Comparison of computer tomographic volumetry versus nuclear split renal function to determine residual renal function after living kidney donation.

Patankar K, Low RST, et al.

(Patankar, Ferrari) Department of Nephrology, Fremantle Hospital, University of Western Australia, Perth, WA 6160, Australia (Low, Blakeway) Department of Radiology, Fremantle Hospital, University of Western Australia, Perth, Australia (Ferrari) School of Medicine and Pharmacology, University of Western Australia, Perth, Australia

P. Ferrari, Department of Nephrology, Fremantle Hospital, University of Western Australia, Perth, WA 6160, Australia. E-mail: paolo.ferrari@health.wa.gov.au

Background: Living-donor kidney transplantation is an established practice. Traditionally a combination of renal scintigram and computed tomography (CT) is used to select the kidney that is to be harvested in each donor. Purpose: To evaluate the ability of split renal volume (SRV) calculated from volumetric examination of CT images compared to nuclear split renal function (nSRF) derived from gamma camera scintigram to predict donor residual single kidney function after donor nephrectomy. Material and Methods: This pilot study comprised a retrospective analysis of CT images and renal scintigrams from 12 subsequent live kidney donors who had at least 12 months post-donation renal function follow-up. Results: nSRF derived from the renal scintigram, expressed as the right kidney's function in percent of the total, was 50.2±3.3 (range, 44.1-54.0%) and SRV estimated following analysis of CT imaging was 49.0±2.9 (range, 46.4-52.3%). Although the correlation between nSRF and SRV was moderate (R=0.46), there was 92% agreement on the dominant kidney if a difference of <2% in nSRF versus SRV was considered. Post-donation glomerular filtration rate (GFR) by CKDEPI formula was 92±10 mL/min/1.73m² at 1 year and the correlation between estimated GFR (eGFR) at 1 year and extrapolated single kidney eGFR adjusted by nSRF (R²=0.69, P=0.0007) or SRV (R²=0.74, P=0.0003) was similar. Conclusion: Calculation of SRV from pre-donation CT examination is a valid method to estimate nSRF with good concordance with nSRF determined by renal scintigram and could replace the latter in the assessment of potential kidney donors. The Foundation Acta Radiologica 2013.

PMID:2014542484


Australian population trends and disparities in cholinesterase inhibitor use, 2003 to 2010.


Centre for Population Health Research, Curtin University, Western Australia, Perth, Australia. Electronic address: r.zilkens@curtin.edu.au.

Centre for Population Health Research, Curtin University, Western Australia, Perth, Australia; School of Surgery, University of Western Australia, Western Australia, Perth, Australia.

Curtin Health Innovation Research Institute, Faculty of Health Science, Curtin University, Perth, Western Australia.

Centre for Population Health Research, Curtin University, Western Australia, Perth, Australia. School of Medicine & Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.

BACKGROUND: The Australian Pharmaceutical Benefits Scheme (PBS) first subsidized cholinesterase inhibitors (CEIs) for Alzheimer’s disease in 2001, introducing a novel therapy for a previously untreatable common condition. This study aims to determine Australian rates of CEI use and to assess equality of access to treatment based on socioeconomic status and geographic remoteness.

METHODS: Pharmaceutical claims records were used to identify all Australians prescribed CEIs between January 2003 and December 2010. Age-standardized and sex-adjusted index prescription rates were derived using the total Australian population as the denominator to examine temporal trends and the impacts of socioeconomic and geographic disadvantage on CEI index prescription rates.
RESULTS: Index prescription rates peaked in 2004 at 92.5 per 100,000 person-years, declining to between 70.2 and 73.5 for years 2006 to 2010. Rates were highest in the 85- to 89-year age group and 2.6-fold higher in the least socioeconomic disadvantaged population when compared with the most disadvantaged population. In major cities in Australia, index prescription rates were 1.4 to 1.7 times greater compared with remote areas.

CONCLUSIONS: Increasing geographic remoteness and socioeconomic disadvantage are associated with lower CEI index prescription rates, indicating inequities in the management of Alzheimer's disease in Australia. Copyright 2014 The Alzheimer's Association. Published by Elsevier Inc. All rights reserved.

PMID:23849590


PACSN2 Does Not Influence Thiopurine-Related Toxicity In Patients With Inflammatory Bowel Disease.
Roberts RL, Wallace MC, et al.
1] Department of Surgical Sciences (Dunedin), VU University Medical Center, Amsterdam, The Netherlands [2] On behalf of the Australian and New Zealand Inflammatory Bowel Disease Consortium.
Department of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, The Netherlands.
1] QIMR Berghofer Medical Research Institute, Royal Brisbane Hospital, Brisbane, Queensland, Australia [2] On behalf of the Australian and New Zealand Inflammatory Bowel Disease Consortium.
1] Centre for Inflammatory Bowel Disease, Fremantle Hospital, Fremantle, Western Australia, Australia [2] On behalf of the Australian and New Zealand Inflammatory Bowel Disease Consortium.
1] Flinders Medical Centre, Flinders University of South Australia, Bedford Park, South Australia, Australia [2] On behalf of the Australian and New Zealand Inflammatory Bowel Disease Consortium.
1] Department of Gastroenterology and Hepatology, Royal Adelaide Hospital, Adelaide, South Australia, Australia [2] On behalf of the Australian and New Zealand Inflammatory Bowel Disease Consortium.
1] Department of Gastroenterology, Christchurch Hospital, Christchurch, New Zealand [2] On behalf of the Australian and New Zealand Inflammatory Bowel Disease Consortium.
PMID:24896764


Seroepidemiological study of outdoor recreationists’ exposure to spotted fever group Rickettsia in Western Australia.
Abdad MY, Cook A, et al.
Australian Rickettsial Reference Laboratory, Geelong, Victoria, Australia; School of Population Health, University of Western Australia, Perth, Western Australia, Australia; Fremantle Hospital, Fremantle, Western Australia, Australia; School of Veterinary and Biomedical Science, Murdoch University, Murdoch, Western Australia, Australia yazid.abdad@hotmail.com.
Australian Rickettsial Reference Laboratory, Geelong, Victoria, Australia; School of Population Health, University of Western Australia, Perth, Western Australia, Australia; Fremantle Hospital, Fremantle, Western Australia, Australia; School of Veterinary and Biomedical Science, Murdoch University, Murdoch, Western Australia, Australia.
Bushland activity has previously been linked to rickettsial exposure in eastern and central regions of Australia, whereas little is known about the risks in Western Australia. The isolation of Rickettsia gravesii sp. nov. from Amblyomma triguttatum ticks and anecdotal reports of low-grade illness among bush recreationists raised the possibility of rickettsial transmission in the State. This study investigated rickettsial seroprevalence and potential risk of exposure to the spotted fever group rickettsiae in rogainers. Our results showed that rogainers active in the bush had a significantly higher risk of
seropositivity (immunofluorescence total antibody titer > 128) for the spotted fever group Rickettsia (odds ratio [OR] = 14.02, 95% confidence interval [CI] = 1.38-142.07) compared with a reference population, the overall seroprevalence in the rogainer group being 23.1%. The American Society of Tropical Medicine and Hygiene.

Publication Types: Research Support, Non-U.S. Gov't
PMID:24935947

Confirming cerebral malaria deaths in resource-limited settings.
Laman M, Davis TM, et al.
Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea; University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, Western Australia, Australia.
PMID:24501116

A pilot study for a prospective, randomized, double-blind trial of the influence of anesthetic depth on long-term outcome.
Short TG, Leslie K, et al.
From the *Department of Anaesthesia, Auckland City Hospital, Auckland, New Zealand; +Department of Anaesthesia and Pain Management, Royal Melbourne Hospital, Melbourne, Victoria, Australia; ++Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong, China; Department of Anaesthesia and Pain Medicine, Royal Perth Hospital, Perth; |School of Medicine and Pharmacology, University of Western Australia; PDepartment of Anaesthesia, Fremantle Hospital, Fremantle, Western Australia, Australia; #Department of Statistics, University of Canterbury, Christchurch, New Zealand; **Department of Anaesthesia and Perioperative Medicine, Alfred Hospital, Melbourne; and ++Anaesthesia and Perioperative Medicine, Monash University, Melbourne, Victoria, Australia.
BACKGROUND: Deep general anesthesia has been associated with increased mortality in 5 observational studies. The association may be causal or an epiphenomenon due to increased anesthetic sensitivity in high-risk patients. We conducted a pilot study to assess the feasibility of performing a definitive randomized controlled trial. The aims of the study were to determine whether anesthetic depth targeting in a high-risk group was feasible and to document anesthetic doses and arterial blood pressures associated with "deep" and "light" general anesthesia.
METHODS: ASA physical status III and IV patients, aged >60 years, having surgery lasting >2 hours, with expected hospital stay >2 days, and receiving general anesthesia were randomly allocated to a Bispectral Index (BIS) or spectral entropy (SE) target of 35 ("low" group) or 50 ("high" group). The primary end point was mean BIS or SE. Secondary end points were postanesthesia care unit length of stay and pain scores, quality of recovery score, hospital length of stay, postoperative complications, and death. A composite end point of postoperative complications (pneumonia, myocardial infarction, stroke, pulmonary embolism, heart failure, and death) was determined at 1 year.
RESULTS: One hundred twenty-five patients were recruited. The mean of the median BIS/SE values for each patient during the maintenance phase of anesthesia in the low and high groups was significantly different: 39 vs 48 (mean difference 8 [95% confidence interval {CI95}, 6 to 10], P < 0.001). There was also a significant difference in mean volatile anesthetic administration (minimum alveolar concentration): 0.98 vs 0.64 (mean difference -0.35 [CI95, -0.44 to -0.26], P < 0.001) and target propofol concentrations: 4.0 vs 3.1 mug/mL (mean difference -0.8 [CI95, -1.2 to -0.3], P = 0.004). Intraoperative mean arterial blood pressures were similar (85 vs 87 mm Hg; mean difference 2 [CI95, -2 to 6], P = 0.86), and there were no differences in short-term recovery characteristics or hospital length of stay. There was a significant difference in the incidence of wound infection at 30 days (13% vs 3%; risk difference -10% [CI95, -21 to -0.1], P = 0.04). At 1 year, the composite rates of
complications in the low and high groups were 28% and 17% (risk difference -11 [CI95, -25 to 4], P = 0.15) and mortality rates were 12% and 9%, respectively (risk difference -2 [CI95, -14 to 9], P = 0.70).

CONCLUSIONS: This pilot study demonstrated that depth of anesthesia targeting with BIS or SE was achievable in a high-risk population with adequate separation of processed electroencephalogram monitor targets. The expected incidence of postoperative complications and mortality occurred. We conclude that a large, multicenter, randomized controlled trial is feasible.

PMID:24781568


Radiation safety of outpatient (177)Lu-octreotate radiopeptide therapy of neuroendocrine tumors.
Calais PJ, Turner JH.
Department of Nuclear Medicine, Fremantle Hospital, The University of Western Australia, Alma Street, Fremantle, WA, 6160, Australia.
PURPOSE: To demonstrate the safety of outpatient 7.8 GBq (177)Lu-DOTA-tyr(3)-octreotate radiopeptide therapy of neuroendocrine tumors by measurement of radiation exposures of hospital personnel, carers and members of the public.
METHODS: Seventy-six patients with progressive, metastatic neuroendocrine tumors each received four cycles of prescribed activity of 7.8 GBq (177)Lu-octreotate at 8-week intervals, as an outpatient procedure. Cohorts comprising four patients were treated in one room, each patient remaining in hospital until radiation exposure from them was below the release limit of 25 μSv h(-1) at 1 m. On occasion, a single patient was treated in a single room. Radiation exposures of hospital staff and patient carers were monitored by personal dosimeter, and nearby areas monitored with a survey meter.
RESULTS: Mean whole-body radiation exposures per therapy day ranged from 8 μSv (physicist) to 33 μSv (nurse), with exposures to personnel, carers and members of the public well within the limits recommended by the International Commission on Radiological Protection. Patients excreted a mean of 46 % of the total administered activity of (177)Lu-octreotate within 4 h of therapy.
CONCLUSION: Lutetium-177-octreotate radiopeptide therapy of neuroendocrine tumors can be safely performed as an outpatient treatment.
PMID:24687907


Testicular torsion in a 65-year-old male identified using Doppler ultrasound.
Potent K, Thyer I.
Fremantle Hospital, Fremantle, Western Australia, Australia.
Publication Types: Letter
PMID:24754728


Sex steroids and cardiovascular disease.
Yeap BB.
School of Medicine and Pharmacology, University of Western Australia, Perth and Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle, WA, Australia.
As men grow older, testosterone (T) levels decline and the significance of this change is debated. The evidence supporting a causal role for lower circulating T, or its metabolites dihydrotestosterone (DHT) and estradiol, in the genesis of atherosclerosis and cardiovascular disease (CVD) in men is limited. Observational studies associate low baseline T levels with carotid atherosclerosis, aortic and peripheral vascular disease, and with the incidence of cardiovascular events and mortality. Studies using mass spectrometry suggest that when total T is assayed optimally, calculation of free T might
not necessarily improve risk stratification. There is limited evidence to support an association of
estradiol with CVD. Interventional studies of T therapy in men with coronary artery disease have
shown beneficial effects on exercise-induced myocardial ischemia. However, placebo-controlled,
randomized clinical trials (RCTs) of T therapy in men with the prespecified outcomes of cardiovascular
events or deaths are lacking. Meta-analyses of randomized controlled trials of T published up to 2010
found no increase in cardiovascular events, mortality, or prostate cancer with therapy. Recently, in a
trial of older men with mobility limitations, men randomized to receive a substantial dose of T reported
cardiovascular adverse effects. This phenomenon was not reported from a comparable trial where
men received a more conservative dose of T, suggesting a prudent approach should be adopted when
considering therapy in frail older men with existing CVD. Adequately powered RCTs of T in middle-
aged and older men are needed to clarify whether or not hormonal intervention would reduce the
incidence of CVD.

PMID:24407188

Non-infectious skin disease in Indigenous Australians.
Heyes C, Tait C, et al.
(Heyes, Toholka) Skin and Cancer Foundation, 1/80 Drummond Street, Carlton, VIC 3053, Australia
(Tait) Royal Perth Hospital, Perth, WA, Australia (Gebauer) Fremantle Hospital, Fremantle, WA, Australia
C. Heyes, Skin and Cancer Foundation, 1/80 Drummond Street, Carlton, VIC 3053, Australia. E-mail:
chris.heyes@health.wa.gov.au
The burden of non-infectious skin disease in the Indigenous Australian population has not been
previously examined. This study considers the published data on the epidemiology and clinical
features of a number of non-infectious skin diseases in Indigenous Australians. It also outlines
hypotheses for the possible differences in the prevalence of such diseases in this group compared
with the general Australian population. There is a paucity of literature on the topic but, from the
material available, Indigenous Australians appear to have a reduced prevalence of psoriasis, type 1
hypersensitivity reactions and skin cancer but increased rates of lupus erythematosus, kava
dermopathy and vitamin D deficiency when compared to the non-Indigenous Australian population.
This article profiles the prevalence and presentation of non-infectious skin diseases in the Indigenous
Australian population to synthesise our limited knowledge and highlight deficiencies in our
understanding. 2013 The Australasian College of Dermatologists.
Publication Types: Review
PMID:2014540512

Periorbital allergic contact dermatitis resulting from topical retinoic acid use.
Anderson A, Gebauer K.
Fremantle Hospital, Alma St, Fremantle, Western Australia, Australia.
Contact dermatitis to topical tretinoin or retinoic acid is rarely described. We outline the case of a 20-
year-old woman presenting with bilateral periorbital dermatitis against the background of longstanding
use of retinoic acid for the ocular complications of toxic epidermal necrolysis. Patch testing confirmed
a contact allergy to retinoic acid and the symptoms of the dermatitis resolved after the cessation of
retinoic acid. 2013 The Authors. Australasian Journal of Dermatology 2013 The Australasian College
of Dermatologists.
PMID:23574260

The interface of religion, spirituality and psychiatry.
Background: Psychiatry has traditionally had nothing to do with religion and spirituality. At times, psychiatry was viewed as being hostile to religion and spirituality. Religious and spiritual experiences were often considered part of psychopathology; however, during the past 2 decades, there is growing awareness that religion and spirituality can be immensely helpful to a large proportion of people to effectively cope with various stressful life events. Their role in the management of various psychiatric disorders is also increasingly researched. Objectives: To understand the role of religion and spirituality in current psychiatric practice, as well as in the larger field of mental health. Methods: Critical review of the evolution of the relationship between religion, spirituality and mental health during the past century. Findings: While religious and spiritual experiences are normal for a large number of people, they may lead to mental disturbances in some, and in many with psychiatric disorders: They may be part of psychopathology. The presentation will raise numerous questions for discussion, such as: Should religious beliefs and spiritual experiences be included as part of routine psychiatric assessment? Should there be integration into routine treatment approaches, and if so, how can this be achieved? Should these be included as integral components of training of psychiatrists? Conclusions: There is a need to recognize the importance of religion and spirituality in our patients' lives. There is growing empirical evidence for the beneficial effects of religion and spirituality in the management of a variety of psychiatric disorders.

Publication Types: Conference Abstract
PMID:71565329

Development and evaluation of successful multicultural training.

John A, Yeak S, et al.
(Yeak, Moore) South Metropolitan Health Service, Mental Health Strategy and Leadership Unit, Perth, WA, Australia (John, Isaac) University of WA, Perth, WA, Australia (John) Bentley Health Service, Mental Health, Perth, WA, Australia (Isaac, Kleczkowska) Fremantle Health Service, Mental Health, Perth, WA, Australia (Johri) Armadale Health Service, Mental Health, Perth, WA, Australia
A. John, University of WA, Perth, WA, Australia

Background: Cultural competency in clinical practice is necessary to deliver culturally appropriate care to our increasingly diverse population. The proportion of overseas born and ATSI patients accessing services for mental health issues through WA is significant. After extensive consultation with relevant stakeholders, we initiated a 1-day cultural competency training program for mental health staff in 2004. This evolved into the first mandatory mental health multicultural competency training in Australia. Objectives: To equip the workforce in delivering best and culturally-appropriate care to our patients. Methods: The training was delivered by seven experts in their respective fields. The syllabus and delivery method were regularly reviewed to meet the needs of the workforce. Various methods for systematically evaluating the benefits of the program were incorporated. We extended our training by providing more in-depth Master Classes and have provided accredited training for WA General Practitioners and WA Country Health Service staff, and our partner organisations. Findings: Analysis of feedback and structured evaluation confirmed that our training courses are enormously popular among mental health clinicians, health service staff, government and non-government organisations. Follow-up evaluation of staff showed that these skills were retained and had improved outcomes for patients from CALD backgrounds admitted to our Mental Health Services. Conclusions: A structured multicultural training program has equipped our workforce to deliver culturally appropriate care.

Publication Types: Conference Abstract
PMID:71565323
Religion and spirituality: A friend or foe?


(Johri) Armadale Health Service, South Metropolitan Health Service, Perth, WA, Australia (Johri, Isaac) University of Western Australia, Perth, WA, Australia (Isaac) Fremantle Hospital, South Metropolitan Health Service, WA, Australia (Bender) City Community Mental Health Service, Perth, WA, Australia

N. Johri, Armadale Health Service, South Metropolitan Health Service, Perth, WA, Australia

Background: Religion and spirituality are essential dimensions of human life and intersect with practice of psychiatry at multiple levels. This relationship is complex, and often raises sharp and contrasting opinions within the psychiatric fraternity. Psychiatry is often blamed for ignoring it for too long. In recent times, there is a renewed interest in this area, and several papers are being written in leading journals. Objectives: To vigorously explore and discuss a comprehensive range of issues associated with the interface of religion, spirituality and psychiatric practice; and to derive a robust framework to inform contemporary psychiatric practice, aid in developing training modules for psychiatric trainees and provide direction for future research. Methods: The first speaker will introduce the topic, highlight current controversies and agreements, and draw a broad framework of scope for this symposium, in light of personal experiences and evidence-based research. The second speaker will reference his own qualitative research study on religious beliefs, practices and experiences; and discuss other available research, all of which highlights the usefulness, benefit and positive aspects of this interface. The last speaker will discuss the potential pitfalls and dangers associated with this proposed assimilation of the interface. This will be followed by open discussion with attendees. Conclusions: It is a challenging task to maintain the right balance in between 'too much and too little' in an attempt to assimilate religion and spirituality with psychiatric practice. There is no excuse to remain inert, ignorant or uninvolved about this interface in today's world.

Publication Types: Conference Abstract
PMID:71565328

Spirituality: The missing component in multicultural training.

Johri N, Yeak S, et al.

(Yeak, Moore) South Metropolitan Health Service, Mental Health Strategy and Leadership Unit, Perth, WA, Australia (Johri, John, Isaac) University of WA, Perth, WA, Australia (John) Bentley Health Service, Mental Health, Perth, WA, Australia (Isaac) Fremantle Health Service, Mental Health, Perth, WA, Australia (Johri) Armadale Health Service, Mental Health, Perth, WA, Australia

N. Johri, University of WA, Perth, WA, Australia

Background: Epidemiological studies reveal a virtually universal belief among psychiatric patients in a variety of religious and spiritual beliefs. The significance of religion and spirituality increases when working with multicultural clients and their families. In the 10 years of evolution of mental health multicultural training in WA, there has been a growing interest in further exploration of religion and spirituality. Objectives: To describe the development of a master class in Religion and Spirituality, for understanding and treatment of people with a mental disorder. Findings: Specific course content was developed from existing evidence-based, peer-reviewed literature. The first 1-day workshop was well attended and richly interactive. The evaluation confirmed the interest and need for ongoing training in this area. Further workshops, exploring in more depth particular groups, have been developed as a result of the feedback received. Conclusions: Multicultural training is incomplete without incorporating religion and spirituality in the core module. Clinicians require structured and specific skills enhancement in understanding a plethora of diverse beliefs and practices in clients, which can then be incorporated into a holistic care plan. This module continues to evolve keeping pace with participant's needs, feedback and expert consensus.

Publication Types: Conference Abstract
PMID:71565325
The subcortical connectome: Hubs, spokes and the space between-A vision for further research in neurodegenerative disease.


This article discusses the subcortical connectome as a vision for further research in neurodegenerative disease. The neurodegenerative diseases of ageing, such as Alzheimer disease (AD), neurocognitive disorders/dementias, movement disorders and cerebrovascular disease, have widespread impact on the neuropsychiatric domains of cognition, emotion, behavior and movement. Therapeutic interventions are based on understanding the in vivo neurobiology of these diseases, as a basis for disease modifying, symptomatic and palliative treatments. Thus, there has been much interest in understanding the neurobiology of these diseases and, accordingly, the neural circuit basis of the neurodegenerative dysfunction that characterizes these disorders. To understand the neural circuit basis of neurodegenerative disease, there has been much research modeling the spread of disease using intrinsic connectivity patterns discovered by resting state functional magnetic resonance imaging (rs-fMRI). These studies support a model of trans-neuronal spread of network based vulnerability to disease such as a protein-misfolding aggregation propagated through particular hubs identified by rs-fMRI. (PsycINFO Database Record (c) 2014 APA, all rights reserved).

PMID:2014-11613-003

Evolution and sustainability of multicultural training.

Moore E, Yeak S, et al.


Evolution and sustainability of multicultural training.

Moore E, Yeak S, et al.

Background: At South Metropolitan Health Service, we have been delivering Fundamental Mental Health Multicultural Training (FHMHMT) since 2004. The training syllabus and delivery method are regularly reviewed by a team of experts to meet the needs of our diverse workforce. Sustainability of this training is essential to ensure our workforce continues to be equipped to deal with diverse and often clinically complex issues in mental health. Objectives: This paper describes the process of ensuring sustainability by delivering the Fundamental MHMCT through local clinicians in a Train the Trainer (TtT) model. This allows the Multicultural MH Training team to concentrate on more advanced, in depth Master Classes, which have been identified as a need in our staff feedback. Findings: There
is a need to ensure that the quality of our existing fundamental program is not lost with the move to the TtT model. The existing syllabus and evaluation framework will be reviewed to ensure quality and standards are maintained, so that popularity of the program is not compromised. Participants reported significant gains and confidence in working with people from diverse backgrounds from the existing program, and this data can be used as a baseline for evaluation of this new method. Conclusions: A forward thinking multicultural training program will ensure the continuity in giving our workforce the skills and competencies to deliver culturally appropriate care.

Publication Types: Conference Abstract
PMID:71565324

Bonvenon! successful multicultural training in the most diverse state in Australia.
Moore E, Yeak S, et al.
(Moore, Yeak) South Metropolitan Health Service, Mental Health Strategy and Leadership Unit, Perth, WA, Australia (John, Isaac) University of WA, Perth, WA, Australia (John) Bentley Health Service, Mental Health, Perth, WA, Australia (Johri) Armadale Health Service, Mental Health, Perth, WA, Australia (Isaac, Klczekowska) Fremantle Health Service, Mental Health, Perth, WA, Australia
Background: WA is culturally diverse and rapidly growing. It is a requirement of the National Standards for Mental Health Services to have staff who are equipped to provide the best possible and culturally appropriate care to all consumers, their families and carers. Objectives: This symposium will present the evolution of a very successful multicultural training program for Mental Health Services and partner organisations in WA. Methods: The three papers describe the 10-year evolution of training in this important area, the changing process of delivery and the changing syllabus, to reflect contemporary changes in the culturally and linguistically diverse profile in WA. The papers will describe the change from fundamental mandatory training to a more advanced exploration of cultural psychiatry in our Master Class series. The decision to move fundamental training from a centralized model to a site-based model (incorporating e-learning packages and reduced face to face teaching) will be discussed. We will describe the challenges and benefits of mandatory training, the need to adapt for sustainability and to meet the changing needs and requirements of the community and our staff. Conclusion: This was a successful model that others may wish to consider in their own states or countries.
Publication Types: Conference Abstract
PMID:71565322

Survey of atypical antipsychotic use amongst CAMHS prescribers.
(Rao) CAHS, Fremantle CAMHS, Department of Health, Fremantle, WA, Australia (Chakrabarti) Tees, Esk and Wear Valleys NHS Foundation Trust, Middlesbrough, United Kingdom (Sigalas) Northern Deanery, Newcastle upon Tyne, United Kingdom
Background: In the last decade, the use of atypical antipsychotics in children has increased. The use has been both licensed and 'off label', targeting different symptoms and clinical conditions. Most research around safety and efficacy has been conducted in adults with repeated calls for such research in children being in vain. Objectives: This survey aims to describe current prescribing practices in the 'real world' and to compare the results with existing research, to evaluate the lessons learnt. Methods: The survey consisted of a semi-structured questionnaire that aimed to evaluate the current practices of CAMHS prescribers. The 31 questionnaires sent out yielded 24 completed returns (77.41%). A literature search yielded articles that described prescribing trends over the last decade. Survey results were compared with the literature. Findings: The commonest indication for atypicals
was psychosis (75%). Others included behavioral control (50%), tics (37.5%), attention deficit hyperactivity disorder (ADHD) and anxiety. Atypicals were the commonest first-line medications for behavioural control, with Risperidone (54%) being the preferred agent. Secondline medications included Quetiapine (7%) and Olanzapine (15%). Doses were lower for behavioral control and the atypicals were trialled for up to 8 weeks with duration of treatment extending to 9 months. The most common target symptoms were aggression (85%), agitation (54%) and anxiety (54%), when used for nonpsychotic presentations. Most prescribers cited peer/ expert opinion and own clinical experience as the evidence base for their use. Conclusions: Atypicals continue to be used as first-line medications for psychotic and non-psychotic behavioural presentations, in spite of the absence of clear evidence and repeated calls for in depth research in this population.

Publication Types: Conference Abstract

PMID:71565470


**Sodium-glucose co-transporter inhibitors.**

Davis T.
(Davis) School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, WA, Australia

Inhibition of the sodium-glucose co-transporter 2 in the kidney lowers blood glucose by increasing glucose excretion in the urine. The associated osmotic diuresis and urinary loss of sodium reduces blood pressure. Canagliflozin and dapagliflozin are sodium-glucose co-transporter 2 inhibitors that have been studied as monotherapy and in combination with other drugs for type 2 diabetes. They reduce concentrations of glycated haemoglobin by 6-9 mmol/mol (0.5-0.8%) more than placebo. Patients may lose 2-3 kg during treatment. Hypoglycaemia is more likely to occur if a sodium-glucose co-transporter 2 inhibitor is used in combination with other drugs that lower blood glucose. Low density lipoprotein cholesterol increases during treatment. Glycosuria increases the risk of genitourinary infections. Increased calcium excretion could potentially reduce bone density. Long-term studies are investigating the cardiovascular safety of these drugs. These studies could also yield data about a possible increased risk of malignancy.

PMID:2014094632


**First report of the stapled mesh stoma reinforcement technique (SMART) in a urologic context.**

Chang D, Thyer I, et al.
(Chang, Thyer, Larkin, Wallace, Hayne) Fremantle Hospital, WA, Australia (Wallace, Hayne)
University of Western Australia, WA, Australia
D. Chang, Fremantle Hospital, WA, Australia

Introduction: Parastomal hernia is a common significant complication of ileal conduit formation. High recurrence rates even after traditional surgical repair are reported. Newer techniques of enforcing the stoma trephine with mesh have been shown to significantly reduce the rate of parastomal herniation but can be timeconsuming. The stapled mesh stoma reinforcement technique (SMART) is a novel and quick method of constructing a reinforced stapled trephine. We report the first case utilizing this technique in a urologic context. Methods: A 59 year old lady with an ileal conduit and history of previous parastomal hernia repair presented with increasingly severe parastomal pain, obstruction of the ileal conduit and features of early small bowel obstruction. A midline laparotomy and adhesiolysis was performed. The ileal conduit was dissected free and mobilised, the parastomal hernia reduced and the hernial sac mobilised and the defect repaired. A new stoma aperture on the left side of the abdomen was fashioned; a cylinder of skin and fat was excised, and a cruciate incision was made on the anterior rectus sheath. A 25 mm CS CompactEA circular stapler was used to secure
a ProLite Ultramesh to the staple line on the posterior rectus sheath. The anvil of the stapler was placed in the abdominal cavity and the shaft of the anvil grasped and delivered through the posterior rectus sheath. The stapler trocar was engaged with the anvil shaft and the stapler fired, leaving behind a reinforced stapled trephine consisting of the mesh, posterior rectus sheath and peritoneum. The mesh circumference was secured to the anterior sheath and the ileal conduit passed through the reinforced stoma trephine. A standard stoma appliance was applied. Results: There were no perioperative complications and the re-sited stoma remained healthy and functioned normally. Conclusions: We report the first utilization of the SMART technique in a urologic context. Favorable results with medium term follow-up (reported out to 7 years) with the device in the general surgical context may be applicable to urology. Longer term data is clearly desirable though this technique deserves consideration in the treatment of urologic para-stomal herniae.

Publication Types: Conference Abstract
PMID:71408714

**Successful implementation of a penile rehabilitation program in an Australian public hospital.**
Katz DJ, Thyer I, et al.
(Katz, Thyer, Hayne) Fremantle Hospital, Fremantle, Australia (Katz) Men's Health Melbourne, Melbourne, Australia (Hayne) School of Surgery, University of Western Australia, Perth, Australia
D.J. Katz, Fremantle Hospital, Fremantle, Australia
Introduction: Numerous consensus guidelines recommend penile rehabilitation (PR) after radical prostatectomy. However, implementation of such a program in an Australian public hospital system is challenging because of resource limitations and financial constraints. The aim of this study was to identify the key steps needed to successfully implement a comprehensive PR program in an Australian public hospital. Materials and Methods: From February 2013, we undertook a step-wise consultative approach to determine the processes needed to initiate a PR program. The key steps identified were: 1. Assessing the baseline knowledge of PR amongst staff of the urology unit. 2. Presenting data to staff on the evidence for PR. 3. Identifying resources available within and external to the public hospital network. 4. Designing a PR program based on available resources. 5. Gaining financial support for a PR program. 6. Results: Based on our systematic approach to implementation of a PR program we identified that: * Few staff members knew the rationale or evidence behind PR. * A formal presentation of evidence to key stakeholders - urologists, nursing staff and pharmacy was crucial to gain support. * Financial assistance for the program, especially for regular PDE5I prescriptions, was essential. * Nursing support is critical for ongoing follow-up. * Teaching of, and supporting an intracavernosal injection protocol is difficult in a public hospital framework. * Outsourcing and public private partnerships can overcome public resource limitations. * Publicising the PR program is important for recruitment. Conclusions: Successful implementation of a PR program in an Australian public hospital is possible. Undertaking a step-wise consultative process is important. There are several key components that need to be worked through such as identifying public and private resources, gaining financial support and facilitating nurse led clinics.
Publication Types: Conference Abstract
PMID:71408605

**The urological sequelae of previous radiotherapy: A 5-year study of admissions and interventions at Fremantle Hospital.**
McCombie S, Lim AL, et al.
(McCombie, Lim, McMillan, Hayne) Fremantle Hospital, Fremantle, Australia
S. McCombie, Fremantle Hospital, Fremantle, Australia
Introduction: Radiotherapy is a common treatment for several pelvic malignancies, which carries a significant risk of urological complications. Evidence on the extent of the burden of these sequelae on
urology departments is largely anecdotal. A retrospective audit was therefore conducted to evaluate the impact radiotherapy-related complications have on an inpatient urology service. Patients and Methods: All patients who attended Fremantle Hospital between 2007 and 2011 for urological reasons directly attributable to previous radiotherapy were identified retrospectively from hospital records; their notes and electronic records were reviewed. No patients were excluded from the study. Departmental records for the same period were analysed and compared. Results: Thirty-three patients were identified; the majority (79%) of these had received radiotherapy for prostate cancer, with the remaining patients having had bladder (9%), cervical (6%) or colorectal (6%) cancer. The majority of patients (79%) underwent radiotherapy after 1999. Twenty-five patients were treated for radiation cystitis, 16 were treated for stricture disease, and 1 was treated for a recto-vesical fistula. For patients with radiation cystitis, 9 patients required a total of 223 sessions of hyperbaric oxygen therapy; 95 units of blood were transfused. Ninety-six individual admissions were identified, with a total length of stay of 402 days; this represents 2.6% of all urology bed days over the 5-year period. Average length of stay was 4.2 days in the studied population, as compared with 2.3 days for the department as a whole. Reasons for admission were for elective procedures (49%), haematuria (32%), sepsis (10%) and retention (8%). Eighty-two per cent of patients required at least one operation to treat their complication. Sixty-six procedures were conducted during these admissions, the majority of which (71%) were cystoscopic procedures. Additional procedures of note included 3 cystectomies, 2 laparotomies, 2 embolisations, a urethral ligation, and an internal iliac artery ligation. Conclusions: Approximately 3% of urology bed days are used in the treatment of complications of radiotherapy. Patients with complications of radiotherapy have a longer average length of stay, and are very likely to require operative intervention. Radiation cystitis and stricture disease are the commonest urological complications encountered. In a urology department with 1300 admissions per annum, approximately 1 procedure was carried out per month for radiotherapy-induced complications. Publication Types: Conference Abstract PMID:71408680


The 'one stop' prostate clinic: A report on Fremantle Hospital's first 200 patients.

McCombie S, Logan C, et al. (McCombie, Logan, Hawks, Ling Ooi, Hayne) Fremantle Hospital, Fremantle, Australia

S. McCombie, Fremantle Hospital, Fremantle, Australia

Introduction: Men living in remote areas of Australia suffer from reduced access to specialist urological services; poorer prostate cancer outcomes have been demonstrated in this group. Fremantle Hospital has developed a rapid-access 'One Stop' Prostate Clinic targeted at patients living in rural and regional Western Australia in an attempt to address this problem. Data on our first 200 patients was collected prospectively to assess the efficacy of this model for assessing patients suspected of having prostate cancer. Patients and Methods: The 'One Stop' Prostate Clinic is a fortnightly clinic that allows the initial consultation and prostate biopsies to occur on a single visit. Biopsy results are then delivered telephonically if appropriate, and further follow-up is arranged only if required. Data was collected prospectively on the first 200 patients to access this clinic, between June 2011 and June 2013. No patients were excluded. Additionally, patient satisfaction was assessed and a cost analysis was performed. Results: Sixty-eight per cent of patients were from rural or remote areas and 32% were from metropolitan areas. Mean age was 64 (range 38-86) and mean PSA was 7 mu g/L (range 0-250 mu g/L). Ninety-three per cent of patients underwent biopsies, and 100 new prostate cancer diagnoses were made; 35 patients had Gleason 6, 46 patients had Gleason 7, and 19 patients had Gleason 8-10 disease. An additional 51 patients had prostatic intraepithelial neoplasia (PIN) or atypical small acinar proliferation (ASAP). Forty-four patients subsequently underwent radical prostatectomy, 21 underwent radiotherapy, and 34 were commenced on active surveillance. Forty-eight patients required no further follow-up. A 2% complication rate was noted: 3 patients required admission for urosepsis (2) or haematuria (1), and 1 patient had a UTI treated by their GP. All patients asked (62) rated the service as good. The clinic saved 135 patient assisted transport scheme (PATS)
return visits and 85 Fremantle Hospital outpatient appointments, resulting in estimated savings of at least $70,000. Conclusions: A rapid-access 'One Stop' Prostate Clinic is an effective and cost-effective model for assessing men suspected of having prostate cancer, particularly those living in rural or remote areas. A high incidence of prostate cancer was noted amongst patients presenting to this clinic.

