 [95% confidence interval, 0.87 to 0.98] and 0.94 [95% confidence interval, 0.90 to 0.99] for 3D7 and W2mef, respectively). Using a validated ultra-high-performance liquid chromatography-tandem mass spectrometry assay and 94 day 7 samples from a previously reported intervention trial, the mean plasma DBL was 31.9 nM (range, 1.3 to 123.1 nM). Mean plasma DBL concentrations were lower in children who failed artemether-lumefantrine treatment than in those with an adequate clinical and parasitological response (ACPR) (P = 0.053 versus P > 0.22 for plasma lumefantrine and the plasma lumefantrine-to-DBL ratio, respectively). DBL is more potent than the parent compound and mildly synergistic with dihydroartemisinin. These properties and the relationship between day 7 plasma concentrations and the ACPR suggest that it could be a useful alternative to lumefantrine as a part of artemisinin combination therapy.
Stress and strain behaviour modelling of the carotid bifurcation.

Lawrence-Brown M, Stanley BM, et al.

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Z. Sun, Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University of Technology, GPO Box, U1987 Perth, WA 6845, Australia. E-mail: z.sun@curtin.edu.au

Background: The aim of this study is to investigate the biomechanical stress and strain behaviour within the wall of the artery and its influence on plaque formation and rupture using computational fluid dynamics (CFD). Methods: A three-dimensional finite-element model of the carotid bifurcation was generated to analyse the wall stress and strain behaviour. Both single-layer and multilayer models were created and structural analysis was compared between these two types of models. Systolic pressure of 180mmHg (~24kPa) was applied in the inner boundary of the carotid bifurcation, and CFD analysis was performed to show the wall shear stress and pressure. Results: The highest wall stress was found at the carotid bifurcation. When a high blood pressure (280mmHg) was applied to the carotid CFD model, the results showed that the stress at the carotid bifurcation may reach the rupture value. The multilayer carotid bifurcation model behaved differently from the equivalent single-layer model, with peak stress (Von-Mises) being higher in the multilayer model. Conclusion: The peak stress and strain was located at the origins of the internal and external carotid arteries. Significant shearing occurred between the layers in the wall of the artery at the bifurcation. Intramural shear stress in the CFD multilayer model has potential for intramural vascular injury. This may be responsible for plaque formation, plaque rupture and an injury/healing cycle.

Efficacy of imiquimod cream, 5%, for lentigo maligna after complete excision: A study of 43 patients.

Ly L, Kelly JW, et al.

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L. Ly, Victorian Melanoma Service, Alfred Center, Alfred Health, Commercial Road, Melbourne, VIC 3004, Australia. E-mail: lenaly21@yahoo.com.au

Objective: To determine the efficacy of imiquimod cream, 5%, in the treatment of lentigo maligna (LM).

Design: Open-label before-and-after interventional study. Setting: A multidisciplinary melanoma clinic at a major tertiary hospital. Patients: Forty-three patients with biopsy-proven LM of greater than 5 mm in diameter completed this study. Interventions: Imiquimod cream, 5%, was applied to the lesion 5 days a week for 12 weeks. The original lesion was excised with a 5-mm margin. Main Outcome Measures: The primary outcome was histopathologic evidence of LM in the excision specimen assessed independently by 2 of 3 dermatopathologists. Visible inflammation during treatment and
macroscopic clearance were recorded. Results: When 5 of the 43 patients with discordant histopathologic assessment of the excision specimen were excluded, 20 of 38 patients (53% [95% confidence interval, 36%-69%]) demonstrated histopathologic clearance of LM after imiquimod treatment. Visible inflammation was significantly associated with histopathologic clearance (P=.04), but the positive predictive value was low (62%). Macroscopic clearance showed some association with histopathologic clearance (P=.11). Dermatopathologist concordance for all 43 specimens was substantial (=0.77; 95% confidence interval, 0.57-0.96). Conclusions: Imiquimod cream, 5%, has limited efficacy in the treatment of LM when determined by histopathologic assessment of the entire treated area. The clinical signs of visible inflammation during treatment and apparent lesion clearance cannot be relied on to assess efficacy. Trial Registration: anzctr.org.au Identifier: ACTRN12610000066088 2011 American Medical Association. All rights reserved. PMID:2011579987

Hereditary hemochromatosis is characterized by a clinically definable arthropathy that correlates with iron load.
Carroll GJ, Breidahl WH, et al.
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OBJECTIVE: To determine the frequency and character of arthropathy in hereditary hemochromatosis (HH) and to investigate the relationship between this arthropathy, nodal interphalangeal osteoarthritis, and iron load. METHODS: Participants were recruited from the community by newspaper advertisement and assigned to diagnostic confidence categories for HH (definite/probable or possible/unlikely). Arthropathy was determined by use of a predetermined clinical protocol, radiographs of the hands of all participants, and radiographs of other joints in which clinical criteria were met. RESULTS: An arthropathy considered typical for HH, involving metacarpophalangeal joints 2-5 and bilateral specified large joints, was observed in 10 of 41 patients with definite or probable HH (24%), all of whom were homozygous for the C282Y mutation in the HFE gene, while only 2 of 62 patients with possible/unlikely HH had such an arthropathy (P=0.0024). Arthropathy in definite/probable HH was more common with increasing age and was associated with ferritin concentrations>1,000 g/liter at the time of diagnosis (odds ratio 14.0 [95% confidence interval 1.30-150.89], P=0.03). A trend toward more episodes requiring phlebotomy was also observed among those with arthropathy, but this was not statistically significant (odds ratio 1.03 [95% confidence interval 0.99-1.06], P=0.097). There was no significant association between arthropathy in definite/probable HH and a history of intensive physical labor (P=0.12). CONCLUSION: An arthropathy consistent with that commonly attributed to HH was found to occur in 24% of patients with definite/probable HH. The association observed between this arthropathy, homozygosity for C282Y, and serum ferritin concentrations at the time of diagnosis suggests that iron load is likely to be a major determinant of arthropathy in HH and to be more important than occupational factors. Copyright [copyright sign] 2011 by the American College of Rheumatology. PMID:20954257

The effectiveness of pulsed electrical stimulation in the management of osteoarthritis of the knee: Results of a double-blind, randomized, placebo-controlled, repeated-measures trial.
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R. E. Fary, Curtin Health Innovation Research Institute, School of Physiotherapy, Curtin University,
Objective: To determine the effectiveness of subsensory, pulsed electrical stimulation (PES) in the symptomatic management of osteoarthritis (OA) of the knee. Methods: This was a double-blind, randomized, placebo-controlled, repeated-measures trial in 70 participants with clinical and radiographically diagnosed OA of the knee who were randomized to either PES or placebo. The primary outcome was change in pain score over 26 weeks measured on a 100-mm visual analog scale (VAS). Other measures included pain on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), function on the WOMAC, patient's global assessment of disease activity (on a 100-mm VAS), joint stiffness on the WOMAC, quality of life on the Medical Outcomes Study Short-Form 36 (SF-36) health survey, physical activity (using the Human Activity Profile and an accelerometer), and global perceived effect (on an 11-point scale). Results: Thirty-four participants were randomized to PES and 36 to placebo. Intent-to-treat analysis showed a statistically significant improvement in VAS pain score over 26 weeks in both groups, but no difference between groups (mean change difference 0.9 mm [95% confidence interval -11.7, 13.4]). Similarly, there were no differences between groups for changes in WOMAC pain, function, and stiffness scores (-5.6 [95% confidence interval -14.9, 3.6], -1.9 [95% confidence interval -9.7, 5.9], and 3.7 [95% confidence interval -6.0, 13.5], respectively), SF-36 physical and mental component summary scores (1.7 [95% confidence interval -1.5, 4.8] and 1.2 [95% confidence interval -2.9, 5.4], respectively), patient's global assessment of disease activity (-2.8 [95% confidence interval -13.9, 8.4]), or activity measures. Fifty-six percent of the PES-treated group achieved a clinically relevant 20-mm improvement in VAS pain score at 26 weeks compared with 44% of controls (12% [95% confidence interval -11%, 33%]). Conclusion: In this sample of subjects with mild-to-moderate symptoms and moderate-to-severe radiographic OA of the knee, 26 weeks of PES was no more effective than placebo. Copyright 2011 by the American College of Rheumatology.
intervention and support.
Publication Types: Conference Abstract
PMID:70586801

Sorce: A phase III, randomised, double-blind trial of sorafenib in patients with resected primary renal cell carcinoma at high or intermediate risk of relapse.
Davis I, Blinman P, et al.
(Blinman, Boland, Thompson, Stockler) NHMRC Clinical Trials Centre, University of Sydney, Camperdown, NSW, Australia (Davis, Blinman, Gurney, Boland, Thompson, Stockler) ANZUP Cancer Trials Group Ltd., Camperdown, NSW, Australia (Davis) Austin Health, Heidelberg, VIC, Australia (Stockler) Sydney Cancer Centre, Royal Prince Alfred Hospital, Camperdown, NSW, Australia (Blinman, Stockler) Sydney Cancer Centre, Concord Repatriation General Hospital, Concord, NSW, Australia (Gurney) Westmead Hospital, Westmead, NSW, Australia (Troon) Royal Perth Hospital, Perth, WA, Australia (Eisen) Cancer Research UK, London, United Kingdom (Claringbold) Fremantle Hospital, Fremantle, VIC, Australia (Eisen) Clinical Trials Unit, Medical Research Council, London, United Kingdom
I. Davis, ANZUP Cancer Trials Group Ltd., Camperdown, NSW, Australia
Thirty to fifty percent of patients develop metastatic disease after nephrectomy for intermediate or high risk RCC and there is no treatment proven to reduce this rate of recurrence. Sorafenib is an oral, multi-targeted tyrosine kinase inhibitor that is an effective treatment for metastatic renal cell carcinoma. SORCE is an international, multi-centre, randomised, phase III double-blind placebo-controlled study examining the efficacy and tolerability of sorafenib (Nexavar) in patients with resected RCC at high or intermediate risk of relapse. The trial is designed to answer two main questions: whether one year of sorafenib increases DFS compared with placebo, and whether three years of sorafenib increases DFS compared with one year. Secondary outcomes include RCC-specific survival time, overall survival, cost-effectiveness, toxicity, biological characteristics of resected primary RCC and corroboration of the Leibovich Prognostic Score. International accrual is currently 968 of a planned 1656 patients randomised to 3 years placebo, 1 year sorafenib and 2 years placebo or 3 years sorafenib (2:3:3). Australian accrual is currently 56 of 250 planned participants recruited from 22 sites since August 2009. SORCE includes a UK-led translational correlative sub-study (TRANSORCE) assessing potential biomarkers in renal cell carcinoma. The ANZUP & CTC collaboration is leading a preferences sub-study being conducted in Australia and the UK (PAS in SORCE) to determine the survival benefits patients' and doctors judge necessary to make the side effects and inconvenience of adjuvant sorafenib worthwhile.
Publication Types: Conference Abstract
PMID:70586885

Meta-analysis of the association between single nucleotide polymorphisms in TGF-beta receptor genes and abdominal aortic aneurysm.
Biros E, Norman PE, et al.
(Biros, Moxon, Morris, Golledge) Vascular Biology Unit, School of Medicine, James Cook University, Townsville, QLD 4811, Australia (Norman) School of Surgery, University of Western Australia, Fremantle Hospital, Fremantle, WA 6959, Australia (Jones, van Rij, Yu) Department of Surgery, University of Otago, Dunedin, New Zealand (Blankensteijn) Department of Vascular Surgery, VU Medical Center Amsterdam, Netherlands (van Sterkenburg) Department of Vascular Surgery, Rijnstate Hostipal Arnhem, Netherlands (Baas) Department of Medical Genetics, University Medical Center Utrecht, Netherlands (Baas) Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands
J. Golledge, Vascular Biology Unit, School of Medicine, James Cook University, Townsville, QLD
Objective: The role of transforming growth factor (TGF)-beta in abdominal aortic aneurysm (AAA) is controversial. The aim of this study was to assess the association of single nucleotide polymorphisms (SNPs) within TGFBR1 and TGFBR2 with AAA and infrarenal aortic diameter by combining data from previously published studies. Methods: We performed a meta-analysis using individual subject data from three independent case-control groups from Western Australia (n= 1675), New Zealand (n= 1209), and the Netherlands (n= 1636) with 610, 601, and 693 cases of AAA (maximum infrarenal aortic diameter >=30. mm), respectively. Data were available for two TGFBR1 (rs10819634, rs1571590) and six TGFBR2 (rs304839, rs1346907, rs1036095, rs9831477, rs9843143, rs764522) SNPs. Results: There was marked heterogeneity between studies. The G alleles of the TGFBR2 rs764522 and rs1036095 SNPs were associated with AAA under a recessive model (OR = 1.69, 95% CI 1.28-2.25, P< 0.001 and OR = 1.59, 95% CI 1.23-2.07, P< 0.001) when a fixed effects model was used. Both associations remained significant after adjustment for multiple testing. Conclusion: This study suggests that two common genetic polymorphisms in TGFBR2 are associated with the risk of developing AAA although this association was mainly driven by findings in the Netherlands group and marked between study heterogeneity was detected. 2011 Elsevier Ireland Ltd.

PMID:2011596422

A single nucleotide polymorphism in exon 3 of the kallikrein 1 gene is associated with large but not small abdominal aortic aneurysm.

Biros E, Norman PE, et al. (Biros, Golledge) Vascular Biology Unit, School of Medicine, James Cook University, Townsville, QLD 4811, Australia (Norman) School of Surgery, University of Western Australia, Fremantle Hospital, Fremantle, WA 6959, Australia (Walker) Department of Surgery and Centre for Clinical Research, University of Queensland, Herston, QLD 4006, Australia (Nataatmadja, West) The Cardiovascular Research Group, Department of Medicine, University of Queensland, The Prince Charles Hospital, Brisbane, QLD 4032, Australia

J. Golledge, Vascular Biology Unit, School of Medicine, James Cook University, Townsville, QLD 4811, Australia. E-mail: jonathan.golledge@jcu.edu.au

Objective: Abdominal aortic aneurysm (AAA) is a late onset degenerative condition with an inherited component thought to be due to multiple risk alleles. A locus on chromosomes 19q13 has been previously associated with AAA. The gene encoding kallikrein 1 (KLK1) is located on chromosome 19q13 and the single nucleotide polymorphism (SNP) rs5516 has been previously shown to lead to structural changes in the KLK1 transcription regulatory region. The aim of this study was to investigate whether rs5516 was associated with AAA and aortic diameter. Methods: We performed a case-control study on two independent subject groups from Western Australia (n = 1304) and Queensland (n = 325) of which 609 and 225 had an AAA, respectively. In addition, we analysed RNA extracted from abdominal aortic biopsies from 12 patients undergoing AAA surgery and 6 organ donors. Results: After adjusting for other risk factors the G allele of the rs5516 polymorphism was associated with large but not small AAA using a dominant model in the Western Australian men and a recessive model in Queensland subjects. In subjects with large AAA the G allele was associated with aortic diameter. The short splice variant of KLK1 was upregulated within AAA compared to control biopsies. Conclusion: This study suggests that a genetic polymorphism in KLK1 may contribute to the risk of developing later stage AAA. 2011 Elsevier Ireland Ltd.

PMID:2011406929

Cochlear implants in forty-eight children with cochlear and/or vestibular abnormality.


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Objective: The role of transforming growth factor (TGF)-beta in abdominal aortic aneurysm (AAA) is controversial. The aim of this study was to assess the association of single nucleotide polymorphisms (SNPs) within TGFBR1 and TGFBR2 with AAA and infrarenal aortic diameter by combining data from previously published studies. Methods: We performed a meta-analysis using individual subject data from three independent case-control groups from Western Australia (n= 1675), New Zealand (n= 1209), and the Netherlands (n= 1636) with 610, 601, and 693 cases of AAA (maximum infrarenal aortic diameter >=30. mm), respectively. Data were available for two TGFBR1 (rs10819634, rs1571590) and six TGFBR2 (rs304839, rs1346907, rs1036095, rs9831477, rs9843143, rs764522) SNPs. Results: There was marked heterogeneity between studies. The G alleles of the TGFBR2 rs764522 and rs1036095 SNPs were associated with AAA under a recessive model (OR = 1.69, 95% CI 1.28-2.25, P< 0.001 and OR = 1.59, 95% CI 1.23-2.07, P< 0.001) when a fixed effects model was used. Both associations remained significant after adjustment for multiple testing. Conclusion: This study suggests that two common genetic polymorphisms in TGFBR2 are associated with the risk of developing AAA although this association was mainly driven by findings in the Netherlands group and marked between study heterogeneity was detected. 2011 Elsevier Ireland Ltd.

PMID:2011596422

A single nucleotide polymorphism in exon 3 of the kallikrein 1 gene is associated with large but not small abdominal aortic aneurysm.

Biros E, Norman PE, et al. (Biros, Golledge) Vascular Biology Unit, School of Medicine, James Cook University, Townsville, QLD 4811, Australia (Norman) School of Surgery, University of Western Australia, Fremantle Hospital, Fremantle, WA 6959, Australia (Walker) Department of Surgery and Centre for Clinical Research, University of Queensland, Herston, QLD 4006, Australia (Nataatmadja, West) The Cardiovascular Research Group, Department of Medicine, University of Queensland, The Prince Charles Hospital, Brisbane, QLD 4032, Australia

J. Golledge, Vascular Biology Unit, School of Medicine, James Cook University, Townsville, QLD 4811, Australia. E-mail: jonathan.golledge@jcu.edu.au

Objective: Abdominal aortic aneurysm (AAA) is a late onset degenerative condition with an inherited component thought to be due to multiple risk alleles. A locus on chromosomes 19q13 has been previously associated with AAA. The gene encoding kallikrein 1 (KLK1) is located on chromosome 19q13 and the single nucleotide polymorphism (SNP) rs5516 has been previously shown to lead to structural changes in the KLK1 transcription regulatory region. The aim of this study was to investigate whether rs5516 was associated with AAA and aortic diameter. Methods: We performed a case-control study on two independent subject groups from Western Australia (n = 1304) and Queensland (n = 325) of which 609 and 225 had an AAA, respectively. In addition, we analysed RNA extracted from abdominal aortic biopsies from 12 patients undergoing AAA surgery and 6 organ donors. Results: After adjusting for other risk factors the G allele of the rs5516 polymorphism was associated with large but not small AAA using a dominant model in the Western Australian men and a recessive model in Queensland subjects. In subjects with large AAA the G allele was associated with aortic diameter. The short splice variant of KLK1 was upregulated within AAA compared to control biopsies. Conclusion: This study suggests that a genetic polymorphism in KLK1 may contribute to the risk of developing later stage AAA. 2011 Elsevier Ireland Ltd.

PMID:2011406929


Cochlear implants in forty-eight children with cochlear and/or vestibular abnormality.


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Dettman, Shani: University of Melbourne, Audiology, Hearing and Speech Sciences, 550 Swanston Street Carlton, Melbourne, VIC, Australia, 3053, dettmans@unimelb.edu.au
Dettman, Shani: Department of Otolaryngology, University of Melbourne, Parkville, VIC, Australia Sadeghi-Barzalighi, Ana: Department of Otolaryngology, University of Melbourne, Parkville, VIC, Australia Ambett, Ranjeeta: Fremantle Hospital, University of Western Australia, Crawley, WA, Australia Dowell, Richard: Department of Otolaryngology, University of Melbourne, Parkville, VIC, Australia Trotter, Matthew: Royal Eye and Ear Hospital, East Melbourne, VIC, Australia Briggs, Robert: Department of Otolaryngology, University of Melbourne, Parkville, VIC, Australia CT and MRI scans for 48 children with cochlear and/or vestibular abnormality were classified in decreasing severity; common cavity, Mondini plus enlarged vestibular aqueduct, Mondini dysplasia alone and enlarged vestibular aqueduct alone. No significant relationship between degree of cochlea abnormality and surgical issues (cerebrospinal fluid gusher, depth of insertion, number of electrodes) or speech perception/language outcomes was found. A significant relationship was observed between cerebrospinal fluid gusher and partial electrode insertion, fewer active electrodes and poorer sentence understanding. Optimum language outcomes were associated with younger age at implant. (PsycINFO Database Record (c) 2011 APA, all rights reserved) (journal abstract).
PMID:Peer Reviewed Journal: 2011-15665-003

Dermatology outpatient population profiling: Indigenous and non-indigenous dermatoepidemiology.
Heyes C, Chan J, et al.
Department of Dermatology, Fremantle Hospital, Fremantle Department of Dermatology, Sir Charles Gairdner Hospital Department of Dermatology, Princess Margaret Hospital Department of Dermatology, Royal Perth Hospital, Perth, Western Australia School of Public Health, James Cook University, Townsville, Queensland, Australia.
Background: Little is known about the population using Australian dermatology outpatient services, in particular, Indigenous patients. This information is important to direct the strategic planning of dermatology services. Methods: This study is a multicentre, retrospective audit of all patients attending public, outpatient dermatology clinics over 7 months across four Perth tertiary hospitals. The patient population (4873 patients) was profiled by age, gender, Indigenous status and rural/urban status. Medical records of the Indigenous patient population (104 patients) were reviewed to reveal the most common skin conditions. Results: The population using public, outpatient services had a median age of 48[em space]years, 51.4% were male and 13.6% were from rural areas. Male patient median age was 50 years compared to 45 years for female patients (P = 0.002). Indigenous patients had a median age of 22 years, a female to male ratio of 3:2 and 26.9% were from rural areas. Over 50% of Indigenous patient appointments were missed. Skin infections, eczematous conditions and naevi were the most common skin conditions in Indigenous patients. Conclusions: This data can guide strategies towards improving the provision of dermatology services for the Australian population. Particular attention is required towards improving Indigenous Australians' capacity to access dermatology services. Copyright 2011 The Authors. Australasian Journal of Dermatology Copyright 2011 The Australasian College of Dermatologists.
PMID:21834816

Indigenous dermatology: A review.
Heyes C, Gebauer K.
(Heyes, Gebauer) Department of Dermatology, Fremantle Hospital, Fremantle, WA, Australia (Heyes) School of Public Health, James Cook University, Townsville, QLD, Australia C. Heyes, Department of Dermatology, Fremantle Hospital, Fremantle, WA, Australia Indigenous Australians suffer increased rates of morbidity across a wide range of medical conditions
including many skin conditions. This review assesses the scope of the literature on Indigenous Dermatology. It seeks to highlight what is known about the burden of skin disease in the Indigenous population and to identify areas of uncertainty. A systematic review of research relating to Indigenous Dermatology since 1980 was performed utilizing the databases Ovid Medline, Embase, the Cochrane Library, CINAHL, Australian Institute of Aboriginal and Torres Strait Islander Studies and Australian Indigenous HealthInfoNet. This review provides an overview of what is known about Indigenous dermatology, highlights areas of clinical need and provides direction on areas requiring further research.

Publication Types: Conference Abstract
PMID:70558767


**Classic Kaposi’s sarcoma with negative human herpesvirus-8 serology.**
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(Foxton, Donnelly) Department of Dermatology, Fremantle Hospital, Fremantle, WA, Australia
G. Foxton, Department of Dermatology, Fremantle Hospital, Fremantle, WA, Australia
An 82 year old Mediterranean man presented with a 12 month history of right leg oedema followed by the development of multiple asymptomatic bluish nodules extending from the foot to the thigh. The differential diagnoses included Kaposi's sarcoma (KS), multiple cutaneous metastasis and angiosarcoma. Histopathologic examination showed a dermal proliferation of interlacing atypical spindle cells intimately related to irregular vascular channels with plump endothelial cells raising the possibility of nodular stage KS. Tumour cells demonstrated positive staining to CD31, CD34, D2-40 and factor VIII. HHV-8 and HIV serology was negative and PCR on the paraffin-embedded tissue was performed to confirm the presence of the virus. The patient was referred to the oncologists for definitive management. We present a review of the literature on KS focusing on HHV-8 diagnostic assays and current treatment strategies.

Publication Types: Conference Abstract
PMID:70391715


**Dermatology outpatient population profiling: Indigenous and non-Indigenous dermatoepidemiology.**
Heyes C, Chan J, et al.
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Department of Dermatology, Sir Charles Gairdner Hospital, Perth, WA, Australia (Halbert) Department of Dermatology, Princess Margaret Hospital, Perth, WA, Australia (Clay) Department of Dermatology, Royal Perth Hospital, Perth, WA, Australia
C. Heyes, Department of Dermatology, Fremantle Hospital, Perth, WA, Australia
Introduction: To enhance, direct and plan future dermatology services in Australia it is essential to know the characteristics of the patient population being served. Little is currently known about the patient population utilising Australian dermatology outpatient services, and in particular, the Indigenous patient population. Methods: This study is a multicentre, retrospective audit of all patients attending public, outpatient Dermatology clinics over a seven-month period across the four Perth tertiary hospitals providing such clinics. The patient population (4873 patients) was profiled by age, gender, Indigenous status and rural/urban status. Detailed profiling of the Indigenous patient population (104 patients), through interrogation of medical records revealed the predominant skin conditions affecting this group. Results: The general population utilising public, outpatient services has an median age of 48 years, are predominantly male (51.4%) and 13.8% are from rural areas. Male patients are on average 5 years older than female patients. In contrast, Indigenous patients have a median age of 22 years, have a female to male ratio of 3 : 2 and 26.9% are from rural areas. Over 50% of Indigenous patient appointments are missed. Skin infections (particularly fungal infections),
eczematous conditions and naevi are identified as the most common primary skin conditions in this Indigenous patient population. Conclusions: This dermatoepidemiological data can guide strategic planning towards improving the provision of dermatology services for the Australian population in the future. Particular attention is required towards improving Indigenous Australians' capacity to access specialist dermatology services.

Publication Types: Conference Abstract
PMID:70391791


Clinical dermatology exposure in the undergraduate and prevocational years of medical training.
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C. Heyes, Department of Dermatology, Fremantle Hospital, Perth, WA, Australia
Repeated international studies have identified the limitations of doctors working in General Practice and other medical specialties in the diagnosis and treatment of various skin conditions. This is likely to be due in part to the limited clinical exposure to specialist-led dermatology in the undergraduate and prevocational years of medical training. This study seeks to identify the current exposure of medical students and prevocational doctors to specialist-led clinical dermatology in Australia. The study audits the total number of days of clinical exposure to specialist-led dermatology in each of Australia's medical schools as well as the number of Intern and Resident Medical Officer dermatology rotations available to prevocational doctors in hospitals nationwide. Australian medical students and junior doctors continue to have limited clinical exposure to specialist-led dermatology and this has significant implications upon the standard of dermatology knowledge and skin care in the wider medical community.
Publication Types: Conference Abstract
PMID:70391790


Treatment resistant elephantiasic thyroid dermopathy responding to rituximab and plasmapheresis.
(Heyes, Gebauer) Department of Dermatology, Fremantle Hospital, Perth, WA, Australia (Nolan) Department of Immunology, Fremantle Hospital, Perth, WA, Australia (Leahy) Department of Haematology, Fremantle Hospital, Perth, WA, Australia
C. Heyes, Department of Dermatology, Fremantle Hospital, Perth, WA, Australia
A patient with a severe case of Graves' disease displayed the rare complete triad of peripheral manifestations - namely thyroid eye disease, thyroid dermopathy (pretibial myxoedema) and acropachy. The most severe and rare form of thyroid dermopathy was exhibited, namely elephantiasic dermopathy. This condition is particularly debilitating and is noted to be poorly responsive to treatment. Despite being trialled on extensive recognised therapies over the course of 11 years, the patient's dermopathy progressively worsened. In mid-2006, under the coordinated care of Fremantle Hospital specialists in Immunology, Haematology and Dermatology, the patient was trialled on a novel combination of rituximab and plasmapheresis with good response. Serial subcutaneous thickness ultrasounds, TSH Receptor antibody levels, clinical photographs and patient symptoms revealed significant and rapid improvement under this new regimen. The patient's condition stabilised in October 2009 at the age of 58 and she was able to cease therapy. The success of this regimen suggests its potential as an effective therapeutic option for other patients with this debilitating condition.
A randomised trial of a four-step multidisciplinary approach to the antenatal care of obese pregnant women.
Quinlivan JA, Lam LT, et al.
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BACKGROUND: Obesity is common in pregnancy and results in morbidity to mother and newborn. AIM: To evaluate whether a four-step multidisciplinary protocol of antenatal care for overweight and obese women would reduce the incidence of gestational diabetes. METHODS: Pregnant women were approached at their first antenatal visit, and body mass index (BMI) was calculated to determine whether they were overweight or obese (BMI > 25). Eligible women were randomised to standard obstetric antenatal care or four-step multidisciplinary antenatal care. Clinic protocol included (i) continuity of obstetric provider; (ii) weighing on arrival at each visit; (iii) a five brief minute intervention by a food technologist who asked about the women's eating habits of the previous day, provided information on reading food labels, shopping lists of affordable foods available from local shops and recipes for a healthy pregnancy diet; and (iv) clinical psychology management to assess symptoms of depression and anxiety, stressful life events and determine whether psychological factors were involved in eating patterns. Labour and delivery data were audited from the medical records to determine the final incidence of gestational diabetes. The primary outcomes were gestational diabetes and weight gain. RESULTS: The intervention was associated with a significant reduction in the incidence of gestational diabetes (6 versus 29%, OR 0.17 [CI 0.03-0.95], P = 0.04). It was also associated with reduced weight gain in pregnancy (7.0 versus 13.8 kg, P < 0.0001). Despite this, birthweight of newborns was similar (3.5 ± 0.1 kg versus 3.4 ± 0.1 kg, P = 0.16). CONCLUSION: A four-step management plan adopted with obese women reduces the incidence of gestational diabetes.

Clinical guidelines for the physical care of mental health consumers: a comprehensive assessment and monitoring package for mental health and primary care clinicians.
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Objectives: People with a mental illness are more likely to experience poor physical health as compared to the general population. Currently, Australian mental health patients experience a relatively low level of physical health appraisal, prompting the development of the Clinical guidelines for the physical care of mental health consumers assessment and monitoring package. Method: The Clinical guidelines package takes an holistic approach, with a focus on the key dimensions of medication effects, lifestyle, existing or developing physical disorders, alcohol and illicit drug use, and psychosocial factors. Results: The package consists of a metabolic syndrome algorithm wall chart, a Clinician handbook, a Psychosocial assessment booklet, and a set of three screening forms. Conclusions: By taking a user-friendly, flexible, evidence-based approach, the resource can be used.
by all clinicians involved in the healthcare of people with a mental illness. 
PMID:21980931

The incidence of falls in intensive care survivors. 
Patman SM, Dennis D, et al. 
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S.M. Patman, School of Physiotherapy, The University of Notre Dame Australia, 19 Mouat Street (PO Box 1225), Fremantle, WA 6959, Australia. E-mail: shane.patman@nd.edu.au 
Background: Falling among adults in acute care is an important problem with falls rates in tertiary hospitals ranging from 2% to 5%. Factors that increase the risk of falling, such as advanced age, altered mental status, medications that act on the central nervous system and poor mobility, often characterise individuals who survive a prolonged intensive care unit (ICU) admission. Purpose: To measure the incidence of falls and describe the characteristics of fallers among intensive care survivors. Methods: A comprehensive retrospective chart review was undertaken of 190 adults who were intubated and ventilated for >=168 h and survived their acute care stay. Using a standardised form, several variables were extracted including falls during hospitalisation and risk factors such as age, severity of illness, and length of stay in intensive care and hospital. Findings: Thirty-two (17%, 95% confidence interval 11.5-22.2%) patients fell at least once on the in-patient wards following their ICU stay. Compared with non-fallers, fallers were younger (53.2 +/- 17.9 vs. 44.1 +/- 18.3 years; p = 0.009) and had a shorter duration of inotropic support in ICU (84 +/- 112 vs. 56 +/- 100 h; p = 0.040). The majority of fallers were aged less than 65 years (84%). Both fallers and non-fallers had similar APACHE II scores (20 +/- 8 vs. 21 +/- 7; p = 0.673), length of stay in intensive care (14.2 +/- 8.7 vs. 14.0 +/- 9.7 days; p = 0.667) and hospital length of stay (43.9 +/- 33.1 vs. 41.0 +/- 38.8 days; p = 0.533). Conclusion: Falling during hospitalisation is common in intensive care survivors. Compared with non-fallers, fallers were younger and required inotropes for a shorter duration. Those who survive a prolonged admission to an ICU may benefit from specific assessment of balance and falls risk by the multidisciplinary team. 2011 Australian College of Critical Care Nurses Ltd. 
PMID:21783378

A qualitative exploration of nurse's perception of Critical Outreach Service: A before and after study. 
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Background: Critical Care Outreach Services (CCOS) have been reported to streamline the transfer of
patients from the intensive care unit (ICU) to the wards and provide a follow-up service supporting ward staff to provide optimum care for patients discharged from ICU. Purpose: The aim of this study was to explore the perceptions of nursing staff before and after the introduction of a CCOS at three adult teaching hospitals in Perth, Western Australia. Methods: Exploratory focus groups were conducted with registered nurses (RNs) at each of the participating hospitals prior to and 6 months after the introduction of a CCOS. Framework analysis was used to analyse the transcribed data using a thematic approach with themes developed from the narratives of the participants. Results: Inexperienced RNs in particular voiced positive comments about the CCOS. The role was seen as a senior nurse who was an additional resource for less experienced staff as they educated them on complex procedures that were not common on the general wards. The RNs reported that apprehensions about the role that they had pre-implementation were not borne out in practice and that they believed that the CCOS had positive effects on patient outcomes. Conclusion: The CCOS improved communication processes between members of the multidisciplinary team and units within the hospital, which subsequently enhanced the ward transition process for critically ill patients and ward nursing staff. 2010.
PMID:21074453


**Mental health risk assessment - a guide for GPs.**

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**BACKGROUND** Risk assessment of patients in general practice is a challenging area of clinical practice. Competing interests of managing patient wishes, consideration of duty to warn others and invoking the Mental Health Act while practising in a medicolegally accountable manner can be difficult.