Publication Types: Conference Abstract
PMID:71408577

The conservative management of renal trauma: A literature review and clinical guideline.
McCombie S, Thyer I, et al.
(McCombie, Thyer, Wallace, Kuan, Dyer, Roux, Hayne) Fremantle Hospital, Fremantle, Australia
(Rao) Royal Perth Hospital, Perth, Australia (Rowling) Sir Charles Gairdner Hospital, Nedlands, Australia
S. McCombie, Fremantle Hospital, Fremantle, Australia
Introduction: Over the last 50 years there has been a paradigm shift towards managing increasingly severe renal trauma conservatively. This is because a nonoperative approach has been shown to reduce nephrectomy rate, complications, and hospital stay. However, whilst several studies have shown a conservative approach to be successful, there is little guidance as to what this conservative approach should entail. As such there seems to be a wide variation in practice regarding several aspects of the conservative management of renal trauma. In an attempt to standardize this a literature review was performed, and consensus recommendations are made by a multi-disciplinary panel of experienced clinicians. Patients and Methods: A literature review was conducted utilizing Medline, Embase, and AustHealth; relevant articles published between 1980 and 2012 were examined. Based on this literature review and collective experience, recommendations were constructed by a multi-disciplinary panel of experienced clinicians including urologists, trauma surgeons, radiologists, and infectious disease physicians. These recommendations were subsequently modified following a formal review and debate at the Western Australian USANZ 2013 state conference, to represent a consensus of expert opinion. Renal trauma is classified according to the American Association for the Surgery of Trauma (AAST) kidney injury severity scale. Recommendations are graded using the European Association of Urology (EAU) grading scale. Results: Consensus recommendations were reached regarding five key aspects of the conservative management of renal trauma. These were: 1. Initial monitoring, thromboprophylaxis, bed rest, and discharge criteria 2. Antibiotics 3. Imaging 4. Follow-up 5. Advice on return to activity The recommendations will be presented in full at the conference. Conclusions: Consensus recommendations were reached based on best available evidence and a consensus of opinion amongst experienced clinicians. These recommendations may help standardize the conservative management of renal trauma.
Publication Types: Conference Abstract
PMID:71408679

Safety, efficacy and flow properties of an arthroscopy pump giving set during flexible ureterorenoscopy.
Rukin NJ, Williams K, et al.
(Rukin, Williams, Wright) Royal Wolverhampton Hospital, Wolverhampton, United Kingdom (Rukin, Kuan) Fremantle Hospital, Perth, WA, Australia
N.J. Rukin, Royal Wolverhampton Hospital, Wolverhampton, United Kingdom
Introduction: Flexible ureterorenoscopy (URS) is commonly used in the management of intra-renal stones. Limitations include accessibility and vision, particularly when using a laser. We aim to determine the safety, efficacy and flow properties of a simple arthroscopy giving set with a built in hand held pump. We hypothesise this giving set offers good stone free rates (SFR), with improved
vision and irrigation flow without compromising patient morbidity. Patients and Methods: We examine a single surgeon’s prospective case series of flexible URS performed using the arthroscopy pump giving set. Data was collected for an 18-month period, during 2012-13. All cases were performed for upper urinary tract stones. Primary outcomes measures included: SFR, length of stay, urosepsis rates and complications. We quantify the increase in flow generated by the giving set on a laboratory based bench test model. We define the effect of flexible URS instrumentation (Optical Integrity ScopeSafe 200 mu m laser fibre and a Coloplast no-tip1.5F Nitinol basket) on pump flow characteristics. Flow tests were run five times to ensure accuracy. Statistical analysis was performed using One-way ANOVA (nonparametric) testing with GraphPad Prism. Results: 86 patients underwent flexible URS for upper tract stones. Mean stone size was 10 mm (2-31 mm). Overall SFR was 91.8%, with 3 patients (3.3%) requiring a second flexible URS procedure. With intra-renal stone < 15 mm the SFR was 94% and 80% for those > 15 mm. Median length of stay for flexible URS was 1 day (0-22 days). Two patients (2%) developed postoperative urosepsis, one required inotropes and renal supportive treatment. Other complications include: postoperative colic (2%), acute urinary retention (1%) and haematuria requiring readmission (1%). Significant improvements in flow properties were demonstrated with the pump system. Flow rates (mL/min) increased by 55-62% for standard flexible URS without instrumentation, 73-95% for a 200 mu m Integrity ScopeSafe laser fibre and 126-173% with a 1.5F Coloplast Nitinol basket in the scope (all significant P < 0.0001). Conclusions: By adopting an arthroscopy giving set with a built in pump we achieved good SFR. The rate of urosepsis was low, with no increased morbidity. Flow study tests demonstrate the device delivers a significant improvement in flow rates with instrumentation (200 mu m laser fibre or 1.5F Nitinol basket). This data supports the hypothesis that the giving set offers a safe and effective modality to help improve vision and achieve good SFR during flexible URS.

Publication Types: Conference Abstract
PMID:71408618

BMC Neurology. 2014; 14(1).

Physical activity and associated levels of disability and quality of life in people with multiple sclerosis: A large international survey.
Marck CH, Hadgkiss EJ, et al.
(Marck, Hadgkiss, Weiland, van der Meer, Jelinek) Emergency Practice Innovation Centre, St Vincent's Hospital Melbourne, PO Box 2900, Fitzroy 3065, VIC, Australia (Weiland) Department of Medicine, The University of Melbourne (St Vincent's Hospital), Fitzroy, VIC, Australia (Pereira) Faculty of Medicine, Notre Dame University, Fremantle, WA, Australia (Jelinek) Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC, Australia
C.H. Marck, Emergency Practice Innovation Centre, St Vincent's Hospital Melbourne, PO Box 2900, Fitzroy 3065, VIC, Australia. E-mail: claudia.marck@svhm.org.au

Background: Multiple Sclerosis (MS) is a common neurodegenerative disease, which often has a devastating effect on physical and emotional wellbeing of people with MS (PwMS). Several studies have shown positive effects of physical activity (PA) on disability, health related quality of life (HRQOL), and other outcomes. However, many studies include only people with mild disability making it difficult to generalize findings to those with moderate or severe disability. This study investigated the associations between PA and HRQOL, relapse rate (RR), disability, and demographic variables in PwMS with varying disability.

Methods: Through online platforms this large international survey recruited 2232 participants with MS who completed items regarding PA, MS and other health characteristics. Results: PwMS who were younger (p < .001), male (p = 0.006), and with lower body mass index (BMI) (p < .001) undertook more PA, which was associated with decreased disability (p < 0.001) and increased HRQOL measures (all p < 0.001). For the subsample of people with relapsing-remitting MS, PA was associated with a decreased RR (p = 0.009). Regression analyses showed that increased PA predicted clinically significant improvements in HRQOL while controlling for level of disability, age and gender. More specifically, increasing from low to moderate and to high PA increased estimated mean physical health composite from 47.7 to 56.0 to 59.9 respectively (25.6%
change), mental health composite from 60.6 to 67.0 to 68.8 (13.5% change), energy subscale from 35.9 to 44.5 to 49.8 (38.7% change), social function subscale from 57.8 to 66.1 to 68.4 (18.3% change), and overall QOL subscale from 58.5 to 64.5 to 67.7 (15.7% change). Conclusions: For PwMS, regardless of disability level, increased PA is related to better HRQOL in terms of energy, social functioning, mental and physical health. These are important findings that should be taken into consideration by clinicians treating PwMS. 2014 Marck et al.; licensee BioMed Central Ltd. PMID:2014502058

BMJ Open. 2014; 4(3).
Protocol for the ProCare Trial: A phase II randomised controlled trial of shared care for follow-up of men with prostate cancer.
Emery J, Doorey J, et al.
(Emery, Pirotta) General Practice and Primary Health Care Academic Centre, University of Melbourne, Carlton, VIC, Australia (Emery, Doorey) Department of General Practice, School of Primary, Aboriginal and Rural Health Care, University of Western Australia, Perth, WA, Australia (Jefford) Department of Medical Oncology, Peter MacCallum Cancer Centre, East Melbourne, VIC, Australia (King) Psycho-oncology Co-operative Research Group (PoCoG), School of Psychology, University of Sydney, Sydney, NSW, Australia (Hayne) School of Surgery, University of Western Australia, WA, Australia (Hawkes) Urology Department, Fremantle Hospital, Fremantle, WA, Australia (Martin) NHMRC Clinical Trials Centre, Sydney Medical School, University of Sydney, Sydney, NSW, Australia (Trevena) School of Public Health, University of Sydney, Sydney, NSW, Australia (Lim) Genesis Cancer Care, Royal Perth Hospital, Perth, WA, Australia (Constable) Prostate Cancer Foundation of Australia, Perth, WA, Australia (Hyatt, Schofield) Department of Cancer Experiences Research, Peter MacCallum Cancer Centre, East Melbourne, VIC, Australia (Hamid) Urology Department, Royal Perth Hospital, Perth, WA, Australia (Violet, Gill) Department of Radiation Oncology, Peter MacCallum Cancer Centre, East Melbourne, VIC, Australia (Frydenberg) Department of Surgery, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, VIC, Australia
J. Emery, General Practice and Primary Health Care Academic Centre, University of Melbourne, Carlton, VIC, Australia. E-mail: jon.emery@unimelb.edu.au

Introduction: Men with prostate cancer require long-term follow-up to monitor disease progression and manage common adverse physical and psychosocial consequences of treatment. There is growing recognition of the potential role of primary care in cancer follow-up. This paper describes the protocol for a phase II multisite randomised controlled trial of a novel model of shared care for the follow-up of men after completing treatment for low-moderate risk prostate cancer. Methods and analysis: The intervention is a shared care model of follow-up visits in the first 12 months after completing treatment for prostate cancer with the following specific components: a survivorship care plan, general practitioner (GP) management guidelines, register and recall systems, screening for distress and unmet needs and patient information resources. Eligible men will have completed surgery and/or radiotherapy for low-moderate risk prostate cancer within the previous 8 weeks and have a GP who consents to participate. Ninety men will be randomised to the intervention or current hospital follow-up care. Study outcome measures will be collected at baseline, 3, 6 and 12 months and include anxiety, depression, unmet needs, prostate cancer-specific quality of life and satisfaction with care. Clinical processes and healthcare resource usage will also be measured. The principal emphasis of the analysis will be on obtaining estimates of the treatment effect size and assessing feasibility in order to inform the design of a subsequent phase III trial. Ethics and dissemination: Ethics approval has been granted by the University of Western Australia and from all hospital recruitment sites in Western Australia and Victoria. Results: of this phase II trial will be reported in peer-reviewed publications and in conference presentations. Trial Registration: Australian New Zealand Clinical Trial Registry ACTRN12610000938000. PMID:2014238355
A stepped-wedge cluster randomised controlled trial for evaluating rates of falls among inpatients in aged care rehabilitation units receiving tailored multimedia education in addition to usual care: A trial protocol.

Hill AM, Waldron N, et al.

(Hill) School of Physiotherapy, University of Notre Dame Australia, Fremantle, WA, Australia (Waldron) Department of Rehabilitation and Aged Care, Armadale Kelmscott Memorial Hospital, Perth, WA, Australia (McPhail) Health Strategy and Networks, Strategic System, Policy and Planning, Department of Health, Government of Western Australia, Perth, WA, Australia (Etherton-Beer) School of Medicine and Pharmacology, WA Centre for Health and Ageing, University of Western Australia, Perth, WA, Australia (Ingram) Department of Rehabilitation and Aged Care, Sir Charles Gairdner Hospital, Perth, WA, Australia (Haines) Allied Health Research Unit, Monash Health, Cheltenham, VIC, Australia

Introduction: Falls are the most frequent adverse event reported in hospitals. Approximately 30% of in-hospital falls lead to an injury and up to 2% result in a fracture. A large randomised trial found that a trained health professional providing individualised falls prevention education to older inpatients reduced falls in a cognitively intact subgroup. This study aims to investigate whether this efficacious intervention can reduce falls and be clinically useful and cost-effective when delivered in the real-life clinical environment. Methods: A stepped-wedge cluster randomised trial will be used across eight subacute units (clusters) which will be randomised to one of four dates to start the intervention. Usual care on these units includes patient's screening, assessment and implementation of individualised falls prevention strategies, ongoing staff training and environmental strategies. Patients with better levels of cognition (Mini-Mental State Examination >23/30) will receive the individualised education from a trained health professional in addition to usual care while patient's feedback received during education sessions will be provided to unit staff. Unit staff will receive training to assist in intervention delivery and to enhance uptake of strategies by patients. Falls data will be collected by two methods: case note audit by research assistants and the hospital falls reporting system. Cluster-level data including patient's admissions, length of stay and diagnosis will be collected from hospital systems. Data will be analysed allowing for correlation of outcomes (clustering) within units. An economic analysis will be undertaken which includes an incremental cost-effectiveness analysis. Ethics and dissemination: The study was approved by The University of Notre Dame Australia Human Research Ethics Committee and local hospital ethics committees. Results: The results will be disseminated through local site networks, and future funding and delivery of falls prevention programmes within WA Health will be informed. Results will also be disseminated through peer-reviewed publications and medical conferences.

PMID:2014061348


Procedural sedation: it is not what you do, it is how you do it.

Lamb AR, Harper M.

Fremantle, Western Australia.

PMID:24771785


Exploring the link between pholcodine exposure and neuromuscular blocking agent
anaphylaxis.
Brusch AM, Clarke RC, et al. Department of Clinical Immunology, Fremantle Hospital, Fremantle, WA, Australia; Sir Charles Gairdner Hospital, Perth, WA, Australia.
Neuromuscular blocking agents (NMBAs) are the most commonly implicated drugs in IgE-mediated anaphylaxis during anaesthesia that can lead to perioperative morbidity and mortality. The rate of NMBAA anaphylaxis shows marked geographical variation in patients who have had no known prior exposure to NMBAs, suggesting that there may be external or environmental factors that contribute to the underlying aetiology and pathophysiology of reactions. Substituted ammonium ions are shared among NMBAs and are therefore thought to be the main allergenic determinant of this class of drugs. Substituted ammonium ions are found in a wide variety of chemical structures, including prescription medications, over-the-counter medications and common household chemicals, such as the quaternary ammonium disinfectants. Epidemiological studies have shown parallels in the consumption of pholcodine, a nonprescription antitussive drug which contains a tertiary ammonium ion, and the incidence of NMBAA anaphylaxis. This link has prompted the withdrawal of pholcodine in some countries, with an ensuing fall in the observed rate of NMBAA anaphylaxis. While such observations are compelling in their suggestion of a relationship between pholcodine exposure and NMBAA hypersensitivity, important questions remain regarding the mechanisms by which pholcodine is able to sensitize against NMBAs and whether there are other, as yet unidentified, agents that can elicit similar hypersensitivity reactions. This review aims to explore the evidence linking pholcodine exposure to NMBAA hypersensitivity and discuss the implications for our understanding of the pathophysiology of these reactions. 2013 The British Pharmacological Society.
PMID:24251966

Personalized dosimetry of 131I-rituximab radioimmunotherapy of non-hodgkin lymphoma defined by pharmacokinetics in bone marrow and blood.
Boucek JA, Turner JH. (Boucek, Turner) Department of Nuclear Medicine, University of Western Australia, Fremantle Hospital, Alma Street, Fremantle 6160, Australia
J.H. Turner, Department of Nuclear Medicine, University of Western Australia, Fremantle Hospital, Alma Street, Fremantle 6160, Australia. E-mail: harvey.turner@health.wa.gov.au
Purpose: To report a comparison of SPECT/CT technique with standard blood-based dosimetry methodology in a cohort of non-Hodgkin lymphoma (NHL) patients treated with <sup>131</sup>I-rituximab anti-CD20 chimeric monoclonal antibody. Methodology: Red marrow uptake was measured directly using serial quantitative whole-body imaging in conjunction with SPECT/CT in a cohort of 23 patients undergoing routine <sup>131</sup>I-rituximab radioimmunotherapy of NHL. Absorbed dose measurements were then compared with radiation doses calculated using standard peripheral blood counting methodology. Results: Activity clearance from whole body of 88.7 hours measured by imaging <sup>131</sup>I-rituximab was significantly slower (p<0.001) than the mean effective half-life clearance of 60.8 hours calculated from the sampling peripheral blood. The mean activity concentrations in bone marrow measured using SPECT/CT, and by blood sampling, extrapolated to the time of administration, were, however, concordant. The absorbed self-dose in red marrow, measured using imaging, was 1.02 Gy compared with the dose (0.81 Gy) calculated from blood sampling. Neutrophil toxicity correlated with absorbed dose by SPECT/CT imaging (p=0.01), whereas the blood sampling method demonstrated no correlation with any parameters of hematological toxicity. Conclusion: Radiation dose to red marrow from <sup>131</sup>I-rituximab is inherently underestimated by standard indirect peripheral blood counting methods. Personalized marrow dosimetry by quantitative gamma imaging more accurately predicts of hemopoietic myelotoxicity by direct measurement of the bone marrow activity concentration of <sup>131</sup>I-rituximab. 2014 Mary Ann Liebert, Inc.
PMID:2013801764
Regions of high wall stress can predict the future location of rupture of abdominal aortic aneurysm.

Doyle BJ, McGloughlin TM, et al. (Doyle, Miller) Intelligent Systems for Medicine Laboratory, School of Mechanical and Chemical Engineering, University of Western Australia, 35 Stirling Highway, Perth, WA, Australia (Doyle) Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, United Kingdom (McGloughlin) Department of Mechanical, Aeronautical and Biomedical Engineering, Materials and Surface Science Institute, University of Limerick, Limerick, Ireland (Miller) Institute of Mechanics and Advanced Materials, School of Engineering, Cardiff University, Cardiff, United Kingdom (Powell) Vascular Surgery Research Group, Imperial College, Charing Cross Campus, London, United Kingdom (Norman) School of Surgery, Fremantle Hospital, University of Western Australia, Fremantle, WA, Australia

B.J. Doyle, Intelligent Systems for Medicine Laboratory, School of Mechanical and Chemical Engineering, University of Western Australia, 35 Stirling Highway, Perth, WA, Australia. E-mail: barry.doyle@uwa.edu.au

Predicting the wall stress in abdominal aortic aneurysm (AAA) using computational modeling may be a useful adjunct to traditional clinical parameters that indicate the risk of rupture. Maximum diameter has been shown to have many limitations, and using current technology it is possible to provide a patient-specific computational risk assessment using routinely acquired medical images. We present a case of AAA rupture where the exact rupture point was clearly visible on the computed tomography (CT) images. A blind computational study based on CT scans acquired 4 months earlier predicted elevated wall stresses in the same region that later experienced rupture. 2014 Springer Science+Business Media and the Cardiovascular and Interventional Radiological Society of Europe (CIRSE).

PMID:2014371972

A case of pulmonary hemorrhage due to drug-induced pneumonitis secondary to ticagrelor therapy.

Whitmore TJ, O'Shea JP, et al. (Whitmore) Respiratory Medicine Department, United Kingdom (Edwards) Department of Cardithoracic Surgery, Royal Perth Hospital, Perth, WA, Australia (O'Shea) Department of Cardiovascular Medicine, Fremantle Hospital, Fremantle, WA, Australia (Starac) Western Diagnostic Pathology, Myaree, WA, Australia (Waterer) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia

T.J. Whitmore, Respiratory Medicine Department, United Kingdom. E-mail: timothy.whitmore@health.wa.gov.au

We report a case of significant pulmonary hemorrhage developing shortly after commencing ticagrelor and aspirin therapy and requiring coronary artery bypass grafting to safely cease the antiplatelet therapy. Lung biopsy findings were consistent with druginduced lung injury. Clinicians should be aware of this significant adverse event with this drug class. 2014 American College of Chest Physicians.

PMID:2014174625

Cranial nerve assessment: A concise guide to clinical examination.

Damodaran O, Rizk E, et al. (Damodaran) Department of Neurosurgery, Liverpool Hospital, Sydney, NSW 2170, Australia (Rizk) Penn State University Hershey Medical Center, Department of Neurosurgery Hershey, PA, United States (Rodriguez) Department of Clinical Neurophysiology, Fremantle Hospital, Perth, WA, Australia (Lee) Interhospital Neurosurgical Service, Sir Charles Gairdner Hospital, Perth, Australia (Lee)

Examination of the cranial nerves is an integral and important part of a complete neurological examination. Historically, these skills were crucial for diagnosing specific lesions. With the development of modern imaging modalities, the significance of clinical examination techniques has perhaps been undermined. The authors present an overview of each cranial nerve with a concise summary of examination techniques. Clin. Anat. 27:25-30, 2014. 2013 Wiley Periodicals, Inc. Copyright 2013 Wiley Periodicals, Inc.

Differential associations of testosterone, dihydrotestosterone and oestradiol with physical, metabolic and health-related factors in community-dwelling men aged 17-97 years from the Busselton Health Survey.
Yeap BB, Knuiman MW, et al.
PMID:24428256

Effect of continuous positive airway pressure therapy on sexual function and serum testosterone in males with type 2 diabetes and obstructive sleep apnoea.
School of Medicine and Pharmacology, University of Western Australia, Fremantle, WA, Australia.
OBJECTIVE: There have been no studies of the effect of continuous positive airway pressure (CPAP) therapy on erectile dysfunction (ED) and serum testosterone in men with type 2 diabetes and obstructive sleep apnoea (OSA), a patient group at increased risk of ED and hypogonadism. The aim of this study was to determine whether CPAP improves sexual and gonadal function in males with type 2 diabetes and a pre-CPAP apnoea-hypopnoea index >15/h.
DESIGN: Substudy of a trial assessing the effect of 3 months of CPAP on cardiovascular risk in type 2 diabetes.
PATIENTS: Of 35 males starting CPAP, 27 (mean ± SD age 654 ± 96 years, median [interquartile range] diabetes duration 121 [52-153] years) completed the trial.
MEASUREMENTS: Serum total and free testosterone, responses to the Androgen Deficiency in the Aale (ADAM) and Sexual Health Inventory for Men (SHIM) questionnaires.
RESULTS: There were no significant changes in mean total or free testosterone (baseline concentrations 127 ± 45 nm and 026 ± 007 pm, respectively), or SHIM score (baseline 13 [5-17]), after 3 months of CPAP (P > 020). The ADAM score (baseline 62 ± 21) fell after 1 month (to 50 ± 26) and was maintained at this level at 3 months (P = 0015). The Epworth Sleepiness Scale score decreased and self-reported physical activity increased over 3 months (P < 0017) without a change in body mass index (P = 100).
CONCLUSIONS: These findings imply that CPAP therapy improves somnolence and promotes exercise in men with type 2 diabetes, but that there is no direct benefit for gonadal or sexual function.
2014 John Wiley & Sons Ltd.
PMID:24392703

Factors that affect serum levels of ferritin in australian adults and implications for follow-up.
McKinnon EJ, Rossi E, et al.
(McKinnon, Olynkyk) Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, WA, Australia (Rossi, Beilby) PathWest, Perth, WA, Australia (Beilby) School of Pathology and
Laboratory Medicine, University of Western Australia, Nedlands, WA, Australia (Trinder) School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia, Fremantle, WA, Australia (Trinder) Western Australian Institute of Medical Research, Perth, WA, Australia (Olynyk) Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia (Olynyk) Curtin Health Innovation Research Institute, Curtin University, Bentley, WA, Australia

J.K. Olynyk, Department of Gastroenterology, Fremantle Hospital, PO Box 480, Fremantle, WA 6959, Australia. E-mail: john.olynyk@health.wa.gov.au

Background & Aims: Serum levels of ferritin are commonly measured to assess iron stores but are affected by factors such as obesity and chronic disease. Published reference ranges have not changed in decades, and the number of patients whose levels exceed the upper limits has been increasing. As a result, more patients are evaluated for iron overload. Methods: We compared serum levels of ferritin in 1188 Australian adults who participated in the 2005 Busselton Population Survey with levels from the 1995 survey. Parametric regression was used to assess the effects of body weight and biochemical parameters on serum level of ferritin to derive contemporary population-appropriate reference ranges. Results: In 2005, age-adjusted levels of ferritin were 21% higher in men (P < .0001) and 10% higher in women (P=.01) than in 1995; 31% of men exceeded levels of 300 mug/L, compared with 23% in 1995. Body mass index (BMI) >25 kg/m² was associated with higher levels of ferritin in men >35 years old and in postmenopausal women (P < .002). Serum level of -glutamyltransferase (GGT) correlated with serum level of ferritin (P < .0001). In men, the estimated 95th percentiles ranged from 353 to 495 mug/L (<35 years), from 350 to 511 mug/L (>35 years, BMI <25 kg/m²), and from 413 to 696 mug/L (>35 years, BMI >25 kg/m²) when GGT levels were 10-75 IU/L. In women, the 95th percentiles ranged from 106 to 235 mug/L (premenopausal), from 222 to 323 mug/L (postmenopausal, BMI <25 kg/m²), and from 249 to 422 mug/L (postmenopausal, BMI >25 kg/m²) when GGT levels were 8-45 IU/L. Conclusion: Serum levels of ferritin increased significantly between 1995 and 2005. Reference ranges that accommodate demographic and biomedical variations will assist clinicians in identifying individuals who require further evaluation for iron overload. 2014 AGA Institute.

PMID:2013789917


Acute kidney injury due to decompression illness.

Viecelli A, Jamboti J, et al.

(Viecelli, Jamboti, Ferrari) Department of Nephrology, Fremantle Hospital, Perth, WA, Australia (Jamboti, Ferrari) School of Medicine and Pharmacology, University of Western Australia, Perth, WA, Australia (Waring, Banham) Department of Diving and Hyperbaric Medicine, Fremantle Hospital, Perth, WA, Australia

P. Ferrari, Department of Nephrology, Fremantle Hospital, Perth, WA, Australia. E-mail: paolo.ferrari@health.wa.gov.au

Decompression illness is a rare but serious complication of diving caused by intravascular or extravascular gas bubble formation. We report the first case of acute kidney injury in a 27-year-old diver following three rapid ascents. He presented with transient neurological symptoms and abdominal pain followed by rapidly progressive acute kidney injury (creatinine peak 1210 mumol/L) due to arterial air emboli. He received supportive care and 100% oxygen followed by hyperbaric therapy and recovered fully. Arterial air emboli caused by rapid decompression can affect multiple organs including the kidneys. Early transfer to a hyperbaric unit is important as complications may present delayed.

2014 The Author.

PMID:2014513654


Continuous veno-venous hemofiltration to adjust fluid volume excess in septic shock patients reduces intra-abdominal pressure.
Dabrowski W, Kotlinska-Hasiec E, et al.
(Dabrowski, Kotlinska-Hasiec, Rzecki) Department of Anesthesiology and Intensive Therapy, Medical University of Lublin, Lublin, Poland (Schneditz) Institute of Physiology, Medical University of Graz, Graz, Austria (Zaluska) Department of Nephrology, Medical University of Lublin, Lublin, Poland (De Keulenaer) Intensive Care Unit, Fremantle Hospital, Australia (Malbrain) Intensive Care Unit and High Care Burn Unit, Antwerp Hospital Network, ZNA Campus Stuivenberg/St-Erasmus, Antwerp, Belgium W. Dabrowski, Department of Anesthesiology and Intensive Therapy, Medical University of Lublin, Jaczewskiego 8, 20 - 954 Lublin, Poland. E-mail: w.dabrowski5@yahoo.com

Objective: To analyze the effect and the time course of continuous veno-venous hemofiltration (CVVH) with net ultrafiltration (UF) on intra-abdominal pressure (IAP) body fluid volumes in septic shock patients with acute kidney injury (AKI).

Methods: Patients were studied at baseline and after 6, 12, 24, 48, 72, and 96 hours of CVVH treatment. IAP was measured via the bladder, and abdominal perfusion pressure (APP) was calculated as mean arterial pressure minus IAP. Fluid volume excess (VE), total body water (TBW), extracellular body water (ECW), and intracellular body water (ICW) were derived from wholebody bioimpedance analysis (BIA).

Results: 30 patients entered final analysis, of which 6 died during CVVH (non-survivors). Fluid VE, TBW, ECW, ICW, and IAP significantly decreased in the 24 survivors, whereas these variables remained essentially unchanged in non-survivors. APP slowly increased in survivors, while it did not change in non-survivors. IAP strongly correlated with VE in survivors: The lower the IAP, the lower the fluid volume excess. Conclusion: CVVH with net UF successfully reduced IAP, TBW, ECW, and ICW in critically ill patients who survived 96 h of CVVH. Failure to increase APP was associated with fatal outcome, and, finally, IAP correlated with fluid volume excess. BIA could be helpful to monitor fluid status in patients with AKI. 2014 Dustri-Verlag Dr. K. Feistle.

PMID:2014462987

Critical Care. 2014; 18(2).

Calorie intake and patient outcomes in severe acute kidney injury: Findings from The Randomized Evaluation of Normal vs. Augmented Level of Replacement Therapy (RENAL) study trial.

(Bellomo) Department of Intensive Care, Austin Hospital, Studley Rd, Heidelberg, Melbourne, VIC 3084, Australia (Cass) Nephrology Division, The George Institute for International Health, Level 10, King George V Building, Missenden Road, Camperdown, Sydney, NSW 2050, Australia (Cole) Department of Intensive Care, Nepean Hospital, PO Box 63, Penrith, Sydney, NSW 2715, Australia (Finfer) Department of Intensive Care, Royal North Shore Hospital, Pacific Highway, St Leonards, Sydney, NSW 2065, Australia (Gallagher, Lee) Division of Nephrology, The George Institute for International Health, Level 10, King George V Building, Missenden Road, Camperdown, Sydney, NSW 2050, Australia (Lo) Division of Biostatistics, The George Institute for International Health, Level 10, King George V Building, Missenden Road, Camperdown, Sydney, NSW 2050, Australia (McGuinness) Department of Cardiotoracic and Vascular Intensive Care, Auckland City Hospital, Park Rd, Grafton 1142, Auckland, New Zealand (McGuinness) Department of Critical care Medicine, Auckland City Hospital, Park Rd, Grafton 1142, Auckland, New Zealand (Myburgh) Department of Intensive Care, St George Hospital, Gray Street, Kogarah, Sydney, NSW 2217, Australia (Norton) The George Institute for International Health, Level 10, King George V Building, Missenden Road, Camperdown, Sydney, NSW 2050, Australia (Scheinkestel) Department of Intensive Care, Alfred Hospital, Commercial Rd, Prahran, Melbourne, VIC 3181, Australia (Mitchell, Ashley, Gissane, Malchukova, Ranse) Canberra Hospital, Australian Capital Territory, Australia (Raza, Nand, Sara) Blacktown Hospital, New South Wales, Australia (Millis, Tan, Wong) Concord Hospital, New South Wales, Australia (Harrigan, Crowfoot, Hardie) John Hunter Hospital, New South Wales, Australia (Bhonagiri, Micallef) Liverpool Hospital, New South Wales, Australia (Brieva, Lintott) Mater Calvary Hospital, Newcastle, NSW, Australia (Gresham, Nikas, Weisbrodt) Nepean Hospital, New South Wales, Australia (Shehabi, Bass, Campbell, Stockdale) Prince of Wales Hospital, New South Wales, Australia (Ankers, O'Connor,
Introduction: Current practice in the delivery of caloric intake (DCI) in patients with severe acute kidney injury (AKI) receiving renal replacement therapy (RRT) is unknown. We aimed to describe calorie administration in patients enrolled in the Randomized Evaluation of Normal vs. Augmented Level of Replacement Therapy (RENAL) study and to assess the association between DCI and clinical outcomes.

Methods: We performed a secondary analysis in 1456 patients from the RENAL trial. We measured the dose and evolution of DCI during treatment and analyzed its association with major clinical outcomes using multivariable logistic regression, Cox proportional hazards models, and time adjusted models.

Results: Overall, mean DCI during treatment in ICU was low at only 10.9 + 9 Kcal/kg/day for non-survivors and 11 + 9 Kcal/kg/day for survivors. Among patients with a lower DCI (below the median) 334 of 729 (45.8%) had died at 90-days after randomization compared with 316 of 727 (43.3%) patients with a higher DCI (above the median) (P = 0.34). On multivariable logistic regression analysis, mean DCI carried an odds ratio of 0.95 (95% confidence interval (CI): 0.91-1.00; P = 0.06) per 100 Kcal increase for 90-day mortality. DCI was not associated with significant differences in renal replacement (RRT) free days, mechanical ventilation free days, ICU free days and hospital free days. These findings remained essentially unaltered after time adjusted analysis and Cox proportional hazards modeling.

Conclusions: In the RENAL study, mean DCI was low. Within the limits of such low caloric intake, greater DCI was not associated with improved clinical outcomes. 2014 Bellomo et al.; licensee BioMed Central Ltd.

PMID:2014230804
have attended a renal unit?
Research design and methods:
Fifty-seven citations were independently reviewed by four authors. The inclusion criteria were: (1) the article focused on information flow from nephrologists and/or specialists to general practitioners; (2) it includes the involvement of PCPs in nephrology, including registrars and PCPs with special interests or specialists in any medical field; (3) it was published from 1990 onwards (inclusive) and (4) the study was conducted in the United Kingdom, Canada, The Netherlands, Australia, United States or New Zealand. Selected articles were then reviewed by the fifth author as a measure of inter-rater reliability.
Results:
Eighteen papers in four categories were identified: six audits or observational studies, one meta-analysis; one randomized controlled trial; six qualitative studies; and four position statements or quality improvement tools. Published audits involving feedback to clinicians using validated tools demonstrate the scope for substantial improvement in the amount of information relayed to PCPs. Specialists may not prioritize the letter to the PCP but there is some evidence of a direct impact from limited or inadequate communication on patient outcomes. Only two studies focused on patients attending nephrology clinics.
Conclusions:
There is some evidence that improving the quality of letters from specialists to PCPs may benefit patient care. This review suggests a need for research on communication from nephrologists about patients who have received care at a renal unit regardless of whether or not the patient continues to attend.
PMID:24945721

Anesthesia and ventilation strategies in children with asthma: part I - preoperative assessment.
Regli A, von Ungern-Sternberg BS.
adDepartment of Intensive Care, Fremantle Hospital bSchool of Medicine and Pharmacology, The University of Western Australia cSchool of Medicine, The University of Notre Dame dDepartment of Anesthesia and Pain Management, Princess Margaret Hospital for Children, Perth, Western Australia, Australia.
PURPOSE OF REVIEW: Asthma is a common disease in the pediatric population, and anesthetists are increasingly confronted with asthmatic children undergoing elective surgery. This first of this two-part review provides a brief overview of the current knowledge on the underlying physiology and pathophysiology of asthma and focuses on the preoperative assessment and management in children with asthma. This also includes preoperative strategies to optimize lung function of asthmatic children undergoing surgery. The second part of this review focuses on the immediate perioperative anesthetic management including ventilation strategies.
RECENT FINDINGS: Multiple observational trials assessing perioperative respiratory adverse events in healthy and asthmatic children provide the basis for identifying risk factors in the patient's (family) history that aid the preoperative identification of at-risk children. Asthma treatment outside anesthesia is well founded on a large body of evidence. Optimization and to some extent intensifying asthma treatment can optimize lung function, reduce bronchial hyperreactivity, and minimize the risk of perioperative respiratory adverse events.
SUMMARY: To minimize the considerable risk of perioperative respiratory adverse events in asthmatic children, a good understanding of the underlying physiology is vital. Furthermore, a thorough preoperative assessment to identify children who may benefit of an intensified medical treatment thereby minimizing airflow obstruction and bronchial hyperreactivity is the first pillar of a preventive perioperative management of asthmatic children. The second pillar, an individually adjusted anesthesia management aiming to reduce perioperative adverse events, is discussed in the second part of this review.
PMID:24722006

**Anesthesia and ventilation strategies in children with asthma: part II - intraoperative management.**

Regli A, von Ungern-Sternberg BS.
daDepartment of Intensive Care, Fremantle Hospital bSchool of Medicine and Pharmacology, The University of Western Australia cSchool of Medicine, The University of Notre Dame dDepartment of Anesthesia and Pain Management, Princess Margaret Hospital for Children, Perth, Western Australia, Australia.

**PURPOSE OF REVIEW:** As asthma is a frequent disease especially in children, anesthetists are increasingly providing anesthesia for children requiring elective surgery with well controlled asthma but also for those requiring urgent surgery with poorly controlled or undiagnosed asthma. This second part of this two-part review details the medical and ventilatory management throughout the perioperative period in general but also includes the perioperative management of acute bronchospasm and asthma exacerbations in children with asthma.

**RECENT FINDINGS:** Multiple observational trials assessing perioperative respiratory adverse events in healthy and asthmatic children provide the basis for identifying risk reduction strategies. Mainly, animal experiments and to a small extent clinical data have advanced our understanding of how anesthetic agents effect bronchial smooth muscle tone and blunt reflex bronchoconstriction. Asthma treatment outside anesthesia is well founded on a large body of evidence. Perioperative prevention strategies have increasingly been studied. However, evidence on the perioperative management, including mechanical ventilation strategies of asthmatic children, is still only fair, and further research is required.

**SUMMARY:** To minimize the considerable risk of perioperative respiratory adverse events in asthmatic children, perioperative management should be based on two main pillars: the preoperative optimization of asthma treatment (please refer to the first part of this two-part review) and - the focus of this second part of this review - the optimization of anesthesia management in order to optimize lung function and minimize bronchial hyperreactivity in the perioperative period.

PMID:24686320


**The future of somatoform disorders: somatic symptom disorder, bodily distress disorder or functional syndromes?**

Rief W, Isaac M.
aClinical Psychology and Psychotherapy, University of Marburg, Germany bUniversity of Western Australia, Fremantle Hospital, Fremantle, WA 6160, Australia.

PMID:25023885


**Antecedents, consequences and interventions for workplace bullying.**

Kemp V.