**OBJECTIVE** This article summarises the risk assessment of patients with possible mental disorders and provides suggestions regarding measures that may be undertaken to manage risk in psychiatric emergencies.

**DISCUSSION** The evidence of effectiveness for risk assessment interventions in acute settings is limited. While it is not possible for general practitioners to predict the future, and particularly to predict fatal outcomes, they can be expected to meet a standard of care that identifies those at risk and provide an acceptable clinical response.

PMID:21655480


**Terminal delirium.**

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Delirium is common in terminally ill patients and is associated with increased morbidity and mortality. Often misdiagnosed and poorly managed due to the similarity in presentation with pain and other psychological disorders such as dementia and depression, it is a distressing symptom for patients, their families/caregivers and health care professionals. The pathogenesis of delirium is multifactorial, complex and poorly understood and no single cause has been identified to date. Management of delirium requires accurate assessment and investigation of potential causes and may include both non-pharmacological and pharmacological strategies. Palliative sedation may be required in some cases, but this strategy remains controversial. Difficulties identified included a lack of awareness and poor recognition of delirium, a paucity of definitive assessment tools for both delirium and pain at the end of life and the underuse of assessment tools that are available. The routine use of medications at the end of life may cause or exacerbate delirium.

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A strategy for recruiting subjects to test an innovation in community pharmacy.

Jiwa M, Hughes J, et al.

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Innovations that help the pharmacist identify which patients with lower bowel symptoms should be referred to a doctor may reduce delayed presentation to medical practitioners. This study reports several methods to recruit patients presenting with lower bowel symptoms to a study in community pharmacies.

PMID: 058446926260860

Diagnostic value of SPECT, PET and PET/CT in the diagnosis of coronary artery disease: A systematic review.

Al Moudi M, Sun Z, et al.

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Purpose: The purpose of the study was to investigate the diagnostic value of SPECT, PET and PET/CT in the diagnosis of coronary artery disease, based on a systematic review. Material and Methods: A search of PubMed/Medline and Sciencedirect databases in the English-language literature published over the last 24 years was performed. Only studies with at least 10 patients comparing SPECT, PET or combined PET/CT with invasive coronary angiography in the diagnosis of coronary artery disease (50% stenosis) were included for analysis. Sensitivities and specificities estimates pooled across studies were analysed using a Chisquare test. Results: Twenty-five studies met the selection criteria and were included for the analysis. Ten studies were performed with SPECT alone; while another six studies were performed with PET alone. Five studies were carried out with both PET and SPECT modalities, and the remaining four studies were investigated with integrated PET-CT. The mean value of sensitivity, specificity and accuracy of these imaging modalities for the diagnosis of coronary artery disease was 82% (95%CI: 76 to 88), 76% (95%CI: 70 to 82) and 83% (95%CI: 77 to 89) for SPECT; 91% (95%CI: 85 to 97), 89% (95%CI: 83 to 95) and 89% (95%CI: 83 to 95) for PET; and 85% (95%CI: 79 to 90), 83% (95%CI: 77 to 89) and 88% (95%CI: 82 to 94) for PET/CT, respectively. The diagnostic accuracy of these imaging modalities was dependent on the radiotracers used in these studies, with ammonia resulting in the highest diagnostic value. Conclusion: Our review shows that PET has high diagnostic value for diagnosing coronary artery disease, and this indicates that it is a valuable technique for both detection and prediction of coronary artery disease. 2011 Biomedical Imaging and Intervention Journal. All rights reserved.

Publication Types: Review

PMID: 2011217402

'One stop' haematuria clinic in Fremantle Hospital, Western Australia: a report of the first 500 patients.


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UNLABELLED: What's known on the subject? and What does the study add? Haematuria is a
symptom of urologic cancer particularly bladder cancer and timely diagnosis can prevent disease from progression to a more advanced or incurable stage. The 'One Stop' Haematuria clinic is the first rapid assessment clinic for haematuria in a public hospital in Western Australia. The results from this study have confirmed that it is an efficient and effective model in the streamlined care of patients with haematuria and provides evidence to support a more widespread adoption of this model of care. OBJECTIVE: * To report the prospective outcomes and clinic process for the first 500 patients at a new 'one stop' Haematuria Clinic (OSHC) in a Western Australian public hospital.

PATIENTS AND METHODS: * The first 500 patients who attended the weekly OSHC between May 2008 and February 2011 were included in this paper. * Patients with haematuria were referred by various specialties. Gender, age, outcomes following OSHC attendance, diagnoses and wait times were recorded. RESULTS: * In all, 311 males and 189 females presented to the clinic with visible haematuria (296 cases) and microscopic haematuria (204 cases). * Sixty-six new cancers (13.2%) were diagnosed, 63 urological and three non-urological. * Fifty-one patients (10.2%) were diagnosed with transitional cell carcinoma of the bladder. Further breakdown of staging for bladder transitional cell carcinoma diagnoses were stage Ta (23 patients), stage T1 (21 patients) and stage 2-4 (seven patients). * Sixty-nine patients (13.8%) were diagnosed with urological pathologies requiring surgery. Thirty-four patients (6.8%) were followed up by the nurse practitioner or continence advisors. In all, 61.2% of patients were discharged after a single visit to the OSHC. * Excluding those requiring surgery only 3.4% patients required further urologist follow-up. CONCLUSION: * The results have demonstrated that the first OSHC in a public Western Australian hospital is an efficient and effective model for the streamlined care of patients with haematuria. * We encourage that similar models are adopted in other public hospitals in the region. Copyright 2011 THE AUTHORS. BJU INTERNATIONAL Copyright 2011 BJU INTERNATIONAL. PMID:22085132


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Introduction: Optimal treatment of high grade NMIBC remains controversial. We aim to determine the benefits (efficacy and tolerability) of a combination regime (BCG+MMC) and compare it to standard BCG and maintenance in patients with pT1 or high grade pTa bladder TCC (papillary or solid). Study Design: Pilot study followed by two-stage, multi-centre, phase III RCT. Stage-1 aims to establish feasibility and tolerability in a multi-centre setting. Stage-2 aims to determine which regimen is preferable (endpoints: recurrence, progression, distant metastases, adverse events, quality of life, death). Sample Size: For stage 1, 61 subjects per arm provides 90% power and 95% confidence to distinguish a feasibility rate of <=50% (not worthy of further research) versus >=70% (worthy of further research). For stage 2, 500 subjects gives >80% power to detect a 38% reduction in the risk of recurrence. Methods (pilot): Patients elected to receive the combination regime (n = 10) or standard (n = 5) regime. Four surveillance cystoscopies +/- biopsy were scheduled throughout the treatment. Local and systemic toxicity data including International Prostate Symptom Score (IPSS), Cystitis Score (CS) and visual analogue pain scale (VAP) were prospectively collected. Intervention: See image below. (Figure presented) Results (pilot): Fourteen patients completed induction and ten maintenance. Four patients did not complete allocated treatment; one (BCG/MMC) progressed during induction requiring cystectomy, another (BCG/MMC) developed reactive arthritis after induction and completed scheduled MMC only, and two (BCG) declined scheduled maintenance after induction. Median baseline IPSS,
CS and VAP for BCG vs. BCG/MMC groups were similar and did not change significantly at six weeks, three or six months. Conclusion: No difference in toxicity between the two regimes has been demonstrated. A multi-centre RCT is required to confirm this and determine oncological outcomes. This trial will establish a national, standardised protocol for intravesical BCG including maintenance and will determine whether a practical means of adding MMC is beneficial.

Publication Types: Conference Abstract
PMID:70350466

BJU International. 2011; 107(Supplement S1): 11.

Intravesical chemotherapy plus BCG in non-muscle invasive bladder cancer: A systematic review with meta-analysis.
Houghton B, Hayne D, et al.
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B. Houghto, University of Sydney, NHMRC Clinical Trials Centre, Sydney, Australia
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 is planning a trial in this area using the Di Stasi 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. 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:70350422

Blood. 2011; 118 (21).

First-line radio-immunotherapy of newly diagnosed, advanced follicular non-Hodgkin lymphoma with 131I-rituximab: The INITIAL study.
McQuillan AD, MacDonald WBG, et al.
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(MacDonald, Turner) Department of Nuclear Medicine, Fremantle Hospital, Fremantle, Australia
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Introduction: Radio-immunotherapy (RIT) with <sup>131</sup>I-rituximab has demonstrated efficacy in relapsed and refractory non-Hodgkin lymphoma (NHL). <sup>131</sup>I-tositumomab has been shown to be an effective first-line agent in follicular NHL with durable response. We aimed to evaluate the efficacy and safety of first-line <sup>131</sup>I-rituximab RIT and the duration of response in previously untreated patients with follicular NHL, given that this radiolabeled chimeric antibody treatment can be repeated upon relapse. Methods: Fifty consecutive patients with newly diagnosed,
symptomatic, advanced follicular NHL received a prescribed therapy activity of $^{131}$I-rituximab predicated upon a fixed, whole-body radiation dose of 0.75 Gy. All patients were treated as outpatients. All patients received a standard four-week course of rituximab at a dose of 375 mg/m$^2$ in conjunction with the radionuclide therapy, and subsequent rituximab maintenance at 3-monthly intervals for one year. Response was determined by $^{18}$F-FDG PET/CT scans at baseline, and at 3 and 12 months post-treatment. Results: Overall response rate (ORR) at 3 months was 98%, with complete response (CR) seen in 38 patients (76%) and partial response (PR) in 11 patients (22%). Four patients (36%) assessed as having PR at 3 months converted to CR in the year following treatment, so that 84% of patients were in CR at one year. During median follow-up of 33 months (range 12-61 months) only one patient (2.6%) among those who had achieved CR has relapsed, while progressive disease has been seen in seven patients (64%) of those with PR at first post-treatment assessment. Only three of the seven patients with PD have so far required further treatment; one with local radiotherapy and two who have received combination chemotherapy. Median progression-free survival (PFS) has not yet been reached. Toxicity was limited to hematological Grade 4 neutropenia in 5 patients (10%) and thrombocytopenia in 5 patients (10%). One patient received a single platelet transfusion. There were no episodes of bleeding or infection. Three patients have died; one from transformed, aggressive NHL (the only non-responder) and the other two from non-hematological malignancies not apparent at study entry.

Conclusion: First-line $^{131}$I-rituximab RIT of advanced follicular NHL is effective and safe. Early response rates are similar to those observed with combination chemotherapy and rituximab regimens. Durable CR is present in 82% of patients over a median follow-up of 33 months and median PFS has not yet been reached. Of those with documented PR at 3 months, approximately one-third subsequently converted to CR, while the remaining two-thirds developed PD.

Publication Types: Conference Abstract
PMID:70768389


Radioimmunotherapy of indolent non-Hodgkin lymphoma (NHL) has achieved objective response rates in clinical trials comparable with standard rituximab with cyclophosphamide, doxorubicin, vincristine, and prednisone chemotherapy, but is relatively underused in routine practice. In this article, we report our clinical experience in 142 consecutive patients who received iodine-131 rituximab radioimmunotherapy for low-grade, predominantly follicular, relapsed NHL. Objective response rates of 67%, with complete response (CR) in 50% and median overall survival of 32 months, matched the response rates in a phase 2 clinical trial of (131)I-rituximab radioimmunotherapy and compares favorably with those reported for (131)I-lositumomab or (90)Y-ibritumomab tiuxetan. Progression-free survival was 18 months overall and 32 months in CR or CR-unconfirmed patients. Our patients comprised 107 (75%) follicular lymphoma, 21 (15%) small lymphocytic lymphoma, 6 (4%) mucosa-associated lymphoid tissue/marginal zone lymphoma, and 8 (6%) mantle-cell lymphoma, with median follow-up of 32 months and 8-year overall survival of 48%. Toxicity was limited to hematologic grade 4 neutropenia, occurring in 10% and thrombocytopenia in 6%. There were no episodes of bleeding or infection requiring hospital admission. Radioimmunotherapy with (131)I-rituximab in routine clinical outpatient practice provides cost-effective, safe treatment of relapsed/refractory indolent NHL, with half of patients achieving durable, complete remission with potential for repeat radioimmunotherapy on relapse.

PMID:20864582
**Oncocytic carcinoma of the parotid gland with facial nerve invasion.**
Leahy T, Sader C.
Approximately 3% of all head and neck neoplasms originate in the parotid gland and less than 1% are oncocytic. We present the rare case of a 44-year-old man with oncocytic carcinoma of the parotid gland with facial nerve invasion and discuss the characteristics of this rare entity.

**Ingested bony foreign body abutting thoracic aorta.**
Leahy TW, Kuthubutheen J.
The authors present the case of a 38-year-old female who presented with an ingested oesophageal foreign body (lamb bone) following consumption of a casserole. The bone was initially not seen on plain x-ray but CT imaging revealed a 21×20 mm pyramid shaped bone distending the proximal oesophageal mucosa and lodged only 2 mm from the aortic arch. Cardiothoracic surgery services were available on standby to perform an emergency thoracotomy in the event of any haemorrhage. However, the bone was removed successfully with rigid oesophagoscopy and the patient made a full recovery.

**A rare case of bilateral malignant otitis externa and osteomyelitis with lower cranial nerve sequelae.**
Leahy TW, Sader C.
ENT Department, Fremantle Hospital, Perth, Western Australia, Australia.
The authors present the case of a 76-year-old male who presented with right-sided recurrent malignant otitis externa (MOE) and skull-base osteomyelitis. His management involved aggressive antimicrobial therapy and multiple hyperbaric oxygen treatments. After resolution of his right-sided infection, the patient returned a short time later with symptoms and findings consistent with new, left-sided MOE with involvement of the left skull-base. With repeat treatment, the patient is now cured of his infection but poses a challenge to the treating team about future management.

**Quality use of medicines and health outcomes among a cohort of community dwelling older men: an observational study.**
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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT *Adverse drug reactions and polypharmacy are common, particularly later in life. Suboptimal use of medicines may be associated with adverse health outcomes. WHAT THIS STUDY ADDS *Markers of potentially suboptimal medication use (both medication over-use and under-use) were observed frequently among a cohort of community dwelling older men. Potentially suboptimal medication appeared to be independently associated with important adverse health outcomes. AIM To determine the prevalence of potentially suboptimal medication use and association with adverse outcomes. METHODS A prospective, observational cohort study of 4260 community-dwelling older men from Perth, Western Australia (mean age of 77 +/- 3.6 years) was conducted. Follow-up was for 4.5 years (or until death, if sooner). Cox proportional hazard models were used to explore associations between suboptimal medication use and prospective clinical
outcomes. Logistic regression analyses were used to explore predictors of a fall in the previous 12 months. RESULTS Use of potentially inappropriate medicines (48.7%), polypharmacy (≥5 medications, 35.8%) and potential under-utilization (56.7%) were highly prevalent, and overall 82.3% of participants reported some form of potentially suboptimal medication use. A self-reported history of falls in the previous 12 months was independently associated with the number of medicines taken (odds ratio [OR] = 1.06, 95% confidence interval [CI] 1.02, 1.09) and use of one or more potentially inappropriate medicines (OR = 1.23, 95% CI 1.04, 1.45). After adjusting for age, co-morbidity, smoking status, body mass index, hypertension and educational attainment, the number of medicines reported was associated with admission to hospital (hazard ratio [HR] = 1.04, 95% CI 1.03, 1.06), cardiovascular events (HR = 1.09, 95% CI 1.06, 1.12) and all cause mortality (HR = 1.04, 95% CI 1.00, 1.07). Use of one or more potentially inappropriate medicines was associated with admission to hospital (HR = 1.16, 95% CI 1.08, 1.24). Potential under-utilization was associated with cardiovascular events (HR = 1.20, 95% CI 1.03, 1.40). CONCLUSIONS These data suggest that both medication over-use and under-use occur frequently among older men and may be harmful. Copyright 2011 The Authors. British Journal of Clinical Pharmacology Copyright 2011 The British Pharmacological Society. PMID:21395652


Cost-effectiveness of artemisinin combination therapy for uncomplicated malaria in children: Data from Papua New Guinea.

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Objective To compare the cost-effectiveness of conventional antimalarial therapy with that of three artemisinin combination treatment regimens in children from Papua New Guinea aged 6 to 60 months. Methods An incremental cost-effectiveness analysis was performed using data from 656 children with Plasmodium falciparum and/or P. vivax malaria who participated in a large intervention trial in two clinics in northern Papua New Guinea. The children were randomized to one of the following groups: (i) conventional treatment with chloroquine plus sulfadoxine plus pyrimethamine (CQ+S+P); (ii) artesunate plus S plus P; (iii) dihydroartemisinin plus piperaquine (DHA+PQ); and (iv) artemether plus lumefantrine (A+L). For treatment outcomes, World Health Organization definitions were used. The cost of transport between home and the clinic plus direct health-care costs served as a basis for determining each regimen’s incremental cost per incremental treatment success relative to CQ+S+P by day 42 and its cost per life year saved. Findings A+L proved to be the most effective regimen against P. falciparum malaria and was highly cost-effective at 6.97 United States dollars (US$) per treatment success (about US$ 58 per life year saved). DHA+PQ was the most effective regimen against P. vivax malaria and was more cost-effective than CQ+S+P. Conclusion A+L and DHA+PQ are highly cost-effective regimens for the treatment of paediatric P. falciparum and P. vivax malaria, respectively, in parts of Papua New Guinea. Future research will be required to determine if these findings hold true for other territories in Asia and Oceania with similar malaria epidemiology. PMID:2011132821


Using the Burn Specific Health Scale-Brief as a measure of quality of life after a burn - What score should clinicians expect?

Kvannli L, Finlay V, et al.
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Background: How do clinicians determine the acceptable level of recovery of quality of life (QoL) after a burn? Many use the Burn Specific Health Scale (BSHS). The aim of this study was to examine normative values of the BSHS-Brief (BSHS-B) questionnaire in the general population. Methods: Two random samples of the non-burned public were taken. Each individual completed either the physical or the generic questions adapted from the BSHS-B questionnaire. Results: Of the 124 subjects who completed the physical questions, >73% rated themselves 36/36. Group mean (SD) = 34.8 (2.9), median (IQR) = 36 (35-36), range 16-36. Advancing age was associated with reduced physical capability (p = 0.016). In contrast, 7.6% of the 105 subjects who answered the generic questions recorded a full score (84/84). Group mean (SD) = 71.3 (13.8), median (IQR) = 76 (66-80), range 10-84. Conclusion: The study showed the non-burned population do not respond with full scores to all questions in the BSHS-B. The result was more notable in the non-physical questions related to the psychological and environmental factors. The data presented prompts clinicians to collect and define acceptable recovery of quality of life after a burn as measured by the BSHS-B for their local burn population. 2010 Elsevier Ltd and ISBI. All rights reserved.

Laser trabeculoplasty: An investigation into factors that might influence outcomes.


Objective: To examine the effectiveness of argon (ALT) or selective (SLT) laser trabeculoplasty (LTP) in lowering intraocular pressure (IOP) and to determine whether patient-related factors had any impact on outcome. Design: Retrospective review. Participants: 500 patients treated with LTP over 14 years. Methods: This study was conducted at Sunnybrook Health Sciences Centre, University of Toronto. Five patient-related characteristics were used as dependent variables - age, race, gender, pseudophakic status, and pseudoexfoliation. IOP decrease and treatment failure at 12 months were the main outcome variables. Results: 500 eyes of 500 patients were included, 350 after ALT and 150 after SLT. The mean +/- standard deviation baseline IOP was significantly higher in the patients treated by ALT than in those treated by SLT (24.2 +/- 5.4 versus 22.2 +/- 4.6, p < 0.0001) at baseline but not at 1 year (19.6 +/- 5.1 versus 19.5 +/- 6.1, p = 0.41). When the final IOP was examined by multiple regression analysis, there was a significant effect in favor of ALT over SLT (p = 0.03) and for patients with higher baseline IOPs (p < 0.0001). No significant effect was found for any of the demographic subgroupings. However, when the outcome variable was success or failure, only the baseline IOP remained significant. Conclusions: Specific patient characteristics do not significantly influence LTP outcome after 12 months of follow-up. The most powerful predictor of either final IOP or clinical success was a higher baseline IOP, but ALT may have a better ability to lower IOP.

Mentoring and professional support programs in cancer nutrition for regional dietitians.

Increasing numbers of cancer patients are receiving radiotherapy treatment in regional areas, in addition to those requiring long-term local follow-up on treatment completion at metropolitan centres. Dietitians in rural and remote areas are by necessity required to practise a broad range of nutritional interventions. A limited knowledge of specialist cancer nutritional management, particularly for head and neck and upper gastrointestinal cancer, can arise from lack of exposure to a cancer caseload, limited access to professional development and recruitment and retention issues. Mentoring and professional support has been demonstrated to improve confidence, facilitate skill development and build professional networks. Mentoring and professional support programs in head and neck and upper gastrointestinal cancer across various states in Australia assist regional dietitians and other health professionals in improving care for regional cancer patients through support in delivering a high quality and sustainable service.

Publication Types: Review
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Technical considerations and operative aspects of late conversion of endoluminal stent-grafts.
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We present our experience with late abdominal aortic stent-graft conversion to open repair. In particular, the indications for conversion, operative strategies and a review of the pertinent literature. A retrospective analysis of a series of open conversions after endoluminal repair of abdominal aortic aneurysm (AAA), conducted at Royal Perth Hospital and Hollywood Hospital, Western Australia over a 4 year period. Six patients had late open conversion of their endoluminal stent-graft repair. Two patients presented emergently with aneurysm sac rupture secondary to endoleak. Elective conversion for type IV endoleak was performed in two patients. Two patients had graft removal for bilateral limb occlusion. Surgery was challenging and complete graft excision was performed when possible with hybrid grafting techniques utilised after excision of a portion of the endograft. Anastomotic techniques included suture pledgets and graft plugs to strengthen anastomoses particularly at the proximal aortic anastomosis. Five patients recovered from their procedure to be discharged within two weeks of operation. One patient died in the early postoperative period. Late conversion of endoluminal abdominal aortic stent-grafts is not common and can be technically challenging. A variety of techniques can be chosen to deal with the complex anatomical variations.
PMID: 2012122827


The comminuted midshaft clavicle fracture: A biomechanical evaluation of plating methods.
Taylor PRP, Day RE, et al.
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BACKGROUND: The optimal plate location and fixation method for midshaft fractures of the clavicle remains undetermined. The objective of this study was to develop a realistic biomechanical model with
which to compare superior with inferior-medial plate placement, and the failure resistance of locked and against non-locked constructs. METHODS: We estimated implant loads for operated patients in early rehabilitation utilising 3-D mathematical model of the shoulder. During simulation of upper limb motion associated with eating, the fracture opened in an inferior and frontal direction. The peak X, Y, and Z loads from the simulation were reproduced using a materials testing machine. A one centimetre transverse osteectomy was created at the midshaft of forty composite clavicles. Each specimen was then fixed with either (1) non-locked superior plating (n=10), (2) locked superior plating (n=10), (3) non-locked inferior-medial plating (n=10), or (4) locked inferior-medial plating (n=10). Specimens were loaded at 20N/s in four-point bending for 50 cycles to the peak X, Y, Z moment obtained from the computational model (-3.50, 2.46, and -1.00Nm), then loaded to failure at 20N/s. FINDINGS: Inferior-medial unlocked plates were significantly stiffer than superior locked plates (P=0.046).

INTERPRETATION: Operative fixation of midshaft clavicle fractures is controversial, though becoming more widely accepted. Few biomechanical data are available to assist surgical decision-making. Inferior plates may be better equipped to resist the in vivo loads experienced by the clavicle during early rehabilitation after internal fixation, particularly during the shoulder flexion motions associated with eating.

Manning L, Laman M, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Western Australia.
BACKGROUND: In areas of unstable malaria transmission, plasma Plasmodium falciparum histidine-rich protein 2 (PfHRP-2) concentrations parallel total parasite biomass and thus infection severity. However, where transmission is more intense, plasma PfHRP-2 might not reliably predict complications and mortality. METHODS: As part of a prospective case-control study of severe pediatric illness in Madang, Papua New Guinea, we recruited 220 children aged 6 months to 10 years with severe falciparum malaria, 48 with uncomplicated malaria, and 139 healthy controls. Groups were matched by age, sex, and province of parental birth. Plasma PfHRP-2 levels were quantified by validated immunoassay. RESULTS: Detectable plasma PfHRP-2 concentrations were present in 21 healthy controls (15.1%). Although plasma PfHRP-2 levels were higher in the children with clinical malaria (P < .001), there was no difference between those with uncomplicated and severe infections (median, 584 and 456 ng/mL, respectively [interquartile range, 77-1114 and 113-1113 ng/mL, respectively]; P = .43). Log parasitemia, hemoglobin, log plasma bilirubin, and plasma creatinine levels were independently associated with plasma PfHRP-2 levels in multiple regression analysis (P <= .014), but coma, blood lactate level, and plasma bicarbonate level were not. The 1 severely ill child who died had a plasma PfHRP-2 concentration of 483 ng/mL, close to the group median. CONCLUSIONS: The clinical and prognostic utility of plasma PfHRP-2 concentrations depends on the epidemiologic circumstances. In areas of intense malaria transmission, plasma PfHRP-2 reflects recent as well as present infections.
PMID:21216895

Certolizumab pegol in the treatment of Crohn’s disease: Evidence from the PRECiSE clinical trial program.
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Certolizumab is an IgG4-binding pegylated humanized Fab fragment that is the third anti-TNF-alpha agent available for the treatment of Crohn’s disease (CD). It has clearly demonstrated efficacy in the maintenance of CD disease response and remission, with recent data demonstrating that it also has long-term efficacy in CD with no new concerns about its safety. Evidence is mounting for a role of certolizumab pegol in patients who have lost response to infliximab and adalimumab and for a role in the treatment of perianal fistulating disease. Unfortunately, the pivotal double-blinded, placebo-controlled study investigating its efficacy in the induction of response in CD did not fully meet its primary end points, making registration of this agent for use in CD difficult. 2011 Future Science Ltd.


**Serum iron markers are inadequate for guiding iron repletion in chronic kidney disease.**
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BACKGROUND AND OBJECTIVES: Iron (Fe) overload may complicate parenteral Fe therapy used to enhance the efficacy of erythropoietic-stimulating agents in the treatment of anemia of chronic kidney disease. However, serum Fe markers are influenced by inflammation or malignancy and may not accurately reflect the amount of body Fe. DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS: We studied the relationship between parenteral Fe therapy, conventional serum Fe markers, and liver iron concentration (LIC) measured using magnetic resonance R2 relaxometry (FerriScan) in 25 Fe-deficient predialysis chronic kidney disease patients before and 2 and 12 weeks after single high-dose intravenous Fe and in 15 chronic hemodialysis patients with elevated serum ferritin (>500 g/L).

RESULTS: In predialysis patients, there was strong dose dependency between the administered Fe dose and changes in LIC at weeks 2 and 12; however, no dose dependency between Fe dose and changes in ferritin or transferrin saturation (TSAT) were observed. In hemodialysis patients, LIC correlated with the cumulative Fe dose and duration of dialysis but not with current ferritin or TSAT. The cumulative Fe dose remained a significant independent predictor of LIC in a multiple regression model. Two dialysis patients who received >6 g parenteral Fe had substantially elevated LIC >130 mol/g, which is associated with hemochromatosis. CONCLUSIONS: In Fe-deficient predialysis patients, intravenous Fe therapy is associated with increases in LIC unrelated to changes in conventional Fe markers. In hemodialysis patients, TSAT and ferritin are poor indicators of body Fe load, and some patients have LICs similar to those found in hemochromatosis.

PMID:20876673


**How reassuring is a normal breast ultrasound in assessment of a screen-detected mammographic abnormality? A review of interval cancers after assessment that included ultrasound evaluation.**
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Aim: To review factors resulting in a false-negative outcome or delayed cancer diagnosis in women recalled for further evaluation, including ultrasound, after an abnormal screening mammogram.

Materials and methods: Of 646,692 screening mammograms performed between 1 January 1995 and
31 December 2004, 34,533 women were recalled for further assessment. Nine hundred and sixty-four interval cancers were reported in this period. Forty-six of these women had been recalled for further assessment, which specifically included ultrasound evaluation in the preceding 24 months, and therefore, met the inclusion criteria for this study. Screening mammograms, further mammographic views, ultrasound scans, clinical findings, and histopathology results were retrospectively reviewed by two consultant breast radiologists. Results: The interval cancer developed in the contralateral breast (n = 9), ipsilateral breast, but different site (n = 6), and ipsilateral breast at the same site (n = 31) as the abnormality for which they had recently been recalled. In the latter group, 10 were retrospectively classified as a false-negative outcome, nine had a delay in obtaining a biopsy, and 12 had a delay due to a non-diagnostic initial biopsy. Various factors relating to these outcomes are discussed.

Conclusion: Out of 34,533 women who attended for an assessment visit and the 46 women who subsequently developed an interval breast cancer, 15 were true interval cancers, 10 had a false-negative assessment outcome, and 21 had a delay to cancer diagnosis on the basis of a number of factors. When there is discrepancy between the imaging and histopathology results, a repeat biopsy rather than early follow-up would have avoided a delay in some cases. A normal ultrasound examination should not deter the radiologist from proceeding to stereotactic biopsy, if the index mammographic lesion is suspicious of malignancy.

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Are we neglecting extra-vascular pressures?
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PMID:22129295

Grandparental investment: A relic of the past or a resource for the future?
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Coall, David A.: University of Western Australia, Fremantle, WAU, Australia Hertwig, Ralph: University of Basel, Basel, Switzerland
From changing diapers and minding the kids when school is out to providing support when they set fire to the carpet, grandparents can be invaluable to have around. What motivates grandparents to lend a hand? Several disciplines have offered answers. The most important accounts come from life-history theory and evolutionary psychology, sociology, and economics. These accounts exist side-by-side, but there is little theoretical integration among them. But regardless of whether grandparental investment is traced back to ancestral selection pressure or attributed to an individual grandparent's values or norms, one important question is, What impact does it have in industrialized, low-fertility, low-mortality societies? We briefly review the initial evidence concerning the impact of grandparental investment in industrialized societies and conclude that in difficult circumstances, grandparents can provide the support that safeguards their grandchildren's development. Additional cross-disciplinary research to examine the effects of intergenerational transfers in our evolutionarily unique environment of grandparenthood is needed. (PsycINFO Database Record (c) 2011 APA, all rights reserved)
Understanding the Use of Immunosuppressive Agents in the Clinical Management of IBD.
Waters O, Lawrance IC.
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The advent of the biological era has seen many improvements in the management of inflammatory bowel disease (IBD). These agents, however, are not a ubiquitous panacea as they are neither universally available nor are they universally efficacious in the short or long-term. There is, therefore, still a need for other therapies and it is important to remember about the medications that have been effective in the past. The use of azathioprine and 6-mercaptopurine has been the mainstay of long-term therapy for many IBD patients for many years. Their role as steroid sparing agents and in the maintenance of remission is well recognized, and with the advent of metabolite testing their use has been refined. Methotrexate is a second line immunomodulator with less impressive data but still with observed benefits in Crohn's disease (CD) and two newer immunosuppressive agents, mycophenylate mofetil and tacrolimus have sparked some interest as they appear to be efficacious in some patients. As IBD is a chronic incurable condition that primarily presents in young patients, the treating clinician's goal is to induce and maintain long-term remission. So when one agent is ineffective, or unavailable, other agents need to be considered. This review aims to provide clinicians with practical and up to date knowledge about the use of the immunomodulators in the management of IBD, which is vital in order to offer the best management for their patients.
PMID:21291384

Mental health patients at high risk for obesity, type 2 diabetes, and cardiovascular disease: An Australian perspective.
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In Australia, rates of obesity in the general population are on the rise. The growing incidence of obesity and higher rates of metabolic syndrome in mental health patients places this group of people at a much higher risk for type 2 diabetes and cardiovascular disease. Treatment effects via psychotropic medications, and lifestyle factors such as diet and exercise suggests that attention needs to be drawn to this vulnerable population. Assessment and the ongoing monitoring of physical health is essential in the prevention of major physical illness in people with a mental disorder. 2011 Bentham Science Publishers.
PMID:2012112057

Current Opinion in Psychiatry: Editorial introductions.
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L. DeLisi, Department of Psychiatry, Harvard Medical School, Boston, United States
Publication Types: Editorial
Use of 'chronic disease self-management strategies' in mental healthcare.
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PURPOSE OF REVIEW: Medical care for chronic conditions imposes a substantial burden on healthcare systems designed originally for acute illness or injury. The notion of chronic disease self-management (CDSM) has been developed as a means of encouraging individuals with chronic conditions to self-manage their own health. It is known that successful chronic disease management reduces hospital admission rates and improves patients' quality of life. Although recognized widely by other medical disciplines, it is beginning to have an impact on psychiatric practice; therefore, a review of how the CDSM approach is implemented in psychiatry is timely. RECENT FINDINGS: The move toward self-management in general medicine can be seen by and large as a holistic approach that encourages the person to work in partnership with health professionals to improve outcomes and assist patients to better manage their healthcare needs. One of the defining features of CDSM approaches is the active collaboration between the patient and the healthcare professional. Five mechanisms that demonstrate such active collaboration are self-directed care, illness management and recovery, shared decision-making, joint crisis planning and wellness planning. Their use in psychiatry is discussed. SUMMARY: The key feature of CDSM approaches is an active collaboration between healthcare professionals and healthcare consumers. It is a fundamental shift away from traditional active expert/passive patient treatment modes. Each of the five approaches discussed exemplifies the active participation in treatment planning by both consumers and mental health professionals.