(Kemp) School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle Hospital, Alma Street, Fremantle, WA 6160, Australia

V. Kemp, School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle Hospital, Alma Street, Fremantle, WA 6160, Australia. E-mail: vivien.kemp@uwa.edu.au

**PURPOSE OF REVIEW:** The issue of workplace bullying has become an area of research interest in the last 3 decades. Much of the extant literature is published in the business management journals. This is problematic as the targets of workplace bullying may need psychiatric treatment; as a discipline, therefore psychiatrists may benefit from a deeper understanding of the nature of workplace bullying and its sequelae. **RECENT FINDINGS:** There is still no agreed upon definition, although most definitions include similar criteria. Managers and human resources personnel frequently have difficulty identifying and effectively managing workplace bullying. The consequences for the targets of bullying
can be severe; they may need psychiatric treatment and it can have a lifelong impact. There is a paucity of research into effective prevention and intervention programs. Preventive measures that focus on the whole workplace culture or on targets alone have mixed results. Workplace policies and procedures may lessen the prevalence and incidence of bullying, but often competing interests of senior management, human resources personnel, supervisors and workers may mitigate any antibullying interventions. SUMMARY: Although psychiatrists are likely to treat the targets of bullying, bullying has yet to attract much attention as a research topic in psychiatry. Although the consequences of bullying can be severe for both targets and workplaces, prevention strategies are hampered by competing interests. 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins. Publication Types: Review PMID:2014521976

A review of the management of lymphangiomas.
Ha J, Yu YC, et al. (Ha, Lannigan) Princess Margaret Hospital, Roberts Road, Subiaco, WA 6008, Australia (Ha) Sir Charles Gairdner Hospital, Hospital Avenue, Nedlands, WA 6009, Australia (Ha) University of Western Australia, Australia (Yu) Fremantle Hospital, Alma Street, Fremantle, Australia J. Ha, Princess Margaret Hospital, Roberts Road, Subiaco, WA 6008, Australia. E-mail: jenha81@yahoo.com.au
Introduction: Lymphangioma is a rare benign cyst caused by congenital malformation of the lymphatic systems that often occurs in the cervicofacial region. There is no consensus on its management: Observation, aspiration, injection, cryotherapy, electrocautery, radiation, laser, ligation and excision. Methods: We performed a literature search with the keywords "cystic hygroma", "lymphangioma", "management", "OK 432" and "picibanil" from Medline, Embase and PubMed databases. Results: We present a review of the history, signs and symptoms, diagnosis, histology, classification and management options of cystic hygroma. Conclusion: There is no consensus on the treatment options. It should be individualised depending on the size of the lesion, anatomic localisation and complications. 2014 Bentham Science Publishers. PMID:2014528738

Nonlinear relationship between estimated glomerular filtration rate and mortality in type 2 diabetes: The fremantle diabetes study.
Davis TME, Bruce D, et al. (Davis, Bruce, Davis) FremantleAustralia T.M.E. Davis, FremantleAustralia
Previous studies in type 1 diabetes have shown a U-shaped relationship between estimated glomerular filtration rate (eGFR) and all-cause death. Patients with eGFR>120 and <60 mL/min had higher mortality than those with eGFR 60-120 mL/min. We examined whether this applies in type 2 diabetes by analyzing data from 1,296 Fremantle Diabetes Study patients (mean age 64.0+11.3 yrs, 48.6% males, median [IQR] diabetes duration 4.0 [1.0-9.0] yrs) recruited from 1993 to 1996 and followed until end-2012. During 12.9+6.1 (range 0-19.7) yrs of follow-up, 738 (56.9%) died. In a Cox proportional hazards model with age as timeline, independent predictors of death were male sex, Aboriginality, current smoking, prior ischemic heart disease, peripheral arterial disease, albuminuria, and systolic BP (inversely) (P<0.001), and retinopathy, diastolic BP, BMI, and exercise (inversely) (P<0.035). There was also a U-shaped relationship between eGFR and death. (Table presented) Given the present patients were on average >25 years older than those in type 1 studies and the 0.75 mL/min/yr decline in eGFR with age, the present data parallel those in type 1 diabetes. We conclude that i) a relatively high eGFR in type 2 diabetes indicative of past/present hyperfiltration is an adverse prognostic indicator, and ii) inclusion of eGFR in multivariable analysis of outcomes such as death.
Persons with diabetes are at increased risk of depression, although no clear consensus exists regarding the extent of any increased risk of suicide. In a British study, compared to those in the general population, individuals with type 1 diabetes had 11 times the suicide rate (1), whilst, in a U.S. study, adolescents with diabetes had an increased rate of suicidal ideation but comparable rate of attempts (2). We investigated suicide risk in diabetic versus non-diabetic adult residents from a community-based cohort. We studied 1,413 adult participants (mean+SD age 62.3+12.8 years, 49.8% male, 91.4% type 2 diabetes, median [inter-quartile range] diabetes duration 4.0 [1.0-10.0] years) from the longitudinal observational Fremantle Diabetes Study (FDS) and 5,631 age, sex and postcode matched de-identified nondiabetic residents. All deaths in the state of Western Australia (WA) are recorded in the WA Data Linkage System. The main outcome measure was death from suicide after FDS study entry (1993-6) until end 2012. During 13.1+6.1 years' follow up, 4 (0.28%) diabetic residents committed suicide (21.6/100,000 patient-years) versus 14 (0.25%) matched non-diabetic residents during 14.9+5.6 years' follow up (16.7/100,000 patient-years). The risk of suicide was a statistically non-significant 28% higher in the FDS diabetic residents (hazard ratio (HR; 95% CI), 1.28 (0.42-3.90), P=0.66). Adjusting for the competing risk of dying from other causes, the risk was further attenuated (sub (s) HR 1.13 (0.37-3.45), P=0.83). Men, however, had a 17-fold increased risk of suicide compared with women, independent of diabetes status (sHR 16.5 (2.2-124.5), P=0.006). Suicide is a rare event in adults with and without diabetes. Adults with diabetes had no statistically significant increased risk of suicide compared with non-diabetic adults, but men were at much higher risk than women, irrespective of diabetes status.

HDL-C and HDL-C/ApoA-I Predict Long-Term Progression of Glycemia in Established Type 2 Diabetes.

Objective: Low HDL cholesterol (HDL-C) and small HDL particle size may directly promote hyperglycemia. We evaluated associations of HDL-C, apolipoprotein A-I (apoA-I), and HDL-C/apoA-I with insulin secretion, insulin resistance, HbA1c, and long-term glycemic deterioration, reflected by initiation of pharmacologic glucose control.

Research design and methods: The 5-year Fenofibrate Intervention and Event Lowering in
Diabetes (FIELD) study followed 9,795 type 2 diabetic subjects. We calculated baseline associations of fasting HDL-C, apoA-I, and HDL-C/apoA-I with HbA1c and, in those not taking exogenous insulin (n = 8,271), with estimated beta-cell function (homeostasis model assessment of beta-cell function [HOMA-B]) and insulin resistance (HOMA-IR). Among the 2,608 subjects prescribed lifestyle only, Cox proportional hazards analysis evaluated associations of HDL-C, apoA-I, and HDL-C/apoA-I with subsequent initiation of oral hypoglycemic agents (OHAs) or insulin.

RESULTS: Adjusted for age and sex, baseline HDL-C, apoA-I, and HDL-C/apoA-I were inversely associated with HOMA-IR (r = -0.233, -0.134, and -0.230; all P < 0.001; n = 8,271) but not related to HbA1c (all P > 0.05; n = 9,795). ApoA-I was also inversely associated with HOMA-B (r = -0.063; P = 0.002; n = 8,271) adjusted for age, sex, and HOMA-IR. Prospectively, lower baseline HDL-C and HDL-C/apoA-I levels predicted greater uptake (per 1-SD lower: hazard ratio [HR] 1.13 [CI 1.07-1.19], P < 0.001; and HR 1.16 [CI 1.10-1.23], P < 0.001, respectively) and earlier uptake (median 12.9 and 24.0 months, respectively, for quartile 1 vs. quartile 4; both P < 0.01) of OHAs and insulin, with no difference in HbA1c thresholds for initiation (P = 0.87 and P = 0.81). Controlling for HOMA-IR and triglycerides lessened both associations, but HDL-C/apoA-I remained significant.

CONCLUSIONS: HDL-C, apoA-I, and HDL-C/apoA-I were associated with concurrent insulin resistance but not HbA1c. However, lower HDL-C and HDL-C/apoA-I predicted greater and earlier need for pharmacologic glucose control. 2014 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered.

PMID:24804699

Diabetes Technology & Therapeutics. 2014; 16(9): 604-10.

Carotid Artery Ultrasonographic Assessment in Patients from the Fremantle Diabetes Study Phase II with Carotid Bruits Detected by Electronic Auscultation.

Knapp A, Cetrullo V, et al.
1 School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.

UNLABELLED: Abstract Background: Electronic auscultation appears superior to acoustic auscultation for identifying hemodynamic abnormalities. The aim of this study was to determine whether carotid bruits detected by electronic stethoscope in patients with diabetes are associated with stenoses and increased carotid intima-medial thickness (CIMT).

SUBJECTS AND METHODS: Fifty Fremantle Diabetes Study patients (mean+SD age, 73.7+10.0 years; 38.0% males) with a bruit found by electronic auscultation and 50 age- and sex-matched patients with normal carotid sounds were studied. The degree of stenosis and CIMT were assessed from duplex ultrasonography.

RESULTS: Patients with a bruit were more likely to have stenosis of >50% and CIMT of >1.0mm than those without (odds ratios [95% confidence intervals]=14.0 [1.8-106.5] and 5.3 [1.8-15.3], respectively; both P=0.001). For the six patients with stenosis of >70%, five had a bruit, and one (with a known total occlusion) did not (odds ratio=5.0 [0.6-42.8]; P=0.22). The sensitivity and specificity of carotid bruit for stenoses of >50% were 88% and 58%, respectively; respective values for stenoses of >70% were 83% and 52%. The equivalent negative predictive values were 96% and 98%, and positive predictive values were 30% and 10%, respectively.

CONCLUSIONS: Electronic recording of carotid sounds for later interpretation is convenient and reliable. Most patients with stenoses had an overlying bruit. Most bruits were false positives, but ultrasonography is justified to document extent of disease; CIMT measurement will identify increased vascular risk in most of these patients. The absence of a bruit was rarely a false-negative finding, suggesting that these patients can usually be reassured that they do not have hemodynamically important stenosis.

PMID:24988112

Dipeptidyl peptidase-4 inhibitors: pharmacokinetics, efficacy, tolerability and safety in renal impairment.

Davis TM.

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

The dipeptidyl peptidase-4 (DPP-4) inhibitors are a new class of blood glucose-lowering therapy with proven efficacy, tolerability and safety. Four of the five commercially available DPP-4 inhibitors are subject to significant renal clearance, and pharmacokinetic studies in people with renal impairment have led to lower recommended doses based on creatinine clearance in order to prevent drug accumulation. Data from these pharmacokinetic studies and from supratherapeutic doses in healthy individuals and people with uncomplicated diabetes during development suggest, however, that there is a wide therapeutic margin. This should protect against toxicity if people with renal impairment are inadvertently prescribed higher doses than recommended. Doses appropriate to renal function are associated with reductions in HbA1c that are equivalent to those observed in people with type 2 diabetes who do not have renal impairment. Recent large-scale cardiovascular safety trials of saxagliptin and alogliptin have identified heart failure as a potential concern and renal impairment may increase the risk of this complication. Although the incidence of pancreatitis does not appear to be significantly increased by DPP-4 inhibitor therapy, renal impairment is also an independent risk factor. Additional data from other ongoing DPP-4 inhibitor cardiovascular safety trials should provide a more precise assessment of the risks of these uncommon complications, including in people with renal impairment. 2014 John Wiley & Sons Ltd.

PMID:24684351

Diabetes, Obesity and Metabolism. 2014; 16(5): 426-432.

Intensification of medication and glycaemic control among patients with type 2 diabetes-The ADVANCE trial.

van Dieren S, Kengne AP, et al.

(van Dieren, Kengne, Chalmers, Patel, Neal, Woodward, Zoungas) The George Institute for Global Health, University of Sydney, Sydney, Australia (van Dieren, Kengne, Beulens, Peelen, van der Schouw) Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands (Kengne) Department of medicine, South African Medical Research Council, University of Cape Town, Cape Town, South Africa (Davis) School of Medicine and Pharmacology, Fremantle Hospital, University of Western Australia, Fremantle, Australia (Fulcher) Department of Diabetes, Endocrinology and Metabolism, Royal North Shore Hospital, Sydney, Australia (Heller) Academic Unit of Diabetes, Endocrinology and Metabolism, School of Medicine and Biomedical Sciences, Sheffield, United Kingdom (Colagiuri) Boden Institute for Obesity, Nutrition and Exercise, Sydney University, Sydney, Australia (Hamet) Research Centre, Centre hospitalier del'Universite de Montreal, Montreal, Canada (Mancia) IRCCS Istituto Auxologico Italiano, Milan, Italy (Marre) Department of Endocrinology, Diabetology and Nutrition, Hopital Bichat-Claude Bernard, Universite Paris 7, Paris, France (Williams) School of Medicine, University of Leicester, Leicester, United Kingdom (Zoungas) School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia

S. Zoungas, The George Institute for Global Health, University of Sydney, PO Box M201, Missenden Road, NSW 2050 Sydney, Australia. E-mail: szoungas@georgeinstitute.org.au

Aims: The aim of this study was to assess associations between patient characteristics, intensification of blood glucose-lowering treatment through oral glucose-lowering therapy and/or insulin and effective glycaemic control in type 2 diabetes. Methods: 11140 patients from the Action in Diabetes and Vascular disease: preterAx and diamicron-MR Controlled Evaluation (ADVANCE) trial who were randomized to intensive glucose control or standard glucose control and followed up for a median of 5 years were categorized into two groups: effective glycaemic control [haemoglobin A1c (HbA1c)<7.0% or a proportionate reduction in HbA1c over 10%] or ineffective glycaemic control
(HbA1c>7.0% and a proportionate reduction in HbA1c less than or equal to 10%). Therapeutic intensification was defined as addition of an oral glucose-lowering agent or commencement of insulin. Pooled logistic regression models examined the associations between patient factors, intensification and effective glycaemic control. Results: A total of 7768 patients (69.7%), including 3198 in the standard treatment group achieved effective glycaemic control. Compared to patients with ineffective control, patients with effective glycaemic control had shorter duration of diabetes and lower HbA1c at baseline and at the time of treatment intensification. Treatment intensification with addition of an oral agent or commencement of insulin was associated with a 107% [odds ratio, OR: 2.07 (95% confidence interval, CI: 1.95-2.20)] and 152% [OR: 2.52 (95% CI: 2.30-2.77)] greater chance of achieving effective glycaemic control, respectively. These associations were robust after adjustment for several baseline characteristics and not modified by the number of oral medications taken at the time of treatment intensification. Conclusions: Effective glycaemic control was associated with treatment intensification at lower HbA1c levels at all stages of the disease course and in both arms of the ADVANCE trial. 2013 John Wiley & Sons Ltd.


Incidence and precipitants of hospitalization for pancreatitis in people with diabetes: the Fremantle Diabetes Study.
Davis TM, Drinkwater J, et al.
University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, Australia.

AIMS: To determine the relative risk of pancreatitis in diabetes, and to establish whether diabetes-related as well as recognized risk factors contribute.

METHODS: We studied 1426 participants [mean (sd) age 62.1 (13.3) years, 49.6% male, 90.9% Type 2 diabetes, median (interquartile range) diabetes duration 4.0 (1.0-10.0) years] from the community-based Fremantle Diabetes Study Phase I and 5663 matched residents without diabetes from the same geographical area. Pancreatitis hospitalizations between 1982 and 2010 were ascertained using validated data linkage. For Fremantle Diabetes Study Phase I participants, chart review provided data on the likely causes of pancreatitis.

RESULTS: A total of 21 Fremantle Diabetes Study Phase I participants (1.5%) were hospitalized for pancreatitis before study entry vs 29 (0.5%) of contemporaneous residents without diabetes. During a mean (sd) of 12.1 (5.4) years of follow-up from entry, 22 (1.6%) Fremantle Diabetes Study Phase I participants were hospitalized for a first-ever episode of pancreatitis on 37 occasions (1.31/1000 person-years) compared with 58 (1.0%) residents without diabetes on 81 occasions during a mean (sd) 13.6 (4.8) years (0.75/1000 person-years). The age- and sex-adjusted hazard ratio (95% CI) for first-ever pancreatitis hospitalization in Fremantle Diabetes Study Phase I participants was 1.73 (1.06-2.83; P=0.029). Chart review of 17 of the 22 Fremantle Diabetes Study Phase I participants (77%) with incident pancreatitis and available case notes revealed that four (24%) presented without objective evidence of pancreatitis, seven (41%) presented with cholelithiasis, three (18%) with excessive alcohol consumption, two (12%) as a complication of elective endoscopic retrograde cholangiopancreatography, and one (6%) with hypertriglyceridaemia.

CONCLUSION: Consistent with previously published data, the risk of pancreatitis was higher in community-dwelling Fremantle Diabetes Study Phase I participants but conventional precipitants accounted for confirmed cases. These data question whether diabetes-specific risk factors cause or contribute to pancreatitis. 2014 The Authors. Diabetic Medicine 2014 Diabetes UK.

PMID:24661305


Ethnicity and long-term vascular outcomes in Type 2 diabetes: A prospective observational study (UKPDS 83).
Aims: Evidence of ethnic differences in vascular complications of diabetes has been inconsistent. The aim of this study was to examine the relationship between ethnicity and long-term outcome in a large sample of individuals with newly diagnosed Type 2 diabetes. Methods: In a prospective observational study of 4273 UK Prospective Diabetes Study participants followed for a median of 18 years, 3543 (83%) were White Caucasian, 312 (7%) Afro-Caribbean and 418 (10%) Asian Indian. Relative risks for predefined outcomes were assessed comparing Afro-Caribbean and Asian Indian with White Caucasian using accelerated failure time models, with adjustment for cardiovascular risk factors and other potentially confounding variables. Results: During follow-up, 2468 (58%) participants had any diabetes-related end point, 1037 (24%) a myocardial infarction and 401 (9%) a stroke, and 1782 (42%) died. Asian Indian were at greater risk (relative risk, 95% confidence interval) for any diabetes-related end point (1.18, 1.07-1.29), but at lower risk of all-cause mortality (0.89, 0.80-0.97) and peripheral vascular disease (0.43, 0.23-0.82), vs. White Caucasian. Afro-Caribbean participants were at lower risk for all-cause mortality (0.84, 0.76-0.93), diabetes-related death (0.75, 0.64-0.88), myocardial infarction (0.55, 0.43-0.71) and peripheral vascular disease (0.55, 0.33-0.93) vs. White Caucasian. No ethnicity-related associations were found for stroke or microangiopathy. Conclusions: Asian Indian ethnicity is associated with the greatest burden of disease, but not with an increased risk of major vascular complications or death. Afro-Caribbean ethnicity is associated with reduced risk of all-cause and diabetes-related death, myocardial infarction and peripheral vascular disease, suggesting an ethnicity-specific protective mechanism. 2013 Diabetes UK. PMID:2014048534

Personality traits, self-care behaviours and glycaemic control in Type 2 diabetes: The Fremantle Diabetes Study Phase II.

Aims: To determine whether the personality traits of conscientiousness and agreeableness are associated with self-care behaviours and glycaemia in Type 2 diabetes. Methods: The Big Five Inventory personality traits Agreeableness, Conscientiousness, Extraversion, Neuroticism and Openness were determined along with a range of other variables in 1313 participants with Type 2 diabetes (mean age 65.8 + 11.1 years; 52.9% men) undertaking their baseline assessment as part of the community-based longitudinal observational Fremantle Diabetes Study Phase II. Age- and sex-adjusted generalized linear modelling was used to determine whether personality was associated with BMI, smoking, self-monitoring of blood glucose and medication taking. Multivariable regression was used to investigate which traits were independently associated with these self-care behaviours and HbA<sub>1c</sub>. Results: Patients with higher conscientiousness were less likely to be obese or smoke, and more likely to perform self-monitoring of blood glucose and take their medications (P < 0.019), with similar independent associations in multivariate models (P < 0.024). HbA<sub>1c</sub> was independently associated with younger age, indigenous ethnicity, higher BMI, longer diabetes duration, diabetes treatment, self-monitoring of blood glucose (negatively) and less medication taking (P < 0.009), but no personality trait added to the model. Conclusions: Although there was no independent association between personality traits and HbA<sub>1c</sub>, the relationship between
high conscientiousness and low BMI and beneficial self-care behaviours suggests an indirect positive effect on glycaemia. Conscientiousness could be augmented by the use of impulse control training as part of diabetes management. 2013 Diabetes UK.


Incidence and predictors of hospitalization for tendon rupture in Type 2 diabetes: the Fremantle Diabetes Study.
Zakaria MH, Davis WA, et al.
University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, Australia.

AIMS: To determine the incidence and predictors of tendon ruptures requiring hospitalization of representative patients with Type 2 diabetes.

METHODS: A total of 1296 patients from the longitudinal observational Fremantle Diabetes Study, Phase I, and 5159 de-identified age- and sex-matched control subjects without diabetes from the same urban area were studied. The patients’ mean (sd) age was 64.0 (11.3) years and 48.6% of them were male. Their median (interquartile range) diabetes duration was 4.0 (1.0-9.0) years. The main outcome assessed was any tendon rupture requiring hospitalization in the Fremantle Diabetes Study subjects and the matched control subjects. Independent predictors of spontaneous ruptures in the patients from the Fremantle Diabetes Study were assessed using Cox proportional hazards modelling.

RESULTS: The incidence rate ratio for any tendon rupture requiring hospitalization in patients vs control subjects was 1.44 (95% CI 1.10-1.87; P = 0.005). Independent predictors of spontaneous ruptures in patients were BMI [hazard ratio 1.05 (95% CI 1.002-1.10] for 1 kg/m(2) increase; P = 0.010] and alcohol consumption [hazard ratio 1.52 (95% CI 1.11-2.09) for 1 standard drink/day increase; P = 0.010]. Adjustment of the incidence rate ratio for overall rupture requiring hospitalization for these variables using the BMI and alcohol consumption data from the contemporary Australian general population suggested it could be as high as 1.84.

CONCLUSIONS: There is a greater risk of tendon rupture requiring hospitalization in people with Type 2 diabetes. Alcohol consumption and adiposity are potentially modifiable risk factors of spontaneous ruptures in patients with diabetes. 2013 The Authors. Diabetic Medicine 2013 Diabetes UK.


Type 2 diabetes and associated complications in Western Australian children: A population based study (1990-2012).
(Haynes, Kalic, Curran, Paramalingam, Shah, Jones, Davis) Department of Endocrinology and Diabetes, Princess Margaret Hospital, Perth, Australia (Haynes, Paramalingam, Jones, Davis) Telethon Kids Institute, Perth, Australia (Bulsara) Institute of Health and Rehabilitation Research, Fremantle, Australia

A. Haynes, Department of Endocrinology and Diabetes, Princess Margaret Hospital, Perth, Australia

Background and aims: Data on childhood diabetes are available from the Western Australian Children's Diabetes Database (WACDD), maintained by the only tertiary paediatric hospital in Western Australia servicing all children diagnosed with diabetes throughout the State. This study aimed to describe the incidence of type 2 diabetes in Western Australian children and examine the prevalence of complications of diabetes. Materials and methods: The study included children aged 0-16 years diagnosed with type 2 diabetes at our hospital, between 1990 to 2012, in a population- based sample. Incidence rates per 100,000 person-years at risk were calculated by Indigenous status and year of diagnosis. Mean (+SD) were estimated for age, BMI Z-score and HbA1C at diagnosis. Prevalence of microalbuminuria and hypertension were evaluated for patients at different time points for all available complications screening data. Results: From 1990 to 2012, there were 135 (82 F:53 M) incident cases
of type 2 diabetes in children aged <17 years. Although Indigenous children make up ~6% of the general population, they were grossly over-represented, accounting for 56% of cases. The mean incidence of type 2 diabetes was 0.6 per 100,000 (95%CI: 0.5-0.8) in non-Indigenous children compared to 12.6 per 100,000 (95%CI: 10.0-15.8) in Indigenous children. The mean age at diagnosis was 13.3(+2.0) years. At diagnosis, the mean BMI Z-score was 2.0(+0.6), with 12% of cases classified as being overweight and 61% obese. Mean HbA1c at diagnosis was 9.0%(+2.8%) compared to 7.7%(+2.5%) 3-12 months postdiagnosis. Hypertension was observed in 15/75 (20%) of cases at the time of diagnosis and in 19% of cases 2 years post-diagnosis. Similarly, microalbuminuria was detected in 11/61 (18%) of cases at the time of diagnosis and 23% of cases 2 years post-diagnosis. Conclusion: In keeping with other populations, the incidence of childhood type 2 diabetes is increasing in Western Australia, the highest incidence being observed in Indigenous children. Despite their youth, complications of diabetes were already present in this cohort at diagnosis and their prevalence increased markedly even with short duration of disease. There is presently no screening program for children at increased risk of developing type 2 diabetes in Western Australia, and older adolescents with type 2 diabetes may not be ascertained by the paediatric service. Therefore, undiagnosed cases are likely to exist in the study population, and these data represent a likely underestimation.

Publication Types: Conference Abstract
PMID:71595906


Serum endostatin concentrations are higher in men with symptoms of intermittent claudication.

Golledge J, Clancy P, et al. The Vascular Biology Unit, Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville, QLD 4811, Australia ; Department of Vascular and Endovascular Surgery, The Townsville Hospital, Townsville, QLD 4814, Australia. The Vascular Biology Unit, Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville, QLD 4811, Australia. School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6907, Australia ; Department of Neurology, Royal Perth Hospital, Perth, WA 6000, Australia. School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6907, Australia ; Department of Endocrinology, Fremantle Hospital, Fremantle, WA 6160, Australia. School of Surgery, University of Western Australia, Perth, WA 6907, Australia.

Objectives. A cleavage fragment of collagen XVIII, endostatin, is released into the circulation and has been demonstrated to have antiangiogenic effects in animal models. We hypothesized that circulating endostatin would be increased in patients with symptoms of lower limb peripheral artery disease. Design. Cross-sectional study. Participants. Community dwelling older men. Measurements. Intermittent claudication was defined using the Edinburgh Claudication Questionnaire (ECQ). Serum endostatin was measured by a commercial ELISA. The association of serum endostatin with intermittent claudication was examined using logistic regression adjusting for age, diabetes, hypertension, dyslipidemia, coronary heart disease, and stroke. Results. Serum endostatin was measured in 1114 men who completed the ECQ. 106 men had intermittent claudication, 291 had atypical pain, and 717 had no lower limb pain. Mean (+standard deviation) serum endostatin concentrations (ng/mL) were 145.22 + 106.93 for men with intermittent claudication, 129.11 + 79.80 for men with atypical pain, and 116.34 + 66.57 for men with no lower limb pain; P < 0.001. A 70ng/mL increase in endostatin was associated with a 1.17-fold rise in the adjusted odds of having intermittent claudication (OR 1.17, 95% confidence interval 1.00-1.37, and P = 0.050). Conclusions. Serum endostatin is raised in older men who have symptoms of intermittent claudication. The role of endostatin in the genesis and outcome of peripheral artery disease requires further investigation.

PMID:24600079
Discussion on anal fistulas.

Bartolo DC.
University of Western Australia, Fremantle, Western Australia.
PMID:25003299

Marshall EM, O'Loughlin E, et al.
(Marshall) Department of Anaesthesia, Glasgow Royal Infirmary and Stobhill ACH, Glasgow, United Kingdom (O'Loughlin, Swann) Department of Anaesthesia, Fremantle Hospital and Health Service, Fremantle, WA, Australia (O'Loughlin, Swann) School of Medicine and Pharmacology, University of Western Australia, Fremantle, WA, Australia
E.M. Marshall, Department of Anaesthesia, Glasgow Royal Infirmary and Stobhill ACH, Glasgow Royal Infirmary, 2nd Floor, Walton Building, 84 Castle Street, Glasgow Glasgow G4 0SF, United Kingdom. E-mail: elizabeth.marshall6@nhs.net
Objective: The present study aims to study whether using a videolaryngoscope (A.P. Advance) facilitates or hinders intubation by non-anaesthetists inexperienced in its use. Methods: Thirty doctors from Emergency and Intensive Care Medicine backgrounds performed laryngoscopy and tracheal intubation using the Macintosh laryngoscope (MAC), A.P. Advance Normal Blade (AP N) and A.P. Advance Difficult Airway Blade (AP DAB) in simulated normal and difficult airway manikins. The primary outcomes measured were time to successful tracheal intubation and failure to intubate within 3min or three attempts. Secondary outcomes were number of intubation attempts, adjuncts used, glottic view and ease of intubation. Results: There was a higher rate of failed intubation in the simulated difficult airway in participants using the AP N blade than either the MAC or AP DAB (23% vs 3% and 7%, P = 0.031). This was associated with a longer median time to intubate with the AP N and the AP DAB versus MAC (56.6, 50.2 vs 39.9s, P = 0.007 and P = 0.041). In the normal airway median time to intubate was longest with the AP N (27.8s), and this was significantly slower than the MAC (18.1s, P = 0.003) and the AP DAB (17.3s, P < 0.001). No one failed to intubate the normal manikin. Conclusions: The use of the A.P. Advance videolaryngoscope should not be considered, without adequate prior training and experience, in the management of a difficult airway. The level of adequate training has yet to be established. 2014 Australasian College for Emergency Medicine and Australasian Society for Emergency Medicine.
PMID:2014380402

Modified TIMI risk score cannot be used to identify low-risk chest pain in the emergency department: A multicentre validation study.
Macdonald SPJ, Nagree Y, et al.
(Macdonald, Nagree, Fatovich, Brown) Centre for Clinical Research in Emergency Medicine, Western Australian Institute for Medical Research, Perth, WA, Australia (Macdonald, Nagree, Fatovich, Brown) Discipline of Emergency Medicine, University of Western Australia, Perth, WA, Australia (Macdonald) Department of Emergency Medicine, Armadale Health Service, PO Box 460, Armadale, WA 6992, Australia (Nagree) Department of Emergency Medicine, Fremantle Hospital, Fremantle, WA, Australia (Fatovich, Brown) Department of Emergency Medicine, Royal Perth Hospital, Perth, WA, Australia S.P.J. Macdonald, Department of Emergency Medicine, Armadale Health Service, PO Box 460, Armadale, WA 6992, Australia. E-mail: stephen.macdonald@health.wa.gov.au
Aim: The Thrombolysis in Myocardial Infarction (TIMI) risk score (range 0-7), used for emergency department (ED) risk stratification of patients with suspected acute coronary syndrome (ACS), underestimates risk associated with ECG changes or cardiac troponin elevation. A modified TIMI
score (mTIMI, range 0-10), which gives increased weighting to these variables, has been proposed. We aimed to evaluate the performance of the mTIMI score in ED patients with suspected ACS.

Methods: A multicentre prospective observational study enrolled patients undergoing assessment for possible ACS. TIMI and mTIMI scores were calculated. The study outcome was a composite of all-cause death, myocardial infarction or coronary revascularisation within 30 days. Results: Of the 1666 patients, 219 (13%) reached the study outcome. Area under the receiver operating characteristic curve for the composite outcome was 0.80 (0.76 to 0.83) for the mTIMI score compared with 0.71 (0.67 to 0.74) for the standard TIMI score, p<0.001, but there was no significant difference for death or revascularisation outcomes. Sensitivity and specificity for the composite outcome were 0.96 (0.92 to 0.98) and 0.23 (0.20 to 0.26), respectively, at score 0 for TIMI and mTIMI. At score <2, sensitivity and specificity were 0.82 (0.77 to 0.87) and 0.53 (0.51 to 0.56) for mTIMI, and 0.74 (0.68 to 0.79) and 0.54 (0.51 to 0.56) for standard TIMI, respectively. Conclusions: mTIMI score performs better than standard TIMI score for ED risk stratification of chest pain, but neither is sufficiently sensitive at scores >0 to allow safe and early discharge without further investigation or follow-up. Observed differences in performance may be due to incorporation bias.

PMID:2014181720

EuroIntervention. 2014; Conference Publication: (var.pagings).


Meredith IT, Verheye S, et al.

(Meredith, Verheye, Whelan, Legrand, James, Wilkins, Allocco, Dawkins) MonashHeart, Clayton, Australia; 2. Ziekenhuis Netwerk Antwerpen Middelheim, Antwerp, Belgium; 3. Fremantle Hospital, Fremantle, Australia; 4. University Hospital Sart Tilman, University of Liege, Liege, Belgium; 5. Uppsala University Hospital, Uppsala, Sweden; 6. Department of Cardiology, Dunedin Hospital, Dunedin and Department of Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand; 7. Boston Scientific, Marlborough, USA

Aims: Drug-eluting stents improve clinical outcomes compared with bare metal stents; however, durable polymer coatings may be associated with chronic inflammation and delayed arterial healing, leading to an increased risk of late adverse events including stent thrombosis. Coating drug-eluting stents with bioabsorbable polymer will minimise exposure to the polymer and drug, and may reduce clinical events as well as the need for long-term dual-antiplatelet therapy. SYNERGY is the newest generation of drug-eluting stent based on the well-characterised Element platinum chromium stent platform utilising bioabsorbable polymer poly(D,L-lactide-co-glycolide) (PLGA) to deliver everolimus to the arterial wall. The EVOLVE FHU study compared the performance of the SYNERGY stent (2 dose formulations) to the durable polymer PROMUS Element everolimus-eluting stent (EES). Methods and results: The EVOLVE FHU trial enrolled 291 patients with a de novo lesion <28 mm in length in a coronary artery of >2.25 to <3.5 mm diameter. The SYNERGY stent (Boston Scientific Corporation, Natick, MA, USA) releases everolimus from an ultra-thin abluminal bioabsorbable PLGA polymer on a thin-strut, platinum chromium stent platform. The bioabsorbable polymer is absorbed shortly after drug elution is complete at three months. Three patient groups were compared: patients implanted with PROMUS Element, patients receiving SYNERGY stents releasing everolimus at an equivalent dose to PROMUS Element (‘SYNERGY’ group) and patients receiving the SYNERGY stents releasing everolimus at half that dose (‘SYNERGY 1/2 Dose’ group). The 30-day primary clinical endpoint of target lesion failure (defined as cardiac death or myocardial infarction related to the target vessel, or target lesion revascularisation) was 0%, 1.1%, and 3.1% in the PROMUS Element, SYNERGY, and SYNERGY 1/2 Dose groups, respectively (PROMUS Element: vs. SYNERGYP=0.49; vs. SYNERGY 1/2 Dose P=0.25). The 6-month primary angiographic endpoint of in-stent late loss was noninferior between the control and SYNERGY groups (0.15+0.34 mm for PROMUS Element, 0.10+0.25 mm for SYNERGY, and 0.13+0.26 mm for SYNERGY 1/2 Dose; PROMUS Element: vs. SYNERGY P=0.19; vs. SYNERGY 1/2 Dose P=0.56). At 6 months, the rates of resolved, persistent, and late-acquired incomplete stent apposition were 4.4%, 0%, and 2.9%, respectively for PROMUS Element; 0%, 0%,
and 3.2% for SYNERGY, and 0%, 1.6% and 1.6% for SYNERGY 1/2 Dose. No significant differences were found between PROMUS Element and either SYNERGY formulation for these or other measured IVUS parameters including net volume obstruction. At 2 years, the rate of target lesion failure was similar in all 3 groups (PROMUS Element 6.1%, SYNERGY 5.5% and SYNERGY 1/2 Dose 5.2%; PROMUS Element: vs. SYNERGY P=0.85; vs. SYNERGY 1/2 Dose, P=0.81). Other clinical event rates including death, MI and revascularisation were low and not significantly different between groups. No stent thromboses were found in any group through 2 years. Conclusions: Over 2 years, everolimus (at 2 dose levels) delivered from an ultra-thin bioabsorbable abluminal polymer resulted in similar clinical, angiographic and IVUS-related outcomes compared with PROMUS Element. This will be the first presentation of the 3-year clinical results.

Publication Types: Conference Abstract
PMID:71538452


Biostability, durability and calcification of cryopreserved human pericardium after rapid glutaraldehyde-stabilization versus multistep ADAPT(R) treatment in a subcutaneous rat model.
Department of Cardiothoracic Surgery, Fremantle Heart Institute, Fremantle Hospital and School of Surgery, University of Western Australia, Fremantle, WA, Australia.
OBJECTIVES: Autologous pericardium rapidly fixed with glutaraldehyde (GA) in theatre is considered in many cardiac surgery centres the best material currently available for intracardiac, valvular or vascular repair. Implanted non-fixed autologous tissues suffer rapid degeneration, shrinkage and absorption whereas standard xenotypic fixed tissues cause local cytotoxicity and calcification. In the present study, using a subcutaneous rat model, we tested the biostability, durability and calcification potential of four different pericardium patches treated with GA and relevant to current clinical practice.

METHODS: Pericardium samples were divided into four groups according to the method of treatment. Group I consisted of bovine pericardium (BP) fixed with 0.6% GA (control), Group II cryopreserved human pericardium (CHP) rapidly fixed with 0.6% GA for 4 min and detoxified with MgCl2, Group III CHP treated with the multistep ADAPT() process (delipidized, decellularized with Tx-100, deoxycholate, IgePal CA-630 and denucleased, fixed in 0.05% monomeric GA and detoxified) and Group IV BP treated with the multistep ADAPT() process (CardioCel()). Biostability was determined by shrinkage temperature which measures the degree of cross-linking, and durability assessed by resistance to a mixture of proteinases (pronase digestion). Treated pericardium samples (n = 10 in each of Groups I-IV) were implanted in the subcutaneous rat model for 8 and 16 weeks, followed by histology and calcium analysis (atomic absorption spectrophotometry).

RESULTS: The biostability and the durability of both CHP and BP after the multistep ADAPT() treatment remained stable without any microscopic calcification. Extractable calcium levels of CHP were significantly (P < 0.01) reduced in Group II (1.89 + 0.77 mug Ca/mg tissue) compared with Group I (64.37 + 6.25 mug/mg) after 8 weeks. Calcification of CHP (Group III) and BP (Group IV) after the multistep ADAPT() treatment was significantly reduced (1.43 + 0.48 g/mg and 0.75 + 0.10 mug/mg, respectively) compared with Group I (282.52 + 18.26 mug/mg) and the rapidly treated CHP in Group II (11.32 + 3.21 mug/mg) after 16 weeks.

CONCLUSIONS: Improved biostability and durability with reduced calcification of tissues after the multistep ADAPT() tissue treatment suggest improved alternative substitutes to autologous pericardium.
PMID:24431173


TWEAK and LTβ Signaling during Chronic Liver Disease.
Dwyer BJ, Olynyk JK, et al.
Chronic liver diseases (CLD) such as hepatitis B and C virus infection, alcoholic liver disease, and non-alcoholic steatohepatitis are associated with hepatocellular necrosis, continual inflammation, and hepatic fibrosis. The induced microenvironment triggers the activation of liver-resident progenitor cells (LPCs) while hepatocyte replication is inhibited. In the early injury stages, LPCs regenerate the liver by proliferation, migration to sites of injury, and differentiation into functional biliary epithelial cells or hepatocytes. However, when this process becomes dysregulated, wound healing can progress to pathological fibrosis, cirrhosis, and eventually hepatocellular carcinoma. The other key mediators in the pathogenesis of progressive CLD are fibrosis-driving, activated hepatic stellate cells (HSCs) that usually proliferate in very close spatial association with LPCs. Recent studies from our group and others have suggested the potential for cytokine and chemokine cross-talk between LPCs and HSCs, which is mainly driven by the tumor necrosis factor (TNF) family members, TNF-like weak inducer of apoptosis (TWEAK) and lymphotoxin-beta, potentially dictating the pathological outcomes of chronic liver injury.

Publication Types: Review
PMID:24592262

An unusual case of mesenteric ischaemia.
Ayres LRO, Scott M, et al.
Department of Gastroenterology, Gloucestershire Hospitals NHS Foundation Trust, Gloucester, United Kingdom (Ayres) Department of Gastroenterology, Fremantle Hospital, Alma Street Fremantle, WA 6160, Australia (Scott) Department of Surgery, Gloucestershire Hospitals NHS Foundation Trust, Gloucester, United Kingdom (Shepherd) Department of Pathology, Gloucestershire Hospitals NHS Foundation Trust, Gloucester, United Kingdom
L.R.O. Ayres, Department of Gastroenterology, Fremantle Hospital, Alma Street Fremantle, WA 6160, Australia. E-mail: lachlanyayres@hotmail.com
We describe an unusual cause of diarrhoea and segmental colitis in a previous well adult man. Mesenteric inflammatory veno-occlusive disease is a rare cause of gastrointestinal tract ischaemia of unknown aetiology. We review the literature of this condition and other mesenteric venous pathologies.
PMID:2014012496

Hospital costs associated with depression in a cohort of older men living in Western Australia.
Prina AM, Huisman M, et al.
Department of Public Health & Primary Care, Institute of Public Health, Cambridge University, UK; Western Australia Centre for Health & Ageing, Centre for Medical Research, University of Western Australia; Centre for Global Mental Health, Institute of Psychiatry at King's College London, London, UK. Electronic address: matthew.prina@kcl.ac.uk.
Department of Epidemiology & Biostatistics and the EMGO Institute for Health and Care Research,
BACKGROUND: There is lack of information of the hospital costs related to depression. Here, we compare the costs associated with general hospital admissions over 2 years between older men with and without a documented past history of depression.

METHODS: A community-based cohort of older men living in Perth, Western Australia, was assessed at baseline between 2001 and 2004 and followed up for 2 years by prospective data linkage. The participants were selected randomly from the Australia electoral roll. Two-year hospital costs were estimated.

RESULTS: Among 5411 patients, 75% of 339 men with depressive symptoms had at least one hospital admission compared with 61% of 5072 men without depression (P<.001). Two-year median hospital costs in the depressed group were A$4153 compared with A$1671 in participants free from depression (P<.001). In multivariate analysis, the presence of clinically significant depressive symptoms remained an independent predictor of higher cost [incident rate ratios (RR)=1.44, 95% confidence interval (CI): 1.23-1.68] and was associated with being a high-cost user of health services (RR=2.04, 95% CI: 1.43-2.92).

LIMITATIONS: The estimation of costs was solely based on the main diagnosis, potentially leading to underestimates of the real cost differences.

CONCLUSIONS: Hospital care cost was higher for older men with documented evidence of past depression than those without. The issue of depression in later life must be tackled if we want to optimize the use of limited hospital resources available. 2014.

PMID:24113024


Trends and survival for unprotected left main PCI in Western Australia 2000-2005.
Chopra S, Schultz C, et al.
(Chopra, Schultz, Rankin) Cardiology, Royal Perth Hospital, Perth, Australia (Schultz) School of Medicine and Pharmacology, Perth, Australia (Knuiman, Hobbs, Briffa, Sanfilippo) School of Population Health, University of Western Australia, Perth, Australia (Cutlip) Harvard Clinical Research Institute, Boston, United States (Cutlip) Beth Israel Deaconess Medical Centre, Harvard Medical School, Boston, United States (Nguyen) Cardiology, Fremantle Hospital, Perth, Australia (Newman) Cardiothoracic Surgery, Sir Charles Gairdner Hospital, Perth, Australia

S. Chopra, Cardiology, Royal Perth Hospital, Perth, Australia

Introduction: The introduction of drug-eluting stents and advances in catheter techniques may have led to increasing acceptance of percutaneous coronary intervention (PCI) as a viable alternative to coronary artery bypass graft (CABG) for unprotected left main (LM) disease. Objectives: To investigate 5-year trends and outcomes in a population cohort of unprotected LM disease treated with bare metal (BMS) or drug-eluting stents (DES). Methods: Clinical data from all hospitals offering PCI in Western Australia between 2000 and 2005 and linked administrative health data (hospital admissions and death) from the Western Australian Data Linkage System were merged for all patients who had LM coronary artery PCI. Previous treatment with CABG prior to the index LM PCI was identified by
lookback to 1980. Five-year outcomes were death (all-cause) and the composite of death/myocardial infarction (MI) admission/subsequent coronary artery revascularisation (MACE). The risk of 5-year outcomes were calculated using the Kaplan-Meier method and compared using log-rank tests and adjusted Cox proportional hazards regression. Results: In our cohort of 237 patients, unprotected LM PCI increased over time (n=4 unprotected of 18 LM PCIs in 2000 to n=59 of 78 in 2005), whereas protected LM PCI remained stable (n=14 vs n=19 respectively). We excluded 97 patients with a history of CABG leaving 140 patients with unprotected LM PCI (mean age 73 years (range 38-91), 73% males). BMS and DES were implanted in 13.6% and 86.4% patients, respectively. The 5-year all-cause mortality was 36% (52.6% for BMS and 33.1% for DES, p=0.06). MI within 5 years of the LM PCI was seen in 9.3% overall, and in 5.3% vs 9.9% for BMS and DES respectively (p=0.53). Repeat revascularisation within 5 years of the LM PCI was seen in 30.7% overall, and 26.3% vs 31.4% respectively for BMS vs DES (p=0.82). MACE occurred in 60.7% overall and 68.4% BMS vs 59.5% DES (p=0.19). There was a lower risk of 5-year death for DES compared with BMS (adjusted hazard ratio (HR) 0.42, 95% CI 0.20-0.90) and an apparent lower risk for 5-year MACE (HR 0.55, 95% CI 0.29-1.03). Conclusion: In Western Australia, unprotected LM PCI increased substantially, predominantly due to increased use of DES rather than BMS. DES use was associated with lower all-cause death after 5 years. Further analyses are needed to evaluate the separate effects of comorbidities.

Publication Types: Conference Abstract
PMID:71460430


Index and coronary heart disease related readmission costs for percutaneous coronary intervention in Western Australia.
Gardner C, Geelhoed E, et al.
(Gardner, Geelhoed, Knuiman, Hobbs, Briffa, Sanfilippo) School of Population Health, University of Western Australia, Perth, Australia (Rankin) Department of Cardiology, Royal Perth Hospital, Perth, Australia (Nguyen) Department of Cardiology, Fremantle Hospital, Perth, Australia (Newman) Department of Cardiothoracic Surgery, Sir Charles Gairdner Hospital, Perth, Australia (Cutlip) Beth Israel Deaconess Medical Centre, Harvard Medical School, Boston, United States
C. Gardner, School of Population Health, University of Western Australia, Perth, Australia

Introduction: Following the introduction of drug-eluting stents (DES) in Western Australia in 2002, the proportion of percutaneous coronary interventions (PCI) using these stents increased rapidly to 96% in 2005. Although DES are associated with significant reductions in the risk of target vessel revascularisation, they remain considerably more expensive than bare metal stents (BMS). Objectives: To assess the costs of index admissions and readmissions for coronary heart disease (CHD) related diagnoses over 2 years by type of stent for the total population of patients undergoing PCI in Western Australia between 2000-2004. Methods: Clinical and linked administrative data (inpatient admissions and death) were merged for all patients who had their first PCI in Western Australia between 2000-2004. The clinical data were collected from all hospitals in Western Australia where PCI procedures are performed. Costs were assigned using diagnostic related groups (DRGs) for public and private hospitals using versions 4.2 and 5.1 of Australian Refined DRGs published by the Australian Institute of Health and Welfare. Costs were inflated to 2012-2013 Australian dollars using health price indexes published by the Australian Institute of Health and Welfare. We calculated mean individual costs by year and type of stent for index admissions and cumulative readmissions for CHD related diagnoses (ICD 10-AM codes I20-I25) within 2 years of the index admission. Results: Over the five years, there were 9,593 index PCIs (5174 BMS, 53.9% and 4419 DES, 46.1%). The mean age was 65 for patients undergoing PCI with both BMS and DES. The proportion of males was 74% and 68% for BMS and DES patients respectively. 59% of procedures were performed in public hospitals. Index costs were (Graph Presented) similar for both types of stent and remained relatively constant between 2000-2004 at about AU$9000 (see Figure 1) per patient. Two-year costs for CHD-related readmissions were stable for BMS patients, but increased slightly over the period for DES patients. The total 2-year costs
(including cost of the stents) were significantly greater for DES, driven almost entirely by the higher cost of the DES device compared with BMS. Conclusion: Stent cost is the main driver of increased total 2-year costs of PCI procedures employing DES compared with BMS. Longer follow-up is required to determine if the increased initial cost of DES is offset by decreased subsequent costs associated with lower rates of target vessel revascularisation, and possibly better long-term outcomes.

Publication Types: Conference Abstract
PMID:71459824


Long-term outcomes following coronary artery revascularization procedures in diabetics and non-diabetics.
Nguyen M, Rankin J, et al.
(Nguyen) Cardiology, Fremantle Hospital, Australia (Rankin) Cardiology, Royal Perth Hospital, Australia (Knuiman, Nedkoff, Briffa, Geelhoed, Hobbs, Sanfilippo) School of Population Health, University of Western Australia, Australia (Newman) Cardiothoracic Surgery, Sir Charles Gairdner Hospital Perth, Australia (Cutlip) Harvard Clinical Research Institute, Boston, United States (Cutlip) Beth Israel Deaconess Medical Centre, Harvard Medical School, Boston, United States

Introduction: Patients with diabetes are at greater risk of developing coronary artery disease and have been shown to have increased adverse outcomes following coronary artery revascularization procedures (CARPs). Long-term population-based data are needed to determine the real-world effectiveness of CARPs in patients with diabetes. Objectives: Comparison of 4-year outcomes in patients with and without diabetes who had CARPs in Western Australia during 2000-2004. Methods: Clinical data and linked administrative data (hospital admissions and death) from the Western Australian Data Linkage System were merged for all patients who had their first CARP with stents (PCI) or coronary artery bypass graft (CABG) in Western Australia between 2000-2004. A history of diabetes was identified from the linked data using a 10-year lookback period. Clinical data were collected from all hospitals in Western Australia where CARP procedures are performed. We calculated the unadjusted (Kaplan-Meier) and adjusted (Cox) risks for 4-year death (all-cause), admission for myocardial infarction (MI), and the composite outcome of death/MI admission/subsequent CARP (MACE). Results: There were 14,118 patients who had CARPs, with 3,427 (24%) diabetic patients (72% males, mean age 64.5, mean Charlson comorbidity score 2.9) and 10,691 (76%) nondiabetics (78% males, mean age 63.8, mean Charlson score 1.1). In non-diabetics, 9.1% died within 4 years of the index procedure, compared with 13.7% of diabetics (log-rank p<0.0001); 4.8% of non-diabetics had an admission for MI compared with 7.4% of diabetics (p<0.0001); and 13.7% of non-diabetics had a subsequent CARP vs 15.5% of diabetics (p=0.008). For MACE, 23.4% of non-diabetics vs 29.7% of diabetics experienced an event within 4 years of the index procedure (p<0.0001). After adjusting for age, gender, comorbidities and other covariates, diabetics had a lower risk of 4-year mortality than non-diabetics (HR 0.85, 95% CI 0.75-0.96; HR 1.53 95% CI 1.37-1.71 with no comorbidity adjustment). The risk of MACE at 4 years was equivalent (HR 0.96, 95% CI 0.89-1.04), whilst repeat revascularization was higher in the diabetic cohort (HR 1.31, 95% CI 1.17-1.46). Conclusion: In a real world population, patients with diabetes have significantly worse long-term outcomes (death, MI, repeat CARP) following CARPs than non-diabetics. However, after adjustment for comorbidities, only repeat revascularization was increased in the diabetic group.

Publication Types: Conference Abstract
PMID:71460721


Comparison of 4-year outcomes following percutaneous or surgical coronary artery revascularization procedures in patients with diabetes.
Nguyen M, Rankin J, et al.
Introduction: Coronary artery revascularization procedures (CARP) are the cornerstone of treatment for patients with coronary artery disease. However, patients with diabetes have a greater risk of adverse outcomes following CARPs. Long-term outcomes for percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG) require further investigation in a real world cohort of diabetic patients. Objectives: Comparison of 4-year outcomes in a population cohort of patients with diabetes who had PCI or CABG in 2000-2004. Methods: Clinical data and linked hospital admissions and death data from the Western Australian Data Linkage System were merged for all patients who had their first CARP with PCI or CABG in 2000-2004. A history of diabetes was identified from the linked data using a 10-year lookback period. Clinical data were collected from all hospitals in Western Australia where all CARP procedures are performed. We calculated the unadjusted (Kaplan-Meier) and adjusted (Cox regression) risks for 4-year death (all-cause), admission for myocardial infarction (MI), subsequent CARP and the composite outcome of death/MI admission/subsequent CARP (MACE). Results: There were 3427 patients with diabetes (72% males, mean age 64 years, age range 27-93) who were treated with CARP during 2000-2004 (62% PCI vs 38% CABG). The unadjusted risk of death at 4 years for PCI vs CABG was 13.7% vs 13.6% (log-rank p=0.94), for MI was 10.3% vs 2.5% (p<0.0001), and for repeat revascularization was 23.0% vs 3.3% (p<0.0001) respectively. MACE at 4 years was 36.8% vs 18.0% (p<0.0001), respectively. After adjustment for age, gender, co-morbidities and other covariates, there was no difference in 4-year mortality between the PCI and CABG cohorts (HR 0.92, 95% CI 0.72-1.19). However, the PCI cohort still had higher adjusted risks of MI (HR 4.46, 95% CI 2.84-7.00) and subsequent revascularization (HR 8.24, 95% CI 5.78-11.74). Overall, MACE was significantly higher in the PCI cohort (HR 2.39, 95% CI 1.98-2.88). Conclusion: Diabetic patients whose first CARP is PCI rather than CABG have equivalent adjusted risk of mortality, but increased risk of MI and repeat revascularization at 4 years. Further studies are needed to determine if this is due to residual confounding by selection factors.

Publication Types: Conference Abstract
PMID: 71459907


Australian experience with AbsorbTM bioresorbable scaffold technology in "real-world" coronary disease.
(Nguyen, Chia, Whelan, Kanna) Cardiology, Fremantle Hospital, Perth, Australia (Jepson, Pitney, Back) Prince of Wales Hospital, Sydney, Australia (Pitney) Cardiology, Sutherland Hospital, Sydney, Australia (Hendriks) Fremantle Hospital, Perth, Australia (Ooi) Cardiology, Prince of Wales Hospital, Sydney, Australia (Ahmadi) Medicine, Notre Dame University, Perth, Australia
M.C. Nguyen, Cardiology, Fremantle Hospital, Perth, Australia

Introduction: Coronary metallic stents have been the cornerstone of treatment for coronary arterial disease. Bioabsorbable coronary scaffolds represent a novel treatment option that allows the initial restoration of coronary flow and support of the vessel, however with subsequent resorption of the scaffold, the risks of stent thrombosis and need for long-term antiplatelet therapy can be potentially reduced. "Real world" data on the use of this technology in a more complex subset of patients and lesions is lacking. Objectives: We aimed to study the safety and efficacy of the Absorb bioabsorbable scaffold (ABRS) out to 30 days for the treatment of patients presenting with acute coronary syndrome (ACS) and stable angina, in a wide range of lesion subsets including primary PCI, chronic total occlusions (CTOs), bifurcations, long lesions and multi-vessel disease. Methods: Data was
prospectively collected from 3 major tertiary hospitals in Australia (Fremantle Hospital, Western Australia, and Prince of Wales Public Hospital and Sutherland Hospital, New South Wales) between December 2010 and August 2013. Baseline demographics, presentation, as well as procedural data were collected. Both in-hospital and 30 day safety and efficacy outcomes were analysed. Results: In total, 155 patients were treated with 245 scaffolds (mean age 60yrs, 60% male) with 52% presenting with ACS (6% STEMI) and 10% undergoing multi-vessel intervention. There was a mean of 1.6 scaffolds/patient (range 1 to 5) with LAD, LCX, RCA and SVG treated in 39%, 22%, 35%, and 2.3% respectively. There was 100% procedural success and 99% device success (2 device delivery failures with subsequent successful treatment with drug-eluting stents). There were 2 in-hospital myocardial infarcts (Non Q wave, 1.3%) with no mortality. At 30 days, there were a total of 3 myocardial infarcts (1.9%) including 1 scaffold thrombosis (0.6%) requiring target vessel revascularization (0.6%). There was no mortality. Conclusion: This early local experience has demonstrated ABRS therapy to be highly safe and efficacious in a cohort of real-world patients with complex presentations and disease (including ACS, long lesions, multi-vessel disease and CTOs).
overall relative change in median DALYs was higher among both men and women in developing versus developed countries: men: 1.18 (95% CI: 0.82 to 1.65) versus 0.51 (95% CI: 0.30 to 0.81), and women: 1.11 (95% CI: 0.58 to 2.02) versus 1 (95% CI: 0.67 to 1.47). Within developed nations, the overall relative change in median DALY rates was larger in women than in men: +1.00 (95% CI: 0.67 to 1.47) versus +0.51 (95% CI: 0.3 to 0.81). Similarly, the overall relative change in median years of life lost rate in developed countries was larger in women than in men: +1.64 (95% CI: 1.17 to 2.34) versus +0.53 (95% CI: 0.24 to 0.94). The relative increases in median years lived with nonfatal disease disability (YLD) rates in men and women were larger in developing versus developed nations: men: 0.87 (95% CI: 0.59 to 1.2) versus 0.49 (95% CI: 0.29 to 0.73), and women: 0.75 (95% CI: 0.46 to 1.09) versus 0.49 (95% CI: 0.29 to 0.73). Disability and mortality associated with PAD has increased over the last 20 years, and this increase in burden has been greater among women than among men. In addition, the burden of PAD is no longer confined to the elderly population, but now involves young adults. Furthermore, the relative increase in PAD burden in developing regions of the world is striking and exceeds the increases in developed nations.


Sampson UKA, Norman PE, et al.
(Sampson) Department of Medicine, Vanderbilt University Medical Center (VUMC), Nashville, TN, United States (Norman) School of Surgery, University of Western Australia, Fremantle, WA, Australia (Fowkes) Centre for Population Health Sciences, University of Edinburgh, Edinburgh, United Kingdom (Aboyans) Department of Cardiology, Dupuytren University Hospital, INSERM U1094, Limoges, France (Song, Harrell Jr.) Department of Biostatistics, VUMC, Nashville, TN, United States (Forouzanfar, Naghavi, Ezzati, Murray) Institute for Health Metrics and Evaluation, Seattle, WA, United States (Denenberg, Criqui) Department of Family and Preventive Medicine, University of California, San Diego, CA, United States (McDermott) Department of Medicine and Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, United States (Mensah) Center for Translation Research and Implementation Science (CTRIS), National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, United States (Ezzati) School of Public Health, Imperial College London, United Kingdom
U.K.A. Sampson, Department of Medicine, Vanderbilt University Medical Center (VUMC), Nashville, TN, United States. E-mail: u.sampson@vanderbilt.edu

A comprehensive and systematic assessment of the global burden of aortic aneurysms (AA) has been lacking. Therefore, we estimated AA regional deaths and years of life lost (YLL) in 21 regions worldwide for 1990 and 2010. We used the GBD (Global Burden of Disease) 2010 study causes of death database and the cause of death ensemble modeling approach to assess levels and trends of AA deaths by age, sex, and GBD region. The global AA death rate per 100,000 population was 2.49 (95% CI: 1.78 to 3.27) in 1990 and 2.78 (95% CI: 2.04 to 3.62) in 2010. In 1990 and 2010, the highest mean death rates were in Australasia and Western Europe: 8.82 (95% CI: 6.96 to 10.79) and 7.69 (95% CI: 6.11 to 9.57) in 1990 and 8.38 (95% CI: 6.48 to 10.86) and 7.68 (95% CI: 6.13 to 9.54) in 2010. YLL rates by GBD region mirrored the mortality rate pattern. Overall, men had higher AA death rates than women: 2.86 (95% CI: 1.90 to 4.22) versus 2.12 (95% CI: 1.33 to 3.00) in 1990 and 3.40 (95% CI: 2.26 to 5.01) versus 2.15 (95% CI: 1.44 to 2.89) in 2010. The relative change in median death rate was +0.22 (95% CI: 0.10 to 0.33) in developed nations versus +0.71 (95% CI: 0.28 to 1.40) in developing nations. The smallest relative changes in median death rate were noted in North America high income, Central Europe, Western Europe, and Australasia, with estimates of +0.07 (95% CI: -0.26 to 0.37), +0.08 (95% CI: -0.02 to 0.23), +0.09 (95% CI: -0.02 to 0.21), and +0.22 (95% CI: -0.08 to 0.46), respectively. The largest increases were in Asia Pacific high income, Southeast Asia, Latin America tropical, Oceania, South Asia, and Central Sub-Saharan Africa. Women rather than
men drove the increase in the Asia Pacific high-income region: the relative change in median rates was +2.92 (95% CI: 0.6 to 4.35) versus +1.05 (95% CI: 0.61 to 2.42). In contrast to high-income regions, the observed pattern in developing regions suggests increasing AA burden, which portends future health system challenges in these regions. 2014 World Heart Federation (Geneva). Published by Elsevier Ltd. All rights reserved.


Sampson UKA, Norman PE, et al.
(Sampson) Department of Medicine, Vanderbilt University Medical Center (VUMC), Nashville, TN, United States (Norman) School of Surgery, University of Western Australia, Fremantle, WA, Australia (Fowkes) Centre for Population Health Sciences, University of Edinburgh, Edinburgh, United Kingdom (Aboyans) Department of Cardiology, Dupuytren University Hospital, INSERM U1094, Limoges, France (Song, Harrell Jr.) Department of Biostatistics, VUMC, Nashville, TN, United States (Forouzanfar, Naghavi, Ezzati, Murray) Institute for Health Metrics and Evaluation, Seattle, WA, United States (Denenberg, Criqui) Department of Family and Preventive Medicine, University of California, San Diego, CA, United States (McDermott) Department of Medicine and Preventive Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, United States (Mensah) Center for Translation Research and Implementation Science (CTRIS), National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, United States (Ezzati) School of Public Health, Imperial College London, United Kingdom

U.K.A. Sampson, Department of Medicine, Vanderbilt University Medical Center (VUMC), Nashville, TN, United States. E-mail: u.sampson@vanderbilt.edu

The global burden of abdominal aortic aneurysm (AAA) has not been studied previously. Such information is important given the emergence of cardiovascular diseases in developing countries. We conducted a systematic literature review and estimated the global and regional incidence and prevalence of AAA in 21 world regions by age and sex. The search for prevalence and incidence of AAA using standard clinical and epidemiological terms was conducted using MEDLINE (1950 to 2010), EMBASE (1980 to 2010), AMED (1985 to 2010), CINAHL (1982 to 2010), and LILACS (2008 to 2010). Data abstracted from the systematic review served as priors for Bayesian meta-regression analyses. The analysis drew from 26 high-quality studies to estimate AAA prevalence and incidence. In 1990, the global age-specific prevalence rate per 100,000 ranged from 8.43 (95% CI: 7.03 to 10.14) in the 40 to 44 years age group to 2,422.53 (95% CI: 2,298.63 to 2,562.25) in the 75 to 79 years age group; the corresponding range in 2010 was 7.88 (95% CI: 6.54 to 9.59) to 2,274.82 (95% CI: 2,149.77 to 2,410.17). Prevalence was higher in developed versus developing nations, and the rates within each development stratum decreased between 1990 and 2010. Globally, the age-specific annual incidence rate per 100,000 in 1990 ranged from 0.89 (95% CI: 0.66 to 1.17) in 40 to 44 years age group to 176.08 (95% CI: 162.72 to 190.28) in the 75 to 79 years age group. In 2010, this range was 0.83 (95% CI: 0.61 to 1.11) to 164.57 (95% CI: 152.20 to 178.78). The highest prevalence in 1990 was in Australasia and North America high income regions: 382.65 (95% CI: 356.27 to 410.88) and 300.59 (95% CI: 229.83 to 321.54), respectively. Australasia had the highest prevalence in 2010, although the prevalence decreased to 310.27 (95% CI: 289.01 to 332.94). Regional prevalence increased in Oceania, tropical Latin America, Asia Pacific high income, Southern Sub-Saharan Africa (SSA), Central SSA, South Asia, Western SSA, and Central Asia. AAA global prevalence and incidence rates have decreased over the last 20 years. However, rising rates in some regions highlight the need for policies to enhance global disease surveillance and prevention. 2014 World Heart Federation (Geneva). Published by Elsevier Ltd. All rights reserved.

**Stent technology is a strong driver of coronary artery revascularisation procedure rates in Western Australia: Trends 1981-2011.**

Sanfilippo F, Rankin J, et al.
(Sanfilippo, Knuiman, Briffa, Geelhoed, Hobbs) School of Population Health, University of Western Australia, Perth, Australia (Rankin) Cardiology, Royal Perth Hospital, Perth, Australia (Nguyen) Cardiology, Fremantle Hospital, Perth, Australia (Newman) Cardiothoracic Surgery, Sir Charles Gairdner Hospital, Perth, Australia (Cutlip) Harvard Clinical Research Institute, Boston, United States (Cutlip) Beth Israel Deaconess Medical Centre, Harvard Medical School, Boston, United States F. Sanfilippo, School of Population Health, University of Western Australia, Perth, Australia

Introduction: Coronary artery revascularisation procedures (CARP) are the main interventional treatment for coronary artery disease and have evolved with time. Trends in rates of CARP at the population level, particularly after the introduction of drug eluting stents (DES), are largely undocumented in Australia. Objectives: To investigate the changing trends in CARPs from 1981 to 2011 in Western Australia. Methods: We used records of hospital admissions from the Western Australian Data Linkage System to identify all admissions for CARPs in people aged 35 years or over during 1981 to 2011. Age-standardised rates of admission for CARPs were calculated in males and females separately by the direct method using the Western Australian resident population at 30 June 2006 as the standard. The proportion of DES use was calculated from cardiology registers and medical notes in hospitals in which CARPs are performed. Results: Age-standardised rates of CARP have more than doubled since 1981 from 195 per 100,000 person-years in males and 37 per 100,000 person-years in females to 557 and 165 per 100,000 person-years, respectively, in 2011. Coronary artery bypass graft (CABG) rates peaked in 1993 at 305 and 82 per 100,000 person-years in males and females, respectively, but then steadily declined to 100 and 25 per 100,000 person-years, respectively, in 2011. Rates of percutaneous coronary intervention (PCI) increased rapidly following the introduction of bare metal stents (BMS) in 1992 and surpassed those for CABG in 1995. A second period of accelerated growth in PCI rates occurred following the introduction of DES in 2002. DES comprised 26% of total stent use in 2002, increasing rapidly to 96% by 2005 then falling to 88% in 2006, 68% in 2009 and increasing again to 83% by 2011. Decreasing use of DES in 2006-2009 followed publication of registry data suggesting an increased risk of stent thrombosis. More recent increases in DES rates followed publication of trials for the current generation of DES, with one year risk of stent thrombosis of <1% and very low risk of late stent thrombosis. Conclusion: Age-standardised rates of CARP have steadily increased in Western Australia since 1981. The introduction of BMS in 1992 and of DES in 2002 were associated with periods of accelerated growth in total CARPs. Adverse publicity for DES contributed to a transient decline in use of DES between 2006-2009, but DES remains the primary interventional technology for coronary revascularisation.

Publication Types: Conference Abstract
PMID:71460162


**Percutaneous mitral valve repair in a high-risk Australian series.**

Department of Cardiothoracic Surgery, Sir Charles Gairdner Hospital, Nedlands, Western Australia. Department of Cardiovascular Medicine, Sir Charles Gairdner Hospital, Nedlands, Western Australia. Department of Cardiothoracic Surgery, Sir Charles Gairdner Hospital, Nedlands, Western Australia; Notre Dame Medical School, Fremantle, Western Australia. Department of Cardiovascular Medicine, Sir Charles Gairdner Hospital, Nedlands, Western Australia. Electronic address: Eric.Yamen@health.wa.gov.au.

BACKGROUND: The prognosis for patients with symptomatic, severe mitral regurgitation (MR) who have comorbidities precluding mitral valve surgery is poor. Treatment of MR using a percutaneous edge-to-edge technique may improve survival, quality of life and reduce hospitalisations. To date, there are few studies reporting outcomes after percutaneous mitral valve repair in high-risk patients...
and none reported from Australia.

METHODS: The first 25 patients undergoing percutaneous mitral valve repair using the MitraClip in our Institution had follow-up to six months. These patients had severe, symptomatic MR and were deemed too high-risk for mitral valve surgery by a multidisciplinary heart team, including an interventional cardiologist and cardiothoracic surgeon.

RESULTS: There were no peri-procedural deaths; the only peri-procedural morbidity was blood transfusion in three patients. Three patients had died at six months and there were six readmissions to hospital. There was a significant improvement in heart failure symptoms, 6-minute walk test and quality of life at six months. There was a significant improvement in the proportion of patients with MR <2+, but no significant change in other echocardiographic parameters.

CONCLUSIONS: Percutaneous mitral valve repair is safe in patients at high-risk for surgery, and improves symptoms and quality of life. Copyright 2014. Published by Elsevier B.V.

PMID:24704244


Role of TWEAK in coregulating liver progenitor cell and fibrogenic responses.
Tirnitz-Parker JEE, Olynyk JK, et al.
(Tirnitz-Parker, Olynyk) School of Biomedical Sciences, CHIRI Biosciences Research Precinct, Curtin University, Bentley, Australia (Tirnitz-Parker, Olynyk) School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia (Olynyk) Department of Gastroenterology, Fremantle Hospital, Fremantle Australia (Olynyk) Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, Australia (Ramm) School of Medicine, University of Queensland, Brisbane, Australia (Ramm) The Hepatic Fibrosis Group, Department of Cell and Molecular Biology, QIMR Berghofer Medical Research Institute, Brisbane, Australia
School of Biomedical Sciences, CHIRI Biosciences Research Precinct, Curtin University, Bentley, Australia
PMID:2014148159


CX3CR1 reduces choline-deficient, ethionine-supplemented dietinduced liver injury and liver progenitor cell proliferation.
Elsegood CL, Plant GW, et al.
(Elsegood, Yeoh) School of Chemistry and Biochemistry, University of Western Australia, Crawley, Australia (Elsegood, Olynyk) School of Biomedical Sciences, Curtin University, Bentley, WA, Australia (Elsegood, Yeoh) Harry Perkins Institute of Medical Research, Nedlands, Australia (Plant) Department of Neurosurgery, Stanford Partnership for Spinal Cord Injury and Repair, Stanford University, Stanford, CA, United States (Olynyk) Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia (Olynyk) Institute for Immunology and Infectious Diseases, Murdoch University, Murdoch, WA, Australia
C.L. Elsegood, School of Chemistry and Biochemistry, University of Western Australia, Crawley, Australia
Introduction: We have previously reported that expression of CX3CR1 and its cognate ligand, CX3CL1, is elevated in choline-deficient, ethionine-supplemented (CDE) diet-induced liver injury [1]. We showed that Kupffer cells and monocyte-derived macrophages mediate CDE diet-induced injury and liver progenitor cell (LPC) proliferation. Further, CX3CR1 down-regulates liver fibrosis and inflammation [2, 3]. Aim: To establish a link between CX3CR1 and LPC growth in a transgenic mouse model. Methods: We assessed the role of CX3CR1 in liver injury and LPC proliferation by comparing the response of heterozygous CX3CR1gfp/+ (control) and homozygous CX3CR1gfp/gfp (CX3CR1 knockout) mice to the CDE diet after 3 days. Results: Heterozygous CX3CR1gfp/+ mice exhibited markedly reduced CDE diet-induced LPC proliferation when compared to homozygous CX3CR1gfp/gfp mice. Furthermore, liver mRNA expression of the LPC mitogens, TNFalpha and
lymphotoxin b, were also significantly reduced in the heterozygous mice. In contrast, levels of IL-6, interferon c, HGF, and TWEAK were not affected. Heterozygous CX3CR1gfp/+ mice developed less liver injury compared to the homozygous CX3CR1gfp/gfp, as reflected by a reduction in serum alanine transaminase and TUNEL staining, together with a reduction in the number of inflammatory cells such as neutrophils and B cells. However, the numbers of Kupffer cells and monocyte-derived macrophages were similar in the heterozygous and homozygous mice. Likewise, the degree of hepatic steatosis did not differ between the mice. Conclusion: CX3CR1 down-regulates CDE diet-induced LPC proliferation. This may be as a result of the reduction in liver injury and accompanying reduced production of the LPC mitogens, TNFalpha and lymphotoxin b.


Efficacy and safety of an interferon-free regimen of MK-5172 + ribavirin for 12 weeks or 24 weeks in treatment naive, non-cirrhotic subjects with HCV GT1 Infection: The C-SPIRIT Study.

Gane EJ, Ben Ari Z, et al. (Gane) New Zealand Liver Transplant Unit, Auckland City Hospital, Auckland, New Zealand (Ben Ari) Liver Disease Center, Sheba Medical Center, Ramat Gan, Israel (Mollison) Fremantle Hepatitis Services, Fremantle Hospital, Fremantle, WA, Australia (Zuckerman) Liver Unit, Carmel Medical Center, Haifa, Israel (Bruck) Department of Gastroenterology and Liver Diseases, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel (Baruch) Liver Unit, Rambam Healthcare Campus, Haifa, Israel (Wahl) Merck Research Laboratories, Kenilworth, NJ, United States (Bhanja, Hwang, Zhao, Robertson) Merck Research Laboratories, Upper Gwynedd, PA, United States

Purpose: MK-5172 is a potent, pan-genotypic, second generation hepatitis C virus (HCV) NS3/4A protease inhibitor with a high genetic barrier to resistance. Several interferon-free regimens of direct-acting antiviral agents (DAAs) have been reported to achieve high rates of SVR. Efficacy appears to depend on potency, viral genotype (GT), and patient characteristics. This study evaluates the interferon-free, single DAA regimen of MK-5172 + ribavirin (RBV) in patients with HCV GT 1 infection who express the IL28B CC genotype. Methods: Treatment-naive, non-cirrhotic, IL28B CC genotype patients with HCV GT1 infection were randomized to receive 12 or 24 weeks of MK-5172 100 mg QD + weight-based RBV BID. Patients in the 12-week arm with detectable HCV RNA at treatment week (TW) 4 had their treatment duration extended to 24 weeks. Weekly assessments were performed during treatment. Follow-up visits occurred 4, 12, and 24 weeks after end of treatment. HCV-RNA samples were assessed using COBAS TaqMan ci<sup>2</sup>.0. Futility was defined as HCV-RNA > 25 IU/mL at TW4. Results: 26 patients (17 male/9 female) were enrolled. One patient discontinued on day 1 because his wife was pregnant. Of the remaining patients, 12 had HCV GT1a infection and 13 had GT1b. Mean baseline HCV-RNA was approximately 9.0 x 10<sup>6</sup> IU/mL. All but two patients had achieved HCV-RNA of TND by TW6. As of May 28, 2013, 15 subjects had completed TW12. One patient had confirmed viral breakthrough at TW6 and stopped treatment. All remaining patients maintained viral suppression during treatment. The most frequently reported adverse events (> 10 %) were headache (6, 23 %), asthenia (6, 23 %), anemia (3, 12 %), dyspepsia (3, 12 %), nausea (3, 12 %), and insomnia (3, 12 %). There were no SAEs or treatment discontinuations. ALT was elevated at baseline in 16 patients (range, 34-252), but normalized on treatment in all patients. Nine patients had transient, mild (grade 1-2) elevations in total bilirubin on treatment (range, 1.12-2.45). Conclusion: Patients with HCV GT1a or GT1b infection receiving MK-5172 + RBV achieved rapid and sustained HCV-RNA suppression. One patient had viral breakthrough at TW6. SVR12 and resistance data will be presented. These results support further evaluation of IFN-free regimens with MK-5172.

Table Presented.

Publication Types: Conference Abstract
PMID:71384306
The first Australasian experience with boceprevir: Treatment outcomes, adverse events and adherence.