Apathy and Parkinson's disease.
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OPINION STATEMENT: Apathy, a frequent finding in Parkinson's disease (PD), is significantly associated with depression and dementia. Few studies have examined the efficacy of psychotropic or psychological treatments of apathy in PD, and adequate randomized controlled trials are still lacking. There is anecdotal evidence that dopaminergic agonists may be a useful treatment modality. Levodopa may improve the loss of motivation in the "off" motor state, and dopaminergic agonists could be useful to treat apathy after the withdrawal of dopaminergic treatment in patients undergoing deep brain stimulation of the subthalamic nucleus. On the other hand, the selective norepinephrine reuptake inhibitor atomoxetine did not demonstrate efficacy in improving apathy in a randomized controlled trial with apathy as a secondary efficacy measure. Given the significant association between apathy and both depression and cognitive decline, future studies should examine whether improving mood and cognition may also have a positive impact upon apathy in PD. For those PD patients with "pure" apathy, specific psychotherapeutic techniques should be developed.

Diabetes. 2011; 60: A364.
A matched case-control study of the risk of falls in type 2 diabetes: The busselton diabetes study.
Davis TME, Hunter M, et al.
Background: The incidence of falls is increased in diabetes. There is a range of potential risk factors but previous studies have included limited explanatory variables. We have, therefore, determined independent associates of falls in well-characterised type 2 patients in a community-based case-control study. Methods: Residents of Busselton, Australia, with diabetes and age- and sex-matched controls underwent comprehensive assessment including questions on falls in the prior 3 months and fear of falling/its impact on indoor/outdoor activity. Timed up-and-go/balance tests were performed. Univariate associates of falls in cases vs controls were determined, and multiple logistic regression used to assess independent predictors. Zeroinflated negative binomial regression identified associates of fall frequency. Results: 186 cases (mean age 70.3 years, 50% males, median diabetes duration 8.6 years) and 186 controls were assessed. The cases had a higher mean BMI than controls, and greater proportions were on antihypertensive/vasoactive medication and at high sleep apnea risk (P<=0.022). Antidepressant and analgesic use was similar. The cases had a longer up-and-go test (10.5 +/-3.2 vs 9.4 +/-2.0 sec, P<0.001), worse balance (70 vs 56% with significant problems, P=0.002), and greater fear of falling (24 vs 15%, P=0.033) with consequent limitation of indoor (14 vs 5%, P=0.006) and outdoor (17 vs 10%, P=0.07) activity. The proportions self-reporting recent falls were similar (21 vs 17%, P=0.42), but cases had more falls (63 vs 36). In multiple logistic regression, people without falls were younger (P=0.002), less likely to be on antidepressants (P=0.044) and more likely to limit outdoor activities (P<0.001). After adjusting for this group, the incident rate ratio [95% CI] of falls in those with good/moderate vs poor balance was 0.43 [0.21-0.87] (P=0.019). Conclusions: Diabetes does not increase falls risk despite greater balance/mobility impairments, but restriction of outdoor activities because of fear of falls appears strongly protective. Diabetic patients more often report multiple falls but increased fall frequency is primarily explained by poor balance.

Publication Types: Conference Abstract
PMID:70629084

Diabetes. 2011; 60: A354.

Serum vitamin B12 and depression in metformin-treated patients with type 2 diabetes: The Fremantle diabetes study.

Davis TME, Schimke K, et al.

Background: Metformin therapy decreases serum vitamin B<sub>12</sub> which, in turn, is associated with an increased risk of depression in general population studies. The aim of this study was, therefore, to determine whether metformin-associated reductions in serum vitamin B<sub>12</sub> contribute to depression in type 2 diabetes. Methods: We studied 379 metformin-treated patients from the community-based observational Fremantle Diabetes Study (FDS), or 89.2% of those on this therapy at entry. At FDS baseline and annual reviews, a comprehensive assessment was performed including questions on general health/quality of life. Depression was defined as >2 related symptoms on validated questionnaire. Associates of prevalent depression at entry were assessed by multiple logistic regression and of incident depression by Cox proportional hazards modeling. Results: The mean age of the patients at baseline was 62.5 years, 44.6% were male and their median diabetes duration was 5.1 years. Their geometric mean (SD range) serum vitamin B<sub>12</sub> was 363 (242-544) pmol/L; four (1.1%) had a concentration below the reference range (<160 pmol/L). Over one-third (34.3%) was depressed but vitamin B<sub>12</sub> was not associated with prevalent depression when added to the logistic model as a continuous variable (P=0.29) or quartiles (P>=0.14). 170 patients (44.9%) were neither depressed nor on antidepressant drugs at baseline and had at least one annual assessment over the next 5 years. In Cox models, loge(serum vitamin B<sub>12</sub>) was an independent positive predictor of incident depression as...
a continuous variable (hazard ratio [95% CI] 2.41 [1.31-4.23]), with the highest (2.17 [1.16-4.05], P=0.016) but not the other three quartiles showing a significant association. Conclusions: Low-normal serum vitamin B<sub>12</sub> concentrations are not associated with prevalent or incident depression in metformin-treated type 2 patients. The positive association between high vitamin B<sub>12</sub> levels and incident depression parallels data from large-scale general population studies and suggests that excessive vitamin B<sub>12</sub> supplementation may be deleterious. 

Publication Types: Conference Abstract
PMID:70629053


Reduced rates of severe hypoglycemia in children and adolescents with type 1 diabetes over the decade 2000-2009.
O'Connell SM, Cooper MN, et al.
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S.M. O'Connell, PerthAustralia
We have previously reported increased rates of hypoglycemia associated with improved glycemic control in a large population-based sample of children with T1D, however therapeutic improvements may have altered hypoglycemia incidence. In this study, rates of severe hypoglycemia (SH) (an event leading to loss of consciousness or seizure) in a population based sample of childhood onset T1D were examined and clinical associations of these events investigated. Data were extracted from the Western Australia Childhood Diabetes Database. Clinical data, including hypoglycaemia history is prospectively recorded at each 3 monthly visit. Data from 1,683 patients with T1D from 2000-2009 inclusive (age at diagnosis 10.5 +/- 4.2 years [mean +/- SD], range 1-18) were analysed. Rates of SH were investigated with respect to A1c, treatment type, duration of diabetes, age and gender using interaction terms fitted within a negative binomial regression model. In total 7,378 patient-years of data and 780 severe events were recorded. The rate of SH/100 patient years in 2000 was 14.3, peaking at 17.3 in 2001. From 2004 there was a sharp decline, with the lowest rate of 5.8 in 2006. There was a negligible decline in HbA1c levels of 0.07% per year (p = 0.03). Using multivariate analysis optimal recommended A1c (<7%) was significantly associated with higher risk of SH (IRR=3.0, p<0.001; CI 1.9- 4.7) relative to A1c>10%. Compared to previous findings, children <6 years were no longer at increased risk of SH. From 2000 to 2009 the proportion of patients using pump (1% vs 26%) and injections >= 4/day (8% vs 25%) increased. Using interaction models, from age >13 years the estimate for SH events for the prospective 12 month period was 64% lower for patients using pump therapy compared to injections (p <0.001). There has been a decrease in rates of SH over the past decade despite static glycemic control. More intensive blood glucose monitoring, analog insulins, more widespread use of pump therapy are likely to have contributed to the change, but their relative importance cannot be determined.

Publication Types: Conference Abstract
PMID:70628274


Reducing rates of severe hypoglycemia in a population-based cohort of children and adolescents with type 1 diabetes over the decade 2000-2009.
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T.W. Jones, Department of Endocrinology and Diabetes, Princess Margaret Hospital for Children,
OBJECTIVE - To examine rates of severe hypoglycemia (SH) in a large population-based cohort of children with type 1 diabetes and relationships to HbA1c. RESEARCH DESIGN AND METHODS - Data from 1,683 children (mean [SD] age at diagnosis 10.5 [4.2]; range 1-18 years) from 2000 to 2009 were analyzed from the Western Australian Children's Diabetes Database. Rates of SH were related to HbA1c using negative binomial regression. RESULTS - A total of 7,378 patient-years of data and 780 SH events were recorded. The rate of SH per 100 patient-years peaked at 17.3 in 2001 and then declined from 2004 to a nadir of 5.8 in 2006. HbA1c <7% was not associated with higher risk of SH (incidence rate ratio 1.2 [95% CI 0.9-1.6], P = 0.29) compared with HbA1c 8-9%. CONCLUSIONS - In a sample of youth with type 1 diabetes, there has been a decrease in rates of SH and a weaker relationship with glycemic control than previously observed. 2011 by the American Diabetes Association.


Predicting severe hypoglycemia in the community: A review of recent evidence.

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The recent literature relating to predictors of severe hypoglycemia in the community is reviewed. Medline and EMBASE databases were searched for English language papers between 2005 and July 2010 using the terms ('severe hypoglycaemia' or 'symptomatic hypoglycaemia') and ('predictor[s]' or 'predict[s]' or 'prediction', 'determinant[s]' or 'determine[s]' or 'marker[s]' or 'factor[s]' or 'indicator[s]'). All studies meeting the inclusion criteria were included. From 186 papers identified, 13 original studies were considered eligible. Another eligible paper became available online during the review process. Of the 14 studies, six were studies of Type 2 diabetes. Two or more of these studies recognized dementia or severe cognitive impairment, higher HbA1c, low BMI and peripheral neuropathy as predictors of severe hypoglycemia in adults with Type 2 diabetes. Renin-angiotensin system-related risk factors independently predicted the frequency of severe hypoglycemia in adults, but not children or adolescents with Type 1 diabetes. An algorithm derived from self-monitoring of blood glucose data predicted imminent severe hypoglycemia in insulin-using diabetic patients. 2011 Future Medicine Ltd.


Chubb SAP, Van Minnen K, et al.

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The benefits of self-monitoring of blood glucose (SMBG) in type 2 diabetes remain contentious. If SMBG data do not accurately reflect HbA1c, attempts to modify lifestyle/pharmacotherapy will be ineffective. We aimed to determine how well SMBG correlates with HbA1c and fasting serum glucose (FSG). Community-based type 2 patients using SMBG provided their highest and lowest pre- and post-prandial glucose results in the week before detailed assessment. The ability of average pre- and post-prandial SMBG to predict HbA1c>7.0% was determined by linear regression and receiver operating characteristic (ROC) analyses. Of 1286 patients with known SMBG status, 70% reported using SMBG. Pre-prandial SMBG data were obtained from 554 participants and post-prandial SMBG data from 418. The mean SMBG result and HbA1c correlated significantly (pre-prandial r(s)=0.55,
post-prandial $r(s)=0.47$; $P<0.001$). Areas under the ROC curve (95% confidence limits) were 0.78 (0.74-0.83) and 0.74 (0.69-0.78) for pre- and post-prandial SMBG ($P<0.04$). The optimal cut-point was 6.5mmol/L for pre-prandial SMBG (sensitivity 79.3%, specificity 64.4%). Mean pre-prandial SMBG results correlated with FSG ($r(s)=0.64$, $P<0.001$) but were on average 1.4mmol/L lower, consistent with known whole blood vs. plasma differences. Since SMBG values reflect prevailing glycaemia, refinements in their interpretation and application may improve SMBG effectiveness. Copyright 2011 Elsevier Ireland Ltd. All rights reserved.


**Economic impact of moderate weight loss in patients with Type 2 diabetes: The Fremantle Diabetes Study.**

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AIM: To assess the change in the cost of diabetes medication attributable to moderate weight loss in patients with Type 2 diabetes.

METHODS: Longitudinal data collected annually from 590 patients participating in the observational, community-based Fremantle Diabetes Study were examined to determine whether moderate weight loss ($\geq 5\%$ of initial body weight) was independently associated with diabetes medication cost during 4 years' follow-up.

RESULTS: Overall, the weight of the cohort decreased significantly during 4.3 ± 0.4 years' follow-up by 1.3 ± 6.2 kg (-1.4 ± 7.9% baseline body weight; trend $P < 0.001$). Moderate weight loss was achieved by 31%. HbA(1c) improved significantly in the group with moderate weight loss compared with the group without moderate weight loss [-4 ± 16 mmol/mol (-0.3 ± 1.5%) vs. 0 ± 17 mmol/mol (0.0 ± 1.5%), $P = 0.015$]. Mean (bias-corrected 95% confidence intervals) diabetes medication costs were $A820 ($A744-907) during follow-up. As the cost distribution was highly right-skewed and contained zeros, it was square root ($\sqrt{\cdot}$) transformed before multiple linear regression analysis. The most parsimonious model of baseline associates of $\sqrt{\text{diabetes medication cost}}$ included glycaemic control, diabetes treatment, diabetes duration, BMI, systolic blood pressure, serum HDL cholesterol (negative), taking lipid-lowering medication and age (negative) (adjusted $R^2 = 73.6\%$). After adjusting for these variables, $\sqrt{\text{diabetes medication cost}}$ was negatively associated with moderate weight loss ($P = 0.026$). After entering average values for the cohort into the model, the cost of diabetes medications between baseline and fourth review for an average patient with no weight loss was $A752 compared with $A652 for a patient who attained moderate weight loss, a saving of $A100 (-13.3\%).

DISCUSSION: These data highlight the economic and clinical benefits of moderate weight loss in Type 2 diabetes.

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**Effect of initiation of continuous positive airway pressure therapy on cardiovascular risk factors in patients with type 2 diabetes and obstructive sleep apnoea.**

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Background and aims: Diabetes and obstructive sleep apnoea (OSA) are important co-morbid conditions. In people with diabetes, the prevalence of OSA may be as high as 58%. Continuous Positive Airway Pressure (CPAP) is a highly effective treatment for OSA but there are limited data on the effect of CPAP therapy on OSA in type 2 patients. It is possible that CPAP could improve
metabolic control, blood pressure and diabetes-associated complications such as sexual dysfunction in males. We therefore conducted a before-and-after study to determine whether CPAP improves glycaemic control and other cardiovascular risk factors in type 2 patients with confirmed OSA.

Materials and methods: Between April 2009 and March 2010, 59 type 2 diabetes patients from the longitudinal observational Fremantle Diabetes Study considered at high risk for OSA after an overnight home-based sleep study using an ApneaLink had confirmation of the diagnosis by laboratory polysomnography and then consented to participation in a 3-month CPAP intervention study. A detailed medical history, physical examination and biochemical testing were undertaken immediately before, and 1 and 3 months after CPAP commenced. The males completed two sexual dysfunction questionnaires, the sexual health inventory for men and the ADAM questionnaire, on each occasion. Repeated measures statistical analysis was used to compare variables of interest at the three time points. Results: Forty-four (75%) of the original cohort completed the study. They had a mean +/-SD age of 66.1 +/- 8.8 years, 61.4% were male their median [IQR] diabetes duration was 10.1 [3.8-15.3] years, and they had an apnoea hypopnoea index (AHI) of 38 [27-58] and Epworth Sleepiness Scale (ESS) of 9 [5-12] at entry. There were no significant differences between the 44 completers and 15 non-completers in age, sex, diabetes duration, AHI or ESS (P >= 0.29). Blood pressure improved significantly over 3 months of CPAP therapy from 149 +/-23/80 +/-12 mmHg at entry to 140 +/- 18/73 +/-13 mmHg (trend P=0.038/0.013). The change in systolic blood pressure (SBP) was -8 (-18 to 1) mmHg, with significant improvement between 1 month and 3 months (SBP -8 (-14 to -1) mmHg, P=0.012). Most improvement in diastolic blood pressure also occurred between months 1 and 3 (DBP -8 (-15 to -1) mmHg, P=0.015). Pulse rate declined significantly within the first month (pulse rate -6 (-10 to -2) beats/minute, P=0.001). Glycaemic control, serum lipids and urinary albumin:creatinine ratio (ACR) did not improve over the study period but most patients had acceptable HbA1c (<7.0%), LDL-cholesterol (<2.5 mmol/L) and ACR (<3.0 mg/mmol) at entry. The ESS decreased significantly over the study period, specifically between entry and 1 month (ESS=-4.8 (-6.5 to -3.1, P<0.001)). Amongst the 27 males, the median number of symptoms of sexual dysfunction decreased significantly over the study period, from 6.5 to 5.5 (P=0.008). Conclusion: A 3-month trial of CPAP in community-based type 2 patients improved blood pressure, pulse rate, daytime sleepiness, and, in men, sexual function.


Effects of fenofibrate on renal function in patients with type 2 diabetes mellitus: the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) Study.

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AIMS/HYPOTHESIS: Fenofibrate caused an acute, sustained plasma creatinine increase in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) and Action to Control Cardiovascular Risk in Diabetes (ACCORD) studies. We assessed fenofibrate’s renal effects overall and in a FIELD washout sub-study. METHODS: Type 2 diabetic patients (n = 9,795) aged 50 to 75 years were randomly assigned to fenofibrate (n = 4,895) or placebo (n = 4,900) for 5 years, after 6 weeks fenofibrate run-in. Albuminuria (urinary albumin/creatinine ratio measured at baseline, year 2 and close-out) and estimated GFR, measured four to six monthly according to the Modification of Diet in Renal Disease Study, were pre-specified endpoints. Plasma creatinine was re-measured 8 weeks after treatment cessation at close-out (washout sub-study, n = 661). Analysis was by intention-to-treat. RESULTS: During fenofibrate run-in, plasma creatinine increased by 10.0 mol/l (p < 0.001), but quickly reversed on placebo assignment. It remained higher on fenofibrate than on placebo, but the chronic rise was slower (1.62 vs 1.89 mol/l annually, p = 0.01), with less estimated GFR loss (1.19 vs 2.03 ml min(-1) 1.73 m(-2) annually, p < 0.001). After washout, estimated GFR had fallen less from baseline on fenofibrate (1.9 ml min(-1) 1.73 m(-2), p = 0.065) than on placebo (6.9 ml min(-1) 1.73 m(-2), p < 0.001), sparing 5.0 ml min(-1) 1.73 m(-2) (95% CI 2.3-7.7, p < 0.001). Greater preservation of
estimated GFR with fenofibrate was observed with baseline hypertriacylglycerolaemia (n = 169 vs 491 without) alone, or combined with low HDL-cholesterol (n = 140 vs 520 without) and reductions of >= 0.48 mmol/l in triacylglycerol over the active run-in period (pre-randomisation) (n = 356 vs 303 without). Fenofibrate reduced urine albumin concentrations and hence albumin/creatinine ratio by 24% vs 11% (p < 0.001; mean difference 14% [95% CI 9-18]; p < 0.001), with 14% less progression and 18% more albuminuria regression (p < 0.001) than in participants on placebo. End-stage renal event frequency was similar (n = 21 vs 26, p = 0.48). CONCLUSIONS/INTERPRETATION: Fenofibrate reduced albuminuria and slowed estimated GFR loss over 5 years, despite initially and reversibly increasing plasma creatinine. Fenofibrate may delay albuminuria and GFR impairment in type 2 diabetes patients. Confirmatory studies are merited. TRIAL REGISTRATION: ISRCTN64783481. PMID:21052978


Estimated glomerular filtration rate and albuminuria are independent predictors of cardiovascular events and death in type 2 diabetes mellitus: The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study.

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Aims/hypothesis: We investigated effects of renal function and albuminuria on cardiovascular outcomes in 9,795 low-risk patients with diabetes in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study. Methods: Baseline and year 2 renal status were examined in relation to clinical and biochemical characteristics. Outcomes included total cardiovascular disease (CVD), cardiac and non-cardiac death over 5 years. Results: Lower estimated GFR (eGFR) vs eGFR >=90 ml min^{-1}1.73 m^{-2} was a risk factor for total CVD events: (HR [95% CI] 1.14 [1.01-1.29] for eGFR 60-89 ml min^{-1}1.73 m^{-2}; 1.59 [1.28-1.98] for eGFR 30-59 ml min^{-1}1.73 m^{-2}; p<0.001; adjusted for other characteristics). Albuminuria increased CVD risk, with microalbuminuria and macroalbuminuria increasing total CVD (HR 1.25 [1.01-1.54] and 1.19 [0.76-1.85], respectively; p=0.001 for trend) when eGFR >=90 ml min^{-1}1.73 m^{-2}. CVD risk was further modified by renal status changes over the first 2 years. In multivariable analysis, 77% of the effect of eGFR and 81% of the effect of albumin:creatinine ratio were accounted for by other variables, principally low HDL-cholesterol and elevated blood pressure. Conclusions/interpretation: Reduced eGFR and albuminuria are independent risk factors for cardiovascular events and mortality rates in a low-risk population of mainly European ancestry. While their independent contributions to CVD risk appear small when other risk factors are considered, they remain excellent surrogate markers in clinical practice because they capture risk related to a number of other characteristics. Therefore, both should be considered when assessing prognosis and treatment strategies in patients with diabetes, and both should be included in risk models. Springer-Verlag 2010.

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Is colonoscopy still mandatory after a CT diagnosis of left-sided diverticulitis: can colorectal cancer be confidently excluded?

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BACKGROUND: It is routine practice to perform colonoscopy as a follow-up after an attack of diverticulitis, with the main aim to exclude any underlying malignancy. PURPOSE: This study aimed to determine whether colonoscopy is necessary and what additional information is gained from this procedure. DESIGN: This is a study of a retrospective cohort. SETTINGS AND PATIENTS: From January 2003 to June 2009, patients in whom left-sided diverticulitis was diagnosed on CT scan were matched with colonoscopy reports within 1 year from the date of CT by the use of radiology and endoscopy databases. Patients who had colonoscopy within 1 year before the CT scan were excluded. The Western Australian Cancer Registry was cross-referenced to identify patients who subsequently received diagnoses of cancers for whom colonoscopy reports were unavailable. MAIN OUTCOME MEASURES: The main outcome measures were the number of patients in whom colorectal cancers were diagnosed and other incidental findings, eg, polyps, colitis, and stricture. RESULTS: Left-sided diverticulitis was diagnosed in 1088 patients on CT scan, whereas follow-up colonoscopy reports were available for 319 patients. Eighty-two (26%) patients had incidental findings of polyps (9 polyps >1 cm), and 9 patients (2.8%) received diagnoses of colorectal cancers on colonoscopy. After cross-referencing with the cancer registry, the overall prevalence of colorectal cancer among the cohort within 1 year of CT scan was 2.1% (23 cases). The odds of a diagnosis of colorectal cancer were 6.7 times (95% CI 2.4-18.7) in patients with an abscess reported on CT, 4 times (95% CI 1.1-14.9) in patients with local perforation, and 18 times (95% CI 5.1-63.7) in patients with fistula compared with patients with uncomplicated diverticulitis. LIMITATIONS: This study was limited by the unavailability of data for private/interstate hospitals, and the relatively small number of cancer cases reduced the statistical power of the study. CONCLUSIONS: We recommend routine colonoscopy after an attack of presumed left-sided diverticulitis in patients who have not had recent colonic luminal evaluation. The rate of occult carcinoma is substantial in this patient population, in particular, when abscess, local perforation, and fistula are observed.

PMID:21904141

Oxygen toxicity seizures: 20 years' experience from a single hyperbaric unit.

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INTRODUCTION: Oxygen toxicity seizures (OTS) are a known complication of hyperbaric oxygen therapy (HBOT). The incidence of OTS has been variously reported and appears to be related to the duration and pressure of exposure in addition to individual susceptibility factors. METHOD: All OTS occurring in patients undergoing HBOT during the first 20 years of operation of the Fremantle Hospital Hyperbaric Medicine Unit were reviewed. RESULTS: During 41,273 HBOT in 3,737 patients, 25 OTS occurred; a rate of 0.06% (1/1,650 or 6 per 10,000) HBOT exposures. For the initial treatment of dysbarism with United States Navy Treatment Table 6, the rate was 0.56%. (4/714) and for the treatment of carbon monoxide (CO) poisoning was 0.18% overall but 0.49% for the first HBOT. There was an increasing OTS rate with increasing pressure with a statistically significant difference (P < 0.001) in OTS rate at 203 kPa or less versus > 203 kPa (OR 8.5, 95% confidence intervals (CI) 2.0 to 36.1), and for comparison of two commonly used pressures of 203 kPa versus 243 kPa (P = 0.028, OR 5.1, 95% CI 1.1 to 22.8), but not with first versus follow-up HBOT at 284 kPa for dysbarism (P = 0.061) nor CO (P = 0.142). CONCLUSIONS: This study reports all OTS in a single hyperbaric unit
over a 20-year period, the longest observational study period yet reported for OTS during HBOT for all indications. The incidence of OTS in this study compares favourably to previously reported rates, and shows an increasing OTS rate with increasing pressure.

PMID:22183697


Compliance with the emergency department 4-hour target is dependent on access block.
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Western Australia introduced a target to ensure that 98% of patients arriving to an Emergency Department (ED) are to be assessed and admitted, discharged or transferred within four hours from the time of triage ("Four-Hour Target"). A clinical redesign process was undertaken to support compliance with the target. Objectives: To determine the factors influencing compliance with the four-hour target. Methods: Retrospective observational study using electronic patient information system (EDIS) data. Results: Following ED redesign, it was found that compliance with the four-hour target was almost completely dependent on the number of admitted patients sent to the ward within four hours (r = 0.963, p < 0.001) and access block (r = 0.862, p < 0.001). Although 94.8% of discharged patients were sent home within four hours, the number of patients sent home within four hours was less correlated with overall four-hour performance (r = 0.391, p = 0.005). Conclusion: To ensure that four-hour targets are met, attention should be placed on ensuring that admitted patients are sent to the ward within four hours and access block is minimised. Strategies concentrating on discharged patients alone are unlikely to have a high yield.
Publication Types: Conference Abstract
PMID:70834842


Determining the true burden of general practice patients in the emergency department: The need for robust methodology.
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Publication Types: Editorial
PMID:2011211461


Comparison of two clinical scoring systems for emergency department risk stratification of suspected acute coronary syndrome.
Macdonald SP, Nagree Y, et al.
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Australia, Australia.
Objective: To compare two methods of risk stratification for suspected acute coronary syndrome (ACS) in the ED. Methods: A prospective observational multicentre study was undertaken of patients undergoing evaluation in the ED for possible ACS. We compared the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand (NHF/CSANZ) guideline and the Thrombolysis in Myocardial Infarction (TIMI) risk score for differentiating high- and low-risk patients. Composite outcome was all cause death, myocardial infarction or coronary revascularisation within 30 days. Results: Of 1758 enrolments, 223 (13%) reached the study outcome. Area under the receiver operator characteristic (ROC) curve was 0.79 (95% CI 0.76-0.81) for the NHF/CSANZ group and 0.71 (0.68-0.75) for TIMI score based on initial troponin result (P<0.001), and 0.82 (95% CI 0.80-0.84) and 0.76 (0.73-0.79) respectively when the 8-12 h troponin result is included (P<0.001). Thirty day event rates were 33% for NHF/CSANZ high-risk vs 1.5% for combined low/intermediate risk (P<0.001). For TIMI score, 30 day event rates were 23% for a score >=2 and 4.8% for TIMI<2 (P<0.001). The NHF/CSANZ guideline identified more patients as low risk compared with the TIMI risk score (61% vs 48%, P<0.001). Conclusions: The NHF/CSANZ guideline is superior to the TIMI risk score for risk stratification of suspected ACS in the ED. Copyright 2011 The Authors. EMA Copyright 2011 Australasian College for Emergency Medicine and Australasian Society for Emergency Medicine. PMID:22151670


Endoscopy. 2011; 43(5): 412-8. Bowel cleansing for colonoscopy: prospective randomized assessment of efficacy and of induced mucosal abnormality with three preparation agents. Lawrance IC, Willert RP, et al. Centre for Inflammatory Bowel Diseases, Fremantle Hospital, Fremantle, Western Australia. BACKGROUND AND STUDY AIMS: Bowel-cleansing studies are frequently underpowered, poorly designed, and use subjective bowel cleansing assessments. Consensus on efficacy, tolerability, and preparation-induced mucosal abnormalities is lacking. This study aimed to clarify the differences in efficacy and preparation-induced mucosal inflammation of sodium phosphate (NaP), colonLYTLEY (PEG), and Picoprep (Pico). PATIENTS AND METHODS: This was a prospective randomized single-blinded trial of ambulatory patients to assess the efficacy of bowel preparation and preparation-induced mucosal inflammation. Proceduralists who were blinded to the preparation taken, assessed both bowel cleansing by using the Ottawa bowel preparation assessment tool and preparation-induced mucosal inflammation. RESULTS: Of the 634 patients, 98% ingested more than 75% of the bowel preparation and data were complete for colonic preparation scoring in 99%. The preparation used, time of procedure, and patient sex all independently impacted on bowel cleansing. NaP was less efficacious than PEG (P<0.001) and Pico (P<0.001) for morning procedures whereas all bowel preparations were equally efficacious for afternoon procedures. Preparation-induced mucosal inflammation was 10-fold greater with NaP (P=0.03) and Pico (P=0.03) compared with PEG. CONCLUSIONS: This is the largest published prospective randomized blinded study on this topic and the first to evaluate the three major classes of preparation with a validated tool. The bowel preparation used, time of procedure, and patient sex all independently impacted on bowel cleansing. NaP gave
the worst preparation for morning procedures whereas all preparations were equally effective for afternoon procedures. NaP and Pico induced mucosal inflammation 10-fold more frequently than PEG, a finding that requires further investigation. Copyright Georg Thieme Verlag KG Stuttgart. New York.
PMID:21547879

Benefits and safety of long-term fenofibrate therapy in people with type 2 diabetes mellitus and renal impairment - the FIELD study.
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Purpose: Subjects with diabetes and moderate renal impairment (eGFR 30-59 ml/min/1.73m<sup>2</sup>) are at particular cardiovascular (CVD) risk. The safety of long term fenofibrate treatment in patients with renal dysfunction has been of concern due to the drug's propensity to elevate plasma creatinine. As such, safety guidelines vary between countries regarding fenofibrate dosing in the setting of renal impairment. We investigated the effects of fenofibrate on cardiovascular and endstage renal disease (ESRD) events according to renal function, in subjects with type 2 diabetes in the FIELD study. Methods: A total of 9795 patients, aged 50-75 years, with type 2 diabetes and eGFR >= 30 ml/min/1.73m<sup>2</sup> were randomly assigned to fenofibrate 200mg daily (n=4895) or placebo (n=4900) for 5 years. Renal function was estimated twice prior to randomisation and grouped by eGFR range (30-59, 60-89 and >= 90 ml/min/1.73m<sup>2</sup>) using the Modification of Diet in Renal Disease 4 equation. The pre-specified outcome for all subgroup analyses was total CVD events (composite of CVD death, myocardial infarction, stroke, and coronary and carotid revascularisation). At each study follow-up visit, serious adverse events and instances of ESRD (prospectively defined as plasma creatinine >400 mumol/L, dialysis, renal transplant or renal death) were also recorded. Analysis was by intention to treat. Results: Overall, fenofibrate significantly reduced total CVD events compared to placebo [HR 0.89 (95% C.I. 0.80-0.99, p=0.035)] and this benefit was not statistically different in patients with eGFR 30-59 ml/min/1.73m<sup>2</sup> vs eGFR >= 90 ml/min/1.73m<sup>2</sup> [HR 0.85 (95% C.I. 0.70-1.02, p=0.081); p for interaction 0.2]. Patients with eGFR 30-59 ml/min/1.73m<sup>2</sup> allocated fenofibrate had a significantly reduced risk of cardiovascular mortality [HR 0.51 (95% C.I. 0.28-0.93), p=0.028] compared with placebo. There was no difference in ESRD events between treatment arms, irrespective of baseline eGFR group, nor was there any adverse safety signal of fenofibrate use in patients with low eGFR. Conclusions: Patients with type 2 diabetes and moderate renal impairment (eGFR 30-59 ml/min/1.73m<sup>2</sup>) have very high CVD risk and gain significant benefits on long-term fenofibrate, without any excess safety concerns compared to other diabetic patients with no or mild renal impairment. The FIELD data support the efficacy and safety of standard dose fenofibrate in subjects with moderate renal impairment, suggesting that current guidelines for dose modification in this setting may be too restrictive.

Publication Types: Conference Abstract
PMID:70534257

Evaluation of the diagnostic and prognostic value of plasma D-dimer for abdominal aortic aneurysm.
Aims A number of biomarkers have been associated with abdominal aortic aneurysm (AAA), but there has been no assessment of how such markers along with clinical risk factors can be used to stratify the risk of AAA presence and its progression. The aims of this study were to assess the diagnostic, prognostic, and risk stratification potential of plasma D-dimer for AAA presence and growth.

Methods and results We included 1260 subjects (337 with AAA) recruited from a population screening study and 132 (41 with AAA) from a referral clinic. A total of 299 of the population group were followed by repeat ultrasound imaging for a median of 5.5 years to monitor AAA growth. The diagnostic and prognostic potential of plasma D-dimer was assessed by multivariate regression (adjusting for other AAA risk factors), receiver operator characteristic, and classification and regression tree (CART) analyses. In both groups, the dominant risk factor for AAA was D-dimer; thus in the population group, cut-off values of >400 and >900 ng/mL had adjusted odds ratios of 12.1 (95 CI 7.1-20.5) and 24.7 (95 CI 13.7-44.6), respectively. In both groups, CART analyses confirmed the dominating role of plasma D-dimer in defining extreme risk-groups with AAA prevalence as disparate as 3 and 82. Average yearly AAA growth was positively and significantly associated with D-dimer which was able to predict growth as disparate as 0.4 and 2.5 mm/year.

Conclusion This study suggests that plasma D-dimer can play a role in the diagnosis and prognosis of AAA. Published on behalf of the European Society of Cardiology.

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Phase I-II study of radiopeptide 177 Lu-octreotate in combination with capecitabine and temozolomide in advanced low-grade neuroendocrine tumours.


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Background: Low-grade neuroendocrine tumours (NETs) arise predominantly in fore, mid and hind-gut regions and particularly gastropancreatic tissues and small-bowel. Most have somatostatin receptors which can be targeted by octreotide and radiolabelled somatostatin analogues. Recent trials have demonstrated significant NET responsiveness to capecitabine chemotherapy either in combination with temozolomide, or with 177 Lu-octreotate. Methods: All patients received a fixed activity of 7.8 GBq 177 Lu-octreotate each 8 weeks with 14 days of capecitabine 1500 mg/m² for 4 cycles. In phase I, successive cohorts of patients received escalating doses of temozolomide in groupings of 100, 150 and 200 mg/m² in the last 5 days of each capecitabine cycle. In phase II, patients were treated with 200 mg/m² temozolomide. Dose limiting toxicities, adverse events, objective tumour responses by RECIST and serum/urine NET chemistries were evaluated. Results: As of January 2011, 33 patients were enrolled, 25 completed therapy and 8 ongoing. Of 25 evaluable patients: median age 63 years; primary sites: gastropancreatic 12 (48%), bowel 12 (48%), lung 1 (4%); metastatic sites: liver 21 (84%), nodal 9 (36%), other (bone 2, lung 1). Prior treatments octreotide 9 (36%), chemotherapy 4 (16%) or nil 14 (56%). Treatment was well tolerated in all dosage groups. No dose limiting grade 2, 3 or 4 toxicities were seen in cohorts 1 (100 mg/m²) or 2 (150 mg/m²). 19 patients have completed treatment at the 200 mg/m² temozolomide level; 2 patients experienced grade 3 capecitabine-induced angina, otherwise adverse
events were mild to moderate. The commonest toxicities being transient nausea grade 2 (20%) and grade 3 (4%). Myelotoxicity comprised thrombocytopenia grade 2 (16%), neutropenia grade 3 (8%). There were no grade 4 events. 24 of 25 patients were evaluable for tumour response, 13 (54%) achieving partial response (PR) and 9 (38%) minor response or stable disease (SD). 2 patients progressed and have died of their disease. NET site of origin significantly influenced response, 10 of 11 (91%) gastropancreatic NETs showed PR, whilst lower rates were seen with small-bowel 3 PR (25%) and 8 SD (67%). Conclusion: 177 Lu-octreotate in combination with capecitabine 1500 mg/m$^2$ for 14 days and temozolomide 200 mg/m$^2$ for 5 days given each 8 weeks for 4 cycles is well tolerated in patients with advanced, progressive, low-grade NETs and achieves high overall tumour control rates.

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Elevated LH predicts ischaemic heart disease events in older men: The health in men study.
Hyde Z, Norman PE, et al.
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Context: Hypogonadism in men is associated with insulin resistance, elevations in pro-inflammatory cytokines and fibrinogen, and an atherogenic lipid profile. However, it is uncertain whether the age-related decline in testosterone is associated with ischaemic heart disease (IHD) events. Objective: To determine whether testosterone and its associated hormones, sex hormone-binding globulin (SHBG) and LH, predict IHD events in older men. Design: Prospective cohort study. Methods: Between 2001 and 2004, 3637 community-dwelling men aged 70-88 years underwent a clinical assessment of cardiovascular risk factors and biochemical assessment of testosterone, SHBG and LH. Free testosterone was calculated using mass action equations. Participants were followed until December 2008 using electronic record linkage to capture IHD events (hospital admission or death). Results: Mean follow-up was 5.1 years. During this period, 618 men (17.0%; 95% confidence interval (CI) 15.8, 18.3%) experienced an event, of which 160 were fatal. Men with higher baseline total or free testosterone levels experienced fewer IHD events (hazard ratio (HR)=0.89; 95% CI 0.82, 0.97 and HR=0.86; 95% CI 0.79, 0.94 for each one S.D. increase in total and free testosterone respectively). These associations were maintained after adjustment for age and waist:hip ratio but did not persist after adjustment for prevalent IHD or other cardiovascular risk factors. SHBG was not associated with IHD events. In contrast, higher LH levels were associated with reduced event-free survival in both univariate (HR=1.15; 95% CI 1.08, 1.22) and adjusted analyses (HR=1.08; 95% CI 1.01, 1.15). Conclusions: Dysregulation of the hypothalamic-pituitary-gonadal axis may be a risk factor for IHD. Further studies of men with either elevated LH or low testosterone are warranted. European Society of Endocrinology.
PMID:2011175738
Associations of IGF1 and IGFBPs 1 and 3 with all-cause and cardiovascular mortality in older men: The health in men study.
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Objective: Circulating IGF1 declines with age while ill-health increases. Controversy remains whether differences in the levels of IGF1 and its binding proteins 1 and 3 (IGFBP1 and IGFBP3) determine health outcomes during ageing. We examined associations of IGF1, IGFBP1 and IGFBP3 with all-cause and cardiovascular mortality in older men. Design: We conducted a prospective cohort study of community-dwelling men aged >=70 years. Methods: Plasma collected at baseline (2001-2004) was assayed for total IGF1, IGFBP1 and IGFBP3. Incidence and causes of death from time of recruitment to 31 December 2008 were ascertained using the Western Australian Data Linkage System. Cox regression analyses were performed, adjusting for conventional cardiovascular risk factors. Results: Among 3983 men followed for 5.2 years (median), 694 deaths occurred, 243 from cardiovascular disease (CVD). There was no difference in survival according to quintiles of IGF1. Increased IGFBP1 predicted increased all-cause mortality (highest versus lowest quintile: adjusted hazard ratio (HR)=1.98, 95% confidence interval (CI)=1.52-2.57, P<0.001 for trend) and increased cardiovascular mortality (HR=3.42 (2.03-5.77), P<0.001 for trend). Decreased IGFBP3 predicted increased all-cause mortality (lowest versus highest quintile: HR=1.57, 95% CI=1.23-2.01, P=0.007 for trend). Associations of IGFBP1 and IGFBP3 with all-cause mortality were not attenuated by adjustment for IGF1 levels. Conclusions: In older men, higher IGFBP1 and lower IGFBP3 levels predict overall and CVD-related mortality, while IGF1 levels are not associated with mortality. Further studies are needed to clarify the underlying mechanisms by which IGFBP1 and IGFBP3 levels are associated with mortality risk, and whether this occurs independently of IGF1. 2011 European Society of Endocrinology.

PMID:2011237134

A population-based study of polymorphisms in genes related to sex hormones and abdominal aortic aneurysm.
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Male gender and family history are risk factors for abdominal aortic aneurysm (AAA). We hypothesized that genes involved in sex hormones might be important in AAA. We investigated the association of aortic diameter with single-nucleotide polymorphisms (SNPs) in genes determining circulating sex hormones and their action. We genotyped 74 tagging SNPs across four genes (steroid 5alpha reductase, subfamily A, polypeptide 1 (SRD5A1), cytochrome P450, family 19, subfamily A, polypeptide 1 (CYP19A1), androgen receptor (AR) and estrogen receptor 2 (ESR2)) related to sex hormones.
hormone production and action in 1711 men, 640 of whom had an AAA. One genotype was also assessed in an independent cohort of 782 men, of whom 513 had large AAAs. Associations were assessed adjusting for other risk factors for AAA. One SNP in CYP19A1 was strongly associated with aortic diameter. Subjects who had the rare homozygote genotype (TT) for CYP19A1g.49412370CT (SNP ID rs1961177), had an increased aortic diameter (coefficient 5.058, SE 1.394, P=0.0003, under a recessive model). This SNP was not associated with aortic diameter in an independent cohort, which included patients with larger AAAs. Our findings do not support an important role of genetic polymorphisms in genes determining sex hormones in aortic dilatation in men. The association of one SNP in CYP19A1 with small but not large AAA may suggest differences between AAA formation and progression. This SNP warrants further investigation in another large population, including patients with small AAAs. 2011 Macmillan Publishers Limited. All rights reserved.

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Phase II study of radiopeptide (177)Lu-octreotate and capecitabine therapy of progressive disseminated neuroendocrine tumours.

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PURPOSE: In this phase II study we investigated the safety and efficacy of combination capecitabine and (177)Lu-octreotate for the treatment of disseminated, progressive, unresectable neuroendocrine tumours (NETs). METHODS: Enrolled in the study were 33 patients with biopsy-proven NETs, positive (111)In-octreotide scintigraphy and progressive disease measurable by CT/MRI who were to receive four cycles of 7.8GBq (177)Lu-octreotate 8-weekly, with 14days of 1,650mg/m² capecitabine per day. RESULTS: Of the 33 patients, 25 completed four cycles. Minimal transient myelosuppression at 3-4weeks caused grade 3 thrombocytopenia in one patient but no neutropenia. Nephrotoxicity was absent. Critical organ radiation dosimetry provided median estimates of the dose per cycle to the kidneys of 2.4Gy and to the liver of 4.8Gy, and showed cumulative doses all below toxic thresholds. Objective response rates (ORR) were 24% partial response (PR), 70% stable disease (SD) and 6% progressive disease. Median progression-free survival and median overall survival had not been reached at a median follow-up of 16months (range 5-33months). Survival at 1 and 2years was 91% (95% CI 75-98%) and 88% (95% CI 71-96%), respectively. CONCLUSION: The addition of capecitabine radiosensitizing chemotherapy does not increase the minimal toxicity of (177)Lu-octreotate radiopeptide therapy and led to an ORR of 24% PR and 70% minor response or SD in patients with progressive metastatic NETs. Tumour control and stabilization of disease was obtained in 94% of these patients.

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Interprofessional programmes provide evidence and skills to both health care professionals and consumers in remote and regional Western Australia.

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Background and Aims: Two projects provide metropolitan based Western Australians with evidence-based self-management strategies for spinal pain; (1) Inter-professional low back pain education programme for General Practitioners (gPEP); (2) Preclinic inter-professional group education for
consumers attending tertiary pain medicine units via Self-Training Educative Pain Sessions (STEPS).

Methods: An inter-disciplinary Spinal Pain Implementation working party established by Health Networks (Department of Health, WA) prioritised the funding and delivery of gPEP and STEPS to Health Care Professionals (HCPs) and consumers, respectively, in regional WA. Sixty HCPs from four WA regional areas attended this prospective cohort study (questionnaires baseline and 2 months). More than eighty consumers attended and five weeks after attendance a subset of 15 consumers participated in an independent semi-structured telephone interview. Results: HCPs (n = 49 consented to participate; response rate postintervention 53%) adopted more evidence-based beliefs and self-reported clinical approaches post-intervention, as evidenced by HCPAIRS score differences (mean change = -4.2 +/- 7.4, p < 0.008; baseline 41.4 +/- 9.0) and significant positive shifts on 11 of 12 measures of clinical knowledge and behaviours (p < 0.001 for 10/11 questions; p = 0.011 for 1). Consumers: Five themes identified: (1) central role of the GP; (2) lack of community-based specialist and GP services; (3) use of individual coping strategies; (4) Empowerment, validation of self-acquired coping strategies, and acquisition of new self-management skills (from STEPS); (5) Benefits and drawbacks of the group-based education format. Conclusions: The "Rural Roadshow" was useful for HCPs and consumers in regional WA and highlight the need for community-based health information and services.

Publication Types: Conference Abstract
PMID:70577659

Hopeful, helpless, hyperaroused and holding on - Hospital outpatients' pain management strategies adopted following an interdisciplinary pain management group programme.

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Background and Aims: There is extensive quantitative research on psychological interventions for chronic pain and psychological distress. This research sought to add the patient perspective by: conducting a quantitative and qualitative analysis of an interdisciplinary pain programme's outcomes supplementing the data with a qualitative analysis to ascertain participants' views of the most useful coping strategies. Methods: Participants were outpatients referred to a hospital pain management programme (N = 92). Ten participants (5 females, 5 males) were invited to engage in semi-structured interviews to supplement the quantitative data derived from HADS, IES-R, pain intensity scores and functional activity measures. Statistical analysis (N = 92) included paired sample and independent T-tests, repeated measures, ANOVAs. A qualitative (thematic) analysis of the semi-structured interviews (N = 10) was used to identify themes. Results: Quantitative data showed significant improvement in physical functioning and psychological distress but not in significantly reduced pain intensity. Qualitative analysis revealed that participants tended to cope with their pain and distress and interpret and adopt strategies from a pain programme according to their past psycho-social histories. Hyperaroused participants tended to engage in overactivity or exercise and have difficulty in applying relaxation techniques. The hopeless and helpless tended not to apply any of the suggested self-management techniques and to rely on others for help. Memories of childhood trauma, deprivation or maltreatment were particularly relevant to coping strategies. Conclusion: Results highlight the role of psychosocial influences in the development of persistent pain and psychological distress and the need for targeted interventions to support healthy coping strategies.

Publication Types: Conference Abstract
PMID:70577014

Sequential intravesical
chemoimmunotherapy with mitomycin C and bacillus Calmette-Guerin and with bacillus Calmette-Guerin alone in patients with carcinoma in situ of the urinary bladder: Results of an EORTC Genito-Urinary Group randomized phase 2 trial (30993). Eur Urol 2011;59:438-46. Ooi WL, Stockler M, et al. (Ooi, Hayne) School of Surgery, University of Western Australia, Fremantle Hospital, Alma Street, Fremantle, WA 6160, Australia (Stockler) NHMRC Clinical Trials Centre, C-39 Royal Prince Alfred Hospital, University of Sydney, NSW 2006, Australia
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Publication Types: Letter
PMID:2011304728

Evidence Based Library and Information Practice. 2011; 6(4).
Employers’ perspectives on future roles and skills requirements for Australian health librarians.
Objective – This study, which comprises one stage of a larger project (ALIA/HLA Workforce and Education Research Project), aimed to discover employers’ views on how (or whether) health librarians assist in achieving the mission-critical goals of their organizations; how health librarians contribute to the organization now and into the future; and what are the current and future skills requirements of health librarians.
Methods – Each member of the project group approached between one and five individuals known to them to generate a convenience sample of 22 employers of health librarians. There were 15 semi-structured interviews conducted between October and November 2010 with employers in the hospital, academic, government, private, consumer health and not-for-profit sectors. The interview schedule was sent to each interviewee prior to the interview so that they had time to consider their responses. The researchers wrote up the interview notes using the interview schedule and submitted them to the principal researcher, who combined the data into one document. Content analysis of the data was used to identify major themes.
Results – Employers expressed a clear sense of respect for the roles and responsibilities of library staff in their organizations. Areas of practice such as education and training, scientific research and clinical support were highlighted as critical for the future. Current areas of practice such as using technology and systems to manage information, providing information services to meet user needs and management of health information resources in a range of formats were identified as remaining highly relevant for the future. There was potential for health librarians to play a more active and strategic role in their organizations, and to repackage their traditional skill sets for anticipated future roles. Interpersonal skills and the role of health librarians as the interface between clinicians and information technology were also identified as critical for the future.
Conclusions – Interviews with employers provided valuable insights into the current and future roles and skills requirements of health librarians in Australia, enriching the findings of the earlier stages of the research project. The next step is to work with the stakeholder groups in this project and use the research project’s findings as the evidence base on which to develop a structured, modular education framework comprising a postgraduate qualification in health librarianship and a continuing professional development structure supporting a three-year cycle of certification and revalidation.

Osteocalcin: An endocrine link between bone and glucose metabolism.
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Impaired glucose metabolism is common and contributes to the risk of diabetes and cardiovascular disease. Deletion of the gene for the osteoblast-derived protein, osteocalcin, leads to insulin resistance in mice, while the addition of osteocalcin increases insulin secretion from beta-cells and adiponectin expression in adipocytes. Osteocalcin deficiency in -carboxyl groups, undercarboxylated osteocalcin, was found to improve insulin secretion and sensitivity in experiments. Recent studies have examined the relevance of these findings to glucose metabolism and cardiovascular risk in humans. Low total osteocalcin levels are associated with insulin resistance, diabetes and metabolic syndrome in observational studies. New therapeutic approaches to diabetes and heart disease may be anticipated if this bone-derived protein is involved in the regulation of glucose metabolism and cardiovascular risk. 2011 Expert Reviews Ltd.

Publication Types: Review
PMID:2011152495

Tumor seeding after EUS-guided FNA of pancreatic tail neoplasia.
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PMID:21951481

Polymorphisms associated with normal memory variation also affect memory impairment in schizophrenia.
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Neurocognitive dysfunction is a core feature of schizophrenia with particularly prominent deficits in verbal episodic memory. The molecular basis of this memory impairment is poorly understood and its relatedness to normal variation in memory performance is unclear. In this study, we explore, in a sample of cognitively impaired schizophrenia patients, the role of polymorphisms in seven genes recently reported to modulate episodic memory in normal subjects. Three polymorphisms (GRIN2B rs220599, GRM3 rs2189814 and PRKCA rs8074995) were associated with episodic verbal memory in both control and patients with cognitive deficit, but not in cognitively spared patients or the pooled schizophrenia sample. GRM3 and PRKCA acted in opposite directions in patients compared to controls, possibly reflecting an abnormal brain milieu and/or adverse environmental effects in schizophrenia. The encoded proteins balance glutamate signalling vs. excitotoxicity in complex interactions involving the excitatory amino acid transporter 2 (EAAT2), implicated in the dysfunctional glutamatergic signalling in schizophrenia. Double carrier status of the GRM3 and PRKCA minor alleles was associated with lower memory test scores and with increased risk of schizophrenia. Single nucleotide polymorphism (SNP) rs8074995 lies within the PRKCA region spanned by a rare haplotype associated with schizophrenia in a recent UK study and provides further evidence of PRKCA
contribution to memory impairment and susceptibility to schizophrenia. Our study supports the utility of parsing the broad phenotype of schizophrenia into component cognitive endophenotypes that reduce heterogeneity and enable the capture of potentially important genetic associations. 2011 The Authors. Genes, Brain and Behavior 2011 Blackwell Publishing Ltd and International Behavioural and Neural Genetics Society. PMID:2011310973


Falling Trends in the prevalence, incidence and recurrence of atherothrombotic vascular disease.

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Background: There is a scarcity of data on the combined burden of hospitalised atherothrombotic disease affecting the coronary, cerebrovascular and peripheral arteries. The burden is projected to increase due to improving survival, an aging population and changing risk factor profiles. We determined sex-specific trends in the prevalence, incidence and recurrence of atherothrombotic disease in Western Australia from 2000 to 2007. Methods: Linked hospitalisations for atherothrombotic events statewide were obtained using records from 1985 onwards. Annual sex and age-standardised (35-84 years) prevalence, incidence, and recurrence of admissions for categories of atherothrombotic events were derived using a 15-year lead-in to assess prior disease. Results: In 2007, 45,916 (8.6%) men and 22,782 (4.3%) women had established atherothrombotic disease. From 2000 to 2007 there were 58,656 incident (63.4% men) and 48,920 recurrent events (68.8% men), dominated by coronary disease causing 63.8% and 78.1% of incident and recurrent events respectively. The ratio of incident: recurrent events was 3.1 for cerebrovascular, and 1.0 each for both coronary and peripheral arterial disease. The table shows the major trends. Declining age-standardised prevalence, incidence and recurrence rates were also seen in all categories of monovascular and polyvascular atherothrombotic disease. (Table Presented). Conclusion: The falling trends in a majority of atherothrombotic disease categories and total disease prevalence are likely to indicate improved primary and secondary prevention measures in Western Australia.

Publication Types: Conference Abstract
PMID:70499772


Transthoracic echocardiography inside a hyperbaric chamber.

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Background: Hyperbaric therapy is an established treatment for a variety of conditions including decompression illness, chronic infection and poor wound healing. There are postulated abnormalities of systolic and diastolic left ventricular dysfunction under hyperbaric conditions, including the incompletely understood entity of submersion pulmonary oedema. This study represents the world first use of a modified (to withstand hyperbaric conditions) GE Logiq E transthoracic echocardiograph to assess the haemodynamic effects during hyperbaric oxygen therapy. This study will enroll 20 consecutive patients undergoing hyperbaric therapy at the Fremantle Hospital Hyperbaric Unit. This abstract describes a preliminary analysis of the first four participants (three males). 'Surface' transthoracic (TTE) was followed by repeat TTE at 30 minutes of compression to 2.4 atmospheres pressure on 100% FiO2. Mann-Whitney analysis demonstrates a trend towards reduced left
ventricular outflow tract velocity time integral (as a measure of systolic function), however results did not reach statistical significance ('Surface' mean 18.9+/−2.5; ‘Compression’ mean 16.2+/−1.0; p = 0.07). Diastolic function, measured by mitral pulse wave E/A ratio, did not show any significant change between 'Surface' (mean 1.2+/−0.4) and 'Compression' (mean 1.3+/−0.3; p = 0.65). This study demonstrates a world first environment in which TTE has been used and may provide insight into the changes in physiology experienced during hyperbaric compression that could aid patient selection and best practice for this therapy.

Publication Types: Conference Abstract
PMID:70499650

Cardiovascular risk, renal status and fenofibrate safety in the FIELD study.
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Background: Baseline renal function predicts cardiovascular disease (CVD). In the FIELD study, fenofibrate raised plasma creatinine. We examined the effect of renal status changes on CVD risk and the consequences of fenofibrate administration in moderate renal impairment. Methods: In FIELD, 9795 patients, 50-75 years with type 2 diabetes, were randomly assigned fenofibrate 200mg daily or placebo over five years. The pre-specified outcome for subgroup analysis was total cardiovascular events. Renal status [eGFR (MDRD) and albuminuria (albumin: creatinine ratio)] was examined (baseline, year 2 and close-out). End-stage renal eventswere recorded. Analysis was by intention-to-treat. Results: CVD risk was strongly associated with baseline eGFR (inverse) and albuminuria; and was modified by renal status changes over the first two years. In those whose albuminuria status changed from normal to abnormal, risk significantly increased (p = 0.006) whereas it reduced when albuminuria resolved (p = 0.01). A similar pattern was observed for changing eGFR status between <60 and >=60 ml/min/1.73m2. Overall, fenofibrate reduced total cardiovascular events by 11% (p = 0.035), with comparable benefits seen in all eGFR subgroups (p-interaction = 0.2). The greatest absolute CVD risk reduction (7.5%) was observed with baseline eGFR 30-59 ml/min/1.73m2 (HR 0.68, p = 0.035). End-stage renal disease events were no more common with fenofibrate. Conclusions: Improvements in eGFR and albuminuria over time are associated with lower CVD risk. Fenofibrate slows eGFR loss and does not cause renal injury in diabetes or reduce cardiovascular benefits when creatinine rises. There were large cardiovascular benefits and no renal issues when used in those with moderate renal impairment.

Publication Types: Conference Abstract
PMID:70499664

Heart Lung and Circulation. 2011; 20: S123.
Economic analysis of hospitalisation for transcatheter aortic valve implantation compared to surgical aortic valve replacement in octogenarians.
Yong G, Rankin J, et al.
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Background and objective: Transcatheter Aortic Valve Implantation (TAVI) is a promising alternative to surgical aortic valve replacement (AVR) for treatment of patients with symptomatic severe aortic
stenosis who are at high surgical risk due to age or comorbidities. We aim to evaluate the economic cost of hospitalisation for TAVI compared to surgical AVR in a cohort of octogenarians. Method and results: Since the 2008-2009 financial year in a single centre, 45 octogenarians (mean age 86.4) with severe aortic stenosis were treated with TAVI and 24 (mean age 84.1) were treated with surgical AVR. Direct cost and length of stay for the index hospitalisation for valve replacement were calculated. The median length of stay for TAVI was seven days (IQR 5, 13) compared to surgical AVR of 14 days (IQR 9.3, 27.5) (p < 0.001). The median direct cost of hospitalisation for TAVI was $47615 (IQR 39899, 59622) and for surgical AVR was $47795 (IQR 25839, 76581) (p = NS). Conclusion: in octogenarians, hospitalisation for TAVI is associated with similar cost to surgical AVR but significantly shorter length of stay.

Publication Types: Conference Abstract
PMID:70499477

Heart Lung and Circulation. 2011; 20: S121.

Complementary anatomical suitability for transcatheter aortic valve implant in a program with access to two first generation transcatheter valves.
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Background: Two Transcatheter Aortic Valve Implant (TAVI) devices are currently in use under clinical trial in Australia - Edwards SAPIEN valve (SAPIEN) and Medtronic CoreValve (CoreValve). Anatomical suitability for SAPIEN include: aortic annulus dimension of 18-25mm, iliac-femoral diameter >7-8mm (transfemoral approach using 22-24 Fr RetroFlex system) or >6-6.5mm (transfemoral approach using newer 18-19 NovaFlex system). Anatomical suitability for CoreValve include: aortic annulus dimension of 20-27mm, ascending aorta diameter <=40-43mm, iliac-femoral diameter >6mm (for transfemoral approach) or left subclavian diameter >6mm (for transsubclavian approach). We aim to assess the complementary anatomical suitability in a TAVI program with access to both valves. Methods and results: Fifty-five patients were treated with TAVI in a single centre with simultaneous access to both SAPIEN and CoreValve since February 2009. Twentywere implanted using CoreValve (all transfemoral) and 35 using SAPIEN (12 transapical, 15 transfemoral with RetroFlex system, 8 with NovaFlex system). Aortic annulus was measured using transoesophageal echocardiogram. Iliac-femoral, subclavian, ascending aortic and root anatomy were measured using invasive angiography. Fifty patients (91%) were suitable for SAPIEN valve, with 21 being suitable for transfemoral approach using RetroFlex system and 38 with NovaFlex system. Forty-four patients (80%) were suitable for CoreValve, with 36 being suitable for transfemoral approach. Overall 45 cases were suitable for a transfemoral approach using one or both valves. Conclusion: 9-20% of the patients treated in this centre with access to both transcatheter valves would be unsuitable for treatment if there was access to only one valve. 82% can be treated with a transfemoral approach.

Publication Types: Conference Abstract
PMID:70499471

Hepatology. 2011; 54: 1114A.
The prevalence and metabolic significance of nonalcoholic fatty liver disease in adolescent girls with polycystic ovary syndrome.
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(Ayonrinde, Adams, Mori, Beilin, Hart) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia (Ayonrinde, Olynyk) Gastroenterology and Hepatology, Fremantle Hospital, Fremantle, WA, Australia (Adams) Liver Transplantation Unit, Sir Charles Gairdner Hospital, Nedlands, WA, Australia (Doherty) School of Women's and Infants Health, University of Western
Adolescents with Polycystic Ovary Syndrome (PCOS) are at risk of nonalcoholic fatty liver (NAFLD) and the metabolic syndrome. Objective and Methods: We determined the prevalence and metabolic significance of NAFLD in adolescent girls with PCOS. Community-based adolescents in the Western Australian Pregnancy Cohort (Raine Cohort) Study participated in the menstruation in teenagers study (n=244 females) between ages 14-17 years and in a NAFLD study (n=578 females, 592 males) at age 17 years. Assessments included questionnaires, anthropometric, cardiovascular, pelvic ultrasound, abdominal ultrasound and fasting blood tests. Two hundred and one girls had both ovarian and liver ultrasounds. PCOS was diagnosed using NIH criteria. NAFLD was diagnosed with liver ultrasound.

Results: The prevalence of PCOS and NAFLD in the menstruation study were 16% and 19% respectively. Girls with PCOS had a higher prevalence of NAFLD than those without PCOS (42.3% vs. 14.2%, p=0.001). NAFLD was more prevalent in obese girls with PCOS compared with non-obese girls with PCOS (64.7% vs. 0.0%, p=0.002 using waist circumference, 85.7% vs. 15.4%, p=0.004 using suprailiac skinfold thickness and 83.3% vs. 30.0%, p=0.54 using body mass index (BMI)). Girls with PCOS plus NAFLD had greater adipose tissue (determined by body weight, waist circumference, BMI, suprailiac skinfold thickness), serum leptin and triglycerides but lower serum adiponectin than girls with PCOS without NAFLD (p<0.05 for all). HOMA-IR, serum ALT, CRP, HDL-cholesterol, LDL-cholesterol and glucose levels were similar between the two groups. Girls with PCOS plus NAFLD had similar body weight, waist circumference, waist/hip ratio, BMI, intensity of hepatic steatosis, subcutaneous fat thickness, visceral fat thickness, skinfold thickness, HOMA-IR, serum glucose, insulin, GGT, triglycerides, HDL-cholesterol and adiponectin levels to boys with NAFLD (p>0.05 for all). However, girls had higher serum CRP and leptin whilst boys had higher ALT and AST levels and systolic blood pressure. Free testosterone concentration (FT) was higher in girls diagnosed with NAFLD than those without NAFLD (25.9 vs. 18.9 pmol/L, p=0.02), however FT was not predictive of NAFLD after controlling for obesity. Suprailiac skinfold thickness (odds ratio 1.16, 95% CI 1.08-1.24, p<0.001) and presence of PCOS (odds ratio 3.87, 95% CI 1.09-13.76, p=0.04) were independent predictors of NAFLD in the menstruation study. Conclusions: NAFLD in adolescent females with PCOS is common and has metabolic similarities with male NAFLD. Obesity and PCOS have a dominant effect over testosterone levels in predicting female NAFLD.

Publication Types: Conference Abstract
PMID:70593401

Hepatology. 2011; 54: 466A.

Anthropometric measurements during childhood predict nonalcoholic fatty liver disease in adolescents.

Ayonrinde OT, Olynyk JK, et al.