Nazareth S, Fragomeli V, et al.
(Nazareth) Royal Perth Hospital, Perth, Australia (Fragomeli) Nepean Hospital, Penrith, Australia (Colman) Royal Adelaide Hospital, Adelaide, Australia (Mason) Royal Prince Alfred Hospital, Camperdown, Australia (Morales) Austin Hospital, Heidelberg, Australia (Jones) John Hunter Hospital, New Lambton Heights, Australia (Totten) Fremantle Hospital, Fremantle, Australia (Altus) Flinders Medical Centre, Bedford Park, Australia (Sendall) Cairns Base Hospital, Cairns, Australia (Pham) Cabramatta Practice, Cabramatta, Australia

S. Nazareth, Royal Perth Hospital, Perth, Australia

The approval of direct-acting antiviral agents marks a new era in the treatment of patients with chronic hepatitis C. Clinical trials have revealed significant improvements in treatment outcomes through the addition of boceprevir to pegylated interferon and ribavirin therapy. However treatment is also associated with increased adverse events including anaemia, neutropenia, dysguesia, rash and dry skin. "Real world" studies can provide an insight into treatment and management for a wider spectrum of patients including complex or difficult to treat patients. This study aims to document the first Australasian experience with boceprevir including treatment outcomes, adherence and adverse events. Data was collected from 70 genotype 1 patients across ten Australian liver clinics. Baseline characteristics, pathology results, adverse events, adherence, compliance and treatment outcomes were recorded. Data from all patients were included in the analysis. Mean age was 54 years, 70 % were male and mean baseline weight was 82 kg. Caucasians (n = 54), Asians (n = 15) and Aboriginals (n = 1) were represented. 47 % of participants had cirrhosis and 27 % had advanced fibrosis. 86 % (n = 60) of participants were treatment experienced (27 non-responders). Forty participants (57 %) achieved a sustained virological response (SVR). SVR rates were significantly higher in participants with a low baseline viral load of<800,000 IU/L (relative rate 1.96 [95 % CI, 1.34-2.85; p = 0.002]) and in participants with ribavirin dose reductions (relative rate 1.73 [95 % CI, 1.19-2.53; p = 0.007]). Fibrosis stage was not predictive of SVR. Participants with cirrhosis and advanced fibrosis had higher rates of SVR; however the difference was not significant (relative rate 1.38 [95 % CI, 0.79-2.42] cirrhosis plus advanced fibrosis versus early/no fibrosis). Thirty participants (43 %) ceased treatment early, due to detectable viraemia at week 12 or 24 (n = 17, 24 %), adverse events (n = 9, 13 %) or varied personal reasons (n = 4, 6 %). Six participants with premature discontinuation went on to achieve a SVR. Seven participants (10 %) reported missing doses of boceprevir (0.15-4.5 % of prescribed therapy). Dose reductions to pegylated interferon (n = 13) and ribavirin (n = 28) were initiated due to cytopenias. Anaemia (Hb<10 g/L) was reported in 38 participants (54 %), neutropenia (neutrophils<0.75 x 10<sup>9</sup>/L) in 31 (44 %) and thrombocytopenia in 28 (40 %). Anaemia was managed with ribavirin dose reductions and omissions, transfusion (n = 11) and/or erythropoietin therapy (n = 5). Neutropenia was managed with pegylated interferon dose reductions, plus GCFS (n = 2) and discontinuation in one case. Dysguesia was reported by 55 participants (79 %) with three grade 4 cases. Other adverse events included rash (n = 17, 24 %), dry skin (n = 25, 36 %), depression (n = 17, 24 %), fatigue (n = 10, 59 %), irritability (n = 5, 7 %), diarrhoea (n = 3, 4 %). Serious adverse events included hospitalisation for decompensation (n = 2, 3 %). No deaths were reported. The addition of boceprevir to standard of care substantially increased SVR rates in the clinical setting despite the high representation cirrhotic and treatment experienced patients. Participants reported > 95 % adherence to prescribed doses of boceprevir. Close monitoring is required due to the side effect profile including cytopenias, and liver decompensation.

Publication Types: Conference Abstract
PMID:71384291

Early experience on treatment with direct acting antiviral drugs in chronic hepatitis C-interim analysis in Western Australian tertiary centres.
Background: Direct acting antiviral agents (DAAs)—Telaprevir (TVP) and Boceprevir (BOC) have been approved for the treatment of chronic hepatitis C-genotype 1 patients since April 2013 in Australia. We report our early experience with DAAs in 3 tertiary hospitals in patients treated through early access and patient familiarization programs from September 2011 to May 2013. Aims: To evaluate our experience with telaprevir and boceprevir with reference to (1) virological response (2) host and viral factors affecting response (3) side effect profile Methods: A retrospective descriptive analysis of patients treated with DAAs at 3 tertiary hospitals. Data collected from review of medical records included demographics, IL28B genotype, viral response and side effects. Results: To date 86 patients were treated, of whom 72 % were males. Mean age was 50 years. 55 % were treatment naive. IL28B-homozygous CC genotype (rs12979860) was noted in 30.2 % of the patients. In treatment naive patients with IL28B CC genotype (rs12979860), 80 % treated with Telaprevir and 88 % with Boceprevir achieved SVR 12 or 24. Conclusions: Treatments with DAAs were well tolerated with low discontinuation rate. Rash is common with TVP and dysgeusia in BOC group. Although mild anaemia is more common with BOC, Hb<85 g/L is more common with TVP. Ribavirin dose reduction is common. More patients in BOC than TVP groups received response guided therapy. (Table Presented).

Publication Types: Conference Abstract
PMID:71384258


Direct acting antiviral drugs in chronic hepatitis C and renal toxicity.
(Rao, Kontorinis, Tarquinio, Kong, Nazareth, Cheng) Departments of Gastroenterology and Hepatology, Royal Perth Hospital, Perth, WA, Australia (Mollison, Galhenage, Totten) Departments of Gastroenterology and Hepatology, Fremantle Hospital, Perth, WA, Australia (MacQuillan, Adams, Jeffrey, Vallve) Sir Charles Gairdner Hospital, Perth, WA, Australia

Background: Direct acting antiviral agents (DAAs)—Telaprevir (TVP) and Boceprevir (BOC) have been approved for the treatment of chronic hepatitis C-genotype 1 patients since April 2013 in Australia. In the registration trials, renal dysfunction was not observed. Recent preliminary reports suggested that the incidence of renal impairment may be as high as 5 %, more common in old patients, and with cirrhosis, diabetes and hypertension. We report our early experience with DAAs in 3 tertiary hospitals in patients treated through early access and patient familiarization programs from September 2011 to May 2013. Aims: To determine the incidence and severity of renal dysfunction in patients treated with DAAs. Methods: Retrospective descriptive analysis of patients treated with DAAs at 3 tertiary centres. Data collected from review of medical records included demographics, viral markers, co-morbid conditions & concurrent medications, biochemical investigations and urinalysis. Results: 86 patients were treated, of whom 72 % were males and mean age was 50 years. 34 patients received TVP and 52 BOC. 40.6 % of patients had cirrhosis (hepascore>0.90). 30 % of patients are currently receiving treatment in the TVP group and 3.8 % in the BOC group. 6 % of patients discontinued treatment in TVP group and 5.7 % in BOC group. Only 1 male patient with cirrhosis, aged 75 years, in the telaprevir cohort developed sustained drop in eGFR of 40 % from baseline. He had no significant comorbidities and was not on any concurrent medications. Baseline creatinine was 90 mumol/L (normal: 60-110 mumol/L) and eGFR>60 ml/min/1.73 m<sup>2</sup> (Modification of Diet in Renal Disease formula). Creatinine was noted to rise during week 11 of treatment, peaking at 167 mumol/L; eGFR dropped to 35 ml/min/1.73 m<sup>2</sup>. Urinalysis and renal ultrasonography were normal.
Ribavirin was dose reduced from 1200 mg to 800 mg, Peginterferon to 150 mcg from 180 mcg and Telaprevir was continued at 750 mg thrice daily for a further week. An additional patient with cirrhosis, aged 55 years, in the TVP group was noted to have renal impairment during week 12 of treatment with a 40 % rise in creatinine and 26 % drop in eGFR from baseline. In both patients spontaneous improvement in renal function was noted over the next 2-4 weeks following cessation of TVP with subsequent normalization of creatinine and eGFR to pre-treatment levels. In the Boceprevir cohort, 2 patients, aged 65 & 66 years, both with cirrhosis who had normal pre-treatment creatinine and eGFR were noted to have selfresolving acute kidney injury. One patient developed a 20 % rise in creatinine and 15 % drop in eGFR from baseline at week 12 of treatment. The other patient developed a 23 % rise in creatinine and 10 % drop in eGFR from baseline at week 24 of treatment. In both patients renal function spontaneously improved within 1 to 3 weeks. Conclusion: Treatments with DAAs were well tolerated with low discontinuation rate. Renal dysfunction can be associated with triple therapy and may require ribavirin dose reduction. All 4 patients who developed DAA associated nephrotoxicity had cirrhosis. In TVP treated patients, renal impairment occurred during week 11 and week 12 of treatment and resolved after completion of 12 weeks of therapy.

Publication Types: Conference Abstract
PMID:71384257
characteristics of a novel kindred of five individuals with Muckle-Wells syndrome are described. Response to IL-1 blockade therapy in the proband was evaluated. All five affected family members experienced symptoms of multi-organ inflammation. Lead time between symptom onset and diagnosis was approximately 30 years in the proband. Fever was not a universal feature in all affected family members. Anti-IL-1 therapy in the proband resulted in improvements in patient-reported symptoms, inflammatory markers, auditory acuity and reversal of her infertility. Muckle-Wells syndrome is a rare, multisystem, auto-inflammatory syndrome. Delay in diagnosis prevents effective treatment. We propose reversal of infertility to be among the potential benefits of IL-1 inhibition in this disease. 2013 Springer Science+Business Media New York.

PMID:2014192883


Spontaneous pneumothorax; a multicentre retrospective analysis of emergency treatment, complications and outcomes.

Brown SGA, Ball EL, et al. (Brown, Macdonald) Centre for Clinical Research in Emergency Medicine, Harry Perkins Institute of Medical Research, Perth, WA, Australia (Brown) Department of Emergency Medicine, Royal Perth Hospital, Perth, WA, Australia (Ball) Department of Respiratory Medicine, Royal Perth Hospital, Perth, WA, Australia (Brown, Macdonald) Emergency Medicine, University of Western Australia, Perth, WA, Australia (Macdonald) Department of Emergency Medicine, Armadale Health Service, Perth, WA, Australia (Ball) Department of Respiratory Medicine, Fremantle Hospital, Fremantle, WA, Australia (Wright) Department of Emergency Medicine, Bunbury Regional Hospital, Bunbury, WA, Australia (Mcd Taylor) Department of Emergency Medicine, Austin Hospital, Melbourne, VIC, Australia (Mcd Taylor) Department of Medicine, University of Melbourne, Melbourne, VIC, Australia

S.G.A. Brown, Department of Emergency Medicine, Royal Perth Hospital, GPO Box X2213, Perth, WA 6847, Australia. E-mail: simon.brown@uwa.edu.au

Background: Spontaneous pneumothorax can be managed initially by observation, aspiration or chest drain insertion. Aims: To determine the clinical features of spontaneous pneumothorax in patients presenting to the emergency department (ED), interventions, outcomes and potential risk factors for poor outcomes after treatment. Methods: Retrospective chart review from ED of three major referral and two general hospitals in Australia of presentations with primary spontaneous pneumothorax (PSP) or secondary spontaneous pneumothorax (SSP). Main outcomes were prolonged air leak (>5 days) and pneumothorax recurrence within 1 year. Results: We identified 225 people with PSP and 98 with SSP. There were no clinical tension pneumothoraces with hypotension. Hypoxaemia (haemoglobin oxygen saturation measured by pulse oximetry <92%) occurred only in SSP and in older patients (age >50 years) with PSP. Drainage was performed in 150 (67%) PSP and 82 (84%) SSP. Prolonged air leak occurred in 16% (95% confidence interval 10-23%) of PSP and 31% (21-42%) of SSP. Independent risk factors for prolonged drainage were non-asthma SSP and pneumothorax size >50%. Complications were recorded in 11% (7.5-16%) of those having drains inserted. Recurrences occurred in 5/91 (5%, 1.8-12%) of those treated without drainage versus 40/232 (17%, 13-23%) of those treated by drainage, of which half occurred in the first month after drainage. Conclusion: Pneumothorax drainage is associated with substantial morbidity including prolonged air leak. As PSP appears to be well tolerated in younger people even with large pneumothoraces, conservative treatment in this subgroup may be a viable option to improve patient outcomes, but this needs to be confirmed in a clinical trial. 2014 Royal Australasian College of Physicians.

PMID:2014323929


The impact of lifestyle factors on the physical health of people with a mental illness: a brief review.

Stanley S, Laugharne J.
BACKGROUND: People with a mental illness are much more likely to experience poor physical health when compared to the general population, showing a higher propensity to develop the metabolic syndrome. Past focus has predominantly been upon individuals treated with antipsychotics, yet poor physical health is occurring across diagnoses.

PURPOSE: The purpose of this paper is to draw attention to the major factors within the domain of lifestyle in order to support the need for more detailed and rigorous physical health assessment and ongoing monitoring for people with a mental illness.

METHOD: This paper reviews existing evidence relating to lifestyle factors such as low exercise levels, poor diet and nutrition, high cholesterol levels, tobacco smoking and poor dental care, contributing to poor physical health such as a higher incidence of cardiovascular disease and type 2 diabetes. An integrative review was conducted from a multi-disciplinary search of online databases and journals, focusing upon mental illness and lifestyle issues predominant in the literature.

RESULTS: The findings reviewed here suggest that greater attention should be paid to the physical health assessment and ongoing monitoring of all people with mental health disorders so that preventable illness does not result in higher levels of morbidity and mortality for this disadvantaged population.

CONCLUSION: Early identification aids preventive interventions and assists clinicians and mental health staff to more effectively treat emergent physical health problems.

PMID:23443909


**Delayed vesicovaginal fistula after ring pessary usage.**

Penrose KJ, Yin J, et al.

(Penrose, Yin, Tsokos) Department of Urogynaecology, King Edward Memorial Hospital, Subiaco, WA, Australia (Penrose) Hollywood Private Hospital, Nedlands, WA, Australia (Penrose, Tsokos) University of Notre Dame, Fremantle, WA, Australia (Tsokos) School of Medicine, University of Western Australia, Crawley, WA, Australia (Penrose) 374 Bagot Road, Subiaco 6009, WA, Australia K.J. Penrose, 374 Bagot Road, Subiaco 6009, WA, Australia. E-mail: katherine.penrose@health.wa.gov.au

Vaginal pessaries are commonly used in the conservative management of pelvic organ prolapse, and are generally viewed as safe alternatives to surgery. Serious complications are rare, but can and do arise, typically as a result of the pessary not being fitted and maintained correctly. This case describes delayed development of a vesicovaginal fistula (VVF) 8 months after vaginal ulceration was noted and the ring pessary removed. The 82-year-old patient was managed with a urinary diversion via ileal conduit. This case highlights the importance of meticulous follow-up when a pessary is removed in the setting of ulceration. It is the third documented case of a genitourinary fistula resulting from a vaginal ring pessary, and is the first reported case of this surgical technique being successfully used in this setting. The International Urogynecological Association 2013.

PMID:2014271985


**Effectiveness of an acellular synthetic matrix in the treatment of hard-to-heal leg ulcers.**


(Harding) Wound Healing Research Unit, Institute for Translation, Innovation, Methodologies and Engagement (TIME), Cardiff University, Cardiff, United Kingdom (Aldons, Jenkins) Prince Charles Hospital, Chermside, Australia (Edwards, Finlayson, Gibb) School of Nursing and Midwifery, Queensland University of Technology, Brisbane, Australia (Stacey) Department of Surgery, Fremantle Hospital, University of Western Australia, Fremantle, Australia (Shooter, Lonkhuyzen, Lynam, Upton)
Hard-to-heal leg ulcers are a major cause of morbidity in the elderly population. Despite improvements in wound care, some wounds will not heal and they present a significant challenge for patients and health care providers. A multi-centre cohort study was conducted to evaluate the effectiveness and safety of a synthetic, extracellular matrix protein as an adjunct to standard care in the treatment of hard-to-heal venous or mixed leg ulcers. Primary effectiveness criteria were (i) reduction in wound size evaluated by percentage change in wound area and (ii) healing assessed by number of patients healed by end of the 12 week study. Pain reduction was assessed as a secondary effectiveness criteria using VAS. A total of 45 patients completed the study and no difference was observed between cohorts for treatment frequency. Healing was achieved in 356% and wound size decreased in 933% of patients. Median wound area percentage reduction was 708%. Over 50% of patients reported pain on first visit and 870% of these reported no pain at the end of the study. Median time to first reporting of no pain was 14 days after treatment initiation. The authors consider the extracellular synthetic matrix protein an effective and safe adjunct to standard care in the treatment of hard-to-heal leg ulcers.

Risk factors for nephrotoxicity in patients receiving outpatient continuous infusions of vancomycin in an Australian tertiary hospital.

Norton K, Ingram PR, et al. (Norton, Ingram, Heath, Manning) Department of Microbiology and Infectious Diseases, Royal Perth Hospital, Perth, WA, Australia (Norton) Swan District Hospital, Perth, WA, Australia (Ingram) School of Pathology and Laboratory Medicine, University of Western Australia, Perth, WA, Australia (Heath) School of Medicine and Pharmacology, University of Western Australia, Royal Perth Hospital, Perth, WA, Australia (Manning) School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital Unit, Fremantle, WA, Australia

K. Norton, Department of Microbiology and Infectious Diseases, Royal Perth Hospital, Level 6, South Block, Wellington Street, Perth, WA 6000, Australia. E-mail: katherine.norton@health.wa.gov.au

Objectives: To assess the risk factors for nephrotoxicity caused by vancomycin continuous infusion in a predominantly Caucasian outpatient population. Methods: This was a retrospective cohort study of 155 patient episodes from December 2006 to December 2011. Results: Vancomycin-associated nephrotoxicity (VN) occurred in 26 of 155 (17%) patient episodes. After adjustment for baseline renal function, maximum steady-state vancomycin concentrations >32 mg/L [OR 8.7 (95% CI 3.1-29.6), P < 0.001] and angiotensin receptor blockade [OR 9.78 (95% CI 3.1-39.4), P < 0.001] were independently associated with VN. The cumulative dose and duration of vancomycin therapy were not independent predictors of VN. Conclusions: Cessation of angiotensin receptor-blocking medications in selected patient groups, enhanced monitoring and establishing target steady-state concentrations <30 mg/L to avoid excessive vancomycin exposure may reduce the risk of VN. The Author 2013. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved.

Can interchangeability of lincosamides be assumed in clinical practice? Comparative MICs of clindamycin and lincomycin for Streptococcus pyogenes, Streptococcus agalactiae and Staphylococcus aureus.
Can plate osteosynthesis of periprosthetic femoral fractures cause cement mantle failure around a stable hip stem? A biomechanical analysis.
Department of Orthopaedic Surgery, St. Gallen, Switzerland.
Department of Medical Engineering and Physics, Royal Perth Hospital, Perth, Australia.
Medical Orthopaedic Clinic, Murdoch, Australia.
Fremantle University Hospital, Fremantle, Australia.
Royal Perth Hospital, University of Western Australia, Perth, Australia.
Periprosthetic femoral fractures (PFF) are a serious complication after total hip arthroplasty. Plate fixation with screws perforating the cement mantle is a common treatment option. The study objective was to investigate hip stem stability and cement mantle integrity under dynamic loading. A cemented hip stem was implanted in 17 composite femur models. Nine bone models were osteotomised just distal to the stem and fixed with a polyaxial locking plate the other eight constructs served as the control group. All specimens were tested in a bi-axial material testing machine (100000 cycles). There were no statistically significant differences in axial nor in medial (varus) stem migration. No cement cracks were detected in both groups. Plate fixation of a PFF with a stable, cemented prosthesis did not lead to cement mantle failure in this in vitro study. Copyright 2014 Elsevier Inc. All rights reserved.
PMID:24439999

Yates P.
University of Western Australia, Fremantle, Western Australia, Australia.
PMID:24500595

In older men an optimal plasma testosterone is associated with reduced all-cause mortality and higher dihydrotestosterone with reduced ischemic heart disease mortality, while estradiol levels do not predict mortality.
Yeap BB, Alfonso H, et al.
School of Medicine and Pharmacology (B.B.Y., S.A.P.C., G.J.H., L.F.), University of Western Australia, Perth, Western Australia 6009, Australia; Department of Endocrinology and Diabetes (B.B.Y.), Fremantle Hospital, Fremantle, Western Australia 6160, Australia; Western Australian Centre for Health and Ageing (H.A., O.P.A., L.F.), Centre for Medical Research, University of Western Australia, Perth, Western Australia 6009, Australia; PathWest Laboratory Medicine (S.A.P.C.), Fremantle and Royal Perth Hospitals, Perth, Western Australia 6009, Australia; ANZAC Research Institute (D.J.H.), University of Sydney, Sydney, New South Wales 2139, Australia; School of Psychiatry and Clinical Neurosciences (O.P.A.), University of Western Australia, Perth, Western Australia 6009, Australia; Vascular Biology Unit (J.G.), Queensland Research Centre for Peripheral
Vascular Disease, School of Medicine, James Cook University, Townsville, Queensland 4811, Australia; and School of Surgery (P.E.N.), University of Western Australia, Perth, Western Australia 6009, Australia.

CONTEXT: Testosterone (T) levels decline with age and lower T has been associated with increased mortality in aging men. However, the associations of its metabolites, dihydrotestosterone (DHT) and estradiol (E2), with mortality are poorly defined.

OBJECTIVE: We assessed associations of T, DHT, and E2 with all-cause and ischemic heart disease (IHD) mortality in older men.

PARTICIPANTS: Participants were community-dwelling men aged 70 to 89 years who were residing in Perth, Western Australia.

MAIN OUTCOME MEASURES: Plasma total T, DHT, and E2 were assayed using liquid chromatography-tandem mass spectrometry in early morning samples collected in 2001 to 2004 from 3690 men. Deaths to December 2010 were ascertained by data linkage.

RESULTS: There were 974 deaths (26.4%), including 325 of IHD. Men who died had lower baseline T (12.8±5.1 vs 13.2±4.8 nmol/L [mean±SD], P=.013), DHT (1.4±0.7 vs 1.5±0.7 nmol/L, P=.002), and E2 (71.6±29.3 vs 74.0±29.0 pmol/L, P=.022). After allowance for other risk factors, T and DHT were associated with all-cause mortality (T: quartile [Q] Q2:Q1, adjusted hazard ratio [HR]=0.82, P=.033; Q3:Q1, HR=0.78, P=.010; Q4:Q1, HR=0.86, P>.05; DHT: Q3:Q1, HR=0.76, P=.003; Q4:Q1, HR=0.84, P>.05). Higher DHT was associated with lower IHD mortality (Q3:Q1, HR=0.58, P=.002; Q4:Q1, HR=0.69, P=.026). E2 was not associated with either all-cause or IHD mortality.

CONCLUSIONS: Optimal androgen levels are a biomarker for survival because older men with midrange levels of T and DHT had the lowest death rates from any cause, whereas those with higher DHT had lower IHD mortality. Further investigations of the biological basis for these associations including randomized trials of T supplementation are needed.


Detection of liver injury in IBD using transient elastography.

Thin LW, Lawrance IC, et al.

Centre for Inflammatory Bowel Diseases, Fremantle Hospital, Fremantle, WA, Australia; Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia.

Centre for Inflammatory Bowel Diseases, Fremantle Hospital, Fremantle, WA, Australia; University Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, WA, Australia; Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia. Electronic address: ian.lawrance@uwa.edu.au.

Centre for Population Health Research, Curtin University, Bentley, WA, Australia.

Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia.

Department of Gastroenterology, Fremantle Hospital, Fremantle, WA, Australia; Curtin Health Innovation Research Institute, Curtin University, Bentley, WA, Australia; Institute for Immunology & Infectious Diseases, Murdoch University, Murdoch, WA, Australia.

BACKGROUND: Up to 5% of inflammatory bowel disease (IBD) patients are thought to have clinically significant liver disease due to multifactorial causes, however, this figure may be an underestimate due to reliance on abnormal liver tests (LTs) and/or liver biopsies.

AIMS: Our aim was to evaluate the prevalence of clinically significant liver disease in IBD patients as defined by an increased liver stiffness measurement (LS) >8kPa using transient elastography (TE).

METHODS: 110 IBD patients, and 55 non-IBD control subjects, had their LS recorded using FibroScan (EchoSense, Paris, France) by a single blinded operator trained in TE.

RESULTS: 71 Crohn's disease and 39 ulcerative colitis subjects were included. All demographic variables were similar between the IBD and control groups apart from a significantly higher proportion of IBD patients who smoked (17.3% vs 3.6%, P=0.013). Seven IBD patients (6.4%) had an LS over 8kPa and 3 had persistently elevated LS 6months later. One patient had compensated cirrhosis. No
significant differences in overall LS were observed between the IBD and control groups. Increased BMI and age, however, were independently associated with a higher LS in the IBD but not in the control group (P<0.001 and 0.010 respectively).

CONCLUSION: Using TE, the prevalence of clinically significant liver disease in IBD patients is low. The association of increased BMI and age with increased LS in IBD suggests fatty liver disease being the prevailing aetiology in these patients. Copyright 2014 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved.

PMID:24529605


Relationship between disease severity and quality of life and assessment of health care utilization and cost for ulcerative colitis in Australia: A cross-sectional, observational study.
Gibson PR, Vaizey C, et al.
Alfred Hospital, Australia; Monash University, Clayton, Victoria, Australia. Electronic address: Peter.Gibson@monash.edu.
St. Mark's Hospital, London, United Kingdom. Electronic address: cvaizey@nhs.net.
St. John's University, Queens, New York, USA; Merck Sharp & Dohme Corp., Whitehouse Station, NJ, USA. Electronic address: christopher.black2@merck.com.
OptumInsight, Sydney, New South Wales, Australia. Electronic address: Rebecca.Nicholls@optum.com.
OptumInsight, Sydney, New South Wales, Australia. Electronic address: adel weston@optum.com.
Flinders Private Hospital, Bedford Park, Southern Australia, Australia. Electronic address: peter.bampton@flinders.edu.au.
Alfred Hospital, Australia. Electronic address: M.Sparrow@alfred.org.au.
Centre for Inflammatory Bowel Diseases, School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia. Electronic address: ian.lawrance@uwa.edu.au.
Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia; University of Sydney, Sydney, New South Wales, Australia. Electronic address: warwicks@sydney.edu.au.
IBD Service, Department of Gastroenterology & Hepatology, Royal Adelaide Hospital, Adelaide, South Australia, Australia; School of Medicine, University of Adelaide, Adelaide, South Australia, Australia. Electronic address: Jane.Andrews@health.sa.gov.au.
St. Vincent's Hospital, Sydney, New South Wales, Australia. Electronic address: alissa.walsh@gmail.com.
East Adelaide Medical Centre, Adelaide, Southern Australia, Australia. Electronic address: David.Hetzel@health.sa.gov.au.
Royal Melbourne Hospital, Parkville, Victoria, Australia. Electronic address: Finlay.Macrae@mh.org.au.
Monash University, Clayton, Victoria, Australia; Monash Medical Centre, Clayton, Victoria, Australia. Electronic address: gregory.moore@monash.edu.
Nepean Hospital, University of Sydney, Sydney, New South Wales, Australia. Electronic address: Martin.Weltman@swahs.health.nsw.gov.au.
Concord Hospital, Sydney, New South Wales, Australia. Electronic address: rupertleong@unsw.edu.au.
Merck Sharp & Dohme Corp., Whitehouse Station, NJ, USA. Electronic address: tao_fan@merck.com.

BACKGROUND & AIMS: The burden of ulcerative colitis (UC) in relation to disease severity is not well documented. This study quantitatively evaluated the relationship between disease activity and quality of life (QoL), as well as health care utilization, cost, and work-related impairment associated with UC in an Australian population.

METHODS: A cross-sectional, noninterventional, observational study was performed in patients with a wide range of disease severity recruited during routine specialist consultations. Evaluations included the Assessment of Quality of Life-8-dimension (AQoL-8D), EuroQol 5-dimension, 5-level (EQ-5D-5L),
the disease-specific Inflammatory Bowel Disease Questionnaire (IBDQ), and the Work Productivity and Activity Impairment (WPAI) instrument. The 3-item Partial Mayo Score was used to assess disease severity. Health care resource utilization was assessed by chart review and patient questionnaires.

RESULTS: In 175 patients, mean (SD) AQoL-8D and EQ-5D-5L scores were greater for patients in remission (0.80 [0.19] and 0.81 [0.18], respectively) than for patients with active disease (0.70 [0.20] and 0.72 [0.19], respectively, both Ps<0.001). IBDQ correlated with both AQoL-8D (r=0.73; P<0.0001) and EQ-5D-5L (0.69; P<0.0001). Mean 3-month UC-related health care cost per patient was AUD $2914 (SD=$3447 [mean for patients in remission=$1970; mild disease=$3736; moderate/severe disease=$4162]). Patients in remission had the least work and activity impairment.

CONCLUSIONS: More severe UC disease was associated with poorer QoL. Substantial health care utilization, costs, and work productivity impairments were found in this sample of patients with UC. Moreover, greater disease activity was associated with greater health care costs and impairment in work productivity and daily activities. Copyright 2013 European Crohn's and Colitis Organisation. Published by Elsevier B.V. All rights reserved. PMID:24345767


Short term dose tailoring of anti TNF-a therapy delivers useful clinical efficacy in Crohn's disease patients with secondary loss of response.

(Ghaly) St. Vincent's Hospital, University of New South Wales, Department of Gastroenterology, Sydney, Australia (Costello, Agarwal, Andrews) Royal Adelaide Hospital, Department of Gastroenterology, Adelaide, Australia (Beswick, Headon, Sparrow) Alfred Hospital, Department of Gastroenterology, Melbourne, Australia (Pudipeddi, Walsh) St. Vincent's Hospital, Department of Gastroenterology, Sydney, Australia (Sechi, Connor) Liverpool Hospital, Department of Gastroenterology, Sydney, Australia (Prosser, Bampton) Flinders Medical Centre, Department of Gastroenterology, Adelaide, Australia (Lawrance) Fremantle Hospital, Centre for Inflammatory Bowel Disease, Fremantle, Australia
S. Ghaly, St. Vincent's Hospital, University of New South Wales, Department of Gastroenterology, Sydney, Australia

Background: Dose tailoring of anti TNF therapy in Crohn's disease, by dose escalation or shortening of dosing intervals, may regain clinical response in a proportion of patients. This study examines the impact of dose tailoring on corticosteroid use, the need for surgery and physician perception of clinical efficacy. Methods: This observational multicenter, retrospective study examined the outcomes of dose tailored anti-TNF therapy at six adult teaching hospitals in Australia. Demographics, disease characteristics, medications, indication for, and duration of, dose tailoring and physician's impression of response to treatment were documented. Results: Fifty-five patients were eligible for inclusion with secondary loss of response being the indication in 96%. Patients had escalation of Adalimumab (64%) or Infliximab (36%) for a median of 5 months (1-47), with a median 20 months (3-65) follow up. By 3 months, dose tailoring led to a drop in the mean number of days on high dose steroids (21 vs 11, p < 0.01) and 73% of physicians reported a good clinical efficacy. At the end of follow up, 78% still remained resection free. Deescalation of therapy was possible in 43 subjects, in 28 this was due to successful induction of remission, failure in 8 and inability to fund ongoing therapy in 5. Of those who deescalated therapy due to successful induction of remission, long term (>12 months) follow up and complete data on steroid use was available in 17, of these 13 (77%) remained steroid free at one year. The duration or type of dose tailoring was not predictive of steroid free remission or the need for surgery. Age <30 years was associated with a greater risk of bowel resection despite dose tailoring (OR 5.4, 95% CI 1.27-23, p = 0.02). Absence of prolonged corticosteroid therapy (>6 months) before dose tailoring was predictive of remaining steroid free beyond 12 months (OR 3.5, 95% CI 1.05-12.05, p = 0.04). Conclusions: Short term dose tailoring will regain response in the majority of patients. Of these most will remain free of corticosteroids at one year even when therapy is de-escalated. Younger
patients requiring prolonged steroids appear less likely to benefit.

Publication Types: Conference Abstract
PMID: 71389009


A genome wide association study identifying association of the MHC region with 5-aminosalicylate (5-ASA) induced nephrotoxicity in inflammatory bowel disease.


ethnic outliers and related individuals) compared to a 4,109 controls, matched for disease, imputed to the 1000 genome project and a dedicated HLA-typed cohort. An association signal was identified within the Class II MHC region at rs3135356 (p = 3.99x10^{-8}) with an odds ratio of 2.07. This was robust to principle component correction. Confirmatory single SNP genotyping was undertaken to demonstrate the validity of the imputed genotypes. Conclusions: This is the largest and most detailed study of 5-ASA induced nephrotoxicity to date. Whilst the incidence is low, the morbidity is high with 9% of patients requiring renal replacement therapy and 72% of patients failing to return to a normal creatinine after 5-ASA withdrawal. The genome-wide association study identified association within the Class II MHC region highlighting the underlying adaptive immune system pathogenesis.

Publication Types: Conference Abstract
PMID:71388579


Intra-uterine ExposuRe to Anti-TNF-alpha therapy (ERA study): Infliximab and adalimumab cord blood levels correlate with maternal levels at birth.

Julsgaard M, Christensen LA, et al.
(Julsgaard, Christensen, Grosen) Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus, Denmark (Fallingborg) Aalborg Hospital, Department of Gastroenterology, Aalborg, Denmark (Geary) University of Otago, Christchurch Hospital, Dept. of Medicine (Gastroenterology), Christchurch, New Zealand (Radford-Smith) Royal Brisbane and Women's Hospital, Gastroenterology, Brisbane, QLD, Australia (Julsgaard, Walsh) St Vincent's Hospital, Dept. of Gastroenterology, Sydney, Australia (Kjeldsen) Odense University Hospital, Dept. of Gastroenterology and Hepatology, Odense, Denmark (Sparrow, Gibson, Rosella) Alfred Hospital and Monash University, Dept. of Gastroenterology, Melbourne, Australia (Andrews) Royal Adelaide Hospital, University of Adelaide, IBD Service, Dept of Gastroenterology and Hepatology, Adelaide, Australia (Connor) Liverpool Hospital, University of NSW, Dept. of Gastroenterology, Sydney, Australia (Lawrence) Fremantle Hospital, Centre for Inflammatory Bowel Disease, Fremantle, Australia (Bell) St Vincent's Hospital, University of Melbourne, Gastroenterology, Melbourne, Australia M. Julsgaard, Aarhus University Hospital, Department of Hepatology and Gastroenterology, Aarhus, Denmark

Background: Recent studies suggest no adverse pregnancy outcomes in babies exposed to anti TNF antibodies (ATA). However, the long term implications are unknown. Current guidelines suggest cessation of treatment in the last trimester of pregnancy to reduce fetal exposure but this is difficult for women with IBD who are not in deep remission, as active disease is a greater risk for adverse pregnancy outcome. This study aimed to examine drug levels of ATA in cord blood of newborns exposed to ATA in pregnancy, and to correlate these with maternal levels, the duration of therapy during pregnancy, and time to clearance of ATA in infants. Methods: Women with IBD exposed to infliximab (IFX) or adalimumab (ADA) during pregnancy were included from 2012-present at 11 hospitals in Denmark, Australia and New Zealand. ATA levels were measured using an ELISA in cord and maternal blood at delivery (Matriks Biotek). If positive at birth, the infants were tested every third month until ATA were undetectable. Demographics, disease phenotype, disease activity in pregnancy, duration of ATA use in pregnancy, medication and pregnancy outcomes were prospectively collected by questionnaire and from the treating doctor. Results: 40 mother-baby pairs have been tested (20 IFX and 20 ADA). Drug was ceased prior to gestational week (GW) 30 in 16 (40%) women without disease flares. In them, mean serum concentrations were 1.78 mug/ml (IFX) and 0.15 mug/ml (ADA), and the cord blood level at delivery was <3 mug/ml in 12/16 (75%). There was a strong correlation between cord blood and maternal levels at delivery (IFX: Pearson's r = -0.77, p < 0.0001; ADA: r = -0.753, p < 0.0001). An inverse correlation between duration since last exposure and maternal ATA levels at birth was found (IFX: r = 0.55, p = 0.01; v ADA: r = 0.48, p = 0.04). This was also the case for cord IFX levels at birth (r = -0.532, p = 0.02), but not for cord ADA levels at birth (r = -0.38, p = 0.12). Complete clearance of ATA was seen in 14/17 babies by 6 months and in this group 7 stopped ATA by week 30. To date there has been no detectable ATA levels by 9 months. One woman (2.5%) gave birth preterm
No congenital malformations were detected and all babies are developing normally. Conclusions: Cord blood ATA levels were strongly correlated with maternal level at delivery. Maternal and neonatal ATA levels seem to be inversely correlated with the duration since last exposure. Maternal cessation of ATA prior to week 30 successfully reduced fetal exposure to drug in the majority of cases. Follow up will determine whether high neonatal levels have any negative consequences.


**Pregnancy outcome and counselling of anti-TNF-alpha treated IBD women: An ongoing international multicentre study.**

Julsøgaard M, Christensen LA, et al.