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Publication Types: Conference Abstract
PMID:70593401

Hepatology. 2011; 54: 466A.
diagnosed in adults and are frequently not suspected nor diagnosed during childhood and adolescence despite an association with prevalent or future risk for the metabolic syndrome, nonalcoholic steatohepatitis (NASH), cirrhosis, type 2 diabetes and atherosclerotic cardiovascular disease. Identification of children at increased risk of future NAFLD may guide interventions to prevent adolescent and adult NAFLD and associated metabolic disorders. Objectives and Methods: We sought a relationship between childhood anthropometry (including weight, body mass index (BMI), skinfold thickness (SFT), head circumference (HC), chest circumference (CC) and arm circumference (AC)) and adolescent NAFLD in 1170 serially well characterized 17-year-old adolescents participating in the Western Australian Pregnancy Cohort (Raine Cohort) Study. Case-control analysis was performed using anthropometric measurements serially recorded from birth. NAFLD was diagnosed using liver ultrasound at age 17 years. Results: 150/1170 adolescents (12.8%) were diagnosed with NAFLD. Neither birth weight nor percentage of expected birth weight was associated with NAFLD. There were significant differences in anthropometry acquired during childhood between participants subsequently diagnosed with NAFLD and those without NAFLD. There was a significant mean (sd) body weight difference of 2.7% at age 3 years (15.3 (1.7) kg vs. 14.9 (1.8) kg), progressing to a difference of 24.7% (81.4 (20.5) kg vs. 65.3 (11.5) kg at age 17 years between those with NAFLD and those without NAFLD (p<0.05 at all ages). HC was smaller from age 1 year to 5 years while SFT was greater from age 2 years, BMI and AC from age 3 years and CC from age 5 years onwards (p<0.05 for all). Boys diagnosed with NAFLD at age 17 years had higher systolic blood pressure than boys without NAFLD from age 10 years (p<0.05). Apart from HC, all of these differences persisted and increased through age 17 years. Using multiple logistic regression analysis adjusted for body weight, BMI, AC and CC up to age 5 years, greater suprailiac SFT at age 3 years (OR 1.18, 95% CI 1.05-1.33, p=0.006), CC at age 5 years (OR 1.15, 95% CI 1.08-1.24, p<0.001) and smaller HC at age 1 year (OR 0.65, 95% CI 0.53-0.80, p<0.001) were independent predictors of adolescent NAFLD. Conclusions: Changes in growth and adiposity from as early as one year of age are associated with the future development of NAFLD in 17 year olds. Anthropometric measurements during early childhood may identify individuals predestined to develop NAFLD and allow early targeted intervention.

Publication Types: Conference Abstract
PMID:70592036


Liver and serum iron: Discrete regulators of hepatic hepcidin expression.
Chua ACG, Trinder D, et al.
School of Medicine and Pharmacology Fremantle Hospital University of Western Australia Fremantle, Western Australia, Australia; Western Australian Institute for Medical Research Perth, Western Australia, Australia.
Publication Types: Editorial
PMID:21618572


Gender-specific differences in adipose distribution and adipocytokines influence adolescent nonalcoholic fatty liver disease.
Ayonrinde OT, Olynyk JK, et al.
School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia; Telethon Institute for Child Health Research, Centre for Child Health Research, University of Western Australia, Subiaco, Western Australia, Australia; Department of Gastroenterology and Hepatology, Fremantle Hospital, Fremantle, Western Australia, Australia; Curtin Health Innovation Research Institute, Bentley, Western Australia, Australia. oayonrinde@meddent.uwa.edu.au.
Nonalcoholic fatty liver disease (NAFLD) is a predominantly adult-diagnosed disorder. Knowledge regarding the epidemiology, phenotype, and metabolic risk factors, during adolescence is limited. We sought to determine the prevalence, phenotype, and predictors of NAFLD in 1170 community-based
adolescents in the Western Australian Pregnancy Cohort (Raine) Study (the Raine Cohort) who underwent a cross-sectional assessment that included questionnaires, anthropometry, cardiovascular examinations, blood tests, and abdominal ultrasound examinations. Among the 1170 adolescents assessed, the prevalence of NAFLD was 12.8%. Females compared with males had a significantly higher prevalence of NAFLD (16.3% versus 10.1%, P = 0.004) and central obesity (33.2% versus 9.9%, P < 0.05). The severity of hepatic steatosis was associated with the body mass index, waist circumference, subcutaneous adipose tissue thickness (SAT), serum leptin level, homeostasis model assessment for insulin resistance score (P < 0.001 for all), and serum alanine aminotransferase level (P < 0.005) in both genders, but it was associated with increasing visceral adipose tissue thickness (VAT; P < 0.001) and decreasing serum adiponectin levels (P < 0.05) in males alone. Males and females with NAFLD had similar amounts of SAT (P > 0.05); however, in comparison with females with NAFLD, males with NAFLD had greater VAT, a more severe metabolic phenotype with higher glucose levels and systolic blood pressure and lower adiponectin and high-density lipoprotein cholesterol levels (P < 0.001 for all), and greater measures of liver injury (alanine aminotransferase and aspartate aminotransferase, P < 0.001 for all). Similarly, metabolic syndrome was more common in males than females with NAFLD (24% versus 8%, P = 0.01). Suprailiac skinfold thickness predicted NAFLD independently of the body mass index, insulin resistance, and VAT. Conclusion: Gender differences in adolescent NAFLD are related to differences in adipose distribution and adipocytokines. The male phenotype of NAFLD is associated with more adverse metabolic features and greater visceral adiposity than the female phenotype despite the lower prevalence of NAFLD. (HEPATOLOGY 2011;). Copyright Copyright 2010 American Association for the Study of Liver Diseases. PMID:21374659


Fascin expression in low-grade uterine endometrioid adenocarcinoma: correlation with microcystic, elongated and fragmented (MELF)-type alteration at the deep invasive margin.
Stewart CJR, Crook ML, et al.
Departments of Histopathology, King Edward Memorial Hospital, Perth Fremantle Hospital, Perth, WA, Australia.
Stewart C J R, Crook M L & Manso L (2011) Histopathology59, 73-80 Fascin expression in low-grade uterine endometrioid adenocarcinoma: correlation with microcystic, elongated and fragmented (MELF)-type alteration at the deep invasive margin Aims:[en space] The actin-binding protein fascin appears to potentiate the migratory capacity of both normal and neoplastic cells. It has been suggested that microcystic, elongated and fragmented (MELF) glands might represent areas of active invasion within uterine low-grade endometrioid adenocarcinomas. Therefore, fascin immunoreactivity was investigated in a series of endometrial carcinomas specifically comparing expression in conventional tumour areas, foci of MELF-type invasion and in stromal elements. Methods and results:[en space] Fascin expression was assessed in 28 uterine endometrioid adenocarcinomas and the results compared with cytokeratin (CK) 7 expression and with tumour morphology and distribution. The conventional glandular component of most tumours showed only focal fascin reactivity (<10% cells positive), but staining was more prominent within the peripheral epithelial cells. Foci of squamous/morular type differentiation were also positive. The neoplastic epithelium in MELF-type invasion usually showed strong fascin immunoreactivity, often contrasting with the adjacent negative or more weakly stained conventional tumour glands. There was also staining of reactive stromal cells surrounding MELF foci. Conclusions:[en space] There are distinct micro-anatomical variations in fascin immunoreactivity within endometrial carcinoma. The localized increase in fascin expression in MELF-type epithelium supports the proposal that MELF changes represent areas of active tumour invasion. Copyright 2011 Blackwell Publishing Limited. PMID:21771028
Document delivery the British library withdrawal of service.
Hamill C.
Publishers' perceptions are askew and impacting on the delivery of information between Australian public health libraries and the British Library. Cheryl Hamill provides this update.

The long march... National access to health information online.
Hamill C.
Secretary, Health Libraries Australia Executive, and Western Australian Hospitals Representative, Chief Health Librarians Group
Health Libraries Australia (HLA) has been advocating for almost a decade for a national approach to equitable provision of health information to support clinicians in Australia. Despite ongoing efforts and the adoption of many strategies to influence decision makers, we're 'not there yet'. It's instructive to pause and look in the rear-view mirror before continuing the journey.
PMID:220050685983228

Meeting report: Chief Health Librarians Forum.
Hamill C.
WA Representative, Chief Health Librarians Forum, and Manager, Fremantle Hospital and Health Service, email: Cheryl.Hamill@health.wa.gov.au
Information about the objectives and focus of the Chief Health Librarians Forum (CHLF) in Australia, as well as the work being performed by the forum, is presented.
PMID:131823567075651

Third-party red-cell transfusion in the first 30 days after renal transplantation in patients with DSA is associated with antibody-mediated rejection (AMR).
Ashley I, Samantha F, et al.
(Ashley) Nephrology and Renal Transplant, Royal Perth Hospital, Perth, Australia (Samantha, Campbell, Frank) Department of Immunology, Royal Perth Hospital, Perth, Australia (Paolo) Department of Renal Medicine, Fremantle Hospital, Perth, Australia (Wai) Nephrology and Renal Transplant, Sir Charles Gairdner Hospital, Perth, Australia
I. Ashley, Nephrology and Renal Transplant, Royal Perth Hospital, Perth, Australia
Aim: Exposure to foreign HLA by pregnancy, blood transfusion (BT) and transplant may induce allosensitisation. We hypothesised that BT at the time of renal transplant in sensitised patients with preformed donor specific anti-HLA antibody (DSA) may elicit immune recall and rejection. Methods: We examined post-operative BT and biopsy proven graft rejection (BPAR) in a cohort of 256 patients with DSA (defined as MFI >500 by Luminex SAB) and those without DSA (No-DSA group). Results: 83/219 No-DSA (38%) and 26/37 DSA (70%) P<0.001 were transfused a median of 2U (IQR 2-4) No-DSA and 4U (IQR 2-4) DSA (P=0.13) within the first 30 days after transplant, mostly in the first 2 peri-operative days. There was no difference in patients with delayed graft function (17% No-DSA vs 27% DSA P=0.17), proportion of cadaveric donors (63% nonDSAs vs 76% DSA P=0.13) but 60% DSA vs 32% No-DSA had any BPAR (HR=0.003). The median (IQR) time to rejection from transfusion for No-DSA was 58 (16-362) and DSA 61 (14-461) days (P=0.9). The association between transfusion, DSA and AMR is shown in the Table. (Table presented) Conclusions: Patients with DSA who receive peri-operative BT have significantly higher AMR than non-transfused DSA or transfused No-DSA. Early post-operative 3rd party BT in allosensitised patients with pre-formed DSA maybe harmful, perhaps by additional allo-antigen stimulation and warrants confirmation in other studies.
Immunology and Cell Biology. 2011; 89 (7): A25.

**Initial experience of the Australian paired kidney donation program.**
Paolo F, Samantha F, et al.
(Paolo, Claudia) Department of Nephrology, Fremantle Hospital, Perth, Australia (Paolo, Frank)
School of Medicine, Pharmacology, University of Western Australia, Perth, Australia (Samantha, Frank)
Department of Immunology, Royal Perth Hospital, Melbourne, Australia (Rhonda)
Transplantation Services, Australian Red Cross Blood Service, National Transplantation Services, Melbourne, Australia

F. Paolo, Department of Nephrology, Fremantle Hospital, Perth, Australia

Aims: To review the initial 6 months of activity of the Australian paired Kidney eXchange (AKX) program. Methods: Pairs registered in AKX since August 2010 were reviewed with regard to reason for incompatibility, blood group distribution and degree of sensitisation of participants and match run results. Results: In the first 6 months 54 pairs (VIC 21, NSW 18, QLD 8, WA 7) and 1 altruistic donor (AD) were enrolled in AKX, but 14 pairs left the program (7 donor unsuitable, 3 other live donor transplant, 4 cadaveric transplant). In the two match runs performed to date, 37% of donors and 68% of recipients were blood group O. All recipients were sensitised and most were highly sensitised (63% cPRA >50%, 50% cPRA >75%). In the first match run 22 pairs were included, 5 pairs were matched and 3 proceeded to transplant, a 2-way exchange was refused by one centre. In the second match run 25 pairs and 1 AD were included. No matches were identified using exclusion of HLA antibodies >2000MFI. Using the 8000MFI threshold 9 matches were identified in 5 combinations with 4 recipients having acceptable low-level Class 1 DSAs (all <3500MFI). Only 3 matches would have been possible without inclusion of the AD. Conclusions: Including only sensitised recipients in AKX significantly limits the probability of finding a match of these highly sensitised recipients enrolled in AKX. Inclusion of a single AD can overcome this limitation. In order to increase the match rate of sensitised recipients consideration must be given to include unsensitised ABO incompatible pairs in AKX prior to desensitisation protocols.

Publication Types: Conference Abstract
PMID:70656004

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Immunology and Cell Biology. 2011; 89 (7): A24-A25.

**A flexible approach to matching in paired kidney donation.**
Paolo F, Samantha F, et al.
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F. Paolo, School of Medicine, Pharmacology, University of Western Australia, Perth, Australia

Aims: In the National Organ Matching System (NOMS) paired kidney donation module the agreed matching rule is to exclude from matching any donor against whom a recipient has a HLA donor specific antibody (DSA) >2000MFI. In order to match a pool of highly sensitised patients, a less conservative approach to antibody definition was needed in the second match run of the Australian paired Kidney eXchange (AKX). Methods: DSA, antibody class and crossmatch results of matched pairs were reviewed in the 25 pairs enrolled in the second AKX match run, which included 1 altruistic donor (AD). (Table presented) Results: All recipients were sensitised (mean PRA 70%, range 2-95%), 35% of donors and 68% of recipients were blood group O. No matches were identified using exclusion of DSA with MFI >2000. Using exclusion of DSA with MFI >8000, 12 matches were identified; some
recipients appeared in more than one combination. The matches included 3 recipients with no DSA, 7 recipients with current cumulative DSA <5000MFI and 2 recipients with DSA 5000-10000MFI. However, 5/12 matches resulted in a positive B cell crossmatch (Table 1). Conclusions: Increasing the threshold for exclusion of antibodies increases the chances of identifying a matched pair at the expense of positive crossmatches. A balance is needed between accepting DSA and rejecting those matches, which may have resulted in successful transplantation. Consideration of peak DSA and more knowledge about the significance of cumulative antibody and antibody class is required in order to make an informed decision.

Publication Types: Conference Abstract
PMID:70655999

Inflammatory Bowel Diseases. 2011; 17(12): 2596-7.

**NOD2 and CD.**
Lawrance IC.
Centre for inflammatory Bowel Diseases, Fremantle Hospital Fremantle, Australia; School of Medicine and Pharmacology University of Western Australia, Fremantle Hospital Fremantle, Australia.
Publication Types: Comment
PMID:21509912


**Predictors of fibrostenotic Crohn's disease.**
Rieder F, Lawrance IC, et al.
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F. Rieder, Department of Gastroenterology and Hepatology, Digestive Disease Institute, 9500 Euclid Ave., Cleveland, OH 44195, United States. E-mail: riederf@ccf.org
Intestinal fibrosis is a common and serious complication of Crohn's disease (CD) and as it can occur at any time during the disease course, it is crucial to identify patients at risk. The aim is not only to understand the pathophysiology of fibrogenesis but to be able to accurately inform subjects about their disease course, design future trials of potentially useful antifibrotic therapies, and, most important, identify those CD patients at risk, with the view to early, more aggressive medical therapy. This review summarizes the current status of our understanding and ability to predict fibrostenotic CD. The review encompasses three distinct areas: genetic variants, clinical phenotypes, and serologic markers in order to develop a conceptual framework for an understanding of fibrostenotic CD. It also aims to highlight where our knowledge is insufficient in order to identify areas that require future research. Copyright 2010 Crohn's & Colitis Foundation of America, Inc.
Publication Types: Review
PMID:2011441496

Inflammatory Bowel Diseases. 2011; 17: S23.

**Long-term remission with certolizumab pegol in Crohn's disease: Efficacy over 5 years in patients with no prior anti-TNF agent exposure (precise 3 study).**
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Holstein, Christian
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Purpose: To assess remission rates in patients who received certolizumab pegol for 6 months (26 weeks) in PRECiSE 2, 1 and for a further 4.5 years in PRECiSE 3, and to determine if remission rates are affected in patients without previous TNF inhibitor exposure. Methods: Patients completing PRECiSE 2 (NCT00152425) were eligible to enter PRECiSE 3 (NCT00160524) and receive certolizumab pegol 400 mg every 4 weeks. Efficacy and safety data for patients who received certolizumab pegol in PRECiSE 2 and continued with open-label certolizumab pegol treatment in PRECiSE 3 are presented. The Harvey-Bradshaw Index (HBI) was used to measure disease activity (remission = score of <=4). Remission rates were analyzed from the baseline of PRECiSE 2 in the PRECiSE 3 intent-to-treat population and in a subset of this population who had never received infliximab (IFX-naive). Remission rates were calculated using observed case analyses and nonresponder imputation (NRI). Results: Of the 141 patients in the PRECiSE 3 population, 114 were IFX-naive. At the start of PRECiSE 3 (Week 0), 75% (105/141) and 78% (89/114) of the total and IFX-naive populations were in remission, respectively. Remission rates for the total PRECiSE 3 population after 1, 2, 3, 4, and 5 years (observed case) were 75%, 84%, 82%, 79%, and 91%, respectively, and 76%, 83%, 82%, 81%, and 89%, respectively, for the IFX-naive patients. Remission rates for the total PRECiSE 3 population after 1, 2, 3, 4, and 5 years (NRI) were 65%, 49%, 35%, 23%, and 21%, respectively, and 65%, 47%, 37%, 25%, and 21%, respectively, for the IFX-naive patients. No new safety signals were observed and there were no unexpected serious adverse events. Conclusions: Among patients who initially responded to certolizumab pegol induction therapy and remained in PRECiSE 3, continuous certolizumab pegol 400 mg therapy provided long-term remission for 5 years, including a subset of PRECiSE 3 patients receiving certolizumab pegol with no previous exposure to infliximab.

Publication Types: Conference Abstract
PMID: 70583424

Inflammatory Bowel Diseases. 2011; 17: S51-S52.

**Long-term remission with certolizumab pegol in Crohn's disease: Efficacy over 4.5 years in patients with no prior TNF inhibitor exposure (PRECiSE 3 study).**

Lichtenstein G, Thomsen O, et al.

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Christian Albrechts University, Kiel, Germany (Lawrance)
University of Western Australia, Fremantle Hospital, Fremantle, Australia (Hanauer)
University of Chicago Medical Center, Chicago, IL, United States (Bloomfield)
UCB Pharma, Slough, United Kingdom (Sandborn)
Mayo Clinic, Rochester, MN, United States
G. Lichtenstein, University of Pennsylvania School of Medicine, Philadelphia, PA, United States

**PURPOSE:** To assess remission rates in patients who received certolizumab pegol (CZP) for 6 months (26 weeks) in PRECiSE 2 (NCT00152425) and a further 4 years in PRECiSE 3 (NCT00160524) and to determine whether remission rates are affected in patients without previous TNF inhibitor exposure. **METHODS:** Patients completing PRECiSE 2 were eligible to enter PRECiSE 3 and receive CZP 400 mg every 4 weeks. The Harvey-Bradshaw index was used to measure disease activity (remission = score of less than or equal to 4). Remission rates were analyzed from the baseline of PRECiSE 2 in the PRECiSE 3-CZP population and in a subset of this population who had never received infliximab (IFX-nave). Remission rates were calculated using last observation carried forward (LOCF), observed case (OC), and nonresponder imputation (NRI) analyses. **RESULTS:** Of the 141 patients in the PRECiSE 3-CZP population, 114 were IFX-nave. At the start of PRECiSE 3 (Week 0), 75% (106/141) and 78% (89/114) of the PRECiSE 3-CZP and IFX-naive populations, respectively, were in remission. Remission rates for the PRECiSE 3-CZP population after 1 (Week 26 of PRECiSE 3), 2 (Week 78 of PRECiSE 3), 3 (Week 130 of PRECiSE 3), 4 (Week 182 of PRECiSE 3)
3), and 4.5 (Week 206 of PRECiSE 3) years (LOCF) were 69%, 69%, 64%, 64%, and 63%, respectively, and 69%, 68%, 65%, 65%, and 63%, respectively, for the IFX-nave patients. Remission rates for the PRECiSE 3-CZP population after 1, 2, 3, 4, 2010 IBD Abstracts S51 and 4.5 years (OC) were 74%, 84%, 82%, 79%, and 83%, respectively, and 75%, 83%, 82%, 81%, and 81%, respectively, for the IFX-nave patients. Remission rates for the PRECiSE 3-CZP population after 1, 2, 3, 4, and 4.5 years (NRI) were 65%, 49%, 35%, 23%, and 21%, respectively, and 65%, 47%, 37%, 25%, and 22%, respectively, for the IFX-nave patients. CONCLUSIONS: Continuous CZP 400 mg therapy provided long-term remission for 4.5 years in patients who initially responded to CZP induction therapy. Sustained long-term remission rate was observed in PRECiSE 3 patients receiving CZP as well as in PRECiSE 3 patients receiving CZP with no previous exposure to infliximab.

Publication Types: Conference Abstract
PMID:70316800


Does femoral venous pressure measurement correlate well with intrabladder pressure measurement? A multicenter observational trial.
De Keulenaer BL, Regli A, et al.
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PURPOSE: To investigate if femoral venous pressure (FVP) measurement can be used as a surrogate measure for intra-abdominal pressure (IAP) via the bladder. METHODS: This was a prospective, multicenter observational study. IAP and FVP were simultaneously measured in 149 patients. The effect of BMI on IAP was investigated. RESULTS: The incidences of intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) were 58 and 7% respectively. The mean APACHE II score was 22[NON-BREAKING SPACE]+/-[NON-BREAKING SPACE]10, SAPS 2 score 42[NON-BREAKING SPACE]+/-[NON-BREAKING SPACE]20, and SOFA score 9[NON-BREAKING SPACE]+/-[NON-BREAKING SPACE]40. The mean IAP was 11.2[NON-BREAKING SPACE]+/-[NON-BREAKING SPACE]4.5[NON-BREAKING SPACE]mmHg versus 12.7[NON-BREAKING SPACE]+/-[NON-BREAKING SPACE]4.7[NON-BREAKING SPACE]mmHg for FVP. The bias and precision for all measurements were -1.5 and 3.6[NON-BREAKING SPACE]mmHg respectively with the lower and upper limits of agreement being -8.6 and 5.7. When IAP was above 20[NON-BREAKING SPACE]mmHg, the bias between IAP and FVP was 0.7 with a precision of 2.0[NON-BREAKING SPACE]mmHg (lower and upper limits of agreement -3 and 4.6 respectively). Excluding those with ACS, according to the receiver operating curve analysis FVP[NON-BREAKING SPACE]=[NON-BREAKING SPACE]11.5[NON-BREAKING SPACE]mmHg predicted IAH with a sensitivity and specificity of 84.8 and 67.0% (AUC of 0.83 (95% CI 0.81-0.86) with P[NON-BREAKING SPACE]<[NON-BREAKING SPACE]0.001). FVP[NON-BREAKING SPACE]=[NON-BREAKING SPACE]14.5[NON-BREAKING SPACE]mmHg predicted IAP above 20[NON-BREAKING SPACE]mmHg with a sensitivity of 91.3% and specificity of 68.1% (AUC 0.85 (95% CI 0.79-0.91), P[NON-BREAKING SPACE]<[NON-BREAKING SPACE]0.001). Finally, at study entry, the mean IAP in patients with a BMI less then 30[NON-BREAKING SPACE]kg/m(2) was 10.6[NON-BREAKING SPACE]+/-[NON-BREAKING SPACE]4.0[NON-BREAKING SPACE]mmHg versus 13.8[NON-BREAKING SPACE]+/-[NON-BREAKING SPACE]3.8[NON-BREAKING SPACE]mmHg in patients with a BMI[NON-BREAKING SPACE]>=[NON-BREAKING SPACE]30[NON-BREAKING SPACE]kg/m(2) (P[NON-BREAKING SPACE]<[NON-BREAKING SPACE]0.001). CONCLUSIONS: FVP cannot be used as a surrogate measure of IAP unless IAP is above 20[NON-BREAKING SPACE]mmHg.
PMID:21739341


Matching peep to the degree of intra-abdominal pressure: Effects on the cardiorespiratory
INTRODUCTION. We previously showed that positive end-expiratory pressures (PEEP) up to 15 cmH2O were not able to prevent intra-abdominal hypertension (IAH) induced lung volume decline. In contrast to this, matching PEEP to the corresponding intra-abdominal pressure (IAP) did prevent IAH induced lung volume decline. However, this PEEP strategy was not associated with improved oxygenation in a healthy porcine lung model.

OBJECTIVES. This study examined the effect of IAP matching PEEP on P/F ratio, endexpiratory lung volume (EELV), and cardiac output (CO) in a porcine sick lung model of IAH.

METHODS. Nine adult pigs (48 ± 6 kg) received standardized anesthesia and ventilation. Oleic acid was given intravenously to produce acute lung injury. Two pigs served as controls. In 7 pigs, 3 levels of IAP (baseline, 18, and 22 mmHg) and different levels of PEEP were randomly generated. At baseline IAP, PEEP of 5 and 15 cmH2O were applied. At both levels of IAH, 3 levels of PEEP with varying degrees of matching the corresponding IAP were applied: PEEP = 5 cmH2O, PEEP = IAP (cmH2O) + 5 cmH2O (moderate PEEP), PEEP = IAP (cmH2O) (high PEEP). We measured P/F ratio, EELV, and CO.

RESULTS. Increasing IAP from baseline to 22 mmHg IAH (5 cmH2O PEEP) decreased P/F ratio (-55%), EELV (-45%) and CO (-7%). There was a dose related increase in P/F ratio and EELV and a decrease in CO when IAP matching PEEP was applied. At 22 mmHg IAH, moderate PEEP increased P/F ratio by 60% and EELV by 44% and decreased CO by 12%. High PEEP increased P/F ratio by 162% and EELV by 279% and decreased CO by 30%.

CONCLUSIONS. In a porcine lung injury model, IAP-matching levels of PEEP were able to protect against IAP-induced decline in oxygen level and lung volume but were associated with reduced cardiac function.

Publication Types: Conference Abstract
PMID:70639501

Prenatal maternal stress and infant allergy: An exploratory study.
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Background: Maternal stress in pregnancy is associated with an elevated cord-blood IgE as well as a higher cord-blood lymphoproliferative and stimulated cytokine response to allergens. It has been hypothesised that prenatal stress affects fetal growth and development via activation of the physiological stress response or via effects on the normal Th2-predominant immune response in pregnancy. Method: In our cohort of 230 maternal-infant pairs the Depression, Anxiety, Stress Scale (DASS) and Perceived Stress Scale (PSS) were collected at 37 weeks gestation. At 6 months of age T-cell responses to house dust mite antigen (HDM) and egg ovalbumin antigen (OVA) were assessed in a subset (n = 42). At 12 months of age data on infant allergic disease was collected and skin prick testing (SPT) performed. Results: Ten percent of our cohort was stressed and 5% were depressed. At 1 year the prevalence of allergic disease in the infants was 40.5%, and 22.5% had a positive SPT. At 6 months there was an inverse relationship between prenatal maternal stress and stimulated T-cell IL-13 production to HDM and OVA that approached statistical significance (DASS stress and HDM...
stimulated IL-13 production: $R = -0.42, p = 0.06$; DASS stress and OVA IL-13: $R = -0.31, p = 0.05$; PSS and OVA IL-13: $R = -0.27, p = 0.09$). There was no significant association between prenatal maternal DASS or PSS score and the prevalence of infant allergic disease or positive SPT at 1 year. Conclusion: In our cohort we did not demonstrate a significant association between maternal DASS scores or PSS scores at 37 weeks gestation and infant allergic disease or positive SPT at 12 months of age. However, there was a trend towards significance between stress scores and stimulated 6 month T-cell Th2 cytokine production to allergens supporting the hypothesis that prenatal maternal stress alters the normal Th2 predominance in pregnancy and infancy.

Publication Types: Conference Abstract
PMID:70585942

The dimensions of efficiency and effectiveness of clinical directors: Perceptions of clinical directors and senior management in Western Australian public teaching hospitals.
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Health systems have elected to devolve management to semi-autonomous clinical subunits, known as 'clinical directorates'. This has placed responsibility for managing diminishing healthcare resources primarily in the hands of those who use them the most, notably medical practitioners. This research examines and presents a framework that describes the dimensions of efficient and effective clinical directorship in the context of a devolved management structure. A qualitative research design was employed to explore the perceptions of those involved in the operation of clinical directorates some 10 years after their implementation at three public teaching hospitals in Western Australia. The research found that the clinical insights that medical practitioners bring to the role of clinical director were perceived to be the grounding for clinical directorate effectiveness. Clinical knowledge combined with contextual knowledge, understanding of the politics of healthcare and ability to influence medical peers, were seen as critical. However, having business skills, commitment and good communication skills were perceived to be important to achieve both effectiveness and efficiency. The paper describes the dimensions of clinical director competence as well as the competencies, skills and knowledge perceived to require further development. It highlights the problems and issues that can arise for clinical directors from the perspectives of directors and their management teams. 2011 Radcliffe Publishing.
PMID:2011427294

Impact of the inter-professional team approach in the development of person-centered health care within an orthopaedic out-patient clinic.
Edmondston SJ, Waters S, et al.
Rationale, aims and objectives: High demand for orthopaedic specialist consultation has resulted in long waiting lists in public hospital out-patient clinics. This prospective study with a retrospective cohort analysis was conducted to evaluate the impact of a combined orthopaedic surgeon and physiotherapy triage clinic on waiting time and outcome of the initial consultation.
Methods: Two hundred and thirty-nine patients were assessed in the triage clinic, while the reference group consisted of 136 patients from the same catchment who attended the same outpatient clinic in the previous year. Comparisons in waiting list time and initial clinic outcome were conducted and patient satisfaction with the triage clinic was assessed through a questionnaire.
Results: Mean waiting time over the first 6 weeks of the triage clinic was 10 weeks compared to 4 weeks over the final 6 weeks (p<0.05, 95%CI:1.0 to 11.0). The mean waiting time for the triage clinic patients was 8 (SD=6) weeks, compared to 12 (SD=11) weeks for the control group patients (p<0.0001, 95%CI:2.5 to 6.0). Clinic outcomes were not significantly different between groups (p=0.43-0.92). About one-third of all patients seen in the triage clinic were referred for further consultation with an orthopaedic surgeon (triage 32%, control 36%). Patients reported high levels of satisfaction with the triage clinic.

Conclusion: An inter-professional triage clinic model can significantly reduce orthopaedic outpatient clinic waiting times. Two-thirds of patients attending the clinic were managed without direct consultation with an orthopaedic surgeon. Patient support for the triage clinic was strong based on satisfaction survey responses.


A substantive theory of recovery from the effects of severe persistent mental illness.

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BACKGROUND: This study investigated Western Australian consumer perspectives of recovery from the effects of a severe mental illness. METHOD: The grounded theory method was used to collect and analyze data acquired through 15 face-to-face interviews. DISCUSSION: Participants described recovery as a three-phase process of overcoming loss in biomedical, psychological and/or social dimensions. This process was facilitated by personal protective factors and external mechanisms and further explained in the context of role theory. CONCLUSIONS: Recovery can occur in any one or all of the three dimensions and thus can be complete or partial. It is important to ask, therefore: recovery from what, recovery of what, and recovery to what?

PMID:20659965


Resolution of essential tremor post thalamic stroke.


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Background: Essential tremor is a neurological condition characterised by tremor of the limbs. Previously known as benign essential tremor, the first word was removed due to the often debilitating nature of the condition. Until recently, aetiology was poorly understood however advances in post mortem movement disorder research have shown that the condition involves the cerebellar and cerebellothalamocortical circuits. Accordingly, surgical thalamotomy and deep brain stimulation are recognised therapies for essential tremor. Case: Here we present the case of a 77-year old lady with a long history of essential tremor, primarily affecting her left side. Mrs BW presented to an emergency department in 2010 with left sided weakness and ataxia. MRI revealed a right thalamic stroke. She progressed well with multidisciplinary rehabilitation and was independent with her mobility on discharge. Of note, she had complete resolution of her essential tremor, and her tremor remained absent at last follow-up, 12 months post stroke. Conclusion: This is an interesting case of cure of an essential tremor in which the right thalamic stroke has acted as a thalamotomy, and adds further weight to the involvement of cerebellothalamocortical circuits in essential tremor.

Publication Types: Conference Abstract

PMID:70582545


Negative MRI findings in stroke.
Background: Magnetic resonance imaging (MRI) has a sensitivity for acute stroke which approaches 100%. In cases where the diagnosis of cerebral ischaemia is questionable, MRI can be essential in confirmation. Here we describe eight cases of clinically diagnosed stroke in which MRI was negative for acute ischaemia or other pathology. Aim: To review cases of MRI negative strokes and hypothesise reasons why certain stroke syndromes have no MRI changes. Methods: Cases of assumed ischaemic stroke, primarily internuclear ophthalmoplegia (INO) and lateral medullary syndrome were identified by reviewing the Fremantle Hospital Stroke Unit database from December 2005 to April 2011. Medical records were obtained and reviewed. All MRI scans were reviewed by blinded neuroradiologists. Results: Eight cases of MRI negative stroke were identified; seven were male and one was female. Median time from symptom onset to MRI was 1 day. Cases will be presented in reference to the specific stroke syndrome and will be discussed in detail. Conclusions: MRI is a highly sensitive investigation for acute stroke. We have demonstrated at least two phenotypes of ischaemic stroke in which MRI appears less sensitive. It is important to recognise this, to avoid misdiagnosis and to ensure patients are managed appropriately with regards to further investigations and secondary prevention.

Publication Types: Conference Abstract
PMID:70582514


Human pilot studies reveal the potential of a vitronectin: Growth factor complex as a treatment for chronic wounds.

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Several different advanced treatments have been used to improve healing in chronic wounds, but none have shown sustained success. The application of topical growth factors (GFs) has displayed some potential, but the varying results, high doses and high costs have limited their widespread adoption. Many treatments have ignored the evidence that wound healing is driven by interactions between extracellular matrix proteins and GFs, not just GFs alone. We report herein that a clinical Good Manufacturing Practice-grade vitronectin:growth factor (cVN:GF) complex is able to stimulate functions relevant to wound repair in vitro, such as enhanced cellular proliferation and migration. Furthermore, we assessed this complex as a topical wound healing agent in a single-arm pilot study using venous leg ulcers, as well as several 'difficult to heal' case studies. The cVN:GF complex was safe and re-epithelialisation was observed in all but 1 of the 30 patients in the pilot study. In addition, the case studies show that this complex may be applied to several ulcer aetiologies, such as venous leg ulcers, diabetic foot ulcers and pressure ulcers. These findings suggest that further evaluation is warranted to determine whether the cVN:GF complex may be an effective topical treatment for chronic wounds. 2011 The Authors. 2011 Blackwell Publishing Ltd and Medicalhelplines.com Inc.
PMID:2011520090
Complaints of difficulty to fall asleep increase the risk of depression in later life: The health in men study.
Almeida OP, Alfonso H, et al.
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Objectives: To determine if complaints of poor sleep are associated with incident depression in older men. Methods: Cohort study with an average follow up period of 6 years (range 3 months to 8.5 years). Participants were 5127 community-dwelling Western Australian older men aged 70-90 years who provided information about sleep problems. The primary outcome of interest of the study was a recorded diagnosis of depressive episode, recurrent depressive disorder or dysthymia in the Western Australian Data Linkage System. Participants completed a health questionnaire that included questions assessing difficulty falling asleep, remaining awake, as well as early morning awakening. Other measured factors included age, education, country of birth, living arrangements, social support, smoking, body mass index, and prevalent diabetes, hypertension, arthritis, chronic respiratory diseases, coronary artery disease, stroke, and cancer. Biochemical measurement of C-reactive protein, testosterone and plasma homocysteine were available for 3800 men. Results: We found that 60% of men reported at least one sleep problem and that the unadjusted hazard ratio (HR) of depression was higher in men who complained of difficulties to initiate sleep (HR = 2.19, 95% confidence interval - 95% CI = 1.47-3.27) or who remained awake most of the night (HR = 1.94, 95% CI = 1.15-3.27). There was no association between early morning awakening and incident depression. The association between incident depression and subjective difficulty falling asleep remained after the analyses were adjusted for other measured factors (HR = 1.83, 95% CI = 1.20-2.79). The association between depression and remaining awake was no longer significant once the analyses were adjusted for confounding (HR = 1.43, 95% CI = 0.81-2.53). A sensitivity analysis confirmed these results. Limitations: The evaluation of the exposure (sleep disturbance) was limited to self-rating questions that were not externally validated. The diagnosis of depression was based on administrative record linkage rather than structure clinical interviews. The observational nature of the study limits our ability to ascribe a causal relationship between complaints of poor sleep and incident depression. Conclusions: Complaints of difficulty falling asleep increase the risk of incident depression in older men. Clarifying the mechanisms that underlie this association should become an international research priority, as they may contribute to guide interventions designed to decrease the burden of depression in later life. 2011 Elsevier B.V. All rights reserved.
PMID:2011497565

Honeybee venom immunotherapy in children using a 50-mug maintenance dose.
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Publication Types: Letter
PMID:2011014126
It has been suggested that revision of the femoral component of hip resurfacing after femoral failure would be straightforward and have an outcome comparable to primary total hip arthroplasty (THA). We have compared the outcome of femoral side-only revision resurfacings to the results of primary modular large-bearing metal-on-metal THA. Fourteen consecutive patients underwent revision surgery of the failed femoral component, to a cemented tapered stem (CPT, Zimmer, Warsaw, Indiana) with a large modular metal head (Smith and Nephew Orthopaedics Ltd, Memphis, Tennessee, or Adept, Finsbury Orthopaedics, Surrey, England). The acetabular component was found to be well fixed, well orientated, and was left in situ. The 14 matched patients in the primary THA group received the same components. At a mean follow-up of 49 months (range, 30-60 months), clinical outcome measured using the Oxford and Harris Hip Scores showed no significant difference (P = .11, P = .45, respectively). Operative time and blood loss were comparable for both groups. We conclude that revision of the failed femoral resurfacing component gives excellent results.

PMID:2011619605

Morphology identification using transesophageal echocardiography in migratory renal cell carcinoma surgery.
Fremantle Hospital, Fremantle, Western Australia, Australia.
PMID:20627622

Angiotensin-converting enzyme insertion/deletion polymorphism and severe hypoglycemia complicating type 2 diabetes: the fremantle diabetes study.
Davis WA, Brown SGA, et al.
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Aims/hypotheses: The aim of this study was to determine whether the angiotensin-converting enzyme (ACE) gene I/D polymorphisms independently predict severe hypoglycemia in community-dwelling type 2 patients. Methods: Six hundred and two patients who were ACE genotyped at baseline and assessed in 1998 were followed up to the end of June 2006. Severe hypoglycemia was defined as that requiring documented health service use as the primary diagnosis. Cox proportional hazards modeling was used to determine the predictors of first episode and zero-inflated negative binomial regression modeling identified predictors of frequency. Results: Forty-nine patients (8.1%) experienced 63 episodes of severe hypoglycemia. After adjusting for previously identified significant independent predictors of time to first episode, both ACE DD genotype and ACE inhibitor therapy, but not their interaction, added to the model [hazard ratio (95% confidence interval): 2.34 (1.29-4.26), P = 0.006, and 1.77 (0.99-3.13), P = 0.052, respectively]. Similarly, after adjusting for previously identified risk factors for multiple episodes of severe hypoglycemia, ACE DD genotype was independently associated with increased risk [incidence relative risk (95% confidence interval): 1.80 (1.00-3.24), P = 0.050]. Conclusions/interpretation: ACE DD genotype was associated with an approximately 2-fold
increased risk of the first episode of severe hypoglycemia and its subsequent frequency in well-characterized patients with type 2 diabetes. Consistent with previous case-control studies, ACE inhibitor therapy was a weak predictor of severe hypoglycemia. ACE I/D genotyping might provide useful adjunctive prognostic information when intensive glycemic control measures are contemplated. PMID:21289265


Practical management of antibiotic allergy in adults.
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This review looks at the main issues around immediate hypersensitivity and the role and limitations of testing. The majority of literature on antibiotic hypersensitivity relates to -lactam antibiotics, mainly because of the heavy usage of this class of drugs. Concerns around cross-reactivity always worry clinicians, particularly in the emergency situation. Reasonable data now exist in relation to -lactam antibiotics and derivatives, which enable appropriate risk management to be undertaken. The available literature for other classes of antibiotics is also discussed. PMID:21177267


Discovery and validation of plasma biomarkers for diabesity.
(Winfield, Lipscombe, Bringans, Stoll, Casey) Proteomics International, Perth, Australia (Winfield, Lipscombe, Stoll, Casey, Davis, Hodgson, Morahan, Gan, Leedman) Centre for Food and Genomic Medicine, Perth, Australia (Davis) Princess Margaret Hospital for Children, Perth, Australia (Davis) Fremantle Hospital, Fremantle, Australia (Hodgson, Gan) Royal Perth Hospital, Perth, WA, Australia (Morahan, Leedman) Western Australian Institute for Medical Research, Perth, WA, Australia K. Winfield, Proteomics International, Perth, Australia
Plasma biomarkers in diabesity were sought for use in the prediction of early-onset of the disease and its complications, and ultimately discover new therapeutic targets. Ten cohorts from diverse Western Australian populations were recruited. These cohorts include both children and adults who have either type1 or type 2 diabetes or who are obese. Two cohorts were selected from world recognised large population studies: the Busselton Health Study (16,000 participants) and the Fremantle Diabetes Study (1426 participants) where comparisons of urban verses rural as well as complications of kidney disease are examined. Additional cohorts include subjects from a clinical trial on the benefits of lupin-based foods in the human diet; obese and non-obese children involved in the Growth and Development Study at Princess Margaret Hospital for Children, and children recruited on diagnosis of type 1 diabetes. Plasma from subgroups of each cohort were analysed for differential protein expression following immunodepletion of high-abundance proteins. Candidate biomarkers were identified from iTRAQ labelled samples by 2D-LC-MALDI MS/MS, following the analysis of over 125,000 MS spectra. Verification and validation of potential biomarkers used an orthogonal MRM approach. 200-300 proteins per cohort were identified, and across all studies over 60 proteins showed significant differences in expression when compared to controls. Approximately one third of these proteins have been previously described as involved with diabetes, obesity and their complications. Candidate biomarkers have been identified comparing type 2 diabetics with and without nephropathy and work continues for the evaluation of these biomarkers as either predictive or diagnostic.
Publication Types: Conference Abstract
PMID:70455261
Van Minnen K, Davis WA, et al.
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OBJECTIVE: To assess the accuracy, determinants, and consequences of body weight self-perception in type 2 diabetes. Copyright [copyright sign] 2011 Elsevier Inc. All rights reserved.

METHODS: We studied 1272 community-based patients and a 518-patient overweight/obese subset who returned for >=4 annual reviews. Multiple logistic regression was used to identify baseline predictors of correct weight self-perception and to determine whether correct weight self-perception predicted future weight loss. Overweight and obesity were defined as body mass indices of 25.0-29.9 and >=30.0 kg/m(2), respectively. Copyright [copyright sign] 2011 Elsevier Inc. All rights reserved.

RESULTS: Of the patients who were overweight (40.0%) or obese (41.8%) at baseline, 52.8% and 83.7%, respectively, correctly self-identified their weight category. Overweight/obese participants who self-identified correctly were more likely to have been informed they were overweight (P<.001), predominantly by their general practitioner (80.1%). Overweight participants had less self-awareness if they were not abdominally obese, did not speak English fluently, were male, or had a low income. Obese participants were more likely to consider themselves overweight if they had better diabetes knowledge and higher educational attainment. Correct weight self-perception did not influence subsequent weight loss. Copyright [copyright sign] 2011 Elsevier Inc. All rights reserved.

CONCLUSIONS: Health care professionals can facilitate body weight self-awareness in type 2 diabetes. Education programmes should recognise the impact of gender and socio-demographic variables on accurate weight self-perception. Copyright [copyright sign] 2011 Elsevier Inc. All rights reserved.

PMID:20045657

Reimplantation of a completely extruded talus 8 days following injury: A case report.
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We present the case of a 28-year-old female with 45 months follow-up after reimplantation of a completely extruded talus 8 days following the injury. The extruded talus was recovered at the site of the motor vehicle accident, where it had been embedded in the wreckage and subsequently transported to hospital 3 hours later. Thereafter, the talus was washed in an iodine solution for 5 hours and frozen for a period of 8 days at -80degreeC, after which reimplantation surgery was undertaken. Throughout the extended follow-up period, no evidence of infection ever developed. Three years following her injury, the patient underwent fusion of the subtalar and talonavicular joints. At 45 months postoperative, imaging revealed avascular necrosis of the talar dome without substantial collapse. The patient progressed to the point where, at last follow-up, she was working in an administrative job and was able to bear full weight on the involved foot, despite development of mild pain on physical exertion. Despite the pain, moreover, she remained able to snow ski and to regularly walk 2 kilometers for cardiovascular fitness. We believe this case demonstrates that, in the apparent absence of deep infection, the development of avascular necrosis need not necessarily lead to a poor clinical outcome. Furthermore, this case showed that even after a period of 8 days in the freezer, and following antiseptic cleansing, the extruded talus could be reimplanted with a reasonable degree of clinical success. 2011 American College of Foot and Ankle Surgeons.
PMID:2010695087
Rectally administered topical agents have demonstrated efficacy in the maintenance of distal colitis (DC) and proctitis and as they are rarely associated with significant blood drug levels, side effects are infrequent. The topical 5-aminosalicylic acid (5-ASA) suppositories and enemas target different regions of the distal colon and are effective for proctitis and DC, respectively. They demonstrate clinical results that are better than oral 5-ASAs and are preferred to topical steroids with better clinical, endoscopic and histological outcomes, without the risk of adrenal suppression. Disease resistant to topical agents, however, can be extremely difficult to manage. The addition of oral 5ASAs, steroids, immunosuppressants and the anti-tumor necrosis factor- agents may be effective, but can result in significant side effects and not all patients will respond to the therapies. It is for these patients that new and novel therapies are required. Novel topical agents have been proposed for the management of resistant DC. These agents included butyrate, cyclosporine, and nicotine enemas, as well as tacrolimus suppositories, and tacrolimus, ecabet sodium, arsenic, lidocaine, bismuth, rebamipide and thromboxane enemas. While some of these agents appear to demonstrate impressive outcomes, the majority have only been examined in small open-labeled studies. There is thus a desperate need for more randomized double-blinded placebo controlled studies to investigate the clinical utility of these topical therapies. This review summarizes the efficacy of the established topical therapies, and explores the available data on the new and novel topical agents for the management of DC and proctitis. [copyright sign] 2010 Journal of Gastroenterology and Hepatology Foundation and Blackwell Publishing Asia Pty Ltd.

PMID:21175791
pressure. Free testosterone concentration (FT) was higher in girls diagnosed with NAFLD than those without NAFLD (25.9 vs. 18.9 pmol/L, p = 0.02) but FT was not predictive of NAFLD after controlling for obesity. Suprailiac skinfold thickness (odds ratio 1.16, 95% CI 1.08-1.24, p < 0.001) and presence of PCOS (odds ratio 3.87, 95% CI 1.09-13.76, p = 0.04) were independent predictors of NAFLD in the menstruation study. Conclusions NAFLD is common in adolescent females with PCOS and shares metabolic similarities with male NAFLD. Obesity and PCOS have a dominant effect over testosterone levels in predicting female NAFLD.

**Anthropometric measurements during childhood predict nonalcoholic fatty liver disease in adolescents.**

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Non alcoholic fatty liver disease (NAFLD) is frequently not suspected or diagnosed during childhood and adolescence, however, identification of children at increased risk of future NAFLD, may guide interventions to prevent adolescent and adult NAFLD and associated metabolic disorders. Methods We sought a relationship between childhood anthropometry and subsequent NAFLD in 1170 adolescents, serially well characterized from birth to age 17 years, within the Western Australian Pregnancy Cohort (Raine Cohort) Study. NAFLD was diagnosed using liver ultrasound at age 17 years. Results 150/1170 adolescents (12.8%) were diagnosed with NAFLD. Birth weight was not associated with NAFLD. There was a significant mean (sd) body weight difference of 2.7% at age 3 years (15.3 (1.7) kg vs. 14.9 (1.8) kg), progressing to 24.7% (81.4 (20.5) kg vs. 65.3 (11.5) kg) at age 17 years between the NAFLD and non-NAFLD group (p < 0.05 at all ages). Head circumference (HC) was smaller from age 1 year to 5 years. Skinfold thickness was greater from age 2 years, BMI and arm circumference from age 3 years, chest circumference from age 5 years and systolic blood pressure from age 10 years onwards (p < 0.05 for all) in adolescents subsequently diagnosed with NAFLD. Apart from HC, these differences increased through age 17 years. Suprailiac SFT at age 3 years (OR 1.18, 95% CI 1.05-1.33, p = 0.006), chest circumference at age 5 years (OR 1.15, 95% CI 1.08-1.24, p < 0.001) and HC at age 1 year (OR 0.65, 95% CI 0.53-0.80, p < 0.001) were independent predictors of adolescent NAFLD after controlling for weight and BMI up to age 5 years. Conclusions Changes in growth and adiposity from as early as one year of age are associated with the future development of NAFLD in 17 year olds. Anthropometric measurements during early childhood may identify individuals predestined to develop NAFLD and allow early targeted intervention.

**Colonic interleukin-6 expression is induced by intestinal inflammation and dietary iron.**

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Chronic intestinal inflammation and high dietary iron are associated with a greater risk of developing colorectal cancer. The aim of this study was to investigate the role of IL-6 in iron-induced colonic inflammation and tumourigenesis in a mouse model of colorectal cancer. Methods Mice, fed either an iron-supplemented (1% carbonyl iron) or control (0.01% iron) diet, were treated with dextran sodium sulphate (DSS) and azoxymethane (AOM) to induce intestinal inflammation and cancer. Intestinal inflammation and tumour development were assessed using high-resolution video endoscopy at multiple time-points. Colonic inflammation and tumours were examined histologically and gene expression by real-time PCR. Results Seven days post-AOM/DSS treatment, intestinal inflammation was more severe in iron-loaded mice (p < 0.05). Colonic pro-inflammatory cytokines, IL-6, IFN- and TNFalpha gene expression increased with AOM/ DSS treatment confirming the presence of intestinal inflammation (p < 0.05). Dietary iron loading had an additive effect on the gene expression of IL-6 and other members of this family, IL-11 and IL-17a, in AOM/DSS-treated mice. STAT3 phosphorylation was increased in AOM/DSS-treated mice and this was further enhanced with dietary iron loading. Five weeks after AOM/DSS treatment, iron-loaded mice developed a greater number and larger-sized colonic tumours compared to control mice (p < 0.05). Dietary iron-loading also induced an additive effect on tumour IL-6 gene expression in AOM/DSS-treated mice (p < 0.05). Expression of cellular iron import genes DMT1, Zip14a and Tfr1 was increased and cellular export gene ferroportin was reduced in colonic tumours compared to nontumour tissue from the same animal (p < 0.05), suggesting increased iron uptake by tumours may promote growth. Summary/Conclusions Dietary iron-loading promoted colonic inflammation and tumour formation. The mechanistic basis for the interaction between iron, inflammation and colorectal cancer may involve IL-6/STAT3 signalling.

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Streamlining the referral pathway for patients with suspected gastrointestinal malignancy—a model for optimising coordination of cancer services.

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The pathway from diagnosis to treatment for gastrointestinal (GI) cancer is practically and emotionally challenging for patients and their families. The Endoscopy Unit is often the first point at which patients become aware of a possible diagnosis of cancer, making access to accurate information and support vital. Early referral to the Cancer Nurse Coordination Service (CNCS) has been shown to benefit patients and their families by providing support and education throughout their cancer journey. The WA Cancer and Palliative Care Network propose a clear referral pathway with timely involvement of the multidisciplinary team, ensuring a smooth transition from one service to another. Methods A telephone survey of 10 Endoscopy Units in Perth found direct referral to the CNCS was not practised. An endoscopy nurse-led protocol and flow chart was developed to improve patient support and direct referral to the CNCS. A review of consecutive patients with highly probable GI malignancies diagnosed in the endoscopy unit of a tertiary hospital over 3 months was undertaken to determine the prevalent practice of referral to the CNCS. Specified cancers were colorectal, gastric, oesophageal, and pancreatic. Endoscopic procedure data was prospectively recorded and checked against data obtained from patient medical records. Descriptive statistics were generated and comparisons made between patients directly referred from the endoscopy unit and those that were not. Results Twenty-three patients were identified. Six patients had prior contact with the CNCS before the endoscopic procedure, while 5 patients were never referred. Of the remaining 17 patients (12 male, 5 female), 7/17 patients (41.2%) were referred directly to the CNCS post-endoscopic procedure while 10 were not. The median time to CNC contact was much shorter for directly referred patients compared with patients who
Conclusions Implementation of a protocol-guided patient referral pathway, within the Endoscopy Unit for patients with a probable G1 malignancy streamlines entry into a multidisciplinary treatment pathway. This process is important for the incorporation of early interventions and support via the CNCS prior to definitive therapies.

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The prevalence, characteristics and outcomes of patients presenting with acute upper gastrointestinal bleeding to a secondary health care facility with no emergency endoscopy service.

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There is inadequate Australian data regarding the fate of patients presenting to non-tertiary hospitals with haematemesis or melaena (H or M). We aimed to determine characteristics, management and outcomes of patients presenting with H or M to a busy outer metropolitan general hospital emergency department that has over 70,000 patient presentations per annum but no emergency endoscopy service over a five-year period. Methods Retrospective study of emergency presentations with H or M over a 5-year period (2005-2009). Patients were identified from the Emergency Department database (EDIS) and medical records coding. Patients' records were reviewed from both the presenting hospital and the tertiary referral hospital for gastroscopy. Data collected included demographics, clinical features, laboratory results and gastroscopy findings. The severity of the bleeding event was stratified using the Rockall score and Blatchford score. Clinical outcomes measured included transfusion requirement, length of stay, rebleeding, readmission and 30-day mortality. Results We identified 151 patients. 97 (64.2%) were male. Mean age was 62.9 (SD 19.7) years. 98 (65%) patients presented 'after-hours'. 39% presented with H alone, 40% with M alone and 21% with both. Mean SBP was 124 (range 70-170) mmHg and haemoglobin was 115 (range 46-189) g/L. 123 (81.5%) were transferred for gastroscopy. Gastroscopy was performed urgently in 8.6%. Mean length of stay was 4.5 (range 1-30) days. 30-day mortality was 7 (4.6%). Conclusions Patients presenting to the secondary hospital were younger and 30-day mortality was lower than described in tertiary hospital studies. The total length of stay was similar to tertiary hospitals and did not reflect the severity of bleeding episode. Less than 10% of patients required urgent endoscopy. Further review of outcomes will assist in identification of potential opportunities for quality and cost of care improvement.

Publication Types: Conference Abstract
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An investigation to correlate the activity of Crohn's disease with nutritional status.

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Introduction Malnutrition is often reported in Crohn's disease, however the association between the activity of Crohn's disease, nutritional status and quality of life (QoL) has not been extensively studied.
Nutritional assessment tools may predict development of disease, and nutritional support may be an important therapeutic tool in improving disease outcome and reducing the rates of disease-related complications in these patients. Aim 1. To correlate disease activity, quality of life assessment and disease-related complications with nutritional status in patients with Crohn's disease. 2. To determine if nutritional status improves with improvement in disease activity. 3. To determine if any improvement in nutritional status improves the quality of life and/or varies between different treatment options.

Method All patients were assessed for the activity of Crohn's disease with Crohn's disease activity index (CDAI). Nutritional assessment was carried out with a dietary questionnaire, serum protein and nutrient levels, including prealbumin and retinol-binding protein. Body composition was analysed using body mass index, skin fold thickness, and body fat measurement. QoL was assessed with a validated questionnaire. Results 56 patients with Crohn's disease were enrolled. The average age was 42, male : female ratio was 31:25. Mean CDAI was 168. Kendall's rank correlation coefficient was used: There was minimal association between CDAI and QoL: (b = 0.14; P = 0.43); negative association between CDAI and RBP (b = -0.305 P = 0.0193) and pre-albumin (b =-0.360; P = 0.0054) and minimal association between CDAI and skin fold thickness (b = 0.0912; P = 0.451). There was slight negative association between CDAI and %body fat (b = -0.219: P = 0.0669). Conclusion There was a significant association between CDAI and the serological nutritional status markers prealbumin and retinol binding protein, and a weaker association between morphological assessment tools such as %body fat and skin fold thickness. Further investigation into serological markers of nutritional assessment to clarify their role in the management of Crohn's is suggested.

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Characterisation of patients with cirrhosis in a tertiary hospital general hepatology clinic.
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The burden of chronic liver disease resulting from alcohol, chronic hepatitisC infection (CHC), Nonalcoholic fatty liver disease and chronic hepatitisB infection (CHB) is expected to rise in Australian. We determined the patient characteristics, aetiologies, severity and management of patients with cirrhosis attending a tertiary hospital general hepatology clinic. Methods Patients with cirrhosis attending the hepatology clinic between 2006 and 2011 were identified from the clinic database. Descriptive demographic data, clinical, laboratory and radiological data were recorded. The aetiology of cirrhosis was defined as best possible from available data. Results Two hundred and ninety-nine patients were diagnosed with cirrhosis. More males (69.6%) had cirrhosis compared with females (34.4%). The mean age was similar between genders 55.1 (SD 10.6) years for malesand 57.4 (SD 12.5) years for females. Alcohol related cirrhosis was more common in males than females (51.5% vs. 21.3%, p < 0.05) while NASH related cirrhosis was more common in females than males (25.2% vs.5.6%, p < 0.05). Similar proportions of males and females had CHC associated cirrhosis (females 17.5%, males 19.4%, p > 0.05). Up to age50 years alcohol was the most common cause of cirrhosis in both genders (31.3% of females and 42.4% of males). Over age 50 years alcohol remained the most common cause of cirrhosis in males aged over 50 years (56.2%), while NASH-cirrhosis was most common in females (32.9%). Patients with CHC plus excessive alcohol intake were mostly diagnosed under 50 years (68%). Less common causes of cirrhosis were autoimmune hepatitis, CHB, primary biliary cirrhosis, hereditary haemochromatosis, Wilson's disease and idiopathic cirrhosis. Decompensation of cirrhosis was most common in males with alcohol or CHC associated cirrhosis or older females with NASH-cirrhosis. Conclusions Booze, bulge and CHC (BBC) were the most common causes of cirrhosis in this clinic population. Nevertheless, females aged over 50 were overrepresented in the NASH-cirrhosis group.
Liver non-transferrin bound iron uptake in vivo is iron regulated in hereditary haemochromatosis.

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In hereditary haemochromatosis (HH), a common iron overload disorder, plasma non-transferrin-bound iron (NTBI) levels are increased. NTBI plays an important role in the pathogenesis of liver iron overload in HH however, the mechanism responsible for tissue NTBI uptake remains poorly defined. The aim of this study was to investigate NTBI transport in vivo in murine models of HH. Methods NTBI transport was determined in Hfe knockout (Hfe-/-), Tfr2 Y245X mutant (Tfr2mut) and double mutant (Hfe-/-xTfr2mut) mouse models of HH, as well as wild-type and dietary iron loaded wild-type mice. Initially, serum transferrin was saturated with ferric citrate and then the mice were injected intravenously with NTBI in the form of 59-Fe citrate. Blood samples were collected at 2, 10, 30 min and tissues at 30 min and counted for radioactivity. Plasma NTBI concentration was measured biochemically and liver iron concentration was measured by ICP-atomic emission spectroscopy. Results Plasma NTBI levels were increased in all HH and dietary ironloaded mice compared to wild-type mice (p < 0.01), with the greatest increase (7-fold) observed in Hfe-/-xTfr2mut mice. 59Fe-NTBI was cleared from the plasma in HH and dietary iron loaded mice at a significantly greater rate than wild-type mice (p < 0.01). Most of the 59Fe-NTBI was taken up by the liver, followed by the kidneys, pancreas, heart and duodenum. In the liver, Hfe-/-xTfr2mut mice took up approximately 6-fold more 59Fe-NTBI than wild-type mice, while Hfe-/-, Tfr2mut and dietary iron-loaded mice took up to 3-4 fold more 59Fe-NTBI than wildtype mice (p < 0.01). Liver 59Fe-NTBI uptake was strongly correlated with liver iron concentration in all mice (r = 0.79; p < 0.0001). The amount of 59Fe-NTBI taken up by the kidney, pancreas, heart and duodenum in HH and dietary iron-loaded mice was also significantly increased compared with wild-type mice (p < 0.01). Conclusions This study demonstrates for the first time in vivo NTBI transport in murine models of HH. The liver was the main site of NTBI uptake and it was significantly increased in the mouse models of HH. Liver NTBI uptake was regulated by the liver iron concentration and is likely to contribute to the excessive liver iron deposition in HH.

Colonoscopy with propofol sedation: Better for the patient and for the endoscopist.

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Aim To compare quality-indicator outcomes between patients undergoing colonoscopy with endoscopist-administered sedation and colonoscopy with anaesthetist-administered (propofol) sedation. Methods Consecutive patients undergoing average-risk colonoscopy performed across 2 teaching hospitals in WA were included in this study (single operator, CCRTGE certified). 166 procedures were performed with propofol sedation (propofol group) and 159 with endoscopist-administered sedation (fentanyl group; sedation was performed using Midazolam and Fentanyl). Pain scores were assessed as per the Numerical Pain Rating Score (NRS) by nursing staff in the recovery
area post-procedure. Quality indicators of colonoscopy including caecal intubation rate, polyp
detection rate, and withdrawal time were documented. Time to caecum and total procedure times
were also noted. Complications were documented separately and 30 day hospital readmission rate
was also recorded. Statistical analysis was performed between the 2 groups across key parameters
and p values were calculated. Results The average age of patients in the propofol group was 67 yrs
and the fentanyl group was 64 yrs. Bowel prep was deemed adequate or better in 93% of the propofol
group and 94% of the fentanyl group. Caecal intubation rate was 98.1% in the propofol group and 93%
in the fentanyl group (p value NS). The adenoma detection rate was 44.5% in the propofol group and
34% in the fentanyl group. The nurse assessed pain score, the Numerical Pain Rating Score, NRS (on
average, taken 15 mins post procedure) was scored at 0 in the propofol group and 4 in the fentanyl
(group Range 0-10). No complications were noted in the propofol group, whereas one post
polypectomy bleeding was noted in the fentanyl group. 30 day readmission rates for colonoscopy
related complications (perforation or bleeding) was none across both groups. Conclusion This is only
the second study, to our knowledge, that suggests improvement of adenoma detection rates in
colonoscopies using propofol (First study presented at DDW 2011). Pain score during and post
colonoscopy were lesser in the propofol group. Although the reason for the difference in adenoma
detection rate is not clear, we believe it was likely to be related to the fact that sedation was being
administered by an anaesthetist, whereas the fentanyl group had endoscopist-administered sedation.
We feel that colonoscopy with propofol sedation would lead to better patient and endoscopy outcomes
and validation of the same in a larger cohort across multiple hospitals would be welcome.

Publication Types: Conference Abstract
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Potential 188Re-bombesin radiopeptide therapy of metastatic prostate cancer.
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Objectives: To prepare rhenium-188 radiolabelled bombesin agonist (cys-ma-BBN) and antagonist
demobesin-1 for proof-of-concept prostate tumour localisation in patients with a view to potential
targeted radiopptide therapy. Methods: A cysteine-mercaptoacetic acid chelator was linked to the
bombesin derivative using glycyl-4- aminobenzoic acid (cys-ma-BBN). To a nitrogen-flushed sealed
vial, containing 1 mg SnCl2, 5 mg ascorbic acid and 28 mg sodium oxalate was added cys-ma-BBN
(0.6 µg - 10 µg) and 200 µg 2-mercapto-ethanol. 188ReO4 - (100-200 MBq) was then added and the
vial was heated for 30 minutes at 90 degreeC. Instant thin-layer chromatography and reversed-phase
high-performance liquid chromatography was used to measure radiochemical yield (RCY) and purity
(RCP). HPLC was performed by a linear gradient system consisting of 0.1 % trifluoroacetic acid in
water and acetonitrile. The stability of the radiolabelled derivatives was evaluated by incubating 4 µg
188Re-cys-ma-BBN in 0.5 mL mouse serum at 37 degreeC. Under the same conditions, the effect of
the presence of anti-oxidants such as ascorbic acid and gentisic acid was evaluated. Results: With
optimisation of radiolabelling conditions, the radiochemical purity of 188Re-cys-ma-BBN agonist was
71.0 +/- 3.1 % for 0.6 µg peptide, 91.3 +/- 0.9 % for 2 µg peptide, 93.3 +/- 1.5 for 4 µg peptide, 94.4 +/-
1.3 % for 6 µg peptide, 95.8 +/- 2.4 % for 8 µg peptide and 95.4 +/- 0.5 % for 10 µg peptide. A RCY
and RCP greater than 95 % was obtained using 8 µg demobesin-1. In the presence of mouse serum, the
RCP decreased as a function of time, becoming 51 % after 72 hours. The presence of ascorbic
acid and gentisic acid did not have a significant influence on serum stability. A pilot study of 200 MBq
188Re-demobesin-1 administered intravenously in patients demonstrated no acute toxicity and follow-
up over 2 months was uneventful. In particular, the radiolabelled antagonist showed no
pharmacological response in blood pressure and other vital signs. Conclusion: 188Re-demobesin-1
was synthesised with greater than 95 % yield and 95 % purity, using 8 µg peptide, which had no
measurable pharmacological effect on toxicity in patients after intravenously administration.
Publication Types: Conference Abstract
Automated synthesis of therapeutic activities of 177Lu and 131I radio-pharmaceuticals and 68Ga PET agents in a hospital radiopharmacy.

DeDecker M, Turner JH.