Background: IBD is common in the fertile years. With anti-TNF-alpha therapy it has become possible to rapidly induce and maintain remission. This improved therapy makes it possible for women with IBD to consider pregnancy, but concerns regarding the use of drugs during pregnancy are often raised by IBD patients. We examined outcomes of pregnancy among women with IBD exposed to anti-TNF-alpha during pregnancy. Further, medical treatment, disease activity, and counselling were investigated in an international multicentre study. Methods: 115 women exposed to Infliximab (IFX) or Adalimumab (ADA) during pregnancy who had given birth during a 3 year period were identified at 14 hospitals in Denmark, Australia and New Zealand. Electronic questionnaires were used to investigate diagnosis, medical treatment, disease activity, counselling, and birth outcome. Recruitment is ongoing. Results: 86 (74.8%) of the women filled in the questionnaire of whom 3 had a miscarriage prior to gestational week (GW) 10, leaving a study population of 83 women. The pregnancy was planned in 60 (72.3%) of the cases. 54 (65.1%) and 29 (34.9%) received treatment with IFX and ADA, respectively. Co-medication with thiopurines were used in 25 (30.1%) of the pregnancies. 7 (8.4%) gave birth preterm (GW 32-36). None of the babies were small for gestational age or had congenital malformations. Median Apgar score at 5 minutes was 9.3 (range 7-10). Caesarean section was performed in 52 (60.5%) of the deliveries and in 36 (69.2%) of these cases the women stated IBD as the reason. 19 (22.3%) women experienced a relapse during pregnancy of whom 8 (42.1%) had disease activity at delivery. Anti-TNF-alpha therapy was discontinued during the 1st., 2nd. and 3rd. trimester in 3.9%, 38.2% and 57.9% of the cases, respectively. Counselling on medical treatment with anti-TNF-alpha therapy was given to 72 (83.7%) of the women most frequently by a gastroenterologist (88.9%). The vast majority (98.4%) of women were satisfied with the information provided. 75 (87.2%) of the women would accept treatment with anti-TNF-alpha during a future pregnancy. Conclusions: Maternal anti-TNF-alpha treatment for IBD did not seem to be a risk factor for adverse pregnancy
outcomes. Anti-TNF-alpha was discontinued late in pregnancy. The vast majority of women had received counselling by a gastroenterologist on anti-TNF-alpha treatment during pregnancy and were satisfied with the information provided. A third of the pregnancies were unplanned suggesting risk benefit counselling should be offered to all fertile women at initiation of anti-TNF-alpha therapy.

Publication Types: Conference Abstract
PMID:71389040


**Hard to diagnose and potentially fatal: slow aortic erosion post spinal fusion.**
Ip EW, Bourke VC, et al.
Department of Vascular and Endovascular Surgery, Fremantle Hospital, Fremantle, Western Australia, Australia.
Emergency Department, Fremantle Hospital, Fremantle, Western Australia, Australia.

**BACKGROUND:** Delayed aortic injuries are a rare, but well-recognized complication of spinal surgery. They are a result of slow erosion of osteosynthesis material into the aorta. Although this is a life-threatening complication, patients might present years later with nonspecific symptoms.

**OBJECTIVE:** A complex case of slow aortic injury after thoracic spinal surgery is presented, which highlights the challenges involved in diagnosis and treatment.

**CASE REPORT:** A 62-year-old man had a T6 vertebrectomy and T5-7 anterior spinal fusion for multiple myeloma 5 years earlier. Two years postoperatively, the patient developed intermittent hemoptysis that triggered several presentations to the emergency department and consecutive hospital admissions during a 3-year period. All investigations, including endoscopy, bronchoscopy, and repeated chest computed tomography (CT) scans, were unremarkable. Eventually, the patient presented with frank hemoptysis associated with severe left-sided chest pain. Urgent CT angiography revealed a pseudoaneurysm measuring 34 x 20 mm at the level of the vertebrectomy. The patient underwent emergency surgery and an endoluminal stent graft was successfully placed. The patient remains well after 6 months.

**CONCLUSIONS:** The close proximity of the aorta and spine entertains the risk of aortic injury associated with vertebral osteosynthesis. Long-term complications of slow aortic erosion are extremely difficult to diagnose. The presented patient suffered from an undetected bronchio-aortic fistula with consecutive pseudoaneurysm formation and rupture. Awareness of slow aortic erosion is important for correct diagnostic pathways and subsequent early diagnosis to ensure a positive outcome for the patient. Crown Copyright 2014. Published by Elsevier Inc. All rights reserved.
PMID:24268895


**Distribution of interferon lambda-3 gene polymorphisms in Australian patients with previously untreated genotype 1 chronic hepatitis C: Analysis from the PREDICT and CHARIOT studies.**
Roberts SK, Mitchell J, et al.

(Roberts, Mitchell) Gastroenterology Department, The Alfred, Melbourne, Australia (Thompson)
Gastroenterology Department, St. Vincent's Hospital, Melbourne, Australia (Sievert) Monash University and Gastroenterology Department, Monash Medical Centre, Monash University, Melbourne, Australia (Leung, Booth, George) Storr Liver Unit, Westmead Hospital, Sydney, Australia (Mccaughan) Gastroenterology Department, Royal Prince Alfred Hospital and Centenary Research Institute, Sydney, Australia (Dore) Kirby Institute, Sydney, Australia (Weltman) Gastroenterology Department, Nepean Hospital, Sydney, Australia (Bollipo) Gastroenterology Department, John Hunter Hospital, Newcastle, Australia (Ostapowicz) Gastroenterology Department, Gold Coast Hospital, Southport, Australia (Sloss) Gastroenterology Department, Nambour Hospital, Nambour, Australia (Crawford) Department of Medicine, Greenslopes Hospital, Brisbane, Australia (Cheng) Gastroenterology Department, Royal Perth Hospital, Perth, Australia (Angus) Austin Hospital, VIC, Australia (Dore) St Vincent's Hospital, NSW, Australia (George) Westmead Hospital, NSW, Australia (Haque) Mater
Background and Aims: The aim of this study was to examine the distribution of interferon lambda-3 (IFN-3) gene polymorphisms in previously untreated Australian patients with genotype 1 (Gt1) chronic hepatitis C (CHC) and to compare the IFN-3 genotype frequency among the different ethnic populations.

Methods: This was a prospective, multicenter, observational study undertaken by the Australian Liver Association Clinical Research Network. Eligible subjects had Gt1 CHC and were being considered for and/or undergoing treatment. IFN-3 single nucleotide polymorphisms were genotyped by the Applied Biosystems's Taqman single nucleotide polymorphism genotyping assay.

Results: Between May 2012 and June 2012, 1132 patients were recruited from 38 treatment clinics across Australia. Also, 561 subjects from the CHARIOT (collaborative group hepatitis C study using high dose Pegasys RBV Induction dose in genotype one) study of high-dose interferon who had baseline serum available were retrospectively tested. The overall frequency of IFN-3 rs12979860 CC/CT/TT genotypes was 36%, 52%, and 12%, and that of rs8099917 TT/TG/GG genotypes was 54%, 41%, and 5%, respectively. The prevalence of the favorable IFN-3 rs12979860 CC and rs8099917 TT genotypes in Caucasians, Asians, Aboriginals, Maori/Pacific Islanders, and Mediterraneans was 32% and 52%, 80% and 86%, 33% and 63%, 77% and 88%, and 19% and 29%, respectively. Compared with Caucasians, the frequency of IFN-3 CC was significantly higher among Asians (P<0.0001) and Maori/Pacific Islander subjects (P<0.0001). Conclusions: The distribution of IFN-3 polymorphisms among untreated patients with Gt1 CHC in Australia appears similar to that reported from North America. The frequency of the favorable response alleles varies considerably according to ethnicity, being more common in self-reported Asians and Maori/Pacific Islanders than Caucasians, Aboriginals, and Mediterraneans.
Background and Aims: Non-alcoholic fatty liver disease (NAFLD) and serum 25-hydroxyvitamin D (s25(OH)D) concentrations are both associated with adiposity and insulin resistance (IR) and thus may be pathogenically linked. We aimed to determine the prevalence of vitamin D deficiency in adolescents with NAFLD and to investigate the prospective and cross-sectional associations between s25(OH)D concentrations and NAFLD. Methods: Participants in the population-based West Australian Pregnancy (Raine) Cohort had seasonally adjusted s25(OH)D concentrations determined at ages 14 and then 17 years. NAFLD was diagnosed at 17 years using liver ultrasonography. Associations were examined after adjusting for potential confounders. Odds ratios (ORs) and confidence intervals (CIs) are reported per standard deviation in s25(OH)D concentrations. Results: NAFLD was present in 16% (156/994) of adolescents. The majority of participants with NAFLD had either insufficient (51%) or deficient (17%) vitamin D status. s25(OH)D concentrations at 17 years were inversely associated with risk of NAFLD (OR 0.74, 95% CI 0.56, 0.97; P=0.029), after adjusting for sex, race, physical activity, television/computer viewing, body mass index, and IR. The effect of s25(OH)D concentrations at 17 years was minimally affected after further adjusting for s25(OH)D concentrations at 14 years (OR 0.76, 95% CI 0.56, 1.03; P=0.072). Conclusions: Lower s25(OH)D concentrations are significantly associated with NAFLD, independent of adiposity and IR. Screening for vitamin D deficiency in adolescents at risk of NAFLD is appropriate, and clinical trials investigating the effect of vitamin D supplementation in the prevention and treatment of NAFLD may be warranted.

PMID:2014338937


**IFNL3 polymorphisms predict response to therapy in chronic hepatitis C genotype 2/3 infection.**

Storr Liver Unit, Westmead Millennium Institute and Westmead Hospital, University of Sydney, NSW, Australia.
Storr Liver Unit, Westmead Millennium Institute and Westmead Hospital, University of Sydney, NSW, Australia; Institute of Immunology and Allergy Research, Westmead Hospital and Westmead Millennium Institute, University of Sydney, NSW, Australia.
Unit for The Clinical Management of Digestive Diseases and CIBERehd, Hospital Universitario de Valme, Sevilla, Spain.
Division of Hepatology, Ospedale Casa Sollievo della Sofferenza, IRCCS, San Giovanni Rotondo, Italy.
NIHR Biomedical Research Unit in Gastroenterology and the Liver, University of Nottingham, Nottingham, UK.
Liver Research Group, Institute of Cellular Medicine, Medical School, Newcastle University, Newcastle upon Tyne, UK.
Department of Internal Medicine I, University of Bonn, Sigmund-Freud-Strasse, Bonn, Germany.
Fremantle Hepatitis Services, Fremantle, Australia.
Department of Gastroenterology and Hepatology, Royal Perth Hospital, Western Australia, Australia.
Division of Gastro–Hepatology, S. Giovanni Battista Hospital, Turin, Italy.
Department of Anatomical Pathology, Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital, Sydney, Australia.
Department of Histopathology, University Hospital Queens Medical Centre, Nottingham, UK.
Department is Anatoma Patologica IRCCS, Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy.
Pathologisches Institute, Universitätsklinikum Bonn, Germany.
Institute of Immunology and Allergy Research, Westmead Hospital and Westmead Millennium Institute, University of Sydney, NSW, Australia.
Storr Liver Unit, Westmead Millennium Institute and Westmead Hospital, University of Sydney, NSW, Australia. Electronic address: jacob.george@sydney.edu.au.
BACKGROUND & AIMS: Single nucleotide polymorphisms (SNPs) near the interferon lambda 3 (IFNL3, previously known as IL28B) region are the strongest baseline predictors of sustained virologic response (SVR) to pegylated interferon and ribavirin therapy in hepatitis C virus (HCV) genotype 1 infection. Whether IFNL3 SNPs influence treatment response in genotype 2 and 3 (HCV-2/3) infection remains controversial. This study sought to clarify in a large cohort, whether SNPs in the IFNL3 region are associated with treatment response in HCV-2/3 patients.

METHODS: The cohort comprised 1002 HCV-2/3 Caucasians patients treated with pegylated interferon-alpha and ribavirin who underwent genotyping for the SNPs rs12979860 and rs8099917.

RESULTS: Overall, 736 (73.5%) patients achieved SVR (81.9%, 67.9%, and 57.8% for rs12979860 CC, CT, and TT [p=0.0001]; 78%, 68.7%, and 46.3% for rs8099917 TT, TG, and GG [p=0.0001]). By logistic regression, both rs12979860 CC and rs8099917 TT were independent predictors of SVR with an odds ratio (OR) of 2.39 (1.19-3.81) p=0.0001 and OR 1.85 (1.15-2.23) p=0.0001, respectively. IFNL3 responder genotypes were more frequent in relapsers than null-responders (p=0.0001 for both SNPs). On-treatment rapid virological response (RVR) was predictive of SVR only in those individuals with IFNL3 non-responder genotypes (rs12979860 CT/TT and rs8099917 TG/GG).

CONCLUSIONS: This adequately powered study in patients with HCV genotypes 2 or 3 infection clearly demonstrates that IFNL3 genotypes are the strongest baseline predictor of SVR, in keeping with the known association for genotype 1 infection. IFNL3 genotyping can aid in therapeutic decision making for these patients. Copyright 2014 European Association for the Study of the Liver. Published by Elsevier B.V. All rights reserved.

PMID:24768758

Efficacy and safety of MK-5172 plus ribavirin in treatment-naive patients with hepatitis C virus genotype 1 infection: Final results of the C-spirit study.

Gane E, Ben Ari Z, et al.

Background and Aims: The C-SPIRIT study assessed the interferonfree regimen of MK-5172, a second generation hepatitis C virus (HCV) NS3/4A protease inhibitor, in combination with ribavirin in treatment-naive, non-cirrhotic patients with HCV genotype (G)1 infection and the IL28B CC genotype.

Methods: Patients were randomized to receive MK-5172 100mg QD and ribavirin for 12 or 24 weeks. Patients in the 12 week arm with detectable [not quantifiable, TD(u)] HCV-RNA at treatment week (TW)4 had treatment extended to 24 weeks. The primary end point was sustained virologic response (SVR) at follow-up week 12 (HCV-RNA <25 IU/mL). Results: 26 patients were enrolled, 1 discontinued on Day 1. All other patients had HCV-RNA <25 IU/mL at TW4. In the 12 week arm, 8 patients with undetectable HCV-RNA (<10 IU/mL, TND) at TW4 were treated for 12 weeks (SVR4, n = 7 [88%]; SVR12, n = 5 [63%]). The remaining 4 patients were TD(u) at TW4 and were treated for 24 weeks. Of the patients assigned or extended to 24 weeks of treatment, 13/17 (76%) achieved SVR4 and 10/16 (63%) achieved SVR12 (data pending on 1 patient). To date, seven patients have virologic failure (G1a, n = 5; G1b, n = 2). There were no serious adverse events or treatment discontinuations. Sixteen patients had elevated ALT at baseline but normalized on-treatment; 9 patients had transient, mild elevations in total bilirubin. Conclusions: MK-5172 plus ribavirin was associated with a rapid and sustained suppression of HCV-RNA. These results support further evaluation of MK-5172-based interferon-free regimens.

Publication Types: Conference Abstract

PMID:71444771
**Journal of Infectious Diseases.** 2014; 210(2): 295-305.

**T cells and CD14+ Monocytes Are Predominant Cellular Sources of Cytokines and Chemokines Associated With Severe Malaria.**

Stanisic DI, Cutts J, et al.
Division of Infection and Immunity, Walter and Eliza Hall Institute, Parkville, Victoria, Australia Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea.
Division of Infection and Immunity, Walter and Eliza Hall Institute, Parkville, Victoria, Australia.
Division of Infection and Immunity, Walter and Eliza Hall Institute, Parkville, Victoria, Australia Department of Medical Biology, University of Melbourne, Parkville, Victoria, Australia.
Burnet Institute for Medical Research and Public Health, Prahan, Victoria, Australia.
Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea.
Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.
Division of Infection and Immunity, Walter and Eliza Hall Institute, Parkville, Victoria, Australia Papua New Guinea Institute of Medical Research, Madang, Papua New Guinea Center de Recerca en Salut Internacional de Barcelona (CRESIB), Barcelona, Spain.
Division of Infection and Immunity, Walter and Eliza Hall Institute, Parkville, Victoria, Australia Australian Institute of Tropical Health and Medicine, James Cook University, Queensland, Australia.

**BACKGROUND:** Severe malaria (SM) is associated with high levels of cytokines such as tumor necrosis factor (TNF), interleukin 1 (IL-1), and interleukin 6 (IL-6). The role of chemokines is less clear, as is their cellular source.

**METHODS:** In a case-control study of children with SM (n = 200), uncomplicated malaria (UM) (n = 153) and healthy community controls (HC) (n = 162) in Papua, New Guinea, we measured cytokine/chemokine production by peripheral blood mononuclear cells (PBMCs) stimulated with live Plasmodium falciparum parasitized red blood cells (pRBC). Cellular sources were determined. Associations between immunological endpoints and clinical/parasitological variables were tested.

**RESULTS:** Compared to HC and UM, children with SM produced significantly higher IL-10, IP-10, MIP-1betam and MCP-2. TNF and MIP-1alpha were significantly higher in the SM compared to the UM group. IL-10, IL-6, MIP-1alpha, MIP-1beta, and MCP-2 were associated with increased odds of SM. SM syndromes were associated with distinct cytokine/chemokine response profiles compared to UM cases. TNF, MIP-1beta, and MIP-1alpha were produced predominantly by monocytes and T cells, and IL-10 by CD4(+) T cells.

**CONCLUSIONS:** Early/innate PBMC responses to pRBC in vitro are informative as to cytokines/chemokines associated with SM. Predominant cellular sources are monocytes and T cells. Monocyte-derived chemokines support a role for monocyte infiltrates in the etiology of SM.

PMID:24523513

---


**The importance of validating proposed genetic profiles in IBD.**

Lawrance IC.
Fremantle Hospital, Centre for Inflammatory Bowel Disease, Fremantle, WA, Australia.
Publication Types: Editorial
PMID:24344969

---


**Contact endoscopy as a novel technique in the detection and diagnosis of oral cavity and oropharyngeal mucosal lesions in the head and neck.**

Dowthwaite S, Szeto C, et al.
Objective: We aimed to investigate the diagnostic accuracy of contact endoscopy in evaluating oral and oropharyngeal mucosal lesions. Methods: Between January 2010 and December 2011, 34 patients with lesions of the oral and oropharyngeal mucosa were enrolled in the study. Comparison between initial contact endoscopy results and ‘gold standard’ tissue biopsy was undertaken. Results: Nine patients had histologically confirmed squamous cell carcinoma, 2 had carcinoma in situ, 3 had dysplastic lesions and 20 patients had various benign lesions. Contact endoscopy demonstrated sensitivity and specificity of 89 and 100 per cent respectively in the evaluation of malignant lesions. Benign lesions were correctly categorised in 50 per cent of cases (10/20). The video images from contact endoscopy could not be interpreted in six cases. Conclusions: Contact endoscopy demonstrates high sensitivity and specificity in the imaging of malignant lesions with reduced reliability in the evaluation of benign lesions. Significant shortcomings also exist in the design of current technology that we believe represent a significant barrier to the reliable collection of useful video data.

PMID:24460932


Delayed Presentation of a Congenital Cholesteatoma in a 64-year-old Man: Case Report and Review of the Literature.
Davidoss N, Ha J, et al.
Department of Ear, Nose and Throat, Royal Perth Hospital, Perth, Western Australia, Australia.
Department of Otolaryngology, Princess Margaret Hospital, Perth, Western Australia, Australia.
Department of Otolaryngology, Head and Neck Surgery, Fremantle Hospital, Perth, Western Australia, Australia.
Department of Otolaryngology, University of Western Australia, Crawley, Western Australia, Australia.

Introduction Congenital cholesteatomas of the temporal bone are epidermoid cysts of embryologic origin that result in progressive desquamation and trapping of squamous epithelium behind an intact tympanic membrane. They are benign, slowly progressive lesions that can be found in various areas of the temporal bone. We report a case of a patient with a massive cholesteatoma first detected at the age of 64 years, causing significant destruction of the mastoid and petrous temporal bones, and adjacent occipital bone. Methods We reviewed the literature and a case report of a patient seen in our institution recently. The Medline database was used to search multiple terms including "congenital" and "cholesteatoma." Results The patient's congenital cholesteatoma was detected incidentally on a computed tomography scan when the patient's only symptoms were unilateral conductive hearing loss with a family history of hearing loss. It was subsequently successfully operated on with minimal postoperative complications. Conclusions Congenital cholesteatomas of mastoid origin can often exist for many years in a subclinical state and develop into a massive size before causing symptoms. A high index of suspicion is necessary to detect congenital cholesteatomas in patients with unilateral conductive hearing loss who are otherwise asymptomatic and have a normal tympanic membrane.

PMID:25083369


Lower fructose intake may help protect against development of nonalcoholic Fatty liver in adolescents with obesity.
O'Sullivan T A, Oddy WH, et al.
*School of Exercise and Health Science, Edith Cowan University, Joondalup +Telethon Institute for Child Health Research, Centre for Child Health Research, University of Western Australia, West Perth
OBJECTIVES: Although obesity is a major risk factor for nonalcoholic fatty liver (NAFL), not all individuals with obesity develop the condition, suggesting that other factors such as diet may also contribute to NAFL development. We evaluated associations between fructose and total sugar intake and subsequent diagnosis of NAFL in adolescents with obesity and without obesity in a population-based cohort.

METHODS: Adolescents participating in the Western Australian Pregnancy Cohort (Raine) Study completed 3-day food records and body mass index measurement at age 14 years. At age 17 years, participants underwent abdominal ultrasound to determine NAFL status. Multivariable logistic regression models were used to analyse associations between energy-adjusted fructose and total sugar intake and NAFL status. Food diaries and liver assessments were completed for 592 adolescents.

RESULTS: The prevalence of NAFL at age 17 was 12.8% for the total group and 50% for adolescents with obesity. Fructose intake did not significantly differ between adolescents with or without NAFL in our cohort as a whole. Among adolescents with obesity, those without NAFL had significantly lower energy-adjusted fructose intake at age 14 years compared with those with NAFL (mean + standard deviation [SD] 38.8 + 19.8 g/day, vs 55.7 + 14.4 g/day, P = 0.02). Energy-adjusted fructose intake was independently associated with NAFL in adolescents with obesity (OR [odds ratio] 1.09, 95% CI 1.01-1.19, P = 0.03) after the adjustment for confounding factors. Energy-adjusted total sugar intake showed less significance (OR 1.03, 95% CI 0.999-1.07, P = 0.06). No significant associations were observed in other body mass index categories.

CONCLUSIONS: Lower fructose consumption in adolescents with obesity at 14 years is associated with a decreased risk of NAFL at 17 years. Fructose rather than overall sugar intake may be more physiologically relevant in this association.

PMID:24345826

Angiogenesis inhibition and depression in older men.
Almeida OP, Ford AH, et al.
School of Psychiatry & Clinical Neurosciences, University of Western Australia, Perth; WA Centre for Health & Ageing, Centre for Medical Research, University of Western Australia, Perth; Department of Psychiatry, Royal Perth Hospital, Perth, Australia.
WA Centre for Health & Ageing, Centre for Medical Research, University of Western Australia, Perth School of Medicine and Pharmacology, University of Western Australia, Perth Department of Geriatric Medicine, Royal Perth Hospital, Perth.
School of Medicine and Pharmacology, University of Western Australia, Perth Department of Neurology, Royal Perth Hospital, Perth.
School of Medicine and Pharmacology, University of Western Australia, Perth Department of Endocrinology, Fremantle Hospital, Fremantle.
Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville.
Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville Department of Vascular and Endovascular Surgery, The Townsville Hospital, Townsville, Australia.

BACKGROUND: Cardiovascular diseases have been associated with depression in later life, and a potential mechanism is inhibition of angiogenesis. We designed this study to determine if depression is associated with higher serum concentration of endostatin, an endogenous angiogenesis inhibitor.

METHODS: We performed a cross-sectional examination of a random sample of men aged 69-86 years. Those who scored 7 or higher on the 15-item Geriatric Depression Scale were deemed depressed. We determined the concentration of serum endostatin using a reproducible assay. Other
measures included age, education, body mass index, smoking, history of depression, use of antidepressants, hypertension, diabetes, coronary heart disease and stroke, high sensitivity C-reactive protein, plasma homocysteine, triglycerides and cholesterol. We used logistic regression to investigate the association between endostatin and depression, and adjusted the analyses for confounding factors.

RESULTS: Our sample included 1109 men. Sixty-three (5.7%) men were depressed. Their serum endostatin was higher than that of nondepressed participants (p = 0.021). Men in the highest decile of endostatin had greater adjusted odds of depression (odds ratio [OR] 1.78, 95% confidence interval [CI] 1.03-3.06). A doubling of endostatin doubled the odds of depression (OR 1.93, 95% CI 1.31-2.84). The probability of depression increased with the concentration of endostatin in a log-linear fashion up to a maximum of about 20%-25%.

LIMITATIONS: The cross-sectional design limits the study's ability to ascribe causality to the association between high endostatin and depression.

CONCLUSION: Serum endostatin is associated with depression in older men. It remains to be established whether correction of this imbalance is feasible and could decrease the prevalence of depression in later life.

PMID:24331740


Hormones and cardiovascular disease in older men.
Yeap BB, Flicker L.
School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia; Department of Endocrinology and Diabetes, Fremantle Hospital, Fremantle, Western Australia, Australia. Electronic address: bu.yeap@uwa.edu.au.
School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia; Western Australian Center for Health and Aging, Center for Medical Research, University of Western Australia, Perth, Western Australia, Australia.

Older men have lower circulating testosterone (T) and insulin-like growth factor-I (IGF-I) but higher levels of thyrotrophin (TSH) compared with younger men, and exhibit poorer health. Whether age-associated differences in hormone levels are causally related to cardiovascular disease, or are biomarkers reflecting accumulated ill-health remains under debate. Lower T levels are associated with aortic, peripheral vascular, and cardiovascular disease in middle-aged and older men. In some but not all studies, lower levels of T predict increased incidence of cardiovascular events and mortality. Recently, dihydrotestosterone (DHT) has also been identified as a predictor for peripheral vascular and ischemic heart disease. Small scale randomized clinical trials (RCTs) of T supplementation suggest a protective effect against myocardial ischemia in men with coronary artery disease. There have been no RCTs with the prespecified outcomes of cardiovascular events or mortality. One RCT of T in older men with mobility limitations was stopped due to an excess of cardiovascular adverse events in men receiving T, but other RCTs have not raised similar concerns. Observational studies of testosterone supplementation have reported contrasting results. Levels of IGF-I and its binding proteins 1 and 3 have been variably associated with mortality in some but not all studies, and RCTs of interventions to modulate IGF-I levels are either lacking or lacking in power to examine outcomes of cardiovascular events or mortality. Subclinical hyper- and hypothyroidism predict poorer outcomes, and emerging data implicate higher levels of free thyroxine with other outcomes such as dementia and mortality in older men. However, RCTs that manipulate free thyroxine levels within the normal range are lacking and would be challenging to perform. Further research is needed to clarify the role of these hormones as predictors of cardiovascular outcomes in aging men, and to test whether interventions that modulate levels of T, DHT, IGF-I or free thyroxine would reduce cardiovascular morbidity and mortality. Copyright 2014 American Medical Directors Association, Inc. Published by Elsevier Inc. All rights reserved.

PMID:24529874
International evidence-based recommendations for focused cardiac ultrasound.

BACKGROUND: Focused cardiac ultrasound (FoCUS) is a simplified, clinician-performed application of echocardiography that is rapidly expanding in use, especially in emergency and critical care medicine. Performed by appropriately trained clinicians, typically not cardiologists, FoCUS ascertains
the essential information needed in critical scenarios for time-sensitive clinical decision making. A need exists for quality evidence-based review and clinical recommendations on its use. METHODS: The World Interactive Network Focused on Critical UltraSound conducted an international, multispecialty, evidence-based, methodologically rigorous consensus process on FoCUS. Thirty-three experts from 16 countries were involved. A systematic multiple-database, double-track literature search (January 1980 to September 2013) was performed. The Grading of Recommendation, Assessment, Development and Evaluation method was used to determine the quality of available evidence and subsequent development of the recommendations. Evidence-based panel judgment and consensus was collected and analyzed by means of the RAND appropriateness method.

RESULTS: During four conferences (in New Delhi, Milan, Boston, and Barcelona), 108 statements were elaborated and discussed. Face-to-face debates were held in two rounds using the modified Delphi technique. Disagreement occurred for 10 statements. Weak or conditional recommendations were made for two statements and strong or very strong recommendations for 96. These recommendations delineate the nature, applications, technique, potential benefits, clinical integration, education, and certification principles for FoCUS, both for adults and pediatric patients.

CONCLUSIONS: This document presents the results of the first International Conference on FoCUS. For the first time, evidence-based clinical recommendations comprehensively address this branch of point-of-care ultrasound, providing a framework for FoCUS to standardize its application in different clinical settings around the world. Copyright 2014. Published by Mosby, Inc.

PMID:24951446
Radiotherapy for breast cancer, the TARGIT-A trial - Authors’ reply.
Vaidya JS, Wenz F, et al.
University College London, Division of Surgery and Interventional Science, London W1W 7EJ, UK.
Electronic address: jayant.vaidya@ucl.ac.uk.
Department of Radiation Oncology, University Medical Centre Mannheim, University of Heidelberg, Mannheim, Germany.
Department of Biostatistics, University of Notre Dame, Fremantle, WA, Australia; Clinical Trials Group, Division of Surgery and Interventional Science, University College London, London, UK.
Department of Clinical Oncology, University College London Hospitals, London, UK.
Department of Radiation Oncology, Sir Charles Gairdner Hospital, Perth, WA, Australia.
Publication Types: Comment
Letter
PMID:24835613

Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial.[Erratum appears in Lancet. 2014 Feb 15;383(9917):602].
Vaidya JS, Wenz F, et al.
Clinical Trials Group, Division of Surgery and Interventional Science, University College London, London, UK; Department of Surgery, Royal Free Hospital, London, UK; Department of Surgery, Whittington Hospital, London, UK. Electronic address: jayant.vaidya@ucl.ac.uk.
Department of Radiation Oncology, University Medical Centre Mannheim, University of Heidelberg, Heidelberg, Germany.
Department of Biostatistics, University of Notre Dame, Fremantle, WA, Australia.
Department of Clinical Oncology, University College London Hospitals, London, UK.
Department of Radiation Oncology, Sir Charles Gairdner Hospital, Perth, WA, Australia.
Department of Surgery, Royal Free Hospital, London, UK; Department of Surgery, Whittington Hospital, London, UK.
Department of Breast Surgery, University of Copenhagen, Copenhagen, Denmark.
Department of Surgery, Centro di Riferimento Oncologia, Aviano, Italy.
Department of Surgery, University of California, San Francisco, CA, USA.
Department of Surgery, Sir Charles Gairdner Hospital, Perth, WA, Australia; School of Surgery, University of Western Australia, Perth, WA, Australia.
Department of Gynecology and Obstetrics, Red Cross Hospital, Munich, Germany.
BACKGROUND: The TARGIT-A trial compared risk-adapted radiotherapy using single-dose targeted intraoperative radiotherapy (TARGIT) versus fractionated external beam radiotherapy (EBRT) for breast cancer. We report 5-year results for local recurrence and the first analysis of overall survival.

METHODS: TARGIT-A was a randomised, non-inferiority trial. Women aged 45 years and older with invasive ductal carcinoma were enrolled and randomly assigned in a 1:1 ratio to receive TARGIT or whole-breast EBRT, with blocks stratified by centre and by timing of delivery of targeted intraoperative radiotherapy: randomisation occurred either before lumpectomy (prepathology stratum, TARGIT concurrent with lumpectomy) or after lumpectomy (postpathology stratum, TARGIT given subsequently by reopening the wound). Patients in the TARGIT group received supplemental EBRT (excluding a boost) if unforeseen adverse features were detected on final pathology, thus radiotherapy was risk-adapted. The primary outcome was absolute difference in local recurrence in the conserved breast, with a prespecified non-inferiority margin of 25% at 5 years; prespecified analyses included outcomes as per timing of randomisation in relation to lumpectomy. Secondary outcomes included complications and mortality. This study is registered with ClinicalTrials.gov, number NCT00983684.

FINDINGS: Patients were enrolled at 33 centres in 11 countries, between March 24, 2000, and June 25, 2012. 1721 patients were randomised to TARGIT and 1730 to EBRT. Supplemental EBRT after TARGIT was necessary in 152% [239 of 1571] of patients who received TARGIT (216% prepathology, 36% postpathology). 3451 patients had a median follow-up of 2 years and 5 months (IQR 12-52 months), 2020 of 4 years, and 1222 of 5 years. The 5-year risk for local recurrence in the conserved breast was 33% (95% CI 21-51) for TARGIT versus 13% (07-25) for EBRT (p=0.042). TARGIT concurrently with lumpectomy (prepathology, n=2298) had much the same results as EBRT: 21% (11-42) versus 11% (05-25; p=0.031). With delayed TARGIT (postpathology, n=1153) the between-group difference was larger than 25% (TARGIT 54% [30-97] vs EBRT 17% [06-49]; p=0.069). Overall, breast cancer mortality was much the same between groups (26% [15-43] for TARGIT vs 19% [11-32] for EBRT; p=0.056) but there were significantly fewer non-breast-cancer deaths with TARGIT (14% [08-25] vs 35% [23-52]; p=0.0086), attributable to fewer deaths from cardiovascular causes and other cancers. Overall mortality was 39% (27-58) for TARGIT versus 53% (39-73) for EBRT (p=0.099). Wound-related complications were much the same between groups but grade 3 or 4 skin complications were significantly reduced with TARGIT (four of 1720 vs 13 of 1731, p=0.0029).

INTERPRETATION: TARGIT concurrent with lumpectomy within a risk-adapted approach should be considered as an option for eligible patients with breast cancer carefully selected as per the TARGIT-A trial protocol, as an alternative to postoperative EBRT.

FUNDING: University College London Hospitals (UCLH)/UCL Comprehensive Biomedical Research Centre, UCLH Charities, National Institute for Health Research Health Technology Assessment programme, Ninewells Cancer Campaign, National Health and Medical Research Council, and German Federal Ministry of Education and Research. Copyright 2014 Vaidya et al. Open Access article distributed under the terms of CC BY-NC-ND. Published by Elsevier Ltd. All rights reserved.

Publication Types: Research Support, Non-U.S. Gov't
PMID:24224997
Comparison of three methods for detection of gametocytes in Melanesian children treated for uncomplicated malaria.
Karl S, Laman M, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia. karl@wehi.edu.au.

BACKGROUND: Gametocytes are the transmission stages of Plasmodium parasites, the causative agents of malaria. As their density in the human host is typically low, they are often undetected by conventional light microscopy. Furthermore, application of RNA-based molecular detection methods for gametocyte detection remains challenging in remote field settings. In the present study, a detailed comparison of three methods, namely light microscopy, magnetic fractionation and reverse transcriptase polymerase chain reaction for detection of Plasmodium falciparum and Plasmodium vivax gametocytes was conducted.

METHODS: Peripheral blood samples from 70 children aged 0.5 to five years with uncomplicated malaria who were treated with either artemether-lumefantrine or artemisinin-naphthoquine were collected from two health facilities on the north coast of Papua New Guinea. The samples were taken prior to treatment (day 0) and at pre-specified intervals during follow-up. Gametocytes were measured in each sample by three methods: i) light microscopy (LM), ii) quantitative magnetic fractionation (MF) and, iii) reverse transcriptase PCR (RTPCR). Data were analysed using censored linear regression and Bland and Altman techniques.

RESULTS: MF and RTPCR were similarly sensitive and specific, and both were superior to LM. Overall, there were approximately 20% gametocyte-positive samples by LM, whereas gametocyte positivity by MF and RTPCR were both more than two-fold this level. In the subset of samples collected prior to treatment, 29% of children were positive by LM, and 85% were gametocyte positive by MF and RTPCR, respectively.

CONCLUSIONS: The present study represents the first direct comparison of standard LM, MF and RTPCR for gametocyte detection in field isolates. It provides strong evidence that MF is superior to LM and can be used to detect gametocytaemic patients under field conditions with similar sensitivity and specificity as RTPCR.

Publication Types: Research Support, Non-U.S. Gov't
PMID:25123055

Comparison of an assumed versus measured leucocyte count in parasite density calculations in Papua New Guinean children with uncomplicated malaria.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, PO Box 480, Fremantle 6959, Western Australia, Australia. tim.davis@uwa.edu.au.

BACKGROUND: The accuracy of the World Health Organization method of estimating malaria parasite density from thick blood smears by assuming a white blood cell (WBC) count of 8,000/muL has been questioned in several studies. Since epidemiological investigations, anti-malarial efficacy trials and routine laboratory reporting in Papua New Guinea (PNG) have all relied on this approach, its validity was assessed as part of a trial of artemisinin-based combination therapy, which included blood smear microscopy and automated measurement of leucocyte densities on Days 0, 3 and 7.

RESULTS: 168 children with uncomplicated malaria (median (inter-quartile range) age 44 (39-47) months) were enrolled, 80.3% with Plasmodium falciparum monoinfection, 14.9% with Plasmodium vivax monoinfection, and 4.8% with mixed P. falciparum/P. vivax infection. All responded to allocated therapy and none had a malaria-positive slide on Day 3. Consistent with a median baseline WBC density of 7.3 (6.5-7.8) x 10(9)/L, there was no significant difference in baseline parasite density between the two methods regardless of Plasmodium species. Bland Altman plots showed that, for both species, the mean difference between paired parasite densities calculated from assumed and measured WBC densities was close to zero. At parasite densities <10,000/muL by measured WBC,
almost all between-method differences were within the 95% limits of agreement. Above this range, there was increasing scatter but no systematic bias.

CONCLUSIONS: Diagnostic thresholds and parasite clearance assessment in most PNG children with uncomplicated malaria are relatively robust, but accurate estimates of a higher parasitaemia, as a prognostic index, requires formal WBC measurement.

Publication Types: Research Support, Non-U.S. Gov't
PMID:24739250


**High chlamydia positivity rates in Indigenous people attending Australian sexual health services.**

RPA Sexual Health, Sydney Local Health District, Sydney, NSW, Australia.
catherine.oconnor@unsw.edu.au.
Kirby Institute, University of New South Wales, Sydney, NSW, Australia.
RPA Sexual Health, Sydney Local Health District, Sydney, NSW, Australia.
Melbourne Sexual Health Centre, Melbourne, VIC, Australia.
CaraData Pty Ltd, Brisbane, QLD, Australia.
Sexual Health Service, Fremantle Hospital, Perth, WA, Australia.
Centre for Population Health, Burnet Institute, Melbourne, VIC, Australia.
Baker IDI Heart and Diabetes Institute, Alice Springs, NT, Australia.