Objectives: To minimise radiation exposure to radiopharmaceutical chemists preparing 177Lu radiopeptides, 131I radioimmunotherapeutic agents and 68Ga peptide PET diagnostics. Methods: The Synthera module (IBA Molecular, Belgium) was adapted to prepare routine fully automated preparations of novel therapeutic and diagnostic radiopharmaceuticals under remote shielded sterile conditions. Radiochemical yield and purity was measured by instant thin-layer chromatography and high-performance liquid chromatography. Results: 68Ga-octreotate and 177Lu-octreotate were synthesized, resulting in both a radiochemical yield and radiochemical purity greater than 99%. Synthesis of 131I-rituximab resulted in a yield of 60%, with a radiochemical purity greater than 99%. Using 200 MBq 68GaCl₃ per synthesis, the estimated absorbed body and wrist dose for a manual synthesis was 81 µSv and 11.5 µSv, contrasting with automated synthesis exposure of 7.9 µSv and 1.3 µSv. Using 8000 MBq 177LuCl₃ per synthesis, the estimated absorbed body and wrist dose for a manual synthesis was 334 µSv and 47.7 µSv, contrasting with automated synthesis exposure of 20 µSv and 2.5 µSv. Using 6000 MBq 131I per synthesis, the estimated absorbed body and wrist dose for a manual synthesis was 335 µSv and 83.75 µSv, contrasting with automated synthesis exposure of 54.75 µSv and 10.95 µSv. The reduction in radiation exposure by automated synthesis of radiopharmaceuticals in the Synthera module was at least five fold. Conclusion: Automated synthesis of therapeutic 177Lu and 131I radiopharmaceuticals and 68Ga PET agents in the shielded sterile Synthera module is simple, practical, efficient and virtually eliminates radiation exposure to the radiopharmaceutical chemist. (Figure presented).
examining contact endoscopy for the diagnosis of benign versus malignant head and neck mucosal lesions. These reported a sensitivity and specificity of 77-100%, specificity of 66-100% and an accuracy of 72-92%. Conclusion. Contact endoscopy is a promising optical technology that may be a useful adjunct in the evaluation and diagnosis of benign and malignant head and neck mucosal lesions. Future prospective randomized double-blind studies of this detection method are required. Copyright 2011 Christopher Szeto et al.

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Trabecular bone texture detected by plain radiography and variance orientation transform method is different between knees with and without cartilage defects.

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The objective of this work is to evaluate differences in trabecular bone (TB) texture between subjects with and without tibiofemoral cartilage defects using a variance orientation transform (VOT) method. A case-control study was performed in subjects without radiographic knee osteoarthritis (OA) (K&L grade <2) matched on sex, BMI, age, knee compartment, and meniscectomy where cases (n = 28) had cartilage defects (grade >=2) and controls (n = 28) had no cartilage defects (grade <2). Cartilage defects were assessed from MRI using validated methods. The VOT was applied to TB regions selected on medial and lateral compartments in knee X-rays and fractal signatures (FS) in the horizontal (FS<sub>H</sub>) and vertical (FS<sub>V</sub>) directions, and along the roughest part of TB (FS<sub>Sta</sub>) and texture aspect ratio signatures (StrS), at different trabecular image sizes (0.30-0.70 mm) were calculated. Compared with controls, FS<sub>V</sub> for cases were higher (p < 0.011) at image sizes 0.30-0.40 mm and 0.45-0.55 mm in the medial compartment. In the lateral compartment, FS<sub>H</sub> and FS<sub>Sta</sub> for cases were higher (p < 0.028) than those for controls at 0.30-0.40 mm and 0.45-0.55 mm, while FS<sub>V</sub> was higher (p < 0.02) at 0.30-0.40 mm. TB texture roughness was greater in subjects with cartilage defects than in subjects without, suggesting thinning and fenestration of TB occur early in OA and that the VOT identifies changes in TB in knees with early cartilage damage. No differences in StrS (p > 0.05) were found.

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Angular stability potentially permits fewer locking screws compared with conventional locking in intramedullary nailed distal tibia fractures: a biomechanical study.

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OBJECTIVES: To compare mechanical stability of angle-stable locking construct with four screws with conventional five screw locking in intramedullary nailed distal tibia fractures under cyclic loading.

METHODS: Ten pairs of fresh-frozen human cadaveric tibiae were intramedullary nailed and assigned to either an angle-stable locking construct consisting of four screws or conventional five-screw locking. After simulating an unstable distal two-fragmental 42-A3.1 fracture, the specimens were mechanically tested under quasistatic and cyclic sinusoidal axial and torsional loading. RESULTS: Bending stiffness of the angle-stable and the conventional fixation was 644.3 N/ and 416.5 N/, respectively (P = 0.075, power 0.434). Torsional stiffness of the angle-stable locking (1.91 Nm/) was significantly higher compared with the conventional one (1.13 Nm; p = 0.001, power 0.981). Torsional play of the angle-stable fixation (0.08) was significantly smaller compared with the conventional one (0.46; p = 0.002, power 0.965). The angle-stable locking revealed significantly less torsional deformation in the fracture gap after one cycle (0.74) than the conventional one (1.75; P = 0.005, power 0.915) and also after 1000 cycles (angle-stable: 1.56; conventional: 2.51; p = 0.042, power 0.562). Modes of failure were fracture of the distal fragment, loosening of distal locking screws, nail breakage, and their combination, equally distributed between the groups (P = 0.325).

CONCLUSIONS: Both the angle-stable locking technique using four screws and conventional locking consisting of five screws showed high biomechanical properties. Hence, angle-stable locking reflects a potential to maintain fixation stability while reducing the number of locking screws compared with conventional locking in intramedullary nailed unstable distal tibia fractures.

PMID:21577069


Lifestyle and demographic correlates of poor mental health in early adolescence.
Robinson M, Kendall GE, et al.

(Aim: To determine the constellation of lifestyle and demographic factors that are associated with poor mental health in an adolescent population. Methods: The Raine Study 14-year follow-up involved primary care givers and their adolescent children (n= 1860). The Child Behaviour Checklist (CBCL) was used to assess adolescent mental health. We examined diet, socio-demographic data, family functioning, physical activity, screen use and risk-taking behaviours with mental health outcomes using linear regression. Results: Adolescents with higher intakes of meat and meat alternatives and 'extras' foods had poorer mental health status. Adverse socio-economic conditions, higher hours of screen use and ever partaking in the health risk behaviours of smoking and early sexual activity were significantly associated with increasing CBCL scores, indicative of poorer functioning. Conclusions: By identifying the lifestyle and demographic factors that accompany poorer mental health in early adolescence, we are able to better understand the context of mental health problems as they occur within an adolescent population. 2010 The Authors. Journal of Paediatrics and Child Health 2010 Paediatrics and Child Health Division (Royal Australasian College of Physicians).
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Prevalence and predictors of sexual dysfunction in older men.
Hyde Z, Flicker L, et al.

(Aim: To determine the constellation of lifestyle and demographic factors that are associated with poor mental health in an adolescent population. Methods: The Raine Study 14-year follow-up involved primary care givers and their adolescent children (n= 1860). The Child Behaviour Checklist (CBCL) was used to assess adolescent mental health. We examined diet, socio-demographic data, family functioning, physical activity, screen use and risk-taking behaviours with mental health outcomes using linear regression. Results: Adolescents with higher intakes of meat and meat alternatives and 'extras' foods had poorer mental health status. Adverse socio-economic conditions, higher hours of screen use and ever partaking in the health risk behaviours of smoking and early sexual activity were significantly associated with increasing CBCL scores, indicative of poorer functioning. Conclusions: By identifying the lifestyle and demographic factors that accompany poorer mental health in early adolescence, we are able to better understand the context of mental health problems as they occur within an adolescent population. 2010 The Authors. Journal of Paediatrics and Child Health 2010 Paediatrics and Child Health Division (Royal Australasian College of Physicians).
PMID:2011055112
Context: Hypogonadism in younger men is associated with impaired libido and erectile dysfunction. Testosterone levels decline with age, but the relationship between androgens and sexual dysfunction in older men is controversial. Objective: To determine whether testosterone levels are associated with sexual dysfunction. Design: Prospective cohort study. Setting: Perth, Western Australia. Participants: 1,744 community-dwelling men aged 70-88 years (mean 76 years) at baseline. Methods: Questionnaires in 2001-04 and 2008-09 assessed social and medical factors. Testosterone, SHBG and LH were measured in 2001-04. Sexual dysfunction was assessed by questionnaire in 2008-09 (mean follow-up period 5.2 years). Results: Sexual problems were highly prevalent, with 50.5% (95% CI 48.2-52.9%) reporting erectile dysfunction, 46.5% (95% CI 44.2-48.8%) lacking interest in sexual activity, 38.4% (95% CI 36.1-40.6%) unable to climax, and 22.0% (95% CI 20.1%-24.0%) anxious about their ability to perform sexually. Painful and unpleasurable sex were less common (<5%). In multivariate logistic regression analyses, total testosterone levels in the lowest quintile were associated with lack of interest (OR = 1.59; 95% CI 1.13-2.23), but were not associated with any other sexual problem. Cardiovascular disease, diabetes, and insomnia were the factors most commonly associated with sexual problems. Conclusions: Androgen deficiency is unlikely to be a major cause of sexual dysfunction in older men. However, low testosterone levels may be a causal factor in impaired libido. Clinical trials should investigate this concept.

Publication Types: Conference Abstract
PMID:70579241


Final 5 year follow-up from the RESOLUTE first in man trial.
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Background: RESOLUTE first-in-man (FIM) was the first study to evaluate the Resolute zotarolimus-eluting stent (R-ZES, Medtronic, Inc, Santa Rosa, CA) in 130 patients treated for a single de novo lesion >= 14 mm and <= 27 mm in length, with a reference vessel diameter of >= 2.5 mm and <=3.5 mm. The R-ZES comprises a cobalt-alloy, thin strut, metal stent; and a biocompatible polymer that allows prolonged drug elution; with 85% eluted within the first 60 days, and the remaining exhausted by 180 days. The RESOLUTE FIM study is part of the global RESOLUTE Clinical Trial Program, which comprises at least 5 trials specifically designed with consistent endpoint definitions; standardized data collection, analysis and adjudication methods to promote poolability. To date, the R-ZES has been studied in over 5000 patients; at over 200 investigational sites worldwide. Methods: Patients were enrolled from December 6, 2005 through June 9, 2006 at 12 centers in Australia and New Zealand. The primary endpoint was in-stent late loss at 9 months. The final 5-year follow-up outcomes will be reported. Results: Baseline patient clinical characteristics include hyperlipidemia
(94.6%), hypertension (67.7%), prior MI (45.7%), unstable angina (29.7%), and diabetes (17.7%). Of 131 lesions treated (2 lesions in 1 patient), mean length was 15.49±6.23 mm, 82% were B2/C, and 46.2% of patients had multivessel disease. At 4 years, the cumulative incidence of TLR was 2.3%, TVF was 10.1%, MACE was 14.0%; without any ARC definite and probable ST events at 4 years follow-up. At 4 years, 33.9% of patients were still on dual antiplatelet therapy. Conclusion: The R-ZES has shown long-term effectiveness and safety in a relatively simple patient cohort through 4-year follow-up with a TLR rate of 2.3% and an ARC definite and probable ST rate of 0.0%. We plan to report the final, 5-year clinical outcomes in November, 2011 at the annual meeting of Transcatheter Cardiovascular Therapeutics.

Publication Types: Conference Abstract
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Assessment of reasons for not intensifying antihypertensive treatment in the Taiwanese population.
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Background/Purpose: Despite availability of effective antihypertensives, blood pressure (BP) control is usually inadequate. The Reasons for not Intensifying Antihypertensive Treatment (RIAT) registry evaluated the reasons behind not modifying treatment in an international, cross-sectional study in 16 countries. Methods and results: The Taiwanese cohort of RIAT consisted of 8922 patients with untreated/uncontrolled essential hypertension recruited from 22 centers in the country. At the first visit, physicians selected target BP and antihypertensive treatment, and at the next three visits they measured BP and modified treatment/provided justification for not modifying treatment. Mean target BP selected by physicians was 134.6/84.6±5.1/5.0mmHg, respectively. Patients' individual risk stratification determined the BP goals. More patients achieved targets according to the physicians' opinion than based on actual BP measurements: visit 2-50.6% vs. 48.6%; visit 3-58.4% vs. 55.2%; and visit 4-61.2% vs. 57.0%. At each visit, treatment remained unchanged for >60% patients not reaching target; the most common reason for this at visit 2 was the assumption that the time was too short to assess new drug therapy and at visits 3 and 4 was the assumption that target was reached/had almost been reached. Conclusion: About 40% Taiwanese hypertensive patients in RIAT did not reach BP targets after an average of 4 months' follow-up. The most common reason for not modifying treatment was the assumption that the target had been reached or had almost been reached. 2011.
PMID:2012034900


Reduction of surgical site infection using a microbial sealant: A randomized trial.
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OBJECTIVE: Surgical site infection is a major cause of mortality and morbidity. We have explored the use of a microbial sealant applied before the surgical incision to reduce surgical site infection.
METHODS: We conducted a prospective, randomized, controlled clinical trial to determine the efficacy of a cyanoacrylate sealant in patients undergoing coronary artery bypass grafting. Both left and right long saphenous veins were harvested in individual patients below the knee if 3 or more lengths of vein were required. The sealant (Kimberly-Clark InteguSeal, Roswell, Ga) was applied to 1 leg chosen randomly, and the other leg was prepared in a conventional fashion. Microbiological swabs from the leg wounds were taken at 5 days, and wounds were assessed according to the Southampton score at 30 days by 2 blinded observers. RESULTS: The baseline characteristics of the treated and untreated legs were similar because the procedure was conducted on each individual patient. The study was terminated at 47 patients after review. Patients in whom the sealant was used had 1 (2.1%) wound infection, and there were 12 (25.5%) wound infections in the conventionally prepared leg (P<0.001). There were 13 positive cultures from the treated leg and 22 positive cultures from the untreated site. CONCLUSIONS: The microbial skin sealant applied immediately before the incision significantly reduced the rate of surgical site infection. There was no sensitivity or adverse reaction after application. The treatment was easily integrated with existing routine preoperative procedures. Microbial sealant may thus be a useful addition to a multimodal approach to minimize surgical site infection. Crown Copyright Copyright 2011. Published by Mosby, Inc. All rights reserved.
PMID:21440263

The cardiovascular and prognostic significance of the infrarenal aortic diameter.
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The normal aortic diameter in adults usually ranges from 16 to 18 mm in women and 19 to 21 mm in men. Individuals with diameters outside this range seem to be at increased risk of other cardiovascular disease. There is a graded association between increasing aortic diameter and both cardiovascular mortality and peripheral arterial disease. The magnitude of increased risk of cardiovascular death seems to be about 4% to 6% per mm increase over a diameter of about 23 mm. To a lesser extent, these outcomes are also increased in individuals with aortic diameters below the normal range. While the threshold of 3 cm is useful in the diagnosis of abdominal aortic aneurysm (AAA), it is arbitrary in terms of the vascular biology and pathophysiology of the abdominal aorta. This review examines the risk factors for aortic enlargement and the cardiovascular implications of this enlargement in patients with and without AAAs. The mechanisms underlying the association between aortic diameter and cardiovascular risk and the relevance to screening are also discussed. Copyright Copyright 2011 Society for Vascular Surgery. All rights reserved.
PMID:21944921

Falling rates of hospitalization and mortality from abdominal aortic aneurysms in Australia.
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Background Studies of the population trends for abdominal aortic aneurysms (AAAs) in the period 1970 to 2000 all indicated that the incidence of AAAs was increasing. It is not known whether this
increase has continued. We hypothesized that the incidence of AAAs has begun to fall in Australia.

Methods Age-standardized national trends in mortality from AAAs were estimated for the period 1999 to 2006, and hospital separations (deaths or discharges) for AAAs were estimated for the period 1999 to 2008. Poisson regression models were constructed to estimate the relative change over time.

Results The age-standardized mortality rate from AAAs fell by an average of 6.0% (95% confidence interval [CI], 4.7-7.3) per annum in men and 2.9% (95% CI, 1.0-4.7) in women. After adjusting for age, hospital separations for men decreased by an average of 2.3% (95% CI, 1.4-2.7) per annum for nonruptured AAAs, and 5.9% (95% CI, 5.0-6.6) for ruptured AAAs and for women decreased by an average of 2.2% (95% CI, 1.4-3.0) per annum for nonruptured AAAs, and 5.1% (95% CI, 3.7-6.5) for ruptured AAAs. Ruptured, compared with nonruptured, AAAs were proportionally more common in women compared with men. The age-specific trends in separations from hospital were all downward apart from nonruptured AAAs in individuals aged 80 years and over.

Conclusions The rates of separation from hospital and mortality for AAAs in Australia have fallen since 1999. This suggests a true fall in incidence of AAAs. Although the reasons for this are unknown, it has implications for policy decisions about screening. 2011 Society for Vascular Surgery.

PMID:2011059882

Sensitivity of knee soft-tissues to surgical technique in total knee arthroplasty.

Schirm AC, Jeffcote BO, et al.
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Restricted range of motion and excessive laxity are both potential complications of total knee arthroplasty (TKA). During TKA surgery, the surgeon is frequently faced with the question of how tightly to implant the prosthesis. The most common method of altering implantation tightness is to vary the thickness of the polyethylene inlay after the bone cuts have been made and the trial components inserted. We have sought to quantify how altering the polyethylene thickness may affect post-operative soft tissue tension for a range of prosthetic designs.

Four different prosthetic designs were implanted into fresh-frozen cadaveric knee joints. All four designs were implanted in the standard manner, with a 100 Newton distraction force used to set soft tissue balance. The tibiofemoral force was then recorded at 15degree intervals throughout the passive flexion range. After the standard implantation of each prosthesis, the tibial component was raised or lowered to mimic increasing and decreasing the polyethylene thickness by 2. mm and the force measurements repeated. Tibiofemoral force in extension correlated with implantation tightness for all prosthesis designs. Between 15degree and 90degree of knee flexion, all four designs were insensitive to changes in implantation tightness. Beyond 90degree the effect was more notable in rotating platform mobile-bearing and cruciate-retaining prostheses than in posterior-stabilised mobile-bearing designs.

The findings of this research may be useful in assisting surgical decision-making during the implantation of TKA prostheses. 2010 Elsevier B.V.

PMID:2011215632

New lexicon and criteria for the diagnosis of Alzheimer's disease.

Sohrabi HR, Weinborn M, et al.
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Dyslipidemic diabetic serum increases lipid accumulation and expression of stearoyl-CoA desaturase in human macrophages.

Wong BXW, Kyle RA, et al.
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Type 2 diabetes and dyslipidemia are risk factors for cardiovascular disease. However, mechanisms by which hypertriglyceridemia influences atherogenesis remain unclear. We examined effects of dyslipidemic diabetic serum on macrophage lipid accumulation as a model of foam cell formation. Normal human macrophages were cultured in media supplemented with 10% serum from non-diabetic normolipidemic or non-diabetic hypercholesterolemic adults versus adults with Type 2 diabetes; diabetes and hypertriglyceridemia; or diabetes and hypercholesterolemia. Exposure to diabetic sera resulted in increased macrophage fatty acids (2-3 fold higher, both saturated and unsaturated). Macrophage expression of CD36, scavenger receptor A (SR-A) and stearoyl-CoA desaturase (SCD) was increased, most prominently in macrophages exposed to hypertriglyceridemic diabetic serum (twofold increase in CD36 and fourfold increase in SCD, p<0.05). In these conditions, RNA inhibition of CD36 reduced macrophage free cholesterol (163.9±10.5 vs. 221.9±26.2 mmol free cholesterol/g protein, p=0.04). RNA inhibition of SCD decreased macrophage fatty acid content, increased ABCA1 level and enhanced cholesterol efflux (18.0±3.9% vs. 8.0±0.8% at 48h, p=0.03). Diabetic dyslipidemia may contribute to accelerated atherosclerosis via alterations in macrophage lipid metabolism favoring foam cell formation. Increased expression of CD36 and SR-A would facilitate macrophage lipid uptake, while increased expression of SCD could block compensatory upregulation of ABCA1 and cholesterol efflux. Further studies are needed to clarify whether modulation of macrophage lipid metabolism might reduce progression of diabetic atherosclerosis.

PMID:21674150


Modulation of macrophage fatty acid content and composition by exposure to dyslipidemic serum in vitro.

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Macrophages in arterial walls accumulate lipids leading to the development of atherosclerotic plaques. However, mechanisms underlying macrophage lipid accumulation and foam cell formation are often studied without accounting for risk factors such as dyslipidemia. We investigated the effect of varying
concentrations of triglyceride (TG) within physiological range on macrophage fatty acid (FA) accumulation and expression of cholesterol efflux proteins. Human monocytes were cultured in media supplemented with 10% sera containing low (0.7mmol/L) to high (1.4mmol/L) TG. The resulting macrophages were harvested after 10 days for analysis of FA content and composition and expression of genes involved in lipid metabolism. Exposure to higher TG and lower HDL concentrations in media increased macrophage lipid content. Macrophages exposed to higher TG had increased total FA content compared with controls (876g/mg protein vs. 652g/mg protein) and greater proportions of C16:0, C18:1 and C18:2. Macrophage expression of both ABCA1 and ABCG1 cholesterol efflux proteins were reduced when higher TG concentrations were present in the media. Expression of scavenger receptor CD36, involved in lipoprotein uptake, was also downregulated in macrophages exposed to higher TG. Culturing macrophages in conditions of higher versus lower TG influenced macrophage FA content and composition, and levels of regulatory proteins. Replicating in vitro levels of dyslipidemia encountered in vivo may provide an informative model for investigation of atherogenesis.

PMID:21286835


The mining and burning of coal: effects on health and the environment.
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Australia’s coal conundrum is that all political parties say they are concerned about climate change while sanctioning an unprecedented expansion of coalmining and coal seam gas extraction in Australia. Australia’s coal contributes to climate change and its global health impacts. Each phase of coal’s lifecycle (mining, disposal of contaminated water and tailings, transportation, washing, combustion, and disposing of postcombustion wastes) produces pollutants that affect human health. Communities in which coalmining or burning occurs have been shown to suffer significant health impacts. The health and climate costs of coal are unseen, and when costs to health systems are included, coal is an expensive fuel.

PMID:21929497


Safety of incretin-based therapies for type 2 diabetes.
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Australian database linkages could be used for postmarketing surveillance of antidiabetic therapy side effects.

PMID:21929482


Testosterone and sex in older men.
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Publication Types: Editorial
PMID:2011401949
**Laparoscopic adjustable gastric banding in patients with insulin-treated type 2 diabetes.**
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PMID:21495950

**Bone and metabolic health in patients with non-metastatic prostate cancer who are receiving androgen deprivation therapy.**
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* Androgen deprivation therapy (ADT) in men with prostate cancer increases the risk of osteoporotic fractures, type 2 diabetes and, possibly, cardiovascular events. * There is considerable uncertainty about the risk-benefit ratio of ADT in non-palliative treatment; the benefits of ADT in treating non-metastatic prostate cancer need to be carefully weighed against the risks of ADT-induced adverse events. * Baseline assessment of bone health at the initiation of ADT should include measurement of bone mineral density (BMD) by dual energy x-ray absorptiometry and, in men with osteopaenia, a thoracolumbar spine x-ray. * General measures to prevent bone loss, including regular physical activity, as well as ensuring calcium and vitamin D sufficiency, should be instituted routinely. * All men with a previous minimal trauma fracture should receive pharmacological therapy unless contraindicated; for those who have not sustained a minimal trauma fracture, treatment is advised if the BMD T score is <=-2.0, or if the 10-year risk of a major osteoporotic fracture exceeds 20%. * Men with prostate cancer who are receiving ADT should be closely monitored for weight gain and diabetes; intensive lifestyle intervention is recommended to prevent ADT-induced weight gain and insulin resistance. * Management of the metabolic sequelae of ADT includes optimal reduction of cardiovascular risk factors, with particular attention to weight, blood pressure, lipid profile, smoking cessation, and glycaemic control.
PMID:2011239261

**Western Australian women's perceptions of conflicting advice around breast feeding.**
Objective: to explore women's perceptions of conflicting advice around breast feeding from formal support networks, specifically health professionals involved in postnatal support. Design, setting and participants: a qualitative exploratory design was employed using the critical incident technique. Data were obtained from 62 Western Australian women who responded to an invitation to share incidents of receiving conflicting advice. Women who had breast fed a child within the past 12 months shared their experience through a telephone interview (n=50) or completing a brief questionnaire (n=12) addressing the following questions: Describe a situation in detail where you felt you received conflicting advice about breast feeding from a health professional. How did this situation affect you and/or your breast feeding?

Findings: a modified constant comparison method was used to analyse the critical incidents revealing commonalities under who offered conflicting advice; what contributed to advice being perceived as conflicting; topic areas more inclined to being regarded as conflicting; what protected against advice being perceived as conflicting; the consequences of receiving conflicting advice; and strategies that women used to manage these incidents. Key conclusions and implications for practice: advice that was viewed as conflicting extended beyond the provision of information that was inconsistent or directly contradictory, and included issues around information overload and disparities between the mother's and health professional's expectations. The manner of presenting information or advice, the skills of using effective communication, demonstration of a caring attitude with an empathic approach and focusing upon the woman as an individual were seen to be important to minimise these incidents. Attention to women's perceptions and the consequences of conflicting advice must be addressed, otherwise the credibility and confidence in health professionals' knowledge and ability to support breast feeding is questioned, resulting in a valuable support network being selectively ignored. 2010 Elsevier Ltd.

PMID:20382454

Diagnostic criteria for depression in Parkinson's disease: A study of symptom patterns using latent class analysis.
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Although major depression is one of the most frequent psychiatric disorders among patients with Parkinson's disease, diagnostic criteria have yet to be validated. The main aim of our study was to validate depressive symptoms using latent class analysis for use as diagnostic criteria for major depression in Parkinson's disease. We examined a consecutive series of 259 patients with Parkinson's disease admitted to 2 movement disorders clinics for regular follow-ups. All patients were assessed with a comprehensive psychiatric interview that included structured assessments for depression, anxiety, and apathy. The main finding was that all 9 Diagnostic and Statistical Manual (4th edition) diagnostic criteria for major depression (ie, depressed mood, diminished interest or pleasure, weight or appetite changes, sleep changes, psychomotor changes, loss of energy, feelings of worthlessness or inappropriate guilt, poor concentration, and suicidal ideation) identified a patient class (severe depression group) with high statistical significance. Latent class analysis also demonstrated a patient class with minimal depressive symptoms (no-depression group), and a third patient class with intermediate depressive symptoms (moderate depression). Anxiety and apathy were both significant comorbid conditions of moderate and severe depression. Taken together, our findings support the use of the full Diagnostic and Statistical Manual (4th edition) criteria for major depression.
for use in clinical practice and research in Parkinson's disease and suggest that anxiety may be
included as an additional diagnostic criterion. Copyright 2011 Movement Disorder Society. Copyright
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PMID:21739470


Anxiety rating scales in Parkinson's disease: A validation study of the Hamilton anxiety rating
scale, the Beck anxiety inventory, and the hospital anxiety and depression scale.
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Background: Anxiety is a prevalent and disabling condition in Parkinson's disease (PD). The lack of
anxiety rating scales validated for this population hampers research into anxiety in PD. The aim of this
study is to assess the clinimetric properties of the Hamilton anxiety rating scale (HARS), the Beck
anxiety inventory (BAI), and the hospital anxiety and depression scale (HADS) in PD patients. Design:
Three hundred forty-two PD patients underwent a standardized assessment including a structured
interview for diagnostic and statistical manual diagnoses of anxiety disorders and completion of the
HARS, BAI, and HADS. Inter-rater reliability of the HARS was assessed in 60 patients; test-retest
reliability of the BAI and HADS in 213 and 217 patients, respectively. Results: Thirty-four percent of
patients suffered from an anxiety disorder, whereas an additional 11.4% had clinically significant
anxiety symptoms in the absence of a diagnosis of anxiety disorder. Acceptability, score distribution,
and known groups validity over different levels of anxiety were adequate. Inter-rater reliability for the
HARS and test-retest reliability for the BAI and HADS were good. The HARS, but not the BAI and
HADS, had a satisfactory inter-item correlation, convergent validity and factorial structure. For all
scales, the positive predictive value was poor, and the negative predictive value was moderate.
Conclusions: Given the adequate known groups validity of all three rating scales, each of these scales
is likely to be useful in clinical practice or research for evaluation of symptom severity. Limitations in
the construct validity of the anxiety scales in this study raise questions regarding suitability for their
use in PD. 2011 Movement Disorder Society.
PMID:2011181614


Symptomatology and markers of anxiety disorders in Parkinson's disease: A cross-sectional
study.
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Anxiety is understudied in Parkinson’s disease (PD), which is not justified by the prevalence and impact of anxiety disorders on quality of life in PD patients. In this cross-sectional study, 342 patients suffering from idiopathic PD underwent a research-based assessment including DSM IV criteria for anxiety disorders, the Hamilton anxiety rating scale (HARS) and the beck anxiety inventory (BAI). Thirty-four percent (34%) of subjects met the DSM IV criteria for at least one anxiety disorder; 11.8% met criteria for multiple anxiety disorders; and 11.4% had clinically relevant anxiety symptoms without meeting the criteria for any specific anxiety disorder. Score profiles on the HARS and BAI differed significantly between the disorders, but these differences were associated with different scores on a limited number of items, and the respective symptom profiles were not readily interpretable. Female sex, the presence of motor fluctuations, as well as a previous history of an anxiety disorder were markers for anxiety disorders. The use of a mono-amino oxidase (MAO)-B inhibitor was associated with a reduced prevalence of anxiety disorders. Research into anxiety in PD is hampered by the questionable validity of DSM IV defined anxiety disorders in this population. A first focus for research should therefore be the identification of clinically useful anxiety presentations and their validation in PD. 2011 Movement Disorder Society.

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Meta-analysis identifies 29 additional ulcerative colitis risk loci, increasing the number of confirmed associations to 47.


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University, Institute of Human Genetics, Newcastle Upon Tyne,
Genome-wide association studies and candidate gene studies in ulcerative colitis have identified 18 susceptibility loci. We conducted a meta-analysis of six ulcerative colitis genome-wide association study datasets, comprising 6,687 cases and 19,718 controls, and followed up the top association signals in 9,628 cases and 12,917 controls. We identified 29 additional risk loci (P < 5 x 10^{-8}), increasing the number of ulcerative colitis-associated loci to 47. After annotating associated regions using GRAIL, expression quantitative trait loci data and correlations with non-synonymous SNPs, we identified many candidate genes that provide potentially important insights into disease pathogenesis, including IL1R2, IL8RA-IL8RB, IL7R, IL12B, DAP, PRDM1, JAK2, IRF5, GNA12 and LSP1. The total number of confirmed inflammatory bowel disease risk loci is now 99, including a minimum of 28 shared association signals between Crohn's disease and ulcerative colitis. 2011 Nature America, Inc. All rights reserved.
anaemia in association with medullary nephrocalcinosis and d-RTA, polyclonal hypergammaglobulinaemia, ongoing anaemia, and 24 hrs U Creatinine Clearance at 96 ml/min/1.73 m2. U protein/creatinine ratio was 96 mg/mmol (N < 25 mg/mmol). She reports 6 months intake of high dose ibuprofen in 2005 following back injury and Chinese Herbal medicine until May 2010. Microcytic, hypochromic anaemia was investigated by Haematologist with normal ferritin, T Sat 25% and no specific diagnosis. Alkali supplements and 25OH Vit D therapy for severe 25-OH deficiency (<50 nmol/L). Investigations were consistent with dRTA, normal iron stores, normal Hb electrophoresis, normal serum free light chains, negative autoimmune serology, normal urinary Ca excretion and negative serology for hepatitis. Clinically, she was normotensive with otherwise normal examination. Progressive rise in proteinuria prompted renal biopsy in March 2011. Biopsy was consistent with Membranous GN on light, electron microscopy and immunofluorescence. Investigations for anaemia showed gastric ulcers as cause of anaemia. Patient denies recent ibuprofen intake and urinary metabolite screen is awaited to exclude presence of ibuprofen metabolites. Proteinuria is unchanged on Angiotensin receptor blockers with stable renal function (Creatinine 97 umol/L). Conclusions: We are reporting this case to bring to light this unusual association and to invite feedback from nephrology fraternity.


Nephrotic syndrome and renal failure due to crescentic glomerulonephritis in a lady with rheumatoid arthritis and cryoglobulinemia.


Background: Cryoglobulinemia is characterized by circulating immune complexes which precipitate at cold temperatures in vitro. 'Mixed' Cryoglobulinemia is predominantly associated with Hepatitis C virus infection. Rheumatoid Arthritis is rarely associated with cryoglobulinemia, thus its treatment and prognosis uncertain. Case Report: A 75 year old lady with seropositive, nodular Rheumatoid arthritis presented in with 2 months history of swollen ankles, exertional dyspnea and orthopnea. Examination revealed anasarca, elevated JVP and hypertension with no skin rashes. Chest X-ray revealed pulmonary edema and bilateral minimal pleural effusions. Urinalysis revealed Proteinuria, hematuria and active sediment. Spot Urine Protein/creatinine ratio was 1260 mg/mmol (Normal 13 mg/mmol). Total serum protein was 55 G/L with albumin 20. Urea was 21.4 mmol/L and Creatinine 250 micromol/L. Further investigations revealed strongly positive Rheumatoid factor and presence of Cryoglobulins with hypocomplimentinemia. Hepatitis serology was negative. Renal biopsy revealed Necrotizing Crescentic GN with focal fibrinoid necrosis of the glomerular tuft. Immunofluorescence was consistent with an immunecomplex deposition disease. She reacted adversely to attempted intense immunosuppression with combination therapy with Cyclophosphamide and steroids by developing Neutropenia and Pneumonia. Cyclophosphamide was withdrawn and steroids tapered rapidly. After 24 months of diagnosing with Cryoglobulinic GN, she is progressing satisfactorily on minimal immunosuppression. Her renal function and proteinuria have improved considerably (serum creatinine 155 micromoles/liter and urine protein/creatinine ratio 106 mg/mmol) with improvement in hypoalbuminemia (serum albumin 34G/L) and the nephrotic state. Conclusions: Our case is noteworthy for the rare association of Cryoglobulinemia and Crescentic GN with RA. The optimal treatment of RA associated cryoglobulinic GN is uncertain, although immunosupression in some form targeting antibody production and formation of immune complexes seems logical.

Cholecalciferol therapy in VIT D deficient haemodialysis population: A pilot study.

Light C, Kulkarni H.

(Aim: To study the effect of fixed dose supervised treatment of 25OH-Vit D (25 OHD) deficiency in HD population on biochemical parameters of bone metabolism and ESA use. Background: 25 OH Vitamin D have beneficial effects on bone, cardiovascular and immune functions. 25 OHD is the prevalent non-activated vitamin D in Australia, and its use in haemodialysis (HD) patients deficient in 25OH-D is safe. Methods: 55 of 58 with low Vit D levels were prospectively treated, over 12 months, with Ostelin 18000 U/wk (deficient as 25 OHD: <50 nmol/L) and 6000 U/wk (Insufficient as 25OHD level: 50-75 nmol/L). Hb, ESA use (U/kg/ wk), Ca, P, ALP, and PTH was monitored at baseline and every 3 months. Effect of the 25OHD supplementation was studied over time. PO4 binders, ESA and calcitriol doses were adjusted as per unit protocol. Results: 72.8% and 22.4% of prevalent HD patients in the unit were 25OHD deficient and insufficient respectively. Fixed dose Ostelin therapy was safe. Fixed dose Ostelin therapy improved the 25OHD levels with reduction in PTH, with no effect on Ca, PO4 or Alkaline Phosphatase. 2 patients avoided surgical parathyroidectomy during the period. Fixed dose Ostelin therapy shows improving trend in ESA use with target Hb. Conclusion: 25OHD therapy was safe and showed improving trends in PTH, and ESA use over short period in limited patient population. Larger studies are necessary to confirm these findings. Publication Types: Conference Abstract PMID:70532363

Citrate anticoagulation using ACD solution A during long-term haemodialysis.

Wright S, Steinwandel U, et al.

(Aim: Haemodialysis with regional citrate anticoagulation in patients with contraindications for heparin is increasingly performed in the USA and Europe. Most published protocols use trisodium citrate, which is not readily available nor is it licensed in Australia. We established a protocol for citrate-anticoagulation in haemodialysis using acid citrate dextrose solution A (ACDA), which is approved for apheresis procedures in Australia. The aim of the present study was to assess the safety and efficacy of this protocol for routine use in haemodialysis patients. Methods: Systemic and post-filter blood ionized calcium, serum sodium and bicarbonate and dialyzer clotting score were analyzed prospectively in 14 patients undergoing 150 consecutive haemodialysis treatments with citrate anticoagulation using calcium-free dialysate. A simple algorithm allowed the attending nurse to adjust citrate infusion (to maintain post-filter ionized calcium at 0.2-0.3mmol/L) and i.v. calcium substitution. Scheduled dialysis time was 4h, and point-of-care monitoring of blood ionized calcium during dialysis was done at 0, 15, 60, 120 and 240min. Results: ACDA infusion rates of 300mL/h were used in the first 52 treatments, but resulted in high dialyzer clotting score and 6% of treatments were discontinued due to complete clotting. Thereafter, ACDA infusion rate was increased to 350mL/h, with all 98 subsequent treatments completed successfully. Ionized calcium levels were stable during all procedures with post-dialysis serum sodium averaging 135+/-3mmol/L and bicarbonate 23.8+/-2mmol/L. Conclusion: Routine use of citrate anticoagulation in the setting of a long-term haemodialysis unit is safe and efficient. Point-of-care measurements of ionized calcium levels are critical to safely and successfully perform citrate anticoagulation. Copyright 2011 The Authors. Nephrology Copyright 2011 Asian Pacific Society of Nephrology. PMID:21054668
Effect of donor-recipient age difference on graft function and survival in live-donor kidney transplantation.
Ferrari P, Lim W, et al.
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BACKGROUND: Renal transplant recipients of older deceased-donor kidneys have reduced allograft survival. However, the impact of donor-recipient age difference on live-donor kidney transplant outcomes, where donors are older than recipients, remains unclear. METHODS: Using the Australia and New Zealand Dialysis and Transplant Registry, all primary live-donor kidney transplant recipients in Australia from 1991 to 2006 were studied. Donor-recipient age difference was divided into four categories (donor-recipient<-10, -10-20, 20-29 and >=30 years). Outcome measures included serum creatinine, graft and patient survival. RESULTS: In the adjusted model, donor-recipient age difference of >=30 years showed a trend towards increased risk of graft failure compared with a difference of -10-20 years during the first year post-transplant only (hazard ratio=2.11, 95% CI=1.00-4.47; P=0.05). However, in the multivariate competing risks Cox model, donor-recipient age difference was not associated with increased patient death, death-censored graft failure or serum creatinine at 5 or 10 years, nor was it associated with increased risk of acute rejection within the first 6 months. CONCLUSIONS: Recipients of kidney transplants donated by live donors who are significantly older than recipients have similar graft and patient survivals to recipients from organs of similar vintage. Thus, living kidney donors, who are up to 30 years older than their recipients, provide kidneys of excellent quality. These findings are of relevance when considering paired kidney donation programme because the chance of finding a suitable match should not be unnecessarily limited by unjustified restrictions on the perceived disadvantage of high donor-recipient age difference.

PMID:20601369

The diagnosis of depression in Alzheimer's disease: Review of the current literature.
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Depression is among the most common psychiatric disorders in Alzheimer's disease (AD). Nevertheless, given the overlap between the symptoms of depression and the symptoms of dementia, diagnosing depression is still problematic. Several depression rating scales have been validated for use in AD. Both the Hamilton Depression Rating Scale and the Montgomery-Asberg Depression Rating Scale have been used for screening purposes, to measure the severity of depression, and for assessing response to treatment. The recommendation to diagnose depression in AD is by using structured psychiatric interviews, such as the Structured Clinical Diagnostic Interview for DSM-IV or the Mini International Neuropsychiatric Interview. Based on information obtained from the structured interviews, depression is diagnosed using DSM-IV criteria. Consensus groups suggested specific changes to the diagnostic criteria to account for the overlap of symptoms between depression and dementia, and recent studies validated the DSM-IV criteria for major depression for use in AD.

PMID:2012159762

Localized myxedema of the foot associated with trauma and surgery.
Localized extratibial myxedema is a rare presentation of thyroid disease that manifests with varied symptoms. Previous surgical or radioiodine treatment of hyperthyroidism is linked to the development of localized myxedema, as is prior trauma or surgery. We present the first known case of localized foot myxedema on a background of Graves disease following a traumatic and surgical precipitant and compare and discuss similar cases found in a literature review. Academic Division of Ochsner Clinic Foundation.

Publication Types: Review
PMID:2011328734

Stigmatization of patients with chronic pain: the extinction of empathy.
Cohen M, Quintner J, et al.
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Objective: To address how health professionals may inadvertently contribute to the stigmatization of patients with chronic pain. Setting: Formulation and implementation of the Australian National Pain Strategy. Design: Review of current concepts of stereotyping and stigma, consideration of their relationship to empathy, and how they might impinge upon the clinical encounter. Findings: The extinction of empathy, which we refer to as "negative empathy," can overwhelm health professionals, allowing the entry of negative community stereotypes of chronic pain sufferers and add to their stigmatization. Prevailing dualistic frames of reference encourage this process. Conclusion: Greater awareness by health professionals of their own potential, often inadvertent, contribution to the stigmatization of their patients with chronic pain may serve as a basis for an expanded model of clinical engagement. Wiley Periodicals, Inc.
PMID:22054062

Massive clonidine overdose during refill of an implanted drug delivery device for intrathecal analgesia: a review of inadvertent soft-tissue injection during implantable drug delivery device refills and its management.
Johnson ML, Visser EJ, et al.
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Objectives. The study aims to highlight the potentially serious consequences of inadvertent soft-tissue injection of intrathecal drugs such as clonidine, during refills of implanted drug delivery devices, and to suggest strategies to reduce this complication. Design. Case report and literature review were used. Results. We report the case of a 51-year-old female with chronic arm pain who sustained a massive clonidine overdose (18,000mcg) due to inadvertent soft-tissue injection during a refill of an implanted drug delivery device, resulting in rapid loss of consciousness and significant cardiovascular instability requiring urgent resuscitation, subsequent myocardial infarction, cardiac failure, and other significant
complications. The risks of inadvertent soft-tissue injection of intrathecal drugs during implanted drug delivery device refills and management of such events is poorly documented in the literature.

Conclusion. Inadvertent soft-tissue injection is possibly an underappreciated and underreported complication of intrathecal analgesia via an implanted drug delivery device. Under some circumstances, large doses of other intrathecal drugs such as bupivacaine, opioids, ziconotide, and baclofen may also be delivered by inadvertent soft-tissue injection with potentially life-threatening consequences. We recommend that practitioners, institutions, and professional bodies who manage patients with intrathecal analgesia via intrathecal drug delivery devices highlight and audit this complication and develop systems to manage it. Wiley Periodicals, Inc.

PMID:21672143


An evolutionary stress-response hypothesis for chronic widespread pain (fibromyalgia syndrome).


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Objective. The study aimed to seek a unifying biological basis for the phenomena encompassed in fibromyalgia syndrome (chronic widespread pain and associated morbidities).

Setting. While much progress has been made in the last decade in understanding chronic widespread pain, its pathogenesis remains stubbornly obscure and its treatment difficult. Two themes are gaining currency in the field: that chronic widespread pain is the result of central sensitization of nociception, and that chronic pain is somehow related to activation of a global stress response.

Design. In this article we merge these two ideas within the perspective of evolutionary biology to generate a hypothesis about the critical molecular pathway involved in chronic stress response activation, namely substance P and its preferred receptor, neurokinin-1 (NK-1R), which has many empirically testable implications.

Conclusion. Drawing on diverse findings in neurobiology, immunology, physiology, and comparative biology, we suggest that the form of central sensitization that leads to the profound phenomenological features of chronic widespread pain is part of a whole-organism stress response, which is evolutionarily conserved, following a general pattern found in the simplest living systems. Wiley Periodicals, Inc.

PMID:21692974


Maldynia as a moral judgment?

Quintner J, Buchanan D, et al.

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Publication Types: Letter

PMID:21699648


Preclinic group education sessions reduce waiting times and costs at public pain medicine units.

Davies S, Quintner J, et al.

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Objective. To assess the effects of preclinic group education sessions and system redesign on tertiary pain medicine units and patient outcomes. Design. Prospective cohort study. Setting. Two public hospital multidisciplinary pain medicine units. Patients. People with persistent pain. Interventions. A system redesign from a "traditional" model (initial individual medical appointments) to a model that delivers group education sessions prior to individual appointments. Based on Patient Triage Questionnaires patients were scheduled to attend Self-Training Educatively Pain Sessions (STEPS), a two day eight hour group education program, followed by optional patient-initiated clinic appointments. Outcome Measures. Number of patients completing STEPS who subsequently requested individual outpatient clinic appointment(s); wait-times; unit cost per new patient referred; recurrent health care utilization; patient satisfaction; Global Perceived Impression of Change (GPIC); and utilized pain management strategies. Results. Following STEPS 48% of attendees requested individual outpatient appointments. Wait times reduced from 105.6 to 16.1 weeks at one pain unit and 37.3 to 15.2 weeks at the second. Unit cost per new patient appointed reduced from $1,805 Australian Dollars (AUD) to AUD$541 (for STEPS). At 3 months, patients scored their satisfaction with "the treatment received for their pain" more positively than at baseline (change score=0.88; P=0.0003), GPIC improved (change score=0.46; P<0.0001) and mean number of active strategies utilized increased by 4.12 per patient (P=0.0004). Conclusions. The introduction of STEPS was associated with reduced wait-times and costs at public pain medicine units and increased both the use of active pain management strategies and patient satisfaction. Wiley Periodicals, Inc.

PMID:21087401


System plasticity and integrated care: informed consumers guide clinical reorientation and system reorganization.
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Setting. Two Australian public hospital multidisciplinary pain centers (MPCs) situated on opposite sides of the country. Objective. Restructuring our services to become patient-centred and patient-driven by enabling entry to our MPCs through an education portal, inclusive of both knowledge and self-management skills, and to then be free to select particular treatment options on the basis of evidence of known efficacy (risk/benefit). Design. Group-based education to inform our patients of the current state of uncertainty that exists in Pain Medicine, both in regard to diagnostic and therapeutic practices. Using an interprofessional team approach, we aimed to present practical and evidence-based advice on techniques of pain self-management and existing traditional medical options. Results. Early, resource efficient, group intervention provides many patients with sufficient information to make informed decisions and enables them to partner us in engaging a whole person approach to their care. We have implemented routine comprehensive audits of clinical services to better inform the planning and provision of health care across health services. Conclusions. System plasticity is as important to the process of integrated health care as it is to our understanding of the complexity of the lived experience of pain. Better-informed consumers partnered with responsive health professionals drive the proposed paradigm shift in service delivery. The changes better align the needs of consumers with the ability of health care providers to meet them, thus achieving the twin goals of patient empowerment and system efficiency. Wiley Periodicals, Inc.

PMID:21143757


Is migraine a complex regional pain syndrome of the brain? Migraine prophylaxis with vitamin C?
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INTRODUCTION: subacute sclerosing panencephalitis (SSPE) is a late, rare and usually fatal complication of measles infection. Although a very high incidence of SSPE in Papua New Guinea (PNG) was first recognized 20 years ago, estimated measles vaccine coverage has remained at <= 70% since and a large measles epidemic occurred in 2002. We report a series of 22 SSPE cases presenting between November 2007 and July 2009 in Madang Province, PNG, including localized clusters with the highest ever reported annual incidence. METHODOLOGY/PRINCIPAL FINDINGS: as part of a prospective observational study of severe childhood illness at Modilon Hospital, the provincial referral center, children presenting with evidence of meningo-encephalitis were assessed in detail including lumbar puncture in most cases. A diagnosis of SSPE was based on clinical features and presence of measles-specific IgG in cerebrospinal fluid and/or plasma. The estimated annual SSPE incidence in Madang province was 54/million population aged <20 years, but four sub-districts had an incidence >100/million/year. The distribution of year of birth of the 22 children with SSPE closely matched the reported annual measles incidence in PNG, including a peak in 2002.

CONCLUSIONS/SIGNIFICANCE: SSPE follows measles infections in very young PNG children. Because PNG children have known low seroconversion rates to the first measles vaccine given at 6 months of age, efforts such as supplementary measles immunisation programs should continue in order to reduce the pool of non-immune people surrounding the youngest and most vulnerable members of PNG communities.
FOXP3 correlated with a good disease outcome, better long-term CSS and less adjuvant chemotherapy use in stage II (p<0.0037, <0.0001 and p = 0.04 respectively), but not in stage III CRC. High CD8 and CD45RO expression correlated with better disease outcome in stage II CRC, and better CSS, but the differences were not as marked as for SPARC and FOXP3. CONCLUSIONS: These data suggest that high SPARC and FOXP3 are associated with better disease outcome in stage II CRC and may be prognostic indicators of CSS. Further assessment of whether these markers predict patients at high risk of recurrence with stage II CRC and functional studies of these effects are underway.

PMID:21818290


A sub-microscopic gametocyte reservoir can sustain malaria transmission.

Karl S, Gurarie D, et al.

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Background: Novel diagnostic tools, including PCR and high field gradient magnetic fractionation (HFGMF), have improved detection of asexual Plasmodium falciparum parasites and especially infectious gametocytes in human blood. These techniques indicate a significant number of people carry gametocyte densities that fall below the conventional threshold of detection achieved by standard light microscopy (LM). Methodology/Principal Findings: To determine how low-level gametocytemia may affect transmission in present large-scale efforts for P. falciparum control in endemic areas, we developed a refinement of the classical Ross-Macdonald model of malaria transmission by introducing multiple infective compartments to model the potential impact of highly prevalent, low gametocytaemic reservoirs in the population. Models were calibrated using field-based data and several numerical experiments were conducted to assess the effect of high and low gametocytemia on P. falciparum transmission and control. Special consideration was given to the impact of long-lasting insecticide-treated bed nets (LLIN), presently considered the most efficient way to prevent transmission, and particularly LLIN coverage similar to goals targeted by the Roll Back Malaria and Global Fund malaria control campaigns. Our analyses indicate that models which include only moderate-to-high gametocytemia (detectable by LM) predict finite eradication times after LLIN introduction. Models that include a low gametocytemia reservoir (requiring PCR or HFGMF detection) predict much more stable, persistent transmission. Our modeled outcomes result in significantly different estimates for the level and duration of control needed to achieve malaria elimination if submicroscopic gametocytes are included. Conclusions/Significance: It will be very important to complement current methods of surveillance with enhanced diagnostic techniques to detect asexual parasites and gametocytes to more accurately plan, monitor and guide malaria control programs aimed at eliminating malaria. 2011 Karl et al.

PMID:2011328956

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Body adiposity in later life and the incidence of dementia: The health in men study.

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Objective: To determine if adiposity in later life increases dementia hazard. Methods: Cohort study of 12,047 men aged 65-84 years living in Perth, Australia. Adiposity exposures were baseline body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR). We used the Western Australian Data Linkage System (WADLS) to establish the presence of new cases of dementia between 1996 and 2009 according to the International Classification of Diseases (ICD). Crude and adjusted hazard ratio (HR, 95% confidence interval, 95%CI) of dementia for each adiposity marker was calculated using Cox regression models. Other measured factors included age, marital status, education, alcohol use, smoking, diet, physical activity, and prevalent hypertension, diabetes, dyslipidaemia and cardiovascular disease. Results: Compared with men with BMI<25, participants with BMI between 25-30 had lower adjusted HR of dementia (HR = 0.82, 95% CI = 0.70-0.95). The HR of dementia for men with BMI>=30 was comparable to men with BMI<25 (HR = 0.82, 95%CI = 0.67-1.01). Waist circumference showed no obvious association with dementia hazard. Men with WHR>=0.9 had lower adjusted HR of dementia than men with WHR <0.9 (HR = 0.82, 95%CI = 0.69-0.98). We found a "J" shape association between measures of obesity and the hazard of dementia, with the nadir of risk being in the overweight range of BMI and about 1 for WHR. Conclusions: Higher adiposity is not associated with incident dementia in this Australian cohort of older men. Overweight men and those with WHR>=0.9 have lower hazard of dementia than men with normal weight and with WHR<0.9.

PMID:2011168273

Features and prognosis of severe malaria caused by Plasmodium falciparum, Plasmodium vivax and mixed Plasmodium species in Papua New Guinean children.
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BACKGROUND: Mortality from severe pediatric falciparum malaria appears low in Oceania but Plasmodium vivax is increasingly recognized as a cause of complications and death. The features and prognosis of mixed Plasmodium species infections are poorly characterized. Detailed prospective studies that include accurate malaria diagnosis and detection of co-morbidities are lacking. METHODS AND FINDINGS: We followed 340 Papua New Guinean (PNG) children with PCR-confirmed severe malaria (77.1% P. falciparum, 7.9% P. vivax, 14.7% P. falciparum/vivax) hospitalized over a 3-year period. Bacterial cultures were performed to identify co-incident sepsis. Clinical management was under national guidelines. Of 262 children with severe falciparum malaria, 30.9%, 24.8% and 23.2% had impaired consciousness, severe anemia, and metabolic acidosis/hyperlactatemia, respectively. Two (0.8%) presented with hypoglycemia, seven (2.7%) were discharged with neurologic impairment, and one child died (0.4%). The 27 severe vivax malaria cases presented with similar phenotypic features to the falciparum malaria cases but respiratory distress was five times more common (P[HAIR SPACE]=0.001); one child died (3.7%). The 50 children with P. falciparum/vivax infections shared phenotypic features of mono-species infections, but were more likely to present in deep coma and had the highest mortality (8.0%; P[HAIR SPACE]=0.003 vs falciparum malaria). Overall, bacterial cultures were positive in only two non-fatal cases. 83.6% of the children had alpha-thalassemia trait and seven with coma/impaired consciousness had South Asian ovalocytosis (SAO). CONCLUSIONS: The low mortality from severe falciparum malaria in PNG children may reflect protective genetic factors other than alpha-thalassemia trait/SAO, good nutrition, and/or infrequent co-incident sepsis. Severe vivax malaria had similar features but severe P.
falciparum/vivax infections were associated with the most severe phenotype and worst prognosis. PMID:22216212


Assessment of high-throughput high-resolution MALDI-TOF-MS of urinary peptides for the detection of muscle-invasive bladder cancer.

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Purpose: There is a need for better biomarkers to both detect bladder cancer and distinguish muscle-invasive (stage T2+) from non-invasive (stage Ta/T1) disease. We assess whether MALDI-TOF-MS of the urine peptidome can achieve this. Experimental design: We analysed urine from 751 patients with bladder cancer and 127 patients without bladder cancer. Endogenous peptide profiling was performed using a Bruker Ultraflextreme MALDI-TOF-MS. Results: Significant differences were seen between the spectra of urine from patients with and without T2+ disease. Albumin, total protein and haematuria were also elevated in T2+ patients. Haematuria was detected in 39% of patients with Ta/T1 disease and in 77% of patients with T2+ disease. Class prediction models based on MALDI data produced areas under receiver-operator characteristic curves of up to 0.76 but did not significantly outperform a model based on total protein alone. Many peptides significantly associated with invasive disease are fragments of abundant blood proteins and are also associated with haematuria. Conclusions and clinical relevance: Microscopic haematuria is strongly associated with invasive disease; even traces of blood/plasma strongly influence the urinary peptidome. This needs to be taken into consideration when using 'omic' methods to search for urinary biomarkers as blood proteins may give false-positive results. 2011 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

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Natural history and management of HFE-hemochromatosis.

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Advances in our knowledge of hereditary hemochromatosis (HH) over the past 150 years have revealed new insights into this common genetic disorder. Meticulous family and HLA association studies followed ultimately by cloning of the HFE gene have dramatically changed our understanding of the natural history and manifestations of HH. Cross-sectional studies demonstrated that HH had a highly variable clinical and biochemical penetrance in susceptible individuals of northern European descent. State-of-the-art large longitudinal population studies have accurately defined the natural history. We now recognize that HH is not as discreet an entity as previously thought because genetic

**Chlamydia trends in men who have sex with men attending sexual health services in Australia, 2004-2008.**

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**Background:** In most Australian settings, chlamydia notifications do not contain information on the gender of sexual partners. We assessed trends and predictors of chlamydia testing and positivity among men who have sex with men (MSM), attending sexual health services in Australia. Methods: The Australian Collaboration for Chlamydia Enhanced Sentinel Surveillance (ACCESS) program was established in 2008 to collate demographic and chlamydia testing information from 25 sexual health services. We calculated the proportion tested and chlamydia positivity among MSM and assessed trends from 2004 to 2008 using a chi test and predictors using logistic regression. Results: In the 5-year period, 11,777 MSM attended as new patients (first visit ever to the service) and the proportion tested for chlamydia increased significantly from 71% in 2004 to 79% in 2008 (P < 0.01). Independent predictors of chlamydia testing were younger age, residing in a metropolitan area (adjusted prevalence ratio [APR] = 1.23; 95% confidence interval [CI]: 1.19, 1.27), being Australian-born (APR = 1.03; 95% CI: 1.01, 1.06), being a traveler or migrant (APR = 1.09; 95% CI: 1.06, 1.12), and sex overseas in the past year (APR = 1.05; 95% CI: 1.03, 1.07). Overall chlamydia positivity was 8.6% (95% CI: 8.0%-9.2%). There was no significant trend in chlamydia positivity between 2004 and 2008. Independent predictors of chlamydia positivity were younger age, being a traveler or migrant (APR = 1.52; 95% CI: 1.26-1.84), and exclusive same-sex contact (APR = 1.28; 95% CI: 1.05-1.55). Conclusions: This new national surveillance program demonstrates that the majority of MSM attending sexual health services was offered chlamydia testing and testing has increased over time. The MSM at highest risk of chlamydia were more likely to be tested. Chlamydia transmission was frequent but stable among MSM accessing clinical services. Copyright 2011 American Sexually Transmitted Diseases Association All rights reserved.

PMID:2011176711


**The role of femoral venous pressure and femoral venous oxygen saturation in the setting of intra-abdominal hypertension: a pig model.**

Regli A, De Keulenaer BL, et al.
Femoral venous access is frequently used in critically ill patients. Because raised intra-abdominal pressure (IAP) is also frequently found in this group of patients, we examined the impact of IAP and positive end-expiratory pressure (PEEP) on femoral venous pressure (FVP) and femoral venous oxygen saturation (Sfvo2) in an animal model. Thirteen adult pigs received standardized anesthesia and ventilation. Randomized levels of IAP (3 [baseline], 18, and 26 mmHg) were applied, with levels of PEEP (5, 8, 12, and 15 cmH2O) applied randomly at each IAP level. We measured bladder pressure (IAP), superior vena cava pressure, pulmonary artery pressure, pulmonary artery occlusion pressure, FVP, mixed venous oxygen saturation (Svo2), and Sfvo2. We found that FVP correlated well with IAP (FVP = 4.1 + [0.12 x PEEP] + [1.00 x IAP]; R = 0.89, P < 0.001) with a moderate bias and precision of 5.0 and 3.8 mmHg, respectively. Because the level of agreement did not meet the recommendations of the World Society of Abdominal Compartment Syndrome, FVP cannot currently be recommended to measure IAP, and further clinical trials are warranted. However, a raised FVP should prompt the measurement of the bladder pressure. Femoral venous oxygen saturation did correlate neither with Svo2 nor with abdominal perfusion pressure. Therefore, Sfvo2 is of no clinical use in the setting of raised IAP.

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The important correlates of SWB for men and women were somewhat different. Overall, sociodemographic variables have minimal effect on SWB in urban India and research needs to explore other predictors of SWB. (PsycINFO Database Record (c) 2011 APA, all rights reserved) (journal abstract).


**Paired kidney exchange - An update on the Australian program.**

Fidler SJ, Christiansen FT, et al.

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Living donors are being increasingly used to meet the increasing demand for kidney transplantation. However, due to ABO incompatibility or recipient sensitisation to donor HLA antigens, approximately 30% of potential recipients are incompatible with their intended donor. By paired kidney donor exchange (PKE), two or more incompatible donor/recipient pairs surmount each other's incompatibility problem by simply exchanging donors. Recently an Australian PKE program has been established. To facilitate the program a PKE NOMS matching program has been developed. The algorithm utilizes a virtual crossmatch strategy whereby donors are excluded for recipients with incompatible ABO blood group or donor specific HLA antibodies (DSA) defined by single antigen beads at a defined level of MFI. A matrix of suitable donor/recipient pairs is generated and then all possible combinations of suitable exchanges within this matrix are determined. These combinations are then prioritized according to defined criteria. Final suitability is confirmed by CDC T and B cell crossmatching. An initial evaluation of the program using 32 donor recipient pairs enrolled in the WA PKE program, all recipient DSA were defined using an MFI cut-off of >8000 (run 1) or >2000 (run 2). In run 1, the top ranked combination identified 19 compatible pairs (5 x 3 way and 2 x 2 way exchanges) whilst run 2 identified 17 pairs (5 x 3 way and 1 x 2 way exchanges). This approach has now been applied to the first national matching of 22 highly sensitised pairs using an MFI of >2000 to define DSA. The top ranked combination identified 6 pairs in 2 x 3 way exchanges. Unfortunately, one of the exchanges did not occur due to donor unsuitability. The other exchange was successfully carried out and all recipients are doing well. A second match run is in progress. The National PKE program offers an alternative approach for providing transplants for incompatible live donor recipient pairs.

Publication Types: Conference Abstract

PMID:70652479


**De novo donor specific anti-HLA antibodies (DSA) following renal transplantation are associated with an increase in rejection episodes in a long-term prospective study.**


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Pre-transplant DSA in renal transplant recipients (RTR) is associated with subsequent graft loss. The factors associated with the development post transplantation de novo DSA and the utility of screening for such antibodies are uncertain. The aim of this long-term prospective study was to determine the incidence and significance of de novo post transplant DSA in RTR. A cohort of 272 RTR were screened by Luminex Mixed Screen assay at transplant and at regular time points post transplant for a median follow up of 46 (range 24-74) months. Demographic and relevant clinical data was also collected. The appearance of a de novo DSA was defined as Class I or Class II antibody against
donor HLA detected by Single Antigen beads and a DSA at a MFI >500. One hundred and eighty-five patients who had no antibody at the time of transplant had follow up serum for testing. Nineteen (10%) formed any DSA (CI n = 2, CII n = 11, Both CIII: 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 CII DSA vs 72% without DSA were -DR mismatched. Any biopsy-proven acute rejection (BPAR) occurred in 60% with de novo DSA vs 29% without DSA, and C4d+ve rejection occurred in 23% of new DSA (all Class II) vs 2% without DSA (p < 0.01). In all but 1 case DSA was first detected with or after BPAR. At last follow-up, eGFR for those with DSA was 38 vs 51 mls/min without DSA (p < 0.05). Over a median of 4 years, de novo, predominantly Class II, DSA developed in 10% of RTR and adversely impacted upon graft function. This data suggests improving allocation based upon -DR matching rather than post transplant DSA screening may be a more effective strategy to improve long-term graft outcome.

Publication Types: Conference Abstract
PMID:70652543


Third party blood transfusion before and after renal transplantation: A powerful predictor of rejection and transplant outcome.
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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. The aim of this study was to evaluate the relationship between blood transfusion and transplant outcome in renal transplant recipients (RTR). We determined the BT history of 256 RTR and examined its 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. One hundred and five RTR (41%) never received a BT, 50 (19%) received BT pre-transplant only, 44 (17%) received BT post-transplant only and 57 (22%) received both pre and post transplant BT. Factors associated with transfusion included recipient gender (female), increasing donor and recipient age, re-transplant, 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 HRs 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. BT pre and post transplant are clinically determined and associated with recipient gender, donor and recipient age and donor type. Compared with those never transfused or those transfused pre or post transplant 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:70652525

Transfusion. 2011; 51(10): 2189-2198.
A comparison of self-reported and record-linked blood donation history in an Australian cohort.
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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. The aim of this study was to evaluate the relationship between blood transfusion and transplant outcome in renal transplant recipients (RTR). We determined the BT history of 256 RTR and examined its 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. One hundred and five RTR (41%) never received a BT, 50 (19%) received BT pre-transplant only, 44 (17%) received BT post-transplant only and 57 (22%) received both pre and post transplant BT. Factors associated with transfusion included recipient gender (female), increasing donor and recipient age, re-transplant, 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 HRs 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. BT pre and post transplant are clinically determined and associated with recipient gender, donor and recipient age and donor type. Compared with those never transfused or those transfused pre or post transplant 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:70652525
BACKGROUND: Questionnaire-based studies investigating blood donation history rely on the accurate recall of information from participants for results to be valid. This study aimed to retrieve electronic records from a national blood donation service and link them to self-reported history of donation to assess agreement between the two sources. STUDY DESIGN AND METHODS: Between 2004 and 2006, a sample of participants of northern European descent was selected from the Melbourne Collaborative Cohort Study (n = 31,192) to participate in the "HealthIron" study (n = 1438). A total of 1052 participants completed questionnaires that included questions about blood donation history. In 2009, consenting participants' records were linked to the Australian Red Cross Blood Service (ARCBS) to provide information on blood donations made between 1980 and follow-up (2004-2006). Those who commenced blood donation before 1980 were excluded. RESULTS: A total of 718 participants were available for analysis. Of these, 394 (55%) provided signed consent, including 182 (82%) of the 227 participants who self-reported ever donating blood. The two data sources were concordant for 331 (87%) of participants, with a statistic of 0.74 (SE, 0.05) indicating a high level of agreement. Participants tended to overstate by a factor of 2.0 (95% confidence interval, 1.7-2.2) the number of donations they had made when compared with ARCBS records. CONCLUSION: Participants in studies assessing self-reported blood donation history are likely to correctly indicate whether or not they have ever donated blood. Quantitative estimates are potentially inaccurate and could benefit from validating a sample of records to quantify the bias. 2011 American Association of Blood Banks.