OBJECTIVE: To assess the clinical epidemiology of chlamydia among Aboriginal and Torres Strait Islander (Indigenous) people attending sexual health services around Australia.

DESIGN: Retrospective analysis of routine demographic, behavioural and clinical data, between 1 January 2006 and 31 December 2011.

SETTING: 18 sexual health services in major cities and regional centres in five jurisdictions.

MAIN OUTCOME MEASURES: Attendance, chlamydia testing and positivity rates in patients visiting for the first time, and factors associated with chlamydia positivity.

RESULTS: Of 168,729 new patients, 7,103 (4.2%) identified as Indigenous, of whom 74.3% were tested for chlamydia. Chlamydia positivity was 17.0% in Indigenous women (23.3% in 15-19-year-olds and 18.9% in 20-24-year-olds) and 17.3% in Indigenous men (20.2% in 15-19-year-olds and 24.2% in 20-24-year-olds). There was an increasing trend in chlamydia positivity in Indigenous women from 2006 to 2011 (P for trend = 0.001), but not in Indigenous men. In Indigenous women, factors independently associated with positivity were: younger age, being heterosexual, living in Queensland and attending the service in 2010. In Indigenous men, independent factors associated with chlamydia positivity were younger age, being heterosexual, having sex only in Australia and living in a regional area.

CONCLUSION: The high and increasing chlamydia positivity rates highlight the need for enhanced prevention and screening programs for Indigenous people.

Publication Types: Research Support, Non-U.S. Gov't
PMID:24882492


**Increasing incidence of Clostridium difficile infection, Australia, 2011-2012.**

Engelhardt NE, McGechie DB.
Department of Microbiology, PathWest Laboratory Medicine, Fremantle, WA, Australia.
nelly.engelhardt@health.wa.gov.au.

Department of Microbiology, PathWest Laboratory Medicine, Fremantle, WA, Australia.

PMID:25045987
Dipeptidyl peptidase-4 inhibitors and cardiovascular safety.

Davis TM.
School of Medicine and Pharmacology, University of Western Australia, Fremantle, WA, Australia.
tim.davis@uwa.edu.au.
PMID:24794596

Medical management after control of myocardial ischaemia.

Thompson PL, Judkins C, et al.
(Thompson) Sir Charles Gairdner, Mount Hospitals, Perth, WA, Australia (Thompson) Department of Medicine and Population Health, University of Western Australia, Perth, WA, Australia (Judkins, Thompson) Mount Hospital, Perth, WA, Australia (Judkins) Fremantle Hospital, Fremantle, WA, Australia (Judkins) Heart Research Institute, Sir Charles Gairdner Hospital, Perth, WA, Australia (Thompson) HeartCare WA, Australia

After recovery from myocardial infarction, patients should receive aspirin and statin therapy and be evaluated regarding their need for coronary revascularisation, additional pharmacological treatment and possible device therapy.

Publication Types: Review
PMID:2014289680

A systematic review and individual patient data meta-analysis on intra-abdominal hypertension in critically ill patients: The wake-up project. World initiative on Abdominal Hypertension Epidemiology, a Unifying Project (WAKE-Up!).

Malbrain MLNG, Chiumello D, et al.
(Malbrain, De Laet) Intensive Care Unit, ZiekenhuisNetwerk Antwerpen, ZNA Stuivenberg, Antwerpen, Belgium (Chiumello) Dipartimento di Anestesia, Rianimazione (Intensiva e Subintensiva) e Terapia del Dolore, Fondazione IRCSS Ca’ Granda - Ospedale Maggiore Policlinico, Milan, Italy (Cesana) Biostatistics and Biomathematics Unit, DMMT, University of Brescia, Brescia, Italy (Blaser, Starkopf) Clinic of Anesthesiology and Intensive Care Medicine, Tartu University Hospital, University of Tartu, Tartu, Estonia (Blaser) Department of Intensive Care Medicine University Hospital (Inselspital), University of Bern, Bern, Switzerland (Sugrue) Letterkenny General Hospital, Letterkenny, Ireland (Pelosi, Severgnini) Dipartimento di Scienze Chirurgiche e Diagnostiche Integrate, Universita degli Studi di Genova, Genoa, Italy (Hernandez) Department of Intensive Care Medicine, Pontificia Universidad Catolica de Chile, Santiago, Chile (Brienza) Anesthesia and Intensive Care Unit, Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy (Kirkpatrick) Regional Trauma Services, Foothills Medical Center, Calgary, AB, Canada (Schachtrupp, Kempchen) Department of Surgery, University Hospital RWTH Aachen, Aachen, Germany (Estenssoro, Vidal) Servicio de Terapia Intensiva, Hospital Interzonal de Agudos General San Martin, La Plata, Buenos Aires, Argentina (De Keulenaer) Intensive Care Unit, Fremantle Hospital, Fremantle, WA, Australia (Malbrain) ICU and High Care Burn Unit, ZiekenhuisNetwerk Antwerpen, ZNA Stuivenberg, Lange Beeldkensstraat 267, B-2060 Antwerpen 6, Belgium. E-mail: manu.malbrain@skynet.be

Intra-abdominal hypertension (IAH), defined as a pathologically increase in intraabdominal pressure, is commonly found in critically ill patients. While IAH has been associated with several abdominal as well as extra-abdominal conditions, few studies have examined the occurrence of IAH in relation to mortality. The aim of this paper was to evaluate the prognostic role of IAH and its risk factors at admission in critically ill patients across a wide range of settings and countries. An individual patient meta-analysis of all available data and a systematic review of published (in full or as abstract) medical databases and studies between 1996 and June 2012 were performed. The search was limited to "clinical trials" and "randomized controlled trials", "adults", using the terms "intra-abdominal pressure", "intraabdominal pressure", "abdominal pressure", "intra-abdominal hypertension" and "abdominal hypertension".
"intraabdominal hypertension" combined with any of the terms "outcome" and "mortality". All together data on 2707 patients, representing 21 centers from 11 countries was obtained. Data on 1038 patients were not analysed because of the following exclusion criteria: no LAP value on admission (N.=712), absence of information on ICU outcome (N.=195), age <18 or >95 years (N.=131). Data from 1669 individual patients (19 centers from 9 countries) were analyzed in the meta-analysis. Presence of IAH was defined as a sustained increase in LAP equal to or above 12 mmHg. At admission the mean overall LAP was 9.9+5.0 mmHg, with 463 patients (27.7%) presenting IAH with a mean LAP of 16.3+3.4 mmHg. The only independent predictors for IAH were SOFA score and fluid balance on the day of admission. Five hundred thirteen patients (30.8%) died in intensive care. The independent predictors for intensive care mortality were IAH, SAPS II score, SOFA score and admission category. This systematic review and individual patient data meta-analysis shows that IAH is frequently present in critically ill patients and it is an independent predictor for mortality.

PMID:2014368839


HDL cholesterol and the risk of depression over 5 years.
Almeida OP, Yeap BB, et al.
1] School of Psychiatry and Clinical Neurosciences, University of Western Australia, Perth, WA, Australia [2] WA Centre for Health and Ageing of the Centre for Medical Research, University of Western Australia, Perth, WA, Australia [3] Department of Psychiatry, Royal Perth Hospital, Perth, WA, Australia.
1] School of Medicine and Pharmacology of the University of Western Australia, Perth, WA, Australia [2] Department of Endocrinology, Fremantle Hospital, Fremantle, WA, Australia. Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry of the James Cook University, Townsville, QLD, Australia.
1] WA Centre for Health and Ageing of the Centre for Medical Research, University of Western Australia, Perth, WA, Australia [2] School of Medicine and Pharmacology of the University of Western Australia, Perth, WA, Australia [3] Department of Geriatric Medicine, Royal Perth Hospital, Perth, WA, Australia.
Publication Types: Letter
PMID:23999523


The Parkinson anxiety scale (PAS): Development and validation of a new anxiety scale.
Leentjens AFG, Dujardin K, et al.
(Leentjens) Department of Psychiatry, Maastricht University Medical Center, Maastricht, Netherlands (Dujardin) Neurology and Movement Disorders Unit, Lille University Medical Center, Lille, France (Pontone) Department of Psychiatry and Behavioral Science, Johns Hopkins University School of Medicine, Baltimore, United States (Starkstein) School of Psychiatry, University of Western Australia and Fremantle Hospital, Fremantle, Australia (Weintraub) Departments of Psychiatry and Neurology, Philadelphia Veterans Affairs Medical Center, Perelman School of Medicine at the University of Pennsylvania, Parkinson's Disease Research Education and Clinical Center, Philadelphia, Pennsylvania, United States (Martinez-Martin) Alzheimer Disease Research Unit and CIBERNED, CIEN Foundation, Carlos III Institute of Health, Alzheimer Center Reina Sofia Foundation, Madrid, Spain
A.F.G. Leentjens, Department of Psychiatry, Maastricht University Medical Center, PO Box 5800, 6202 AZ Maastricht, Netherlands. E-mail: a.leentjens@np.unimaas.nl
Existing anxiety rating scales have limited construct validity in patients with Parkinson's disease (PD). This study was undertaken to develop and validate a new anxiety rating scale, the Parkinson Anxiety
Scale (PAS), that would overcome the limitations of existing scales. The general structure of the PAS was based on the outcome of a Delphi procedure. Item selection was based on a canonical correlation analysis and a Rasch analysis of items of the Hamilton Anxiety Rating Scale (HARS) and the Beck Anxiety Inventory (BAI) from a previously published study. Validation was done in a cross-sectional international multicenter study involving 362 patients with idiopathic PD. Patients underwent a single screening session in which the PAS was administered, along with the Hamilton Depression Rating Scale, the HARS, and the BAI. The Mini International Neuropsychiatric Interview was administered to establish Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnoses of anxiety and depressive disorders. The PAS is a 12-item observer or patient-rated scale with three subscales, for persistent, episodic anxiety and avoidance behavior. Properties for acceptability and reliability met predetermined criteria. The convergent and known groups validity was good. The scale has a satisfactory factorial structure. The area under the receiver operating characteristics curve and Youden index of the PAS are higher than that of existing anxiety rating scales. The PAS is a reliable and valid anxiety measure for use in PD patients. It is easy and brief to administer, and has better clinimetric properties than existing anxiety rating scales. The sensitivity to change of the PAS remains to be assessed. 2014 International Parkinson and Movement Disorder Society.

PMID:2014479848

Multiple Sclerosis. 2014; 20 (7): 967.

Associations of physical activity with health outcomes in a large international sample of people with MS.

Marck C, Hadgkiss E, et al.

(Marck, Hadgkiss, Weiland, Van Der Meer, Jelinek) Emergency Practice Innovation Centre, St Vincent's Hospital, Melbourne, VIC, Australia (Weiland) Department of Medicine, University of Melbourne (St Vincent's Hospital), Melbourne, VIC, Australia (Pereira) Faculty of Medicine, Notre Dame University, Fremantle, WA, Australia (Jelinek) Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC, Australia

C. Marck, Emergency Practice Innovation Centre, St Vincent's Hospital, Melbourne, VIC, Australia

Background: People with multiple sclerosis (PwMS) are often advised to rest and conserve energy but recent literature has challenged this view. Several studies have shown positive effects of physical activity (PA) on disability, health related quality of life (HRQOL), and other outcomes, however, some of the evidence is inconclusive. Many studies include only people with mild disability making it difficult to generalize findings to those with moderate or severe disability. Aims: To investigate the associations between PA and HRQOL, relapse rate (RR), disability, and demographic variables in PwMS. Methods: Through online platforms this large international survey recruited 2232 participants with MS who completed items regarding PA, MS and other health characteristics using validated tools such as the International Physical Activity Questionnaire (IPAQ) short form and the Multiple Sclerosis Quality Of Life-54 (MSQOL-54). Participants were over 18 years and consented. The study was approved by the institutional ethics committee. Results: Increased PA was associated with decreased disability (p<0.001), decreased age (p<0.001), male gender (p=0.006), decreased body mass index (BMI) (p<0.001), and increased HRQOL measures of energy, social functioning, mental health and physical health (all p<0.001). For the subsample of people with relapsing remitting MS, PA was associated with a decreased RR (p=0.009). After controlling for disability, increased PA was still associated with decreased BMI, and male gender for those with low and moderate levels of disability but did not reach significance for those in the high disability group. Regression analyses showed that increased PA predicted better QOL regardless of level of disability, age or gender. More specifically, increasing from low to moderate and to high PA increased average physical health scores from 47.7 to 56.1 to 60.0 (25.8% change), mental health scores from 60.6 to 67.0 to 68.8 (13.5% change), energy score from 35.9 to 44.5 to 49.8 (38.7% change), and social function score from 57.8 to 66.1 to 68.4 (18.3% change) (differences between moderate and high PA not significant for mental health and social function scores, all other differences p<0.001). Conclusions: For PwMS, regardless of disability level, increased PA is generally related to better HRQOL in terms of energy, social functioning, mental
Predictors of perioperative blood transfusions in patients with chronic kidney disease undergoing elective knee and hip arthroplasty.

Department of Nephrology, Fremantle Hospital, University of Western Australia, Perth, Western Australia, Australia.

BACKGROUND: Lower preoperative haemoglobin and older age pose a risk for perioperative allogeneic blood transfusions (ABT). The presence of chronic kidney disease (CKD) is associated with low haemoglobin, greater bleeding and ABT utilization.

STUDY DESIGN AND METHODS: The interaction between estimated glomerular filtration rate (eGFR) and haemoglobin on perioperative ABT, length-of-stay and mortality was assessed in 86 patients with CKD stage 3 or higher undergoing elective total knee or hip arthroplasty compared with 294 without CKD. Multivariate analyses for ABT risk with haemoglobin, eGFR, age, gender, duration of surgery and primary versus revision surgery were performed.

RESULTS: Patients with CKD had lower preoperative haemoglobin and higher incidence of ABT. Haemoglobin was independently associated with increased odds of ABT (0.74 (95% confidence interval 0.71-0.77), P=0.001), but eGFR was not (0.98 (0.96-1.02), P=0.089). Length-of-stay and 1 year mortality did not differ between non-transfused CKD patients and controls. Transfused CKD patients had significantly higher length-of-stay compared with transfused controls (25+21 vs 19+16 days, P<0.0001), although 1 year mortality between transfused CKD patients and controls did not differ significantly.

CONCLUSION: CKD alone, in the absence of anaemia, does not predispose to increased risk of ABT or length-of-stay in patients with mild-to-moderate CKD undergoing elective joint surgery. However, low haemoglobin is associated with increased ABT utilization and increased length-of-stay. Considering that 1 in 4 patients undergoing elective hip or knee arthroplasty has CKD, optimal preoperative patient blood management may improve outcome in this population. 2014 Asian Pacific Society of Nephrology.

PMID:24655225


Reno neuro cardio syndrome-fabry's disease: A case report.

Jamboti JS, Forrest CH.
(Jamboti) Department of Renal Medicine, Fremantle Hospital, Fremantle, WA, Australia (Forrest) Path West Laboratory Medicine, Fremantle Hospital, Fremantle, WA, Australia

J.S. Jamboti, Department of Renal Medicine, Fremantle Hospital, Fremantle, WA, Australia

Background: Fabry's disease is a rare X-linked recessive disorder resulting in low levels or absent Lysosomal enzyme Alpha Galactosidase (AGAL) resulting in build up of Globo triaosylceramide in the cells of various organs like kidneys, CNS and heart leading to protean manifestations. Glomerular injury leads to Focal Segmental Glomerulosclerosis (FSGS). Diagnosis is established by low leucocyte AGAL levels. Electron Microscopy (EM) of renal biopsy reveals characteristic diagnostic findings. Case Report: A 21 year old man was referred in 2001 with peripheral oedema and a family history of "nephritis" in his deceased grandfather. Serum creatinine was 150 mumol/L and urinary protein 1.5 g/24 h. Renal biopsy revealed FSGS. Arterio venous fistula was created in March 2011 with stage 4 CKD. Two months later the patient developed Status Epilepticus. MRI revealed multi focal, bi-hemispherical White Matter Lesions. Brain biopsy was performed and patient treated with a diagnosis
of Primary CNS Vasculitis. Patient was found to have severe LVH on ECG during the work up for renal transplantation. Dobutamine stress echocardiogram revealed dynamic left ventricular outflow obstruction. Retinal vein branch occlusion was also detected. With multi-system involvement and positive family history, Fabry’s disease was suspected. Low Leucocyte AGAL levels (0.2 nmol/min/mg protein [normal 0.7-3.3]) confirmed the diagnosis. The initial renal biopsy was reviewed with EM at this point, which revealed the characteristic laminated lipid deposits in endothelial cells and macrophages. Discussion and Conclusions: The diagnosis of Fabry’s disease is often delayed by a decade or more from the initial presentation. Early diagnosis and Enzyme Replacement Therapy might limit the severity of the disease manifestations with improved outcomes. Awareness of the condition and importance of EM in establishing the diagnosis are highlighted.

Publication Types: Conference Abstract
PMID:71588073

Nephrology. 2014; 19: 89.

Acute kidney injury due to decompression illness.
Viecelli A, Jamboti J, et al.
(Viecelli, Jamboti, Ferrari) Department of Nephrology, Fremantle Hospital, Perth, WA, Australia
A. Viecelli, Department of Nephrology, Fremantle Hospital, Perth, WA, Australia

Background: Decompression illness is a rare but serious complication of diving caused by intravascular or extravascular gas bubble formation. Case Report: We report the first case of acute kidney injury in a 27-year-old diver caused by arterial gas emboli formation following three rapid uncontrolled ascents. He presented with transient neurological symptoms including confusion and paralysis followed by abdominal pain (initial lactate 10.8 mmol/L) and rapidly evolving acute kidney injury due to acute tubular necrosis (ATN; initial creatinine 120umol/L, peak at 1210umol/L on day 4 post-diving accident). The diagnosis of ischaemia-induced ATN was supported by a high urinary fractional sodium excretion of 5.5%, elevated LDH (486U/L [125-250]) and a MAG3 scan in keeping with ATN. The absence of myoglobinuria and only moderately elevated creatine kinase (maximum 893U/L [30-170]) made rhabdomyolysis-induced ATN unlikely. He received supportive care with intravenous hydration, sodium bicarbonate and 100% oxygen followed by 7 sessions of hyperbaric therapy and recovered fully without needing dialysis. Conclusions: Arterial air embolism occurs when expanding gas ruptures alveolar capillaries (pulmonary barotrauma) and enters the arterial circulation as a result of rapid decompression. Clinical manifestations depend on the site of embolization and usually include neurological and respiratory symptoms but can also involve the muscles, skin, mesenteric circulation and as shown in this case the kidneys. The diagnosis is made on clinical grounds since gas bubbles are rarely detectable on imaging. Best first aid for decompression illness is 100% oxygen therapy and supportive care but early transfer to a hyperbaric treatment unit is important as symptoms may evolve over time as in our patient.

Publication Types: Conference Abstract
PMID:71588056


Single-centre experience with mammalian target of rapamycin inhibitor (mTORi) in renal transplant recipients.
Wallooppillai D, Ogennis S, et al.
(Wallooppillai, Ogennis, Ferrari) University of Western Australia, Perth, WA, Australia (Ferrari, Kulkarni) Department of Nephrology, Fremantle Hospital, Fremantle, WA, Australia
D. Wallooppillai, University of Western Australia, Perth, WA, Australia

Aim: To review the experience of inhibitors of the mammalian target of rapamycin (mTORi) utilisation in our centre Background: Despite the potential for mTORi to reduce chronic allograft nephropathy and as calcineurin inhibitor (CNI) sparing agents, their use in renal transplant has remained limited. The benefits and effects of mTORi were assessed in our centre’s cohort. Methods: We analysed graft
function, rejection rates, tolerability and discontinuation rates in a retrospective cohort analysis of 44 adult kidney transplant recipients (29 male and 15 female) treated with mTORi between 2006 to 2012.

Results: All patients switched from CNI to mTORi, the reasons for conversion were skin cancers (37%), CNI toxicity/ intolerance (25%), planned reduction in immunosuppression (14%), study trials (7%), BK nephropathy (5%) and others (12%). mTORi had to be discontinued in 15 (34%) patients within 24 months and in 7 (16%) after 24 months because of either rejection, severe proteinuria, oedema, muco-cutaneous effects, leukopenia, pneumonitis, or cerebral venous thrombosis. The eGFR pre-conversion was 56 + 22 mL/min/1.73 m<sup>2</sup> and 63 + 24 mL/min/ 1.73 m<sup>2</sup> (P < 0.01) at 1 month, but did not differ from pre-conversion at 3, 6, 12 and 24 months. Fourteen (32%) patients experienced biopsy proven rejection (n = 9 cellular, 2 mixed and 3 borderline changes) without association to HLA mismatches, or time of conversion after transplantation. Conclusions: In this retrospective analysis of a small subset of patients, mTORi treatment is associated with early adverse effects or acute rejection leading to discontinuation of mTORi in up to 50% of patients. mTOR inhibitors are a reasonable therapeutic alternative to CNIs for a only a subset of renal transplantation recipients.

Publication Types: Conference Abstract
PMID:71588044

**Tolerability and safety of rapid intravenous push bolus administration of iron polymaltose 200mg over 15 minutes on haemodialysis: A pilot study.**

Light C, Kulkarni H.
(Light, Kulkarni) Armadale Health Service, Perth, WA, Australia (Kulkarni) Fremantle Hospital, Perth, WA, Australia
C. Light, Armadale Health Service, Perth, WA, Australia
Aim: To study the safety and tolerability of push dose intravenous iron polymaltose (IVI) 200 mg over 15 minutes on haemodialysis. Background: 200 mg Iron polymaltose are administered as intravenous infusions in 100 ml normal saline over 60 minutes. Prolonged infusions set-ups are time consuming and impact on available resources; limiting its use in non-hospital settings as well as reduced bio-availability due to probable iron loss in the dialysate. Methods: 30 patients (M = 21; F = 9) in a dialysis unit were enrolled after consent in a 12 month prospective, observational study between April 2013 to Mar 2014. 200 mg iron polymaltose diluted with normal saline to 20 mL in a syringe; was administered in the dialysis venous port over 15 minutes as mini boluses. Vital signs and side effect profiles were monitored during, after and prior to the subsequent dialysis. Monthly haemoglobin, erythropoietic stimulating agents (ESA) usages and IV iron doses were recorded. Results: 212 IVI doses were administered at monthly (n = 74), fortnightly (n = 103), or 5 consecutive dialysis (n = 35) intervals. All except 3 doses achieved 15 minutes administration time, with 3 reaching 20 minutes. There were no significant changes in the patients' vital signs and no experience of adverse effects recorded. Median (IQR) ESA use at the start and end of the study were 6924 and 3370 Units/week; Haemoglobin 11.0 and 11.1 g/dL respectively. Conclusions: Push dose of 200 mg Iron over 15 minutes is safe and well tolerated. ESA use was positively affected. 200 mg IVI could be safely administered on dialysis; allowing optimal use of resources.

Publication Types: Conference Abstract
PMID:71588011

Nephrology. 2014; 19: 76.
**Towards a national surveillance network for chronic kidney disease (CKD).**

Hoy WE, Healy HG, et al.
(Hoy, Healy) CKD.QLD, Centre for Chronic Disease, University of Queensland, Brisbane, QLD, Australia (Healy) Renal Services, Metro North Hospital and Health Service, Brisbane, QLD, Australia (Healy, Waugh, Nelson) Electronic Kidney Disease National Audit Alliance (eKiDNAA), Sydney, NSW,
Aim: To describe a collaboration for surveillance of CKD in ambulatory settings across Australia.

Background: Prevention and amelioration of CKD, as well as prediction of future burdens of end stage kidney failure (ESKF) and renal replacement therapy (RRT) depend on knowledge of CKD's distribution and course. However, there are no systems in Australia for systematic surveillance of CKD in the ambulatory (outpatient) setting, nor for following episodes of care in a given patient's journey across outpatient and inpatient settings. Individual health care numbers and electronic health records will ultimately support such functions, but with burgeoning costs of RRT we need evidence-based interventions now. We propose a collaboration of programs that are already collecting CKD data in order to develop regional profiles of CKD and its outcomes in various settings within Australia.

Methods: Membership is open. Potential partners include CKD.QLD, CKD.TAS, CKD.WA, eKiDNA, the Monash-based Registry of Kidney Disease, the St George (Sydney) CKD Chronic Disease Outreach Program, Victoria's eMAP CKD:VIC and the Queensland Aboriginal and Islander Health Council (QAIHC). These systems have already captured data on many thousands of CKD patients in public and private renal practices, as well as chronic disease screening data from primary care settings in Western Victoria and in Aboriginal Health Services (QAIHC and WA). Operating systems include hospital databases, XL, Ferret, Communicare, MMEX and Audit4, PEN-CS, and CDM-Net, with information extractable from all. The initiative is endorsed by KHA, and Amgen funded the consortium's first two meetings. Several partners have collaborated in grant applications to BUPA and NHMRC-CREs. Conclusions: These data will underpin regional maps of CKD and support informed predictions and interventions, before information flows from harmonised electronic approaches.

Publication Types: Conference Abstract
PMID:71588002


**HLA broad antigen and eplet mismatches in determining the risk of acute rejection after kidney transplantation.**


(Do Nguyen, Lim, Fidler, Ferrari, D'Orsogna, Irish) University of Western Australia, Perth, WA, Australia (Lim) Sir Charles Gairdner Hospital, Perth, WA, Australia (Fidler, D'Orsogna, Irish) Royal Perth Hospital, Perth, WA, Australia (Chapman, Craig, Wong) Children's Hospital at Westmead, Sydney, NSW, Australia (Craig, Wong) University of NSW, Sydney, NSW, Australia (Ferrari) Fremantle Hospital, Perth, WA, Australia

H. Do Nguyen, University of Western Australia, Perth, WA, Australia

Aim: To determine the clinical relevance of HLA-ABDR broad antigen and eplet matching for predicting biopsy-proven acute rejection (BPAR) after kidney transplantation. Background: HLAMatchmaker is a computer algorithm that determines structurally-based HLA-antigen compatibility at the epitope level and may better predict the immunological risk of transplant recipients compared to broad HLA antigens matching. Methods: Donor-recipient eplet mismatches at HLA-ABDR were calculated for all kidney transplant (n = 644) recipients in Western Australian between years 2000 and 2010. The test performance characteristics of HLA broad antigen and eplet matching for predicting 12-month BPAR were examined using the Receiver Operating Characteristic (ROC) analysis. Results: Of the 644 kidney transplants recipients over a mean follow-up period of 4 (SD = 3) years, 179 (28%) experienced BPAR. Recipients with higher number of HLA-ABDR broad antigen mismatches (0:17%; 3:35%; 6:30%) or HLA-ABDR eplet mismatches (0-2:19%; 3-9:28%; 10-19:25%; >20:34%)
experienced rejection. The area under the ROC curves (95% CI) for broad antigen (ABDR), eplet (ABDR), broad antigen (DR), eplet (DR) and the combined broad antigen-eplet mismatches were 0.54 (0.49-0.59), 0.54 (0.49-0.60), 0.58 (0.52-0.62), 0.57 (0.52-0.62) and 0.61 (0.56-0.66), respectively. Compared with HLA-ABDR broad antigen matching, the combined HLA-broad antigen-eplet model better predicted BPAR compared to the HLA-ABDR broad antigen model alone (P = 0.01). The optimal balance between test sensitivity and specificity (59% and 44%) of the combined model was achieved using a combined HLA-ABDR (3) and eplet (20) mismatch cut-point. Conclusions: Inclusion of eplet matching to the current allocation algorithm may improve the discriminatory value for predicting BPAR in kidney transplant recipients compared with broad antigen matching alone.

Publication Types: Conference Abstract
PMID: 71587902


Cancer recurrence in kidney transplant recipients.
(Viecelli) Department of Nephrology, Fremantle Hospital, Perth, WA, Australia (Chapman, Craig, Webster, Wong) Centre for Kidney Research, Children's Hospital at Westmead, Sydney, NSW, Australia (Craig, Clayton, Wong) School of Public Health, University of Sydney, Sydney, NSW, Australia (Carroll) Department of Nephrology, Royal Prince Alfred Hospital, Sydney, NSW, Australia (Clayton) Department of Nephrology, Sir Charles Gairdner Hospital, Perth, WA, Australia (Wong) Centre for Transplant and Renal Research, Westmead Millennium Institute, Westmead Hospital, Sydney, NSW, Australia

Background: Clinical guidelines recommend a waiting time of 2-5 years before transplantation in potential recipients who develop cancer, but little is known about the risk of recurrence in recipients. Aim: We aimed to determine the risk of cancer recurrence after kidney transplantation in recipients with a prior cancer and to compare the risk of cancerspecific mortality among recipients with cancer recurrence and those who developed de novo cancers post-transplantation. Methods: Data from the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) was used to assess cancer recurrence risk of all types, excluding non-melanocytic skin cancers, in kidney transplant recipients with a history of cancer pre-transplantation between 1965 and 2012. Results: Of the 21,415 transplant recipients, 651 (3.0%) had cancer prior to transplantation. Nineteen patients (2.9%) experienced cancer recurrence after the first transplant. The median time to first recurrence was 5.8 years [Interquartile range: 7.8 years]. Of all cancer recurrences, 7 (37%) occurred in the first two years posttransplant, 6 (31%) between 2-6 years and the remaining 5 cancers (32%) 6 years after the first transplant. The highest recurrence rates were seen in cancers of the urinary tract system (n = 6, 31%), followed by breast cancer (n = 4, 21.5%) and melanoma (n = 4, 15.8%). Over a median follow-up time of 10.4 years, five recipients (26.1%) died from cancer recurrences. There was an increased risk of cancer death among those with a prior malignancy compared to recipients who developed de novo cancers after transplantation (RR: 1.60; 95%: 1.5-1.8, P < 0.001). Conclusions: Although the risk of cancer recurrence among those who developed cancer prior to transplantation is low, cancer outcomes are inferior to those without pre-existing malignancy.

Publication Types: Conference Abstract
PMID: 71587900

Nephrology. 2014; 19: 44.

Viecelli A, D’Orsogna L, et al.
(Viecelli, Woodroffe, Ferrari) Department of Nephrology, Fremantle Hospital, Perth, WA, Australia
Background: De novo donor-specific HLA antibodies (dnDSA) developing post-transplant are a major cause of late graft loss and often precede renal dysfunction. HLA mismatch is a predictor for the development of dnDSA. In the Australian paired Kidney Exchange (AKX) program HLA matching rules are ignored in favor of a virtual crossmatch. Aim: We aimed to determine whether this approach is associated with increased incidence of dnDSA. Methods: Post-transplant HLA-antibody monitoring in the AKX program has been offered since April 2011. Recipients’ sera collected at 1, 3, 6 and 12 months during the first post-transplant year and yearly thereafter were tested by Luminex Single Antigen Bead (SAB) assay. Results: As of 31 December 2013 there were 60 patients with at least 3 months follow-up. HLA monitoring data was available for 50 patients, sera from 10 patients were not provided to the HLA laboratory. Of the 50 patients whose SAB data were available, 25 had calculated panel reactive antibody >75%, 29 (58%) had performed DSA (preDSA) >500MFI and 7 (14%) had preDSA >2000MFI to the matched donor. After transplantation preDSA became undetectable (<500MFI) in 24 patients, persisted in 3 and increased in strength in 2. The onset of dnDSA with MFI >500 was documented in 5 patients, including 1 without preDSA, 2 with increase in preDSA and 2 who cleared their preDSA. Conclusions: Among mostly sensitised recipients of a kidney paired donation transplant, development of dnDSA early after transplantation is observed in approximately 10% of cases. The relationship between the course of preDSA and dnDSA and graft function and survival requires further analysis.


An observational, non-interventional, multicentre, multinational registry of patients with atypical haemolytic uraemic syndrome (aHUS): Initial characteristics of the Australian cohort. Isbel N, Hughes P, et al. (Isbel) Department of Nephrology, Princess Alexandra Hospital, Brisbane, QLD, Australia (Isbel) University of Queensland, Melbourne, VIC, Australia (Hughes) Department of Nephrology, Royal Melbourne Hospital, Melbourne, VIC, Australia (Ferrari) Department of Nephrology, Fremantle Hospital, Fremantle, WA, Australia (Kausman) Department of Nephrology, Royal Childrens Hospital, Melbourne, VIC, Australia (Lim) Department of Nephrology, Sir Charles Gairdner Hospital, Perth, WA, Australia (Chapman) Renal Transplant Unit, Westmead Hospital, Sydney, NSW, Australia (Licht) Hospital for Sick Children, Toronto, ON, Canada (Fremeaux-Bacchi) Assistance Publique-Hopitaux de Paris, Paris, France (Payne) Alexion Pharmaceuticals, Australia

N. Isbel, Department of Nephrology, Princess Alexandra Hospital, Brisbane, QLD, Australia

Aim: To report baseline demographics of the Australian Cohort of patients with aHUS enrolled into the global aHUS Registry. Background: aHUS is an ultra-rare, genetic, life-threatening disease of chronic complement activation leading to systemic thrombotic microangiopathy, with renal and other end-organ damage. There is a paucity of information on incidence, diagnosis, treatment and patient outcomes. The global aHUS Registry is a multi-centre, multi-national non-interventional registry, initiated in April 2012, prospectively collects information on patients with aHUS. Methods: aHUS patients are eligible for enrolment in a multi-centre, multinational registry. Demographic, disease history, laboratory measures, treatments, efficacy and safety outcome data are collected initially and every 6 months thereafter. Results: By October 8, 2013, 19 Australian patients from 5 centres were enrolled in the aHUS registry. Eighteen (95%) patients were >18 years and 14 (74%) patients were female. 5 patients (26%) had a family member diagnosed with aHUS and 3 patients (16%) had a complement genetic mutation or autoantibody identified. 43% of these patients had received a kidney transplant, 71% received dialysis and 100% had received plasma exchange or infusion. Seven (37%) were treated with eculizumab [ECU] therapy with a median duration of treatment of 1.4 years (0.3-3.6 years). Mean age at ECU treatment initiation was 26 years, and mean time on ECU was 1.5 years. Further analysis of efficacy of therapy and outcomes is ongoing. Conclusions: Analyses of data
obtained through the aHUS Registry will increase our understanding of the history and disease progression in patients with aHUS, and may help optimize management of patients with this rare and lifethreatening disease. New clinical sites are encouraged to participate.

Publication Types: Conference Abstract
PMID:71587859


The effect of pentoxifylline on oxidative stress markers: Substudy of the hero trial.
Zhang L, Pascoe EM, et al.
(Zhang, Pascoe, Badve, Cass, Clarke, Coombes, Ferrari, Mcdonald, Morrish, Pedagogos, Perkovic, Reidlinger, Scaria, Walker, Vergara, Hawley, Johnson) Australasian Kidney Trials Network, University of Queensland, Brisbane, Australia (Zhang, Badve, Hawley, Johnson) Nephrology Department, Princess Alexandra Hospital, Brisbane, Australia (Cass) Menzies School of Health Research, Darwin, Australia (Clarke) Centre for Health Policy, Programs and Economics, University of Melbourne, Melbourne, Australia (Coombes) School of Human Movement Studies, University of Queensland, Brisbane, Australia (Ferrari) Department of Renal Medicine, Fremantle Hospital, Fremantle, Australia (Mcdonald) Department of Nephrology and Transplantation Services, University of Adelaide, Central Northern Adelaide Renal and Transplantation Services, Adelaide, Australia (Pedagogos) Department of Nephrology, Royal Melbourne Hospital, Melbourne, Australia (Perkovic) George Institute for Global Health, Sydney, Australia (Walker) Department of Renal Medicine, Alfred Hospital, Melbourne, Australia

L. Zhang, Australasian Kidney Trials Network, University of Queensland, Brisbane, Australia

Aim: To determine the effect of pentoxifylline on oxidative stress markers in patients with chronic kidney disease (CKD) and erythropoietin stimulating agent (ESA) resistance. Background: ESA-resistant anaemia is common in CKD and associated with adverse outcomes. Enhanced oxidative stress is a putative mechanism for ESA resistant anaemia in CKD. The effect of pentoxifylline on oxidative stress has not been previously reported. Methods: In this multi-centre double-blind, randomized controlled trial, 53 adults with CKD stage 4/5 (including dialysis) and ESA-resistant anaemia (hemoglobin concentration <120g/L and ESA resistance index [ERI] >1.0 IU/kg/week/gHb for erythropoietin and >0.005 mug/kg/week/gHb for darbepoetin) were randomized to pentoxifylline (400 mg daily; n = 26) or matched placebo (n = 27) for 4 months. The primary outcome was ERI. A substudy examined oxidative stress markers: plasma total F2-isoprostanes, protein carbonyls, glutathione peroxidise (GPX) and superoxide dismutase (SOD) activities; 15/ 26 patients in pentoxifylline arm and 17 /27 in control arm had data available for analysis. Results: No differences in ERI, ESA dose, serum ferritin, serum transferrin saturation and reticulocyte count were observed between the groups. Pentoxifylline significantly increased haemoglobin concentration (MD 7.24 g/L, 95% CI 0.32 to 14.16, P = 0.04). The adjusted mean differences [MD] in markers of oxidative stress comparing pentoxifylline-treated patients to controls were: total F2-isoprostanes, adjusted MD 35.01 pg/mL, 95% CI -8.12 to 78.15, P = 0.108; SOD activity, adjusted MD 0.82 U/mL, 95% CI -0.08 to 1.71, P = 0.073; GPX activity, adjusted MD -0.06 U/L, 95% CI -13.0 to 0.89, P = 0.085; protein carbonyls, adjusted MD -0.04 nmol/mg, 95% CI -0.16 to 0.08, P = 0.523. Conclusions: This study did not provide sufficient evidence for pentoxifylline to have an effect on oxidative stress markers despite increasing haemoglobin concentration.

Publication Types: Conference Abstract
PMID:71587847


Association between serum alkaline phosphatase and resistance to erythropoiesis stimulating agents in chronic kidney disease: A post-hoc analysis of the hero trial.
Badve SV, Pascoe EM, et al.
(Badve, Pascoe, Cass, Clarke, Coombes, Ferrari, Mcdonald, Morrish, Pedagogos, Perkovic,
Aim: To study the determinants of primary resistance to erythropoiesis stimulating agent (ESA) in chronic kidney disease (CKD). Background: The causes of ESA-resistant anaemia include nutritional deficiencies, infection, inflammation, neoplasia, severe hyperparathyroidism, and bleeding. After excluding these conditions, 10% of CKD patients exhibit primary ESA-resistant anaemia, associated with increased risks of morbidity and mortality. Methods: The study included 53 adult patients with CKD stage 4 or 5 and primary ESA-resistant anaemia (haemoglobin <120g/L and ESA resistance index [ERI] >1.0 IU/kg/week/gHb for erythropoietin and >0.005 mug/kg/week/gHb for darbepoeitin). Participants were divided into tertiles of ERI (low, medium and high ERI). Multinomial logistic regression was used to analyse the determinants of ERI tertiles. Results: The mean (SD) ERI (IU/kg/week/gHb) in the low (n = 18), medium (n = 18) and high (n = 17) ERI tertiles were 1.4 (0.3), 2.3 (0.2) and 3.5 (0.8), respectively (P < 0.001). There were no significant differences in age, diabetes, BMI, ferritin, transferrin saturation, parathyroid hormone, albumin, liver enzymes, calcium, phosphate or markers of oxidative stress and inflammation (CRP, total F2-isoprostanes, glutathione peroxidise activity, superoxide dismutase activity and protein carbonyls) between the ERI tertiles. The median (interquartile range) serum alkaline phosphatase (U/L) in the low, medium and high ERI tertiles were 89 (64, 121), 99 (76, 134) and 148 (87, 175), respectively (P = 0.05). There was a weak but statistically significant association between ERI and alkaline phosphatase (Pseudo R\(^2\) = 0.06, P = 0.03). The risk of being in the high ERI tertile relative to the low ERI tertile increased with increasing alkaline phosphatase levels (P = 0.02). No other variables were significantly associated with ERI. Conclusions: Serum alkaline phosphatase may be associated with primary ESAresistance. Large prospective studies are required to confirm this association.

Publication Types: Conference Abstract
PMID:71587838
Aim: To determine whether pentoxifylline results in a reduction in erythropoiesis resistance index (ERI) in patients with chronic kidney disease (CKD) and erythropoiesis stimulating agent (ESA)-resistant anaemia. Background: ESA-resistant anaemia is common in CKD and associated with increased risks of hospitalization, cardiovascular events and mortality. Pentoxifylline shows promise as a treatment but has not been rigorously evaluated. Methods: In this multi-centre, double-blind, randomized controlled trial, adults with CKD stage 4 or 5 (including dialysis) and ESA-resistant anemia (hemoglobin concentration <120g/L and ESA resistance index [ERI] > 1.0 IU/kg/week/gHb for erythropoietin-treated patients and > 0.005 mg/kg/week/gHb for darbepoeitin-treated patients) were randomized to pentoxifylline (400 mg daily; n = 26) or matching placebo (control n = 27) for 4 months. The primary outcome was ERI. Results: While ERI was 15% lower in pentoxifylline-treated patients compared to controls, the difference was not statistically significant (adjusted mean difference [MD] -0.39 IU/kg/gHb, 95% CI -0.89 to 0.10, P = 0.1). Pentoxifylline significantly increased haemoglobin concentration (MD 7.6 g/L, 95% CI 1.7 to 13.5, P = 0.01) and non-significantly reduced ESA dose relative to controls (-20.8 IU/kg/week, 95% CI 67.2 to 25.7, P = 0.4). No differences in blood transfusion requirements, adverse events or quality of life were observed between the groups. Pentoxifylline cost $88 per person over the trial and produced mean savings in the cost of ESA of $1332. The overall economic impact over the trial period was a saving of $1244 per person for the pentoxifylline group compared to controls. Conclusions: Pentoxifylline did not significantly modify ESA resistance, but safely increased hemoglobin concentration. Pentoxifylline offers a safe and economical method by which haemoglobin concentration can be increased in ESA-resistant anaemia without needing to increase ESA dose.

Publication Types: Conference Abstract
PMID:71587827


Intravenous calcium infusions (IV-CA) following surgical parathyroidectomy (sPTX) in advanced chronic kidney disease (CKD): A centre experience.
(Graves, Lisweski, Adris, Ferrari, Kulkarni) Fremantle Hospital, Fremantle, WA, Australia
A. Graves, Fremantle Hospital, Fremantle, WA, Australia
Aim: To study the incidence of sPTX induced hypocalcaemia and need for IV-Ca post introduction of a new protocol with increased threshold of albumin corrected serum calcium (sCa) mandating intervention. Background: Hypocalcaemia is a frequent consequence of sPTX in patients with tertiary hyperparathyroidism. No consensus exists on when to institute IV-Ca. Our institution introduced a new protocol with IV-Ca indicated at sCa < 1.8 mmol/L in November 2010. Methods: We analysed the incidence of hypocalcemia, need for IV-Ca, adherence with planned preloading and re-admissions within the subsequent 3 months in a retrospective cohort analysis of 40 CKD [n: 35 (dialysis), 3 (pre-dialysis), 2 (post-transplant)] between Mar 2009 and Oct 2013; before (n 12) and after (n 28) protocol introduction. Results: IV-Ca usage declined from 69% to 28% after introduction of protocol, with no episodes of symptomatic hypocalcaemia or increased readmission rates. Compliance with preloading was poorly documented (36%) or absent (21%). Central venous catheter (CVC) placement reduced from 92% (pre-protocol) and 87% (post-protocol until February 2013) to 16% (since March 2013). Conclusions: In this retrospective analysis of a small subset of patients, IV-Ca infusion is not necessary for asymptomatic hypocalcemia with sCa > 1.9 mmol/L. Early cessation of calcimimetic therapy and aggressive preoperative calcium loading seems to obviate need for IV-Ca infusions. CVC placement should be mandated in a select few only.
Publication Types: Conference Abstract
PMID:71587798


Comparative survival benefits and costs of an eplet-based and broad-antigen matching system
in deceased donor kidney allocation among indigenous Australians.
(Do Nguyen, Fidler, Ferrari, D’Orsogna, Irish, Lim) University of Western Australia, Perth, WA, Australia
(Wong, Chapman, Craig) Children’s Hospital at Westmead, Sydney, NSW, Australia
(Wong, Craig) University of NSW, Sydney, NSW, Australia
(Fidler, D’Orsogna, Irish) Royal Perth Hospital, Perth, WA, Australia
(Australia) Fremantle Hospital, Perth, WA, Australia
(H. Do Nguyen, University of Western Australia, Perth, WA, Australia
Aim: To compare the benefits and costs of incorporating an Eplet-based matching algorithm with the current allocation algorithm for deceased donor kidney allocation in indigenous Australians.
Background: The overall waiting time for transplantation among indigenous Australians is at least six times longer than the non-indigenous Australians with end-stage kidney disease. Such disparities are largely attributed to the HLA antigen mismatch between donors and potential indigenous transplant candidates. Structural matching at the epitope level known as eplets, particularly at the HLA-DR locus may provide a more accurate assessment of immunological risk compared to HLA matching at the broad antigen level. Methods: Using deterministic decision analytical and simulation modelling, we compared the average waiting time for transplantation, the overall survival gains (in life years saved [LY] and quality-adjusted life years [QALYs] gained) and the costs of integrating an Eplet-based allocation for deceased donor kidneys compared with the current allocation algorithm. The Eplet-based model simulated allocation of kidneys to indigenous recipients focusing only on HLA-DR eplet mismatches using predefined cut-offs of <2 and <10 eplet mismatches. Results: The average waiting time for transplantation reduced by an average of 23 (SD = 22) and 22 (SD = 17) months using the eplet-based allocation algorithm with <2 and <10 HLA-DR eplet cut-offs respectively. The average gain in QALY using the eplet-based algorithm varied between 0.01 and 0.05 QALYs, with average savings of $644 to $6,624 depending on the specified threshold. There was a small consequential loss of up to 0.01 QALYs and extra costs of $368 for non-indigenous Australians. Conclusions: Alternative allocation for indigenous kidney transplant recipients are associated with a reduction in transplant waiting-time with improved health benefits without disadvantaging non-indigenous recipients.
Publication Types: Conference Abstract
PMID:71587787

Successful treatment of renal allograft and bladder malakoplakia with minimization of immunosuppression and prolonged antibiotic therapy.
Graves AL, Texler M, et al.
Renal Unit, Fremantle Hospital, Perth, Western Australia, Australia.
Malakoplakia is an unusual granulomatous inflammatory disorder associated with diminished bactericidal action of leucocytes that occurs in immunosuppressed hosts. Cases of renal allograft malakoplakia are generally associated with a poor graft and patient survival. We present the case of a 56-year-old female with allograft and bladder malakoplakia occurring two years after renal transplantation complicated by an early antibody mediated rejection. Following a number of symptomatic urinary tract infections caused by resistant Gram-negative bacilli, a diagnosis of malakoplakia was made by biopsy of a new mass lesion of the renal allograft. Cystoscopy also revealed malakoplakia of the bladder wall. Immunosuppressant regimen was modified. Mycophenolate mofetil was ceased, prednisolone reduced to 5mg/day and tacrolimus concentrations were carefully monitored to maintain trough serum concentrations of 2-4mg/L. Concurrently, she received a prolonged course of intravenous antibiotics followed by 13 months of dual oral antibiotic therapy with fosfomycin and faropenem. This joint approach resulted in almost complete resolution of allograft malakoplakia lesions and sustained regression of bladder lesions on cystoscopy with histological resolution in bladder lesions. Her renal function has remained stable throughout the illness. If treated with sustained antimicrobial therapy and reduction of immunosuppression, cases of allograft malakoplakia may not necessarily be associated with poor graft survival.

PMID:71587787
Differential disruption of blood-brain barrier in severe traumatic brain injury.


(Saw) Intensive Care Unit, Fremantle Hospital, PO Box 480, Fremantle, WA 6959, Australia
(Chamberlain, Barr, Ho) Intensive Care Unit, Royal Perth Hospital, GPO Box X2213, Perth, WA 6001, Australia
(Morgan) School of Medicine, Cardiff University, Henry Wellcome Building, Heath Park, Cardiff CF14 4XN, United Kingdom
(Burnett) Department of Clinical Biochemistry, PathWest Laboratory Medicine, Royal Perth Hospital, Perth, WA, Australia
(Morgan) School of Medicine, University of Western Australia (M570), 35 Stirling Highway, Crawley, WA 6009, Australia
(Ho) School of Population Health, University of Western Australia, Perth, WA, Australia

M.M. Saw, Intensive Care Unit, Fremantle Hospital, PO Box 480, Fremantle, WA 6959, Australia. E-mail: melanie.saw@health.wa.gov.au

Background: Traumatic brain injury (TBI) is a significant cause of death and disability in young adults, but not much is known about the incidence and characteristics of blood-brain barrier (BBB) dysfunction in this group. In this proof of concept study, we sought to quantify the incidence of BBB dysfunction (defined as a cerebrospinal fluid (CSF)-plasma albumin quotient of >0.007) and examine the relationship between plasma and CSF levels of proteins and electrolytes, in patients with severe TBI.

Methods: We recruited 30 patients, all of whom were receiving hypertonic 20% saline infusion for intracranial hypertension and had external ventricular drains in situ. Simultaneous CSF and blood samples were obtained. Biochemical testing was performed for sodium, osmolality, potassium, glucose, albumin, immunoglobulin-G, and total protein.

Results: Eleven patients (37%) showed evidence of impairment of passive BBB function, with a CSF-plasma albumin quotient of >0.007. There were strong positive correlations seen among CSF-plasma albumin quotient and CSF-plasma immunoglobulin-G quotient and CSF-plasma total protein quotient (r = 0.967, P < 0.001 and r = 0.995, P < 0.001, respectively). We also found a higher maximum intracranial pressure (24 vs. 21 mmHg, P = 0.029) and a trend toward increased mortality (27 vs. 11%, P = 0.33) in patients with BBB disruption.

Conclusions: In summary, passive BBB dysfunction is common in patients with severe TBI, and may have important implications for effectiveness of osmotherapy and long-term outcomes. Also, our results suggest that the CSF-plasma total protein quotient, a measurement which is readily available, can be used instead of the CSF-plasma albumin quotient for evaluating BBB dysfunction. 2013 Springer Science+Business Media.

Hematological toxicity of combined lu-octreotate radiopeptide chemotherapy of gastroenteropancreatic neuroendocrine tumors in long-term follow-up.


Department of Hematology, Fremantle Hospital, The University of Western Australia, Fremantle, W.A., Australia.

BACKGROUND: The combination of radiopptide therapy [peptide receptor radionuclide therapy (PRRT)] with radiosensitzing chemotherapy of gastroenteropancreatic neuroendocrine tumors (GEP NETs) may improve efficacy, but has the potential to increase myelotoxicity. In a prospective clinical study of GEP NET patients treated with (177)Lu-octreotate PRRT in combination with capecitabine and temozolomide, as a prelude to a planned Australasian Gastro-Intestinal Trials Group (AGITG) international randomized controlled trial, we characterized the incidence and degree of hematological toxicity.

MATERIALS AND METHODS: Well-differentiated progressive metastatic GEP NETs in 65 patients were treated with 4 cycles of 7.8 GBq (177)Lu-octreotate, 1,650 mg/m(2) capecitabine (n = 28) and 1,500 mg/m(2) capecitabine with 200 mg/m(2) temozolomide (n = 37), and monitored for
hematological toxicity over a 5-year period.

RESULTS: Short-term, self-limited hematological toxicity grade 3/4 comprised anemia in 1 patient (3.5%) in the 28 patient-cohort of patients treated with (177)Lu-octreotate and capecitabine. One of these patients (3.5%) later developed significant anemia and one developed thrombocytopenia (3.5%) over a median follow-up of 60 months (SD 20). The incidence of short-term grade 3/4 reversible myelosuppression in 37 patients after (177)Lu-octreotate/capecitabine/temozolomide was zero. Long-term follow-up for a median of 36 months (SD 11) showed significant thrombocytopenia in 2.7% and neutropenia in 2.7% of the patients and anemia in 10.8% of the patients (n = 4). The 3-year median hemoglobin and platelet and neutrophil counts trended downwards, but remained within normal ranges. Two patients in this cohort developed myelodysplastic syndrome.

CONCLUSION: The modest reversible hematological toxicity of PRRT of GEP NETs is not significantly increased by the addition of radiosensitizing chemotherapy with capecitabine and temozolomide in combination with (177)Lu-octreotate, which has the potential to enhance the efficacy of radiopeptide therapy. 2014 S. Karger AG, Basel.

PMID:24714208

Neurology. 2014; 82(12): 1038-44.

Alcohol consumption and cognitive impairment in older men: a mendelian randomization study.

Almeida OP, Hankey GJ, et al.

From the School of Psychiatry & Clinical Neurosciences (O.P.A.), and School of Medicine and Pharmacology (G.J.H., B.B.Y., L.F.), University of Western Australia, Perth; WA Centre for Health & Ageing (O.P.A., L.F.), Centre for Medical Research, Perth; Departments of Psychiatry (O.P.A.) and Geriatric Medicine (L.F.), Royal Perth Hospital; Department of Neurology (G.J.H.), Sir Charles Gairdner Hospital, Perth; Department of Endocrinology (B.B.Y.), Fremantle Hospital, Fremantle; Queensland Research Centre for Peripheral Vascular Disease (J.G.), School of Medicine and Dentistry, James Cook University, Townsville; and Department of Vascular and Endovascular Surgery (J.G.), The Townsville Hospital, Townsville, Australia.

OBJECTIVE: To determine whether alcohol consumption is causally associated with cognitive impairment in older men as predicted by mendelian randomization.

METHODS: Retrospective analysis of a cohort study of 3,542 community-dwelling men aged 65 to 83 years followed for 6 years. Cognitive impairment was established by a Mini-Mental State Examination score of 23 or less. Participants provided detailed information about their use of alcohol during the preceding year and were classified as abstainers, occasional drinkers, and regular drinkers: mild (<15 drinks/wk), moderate (15-27 drinks/wk), heavy (28-34 drinks/wk), and abusers (>35 drinks/wk). We genotyped the rs1229984 G->A variant of the alcohol dehydrogenase 1B (ADH1B) gene, which is associated with lower prevalence of alcohol abuse and dependence. Other measures included age, education, marital status, smoking and physical activity, body mass index, diabetes, hypertension, and cardiovascular diseases.

RESULTS: At study entry, rs1229984 G->A polymorphism was associated with lower prevalence of regular use of alcohol and decreased consumption among regular users. Six years later, 502 men (14.2%) showed evidence of cognitive impairment. Abstainers and irregular drinkers had higher odds of cognitive impairment than regular drinkers (odds ratio [OR] = 1.23, 95% confidence interval [CI] = 1.00-1.51, after adjustment for other measured factors). The rs1229984 G->A polymorphism did not decrease the odds of cognitive impairment (AA/GG OR = 1.35, 95% CI = 0.29-6.27; GA/GG OR = 1.05, 95% CI = 0.71-1.55).

CONCLUSIONS: Alcohol consumption, including heavy regular drinking and abuse, is not a direct cause of cognitive impairment in later life. Our results are consistent with the possibility, but do not prove, that regular moderate drinking decreases the risk of cognitive impairment in older men.

Publication Types: Research Support, Non-U.S. Gov't
PMID:24553426
Assessment of mortality in sporadic inclusion body myositis: A delphi panel technique.


(De Visser) Academic Medical Center, Amsterdam, Netherlands (Mastaglia) Australian Neuromuscular Research Institute, Nedlands, Australia (Needham) Australian Neuromuscular Research Institute, Murdoch University and Fremantle Hospital, Nedlands, Australia (Sivakumar) Barrow Neurological Institute, St Joseph's Hospital Phoenix, Phoenix, AZ, United States (Corbett) Concord Hospital, Concord, Australia (Lundberg) Rheumatology Unit, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden (Benveniste) Hopital Pitie-Salpetriere, APHP, UPMC, Paris, France (Hilton-Jones) John Radcliffe Hospital, Oxford, United Kingdom (Christopher-Stine) Assistant Department of Medicine and Neurology, Johns Hopkins Hospital, Baltimore, MD, United States (Lloyd) Johns Hopkins School of Medicine, Baltimore, MD, United States (Barghout) Novartis AG, Morristown, NJ, United States (Tseng) Musculoskeletal Diseases Novartis, Institute of Biomedical Research NIBR, Cambridge, MA, United States (Demuro) RTI Health Solutions, Quakertown, PA, United States (Price) Department, Surveys and Observational Studies, RTI Health Solutions Research, Triangle Park, NC, United States (Schmidt) University Medical Center Goettingen, Goettingen, Germany (Mozaffar) University of California Irvine, Orange, CA, United States (Kissel) Wexner Medical Center, Ohio State University, Columbus, OH, United States

V. Barghout, Novartis AG, Morristown, NJ, United States

OBJECTIVE: We performed a Delphi process with neuromuscular disease experts following patients with sporadic inclusion body myositis to obtain estimates of survival and mortality based on panelists' clinical experience.

BACKGROUND: Few published studies in the literature report on the natural history of sIBM, and there is a paucity of mortality data in these patients. Existing studies have been limited by small sample sizes and short follow-up periods.

DESIGN/METHODS: Two online iterative rounds were completed by a total of 13 experts who actively follow patients with sIBM in a total of 7 countries (Australia, France, Germany, the Netherlands, Sweden, the UK and the US). Demographics, comorbidities, and cause of death were collected as were data on assistive devices, injurious falls, and end of life setting.

RESULTS: Panelists' responses were based upon following a total of 585 living patients with sIBM and 149 patients with sIBM who are deceased. Eight of 13 panelists indicated that some patients with sIBM have a shortened lifespan compared with the general population. Two additional panelists indicated that all patients with sIBM have a shortened lifespan. Twelve of the 13 panelists responded that patients with sIBM who have bulbar dysfunction, dysphagia, and/or oropharangeal involvement have a shorter lifespan. Standard mortality ratios of patients with sIBM were calculated as 6.58 for patients aged 41+, and 4.82 for patients over 70. Most panelists agreed that these features of sIBM may result in shortened lifespan for some patients with sIBM when compared with the general population: Younger age at symptom development or diagnosis; Severe symptoms and severe onset of symptoms; Injurious falls.

CONCLUSIONS: To our knowledge, this is the largest sample of patients with sIBM studied, contributing to the body of literature describing the impact of sIBM on mortality. This study identified a shorter lifespan in patients with sIBM compared with the general population. Additional patient demographics were also identified that impact further on lifespan.

Publication Types: Conference Abstract
PMID: 71466490

Authors respond.


(Ho) Radiology Department, Fremantle Hospital, United States (Lawn, Lee, Dunne) Department of Neurology, Royal Perth Hospital, Australia (Bynevelt) Radiology Department, Sir Charles Gairdner Hospital, Perth, WA, Australia

Publication Types: Letter
PMID: 2014175400
Identification of neuropathic pain in cervical radiculopathy - Application of quantitative sensory testing and a screening tool.

Tampin B, Slater H, et al.
(Tampin, Slater, Briffa) School of Physiotherapy and Exercise Science, Curtin University, Australia
(Tampin) Department of Physiotherapy, Sir Charles Gairdner Hospital, Australia
(Tampin) Department of Neurosurgery, Sir Charles Gairdner Hospital, Perth, Australia
(Slater) Pain Medicine Unit, Fremantle Hospital and Health Service, Fremantle, WA, Australia

Objectives: To investigate the presence of neuropathic pain (NeP) in patients with painful cervical radiculopathy (CxRAD), using quantitative sensory testing (QST) and the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) screening questionnaire. Methods: Twenty-three patients (8 females, 46 ± 10 years) with a unilateral painful C6 or C7 cervical radiculopathy (clinical signs of sensory and motor nerve root impairment with a demonstrable clinically relevant abnormality on imaging studies) participated. The LANSS was completed before QST. The QST protocol of the German Research Network on Neuropathic Pain was performed in the maximal pain area. Reference data were obtained in 31 healthy control (HC) subjects. QST data were z-transformed using the included HC data. The study was approved by Ethics Committees of all participating institutions and all participants signed written informed consent. Results: Patients with CxRAD were characterized by a loss of function (thermal, mechanical, vibration detection P < 0.009) and cold hypersensitivity (P = 0.001) in the maximal pain area. All patients demonstrated at least one sensory alteration outside the 95% HC confidence interval. These sensory alterations were confirmative for the presence of NeP. Five (22%) patients with CxRAD demonstrated a NeP component according to the LANSS score. Conclusion: QST data suggest that NeP is likely to be observed in patients with painful CxRAD. The LANSS failed to identify the majority of patients with NeP. Acknowledgement: This study was supported by the National Health and Medical Research Council (Grant 425560), Arthritis Australia and the Physiotherapy Research Foundation.

Publication Types: Conference Abstract
PMID:71512605

Immunoglobulin G is the only anti-beta-2-glycoprotein I isotype that associates with unprovoked thrombotic events among hospital patients.

Brusch A, Bundell C, et al.
1PathWest and Department of Clinical Immunology, Fremantle Hospital, Fremantle
2PathWest and Department of Clinical Immunology, Sir Charles Gairdner Hospital, Nedlands
3School of Pathology and Laboratory Medicine, University of Western Australia, Perth, WA, Australia.

SUMMARY: This study aimed to determine the strength of association between anti-beta-2-glycoprotein I (anti-beta2GPI) isotypes and thrombotic events by phenotyping hospital patients tested for diagnostic purposes with at least one positive anti-beta2GPI isotype. A laboratory database search identified patients who had undergone anti-beta2GPI testing during a 3 year period. Medical records of patients with a positive anti-beta2GPI result were reviewed and clinical events ascertained. Thromboses were subdivided into provoked and unprovoked, depending on the stated aetiology. A total of 128 patients had at least one positive anti-beta2GPI isotype. There was a higher proportion of unprovoked thromboses among patients who were IgG anti-beta2GPI positive compared to those who lacked IgG anti-beta2GPI (20/30 versus 20/98). Median IgG anti-beta2GPI levels were higher among patients with unprovoked events compared to those without (22.5 SGU versus 2 SGU). Retrospective assessment of anti-beta2GPI testing strategies showed that testing IgM and/or IgA anti-beta2GPI after IgG anti-beta2GPI captured a greater number of non-thrombotic events and provoked thromboses than unprovoked thromboses. IgG anti-beta2GPI associates most strongly with clinical events characteristic of antiphospholipid syndrome (APS). These results suggest that IgG anti-beta2GPI is superior to IgM and IgA anti-beta2GPI in the assessment of hospital patients with potential APS.
Towards optimising the provision of laboratory services for bone turnover markers.
Vasikaran SD, Chubb SA, et al.
1Department of Clinical Biochemistry, PathWest Laboratory Medicine, Royal Perth and Fremantle Hospitals, Perth 2School of Pathology and Laboratory Medicine, University of Western Australia, Nedlands 3School of Medicine and Pharmacology, University of Western Australia, Nedlands, WA 4Clinical Biochemistry Unit, Alfred Pathology Service, Melbourne 5Monash University, Melbourne, Vic, Australia.

SUMMARY: Bone turnover markers (BTMs) are either secreted by osteoblasts during bone formation or released by degradation of the collagen matrix of bone during bone resorption, and may be measured in blood or urine to provide an estimate of the rate of bone remodelling. Increased bone remodelling rate is often associated with bone loss which can result in osteoporosis; however, lack of data preclude the inclusion of BTMs in fracture risk algorithms. The changes in BTMs following therapy for osteoporosis may be useful for monitoring. Serum procollagen type I amino-terminal propeptide (s-PINP) and serum carboxy-terminal cross-linking telopeptide of type I collagen (s-betaCTX) have been designated as reference standard markers of bone formation and resorption respectively in osteoporosis; further research is needed for their routine use in osteoporosis. BTMs are useful in diagnosing and monitoring Paget's disease of bone and other bone diseases associated with abnormal bone formation and/or resorption. Standardised patient preparation is required to mitigate the effect of biological variation, and appropriate sample handling and storage are important to minimise sample degradation. Significant inter-method differences exist for BTMs, and harmonisation of methods for the reference BTMs is being pursued. This will help develop universally accepted decision limits and treatment goals. Australian consensus reference intervals have been developed for some methods for s-PINP and s-betaCTX.

Environmental risk factors by gender associated with attention-deficit/ hyperactivity disorder.
Silva D, Colvin L, et al.
(Silva, Colvin, Bower) Telethon Institute for Child Health Research, Centre for Child Health Research, PO Box 855, West Perth, WA 6872, Australia (Silva, Bower) School of Paediatrics and Child Health, University of Western Australia, Perth, Australia (Hagemann) Fremantle Speech Pathology Services, Fremantle, Australia
D. Silva, Telethon Institute for Child Health Research, Centre for Child Health Research, PO Box 855, West Perth, WA 6872, Australia. E-mail: desirees@ichr.uwa.edu.au

BACKGROUND: Early environmental risk factors associated with attention-deficit/ hyperactivity disorder (ADHD) have been increasingly suggested. Our study investigates the maternal, pregnancy, and newborn risk factors by gender for children prescribed stimulant medication for treatment of ADHD in Western Australia. METHODS: This is a population-based, record linkage case-control study. The records of all non-Aboriginal children and adolescents born in Western Australia and aged <25 years who were diagnosed with ADHD and prescribed stimulant medication (cases = 12 991) were linked to the Midwives Notification System (MNS) to obtain maternal, pregnancy, and birth information. The control population of 30 071 children was randomly selected from the MNS. RESULTS: Mothers of children with ADHD were significantly more likely to be younger, be single, have smoked in pregnancy, have labor induced, and experience threatened preterm labor, preeclampsia, urinary tract infection in pregnancy, or early term delivery irrespective of the gender of the child, compared with the control group. In the fully adjusted model, a novel finding was of a possible protective effect of oxytocin augmentation in girls. Low birth weight, postterm pregnancy, small for gestational age infant, fetal distress, and low Apgar scores were not identified as risk factors.
CONCLUSIONS: Smoking in pregnancy, maternal urinary tract infection, being induced, and experiencing threatened preterm labor increase the risk of ADHD, with little gender difference, although oxytocin augmentation of labor appears protective for girls. Early term deliveries marginally increased the risk of ADHD. Studies designed to disentangle possible mechanisms, confounders, or moderators of these risk factors are warranted. Copyright 2014 by the American Academy of Pediatrics.

PMID:2014018340


Long-Term Survival and Dialysis Dependency Following Acute Kidney Injury in Intensive Care: Extended Follow-up of a Randomized Controlled Trial.


(Gallagher, Cass, Finfer, Gattas, Lee, Lo, Myburgh, Rajbhandari) The George Institute for Global Health, Sydney, Australia (Gallagher, Finfer) University of Sydney, Sydney, Australia (Cass) Menzies School of Health Research, Darwin, Australia (Bellomo) Austin Hospital, Heidelberg, Australia (Gattas) Royal Prince Alfred Hospital, Camperdown, Australia (McGuinness, Parke) Auckland City Hospital, Auckland, New Zealand (Myburgh) St. George Clinical School, University of New South Wales, Sydney, Australia (Mitchell, Taylor, Whyte) The Canberra Hospital, Australian Capital Territory, Australia (Raza, Nand, Sara) Blacktown Hospital, New South Wales, Australia (Millis, Wong) Concord Hospital, New South Wales, Australia (Harrigan, Hardie, Whitaker) John Hunter Hospital, New South Wales, Australia (Bhonagiri, Micallef) Liverpool Hospital, New South Wales, Australia (Ellem, Lintott) Mater Calvary Hospital, Newcastle, NSW, Australia (Cole, Cuzner, Weisbrodt, Whereat) Nepean Hospital, New South Wales, Australia (Shehabi, Bass, Edhouse, Jenkins) Prince of Wales Hospital, New South Wales, Australia (Finfer, Bird, O'Connor) Royal North Shore Hospital, New South Wales, Australia (Totaro, Honesett, Rajbhandari) Royal Prince Alfred Hospital, New South Wales, Australia (Myburgh, Inskip, Sidoli) St George Hospital, New South Wales, Australia (Nair, Reynolds) St Vincent's Hospital, New South Wales, Australia (Banerjee, Kong, Skelly) Westmead Hospital, New South Wales, Australia (McGuinness, Brown, Gilder, Parke) Auckland City Hospital/CVICU, New Zealand (McArthur, Newby, Simmonds) Auckland City Hospital/DCCM, New Zealand (Henderson, Mehrtens, Sugden) Christchurch Hospital, New Zealand (Kalkoff, McGregor, Shaw) Whangarei Hospital, New Zealand (Morgan, Gregory, Sutton) Mater Adult and Mater Private Hospital, Queensland, Australia (Garrett, Buckley, McDonald) Nambour General Hospital, Queensland, Australia (Joyce, Harward, Sexton, Perkins) Princess Alexandra Hospital, Queensland, Australia (Lipman, Dunlop, Lassig-Smith, Starr) Royal Brisbane Hospital, Queensland, Australia (Flabouris, O'Connor, Rivett) Royal Adelaide Hospital, South Australia, Australia (Turner, McAllister, Trubody) Royal Hobart Hospital, Tasmania, Australia (Bellomo, Eastwood, Peck) Austin Hospital, Victoria, Australia (Fletcher) Bendigo Hospital, Victoria, Australia (Ihle, Ho, Micallef, Murray) Epworth Hospital, Victoria, Australia (Botha, Allsop, Vuat) Frankston Hospital, Victoria, Australia (Cattigan, Elderkin) Geelong Hospital, Victoria, Australia (Walker, Galt, Gillies) Monash Medical Centre, Victoria, Australia (Harley, Barge, Caf, Jordon) Royal Melbourne, Victoria, Australia (Santamaria, Holmes, Smith) St Vincent's Hospital Melbourne, Victoria, Australia (Scheinkestel, Donaldson, Vallance) The Alfred Hospital, Victoria, Australia (French, Bates, Butler) Western Hospital, Victoria, Australia (Breheny, Palermo) Fremantle Hospital, Western Australia, Australia (Dobb, Chamberlain, Lord) Royal Perth Hospital, Western Australia, Australia (Jun, Yianni, D'Haeseleer) The George Institute, United States M. Gallagher, The George Institute for Global Health, Sydney, Australia. E-mail: mgallagher@georgeinstitute.org.au

Background: The incidence of acute kidney injury (AKI) is increasing globally and it is much more common than end-stage kidney disease. AKI is associated with high mortality and cost of hospitalisation. Studies of treatments to reduce this high mortality have used differing renal replacement therapy (RRT) modalities and have not shown improvement in the short term. The reported long-term outcomes of AKI are variable and the effect of differing RRT modalities upon them is not clear. We used the prolonged follow-up of a large clinical trial to prospectively examine the long-
term outcomes and effect of RRT dosing in patients with AKI.

Methods and Findings: We extended the follow-up of participants in the Randomised Evaluation of Normal vs. Augmented Levels of RRT (RENAL) study from 90 days to 4 years after randomization. Primary and secondary outcomes were mortality and requirement for maintenance dialysis, respectively, assessed in 1,464 (97%) patients at a median of 43.9 months (interquartile range [IQR] 30.0-48.6 months) post randomization. A total of 468/743 (63%) and 444/721 (62%) patients died in the lower and higher intensity groups, respectively (risk ratio [RR] 1.04, 95% CI 0.96-1.12, p = 0.49). Amongst survivors to day 90, 21 of 411 (5.1%) and 23 of 399 (5.8%) in the respective groups were treated with maintenance dialysis (RR 1.12, 95% CI 0.63-2.00, p = 0.69). The prevalence of albuminuria among survivors was 40% and 44%, respectively (p = 0.48). Quality of life was not different between the two treatment groups. The generalizability of these findings to other populations with AKI requires further exploration.

Conclusions: Patients with AKI requiring RRT in intensive care have high long-term mortality but few require maintenance dialysis. Long-term survivors have a heavy burden of proteinuria. Increased intensity of RRT does not reduce mortality or subsequent treatment with dialysis. Trial registration: http://www.ClinicalTrials.gov NCT00221013 Please see later in the article for the Editors' Summary. 2014 Gallagher et al.

PMID: 2014160708


Reported high salt intake is associated with increased prevalence of abdominal aortic aneurysm and larger aortic diameter in older men.

Golledge J, Hankey GJ, et al.
Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville, Australia; Department of Vascular and Endovascular Surgery, The Townsville Hospital, Townsville, Australia.
School of Medicine and Pharmacology, University of Western Australia, Perth, Australia; Department of Neurology, Royal Perth Hospital, Perth, Australia.
School of Medicine and Pharmacology, University of Western Australia, Perth, Australia; Department of Endocrinology, Fremantle Hospital, Fremantle, Australia.
School of Psychiatry & Clinical Neurosciences, University of Western Australia, Perth, Australia; WA Centre for Health & Ageing, Centre for Medical Research, Perth, Australia; Department of Psychiatry, Royal Perth Hospital, Perth, Australia.
School of Medicine and Pharmacology, University of Western Australia, Perth, Australia; WA Centre for Health & Ageing, Centre for Medical Research, Perth, Australia; Department of Geriatric Medicine, Royal Perth Hospital, Perth, Australia.
School of Surgery, University of Western Australia, Perth, Australia.

BACKGROUND: Salt intake has been implicated in the pathogenesis of abdominal aortic aneurysm (AAA) through studies in rodent models but not previously studied in humans. The aim of this study was to examine the association between reported addition of salt to food and the prevalence of AAA.

METHODS: A risk factor questionnaire which contained a question about salt intake was included as part of a population screening study for AAA in 11742 older men. AAA presence was assessed by abdominal ultrasound imaging using a reproducible protocol.

RESULTS: The prevalence of AAA was 6.9, 8.5 and 8.6% in men who reported adding salt to food never, sometimes and always, respectively, p = 0.005. Addition of salt to food sometimes (odds ratio [OR]: 1.22, 95% confidence interval [CI]: 1.03-1.44) or always (OR: 1.23, 95% CI 1.04-1.47) was independently associated with AAA after adjustment for other risk factors including age, waist-hip ratio, blood pressure, history of hypertension, high cholesterol, angina, diabetes, myocardial infarction and stroke. Salt intake was also independently associated with aortic diameter (beta 0.023, p = 0.012). In men with no prior history of hypertension, high cholesterol, angina, myocardial infarction or stroke (n = 4188), the association between addition of salt to food sometimes (OR: 1.41, 95% CI 0.96-2.08) or always (OR: 1.52, 95% CI 1.04-2.22) and AAA remained evident.

CONCLUSION: Reported salt intake is associated with AAA in older men. Additional studies are needed to determine whether reducing salt intake would protect against AAA.
Continuous infusions of meropenem in ambulatory care: clinical efficacy, safety and stability.
Manning L, Wright C, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia; Department of Infectious Diseases, Fremantle Hospital and Health Service, Fremantle, Western Australia, Australia.
Pharmacy Department, Fremantle Hospital and Health Service, Fremantle, Western Australia, Australia.
Department of Microbiology and Infectious Diseases, Royal Perth Hospital, Perth, Western Australia, Australia; School of Pathology and Laboratory Medicine, University of Western Australia, Perth, Western Australia, Australia.
Department of Microbiology and Infectious Diseases, Royal Perth Hospital, Perth, Western Australia, Australia.
Department of Microbiology and Infectious Diseases, Royal Perth Hospital, Perth, Western Australia, Australia; School of Medicine and Pharmacology, University of Western Australia, Royal Perth Hospital, Perth, Western Australia, Australia.
School of Pharmacy, Curtin University, Bentley, Western Australia, Australia.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.
Department of Infectious Diseases, Fremantle Hospital and Health Service, Fremantle, Western Australia, Australia.
OBJECTIVES: Concerns regarding the clinical impact of meropenem instability in continuous infusion (CI) devices may contribute to inconsistent uptake of this method of administration across outpatient parenteral antimicrobial therapy (OPAT) services.
METHODS: We retrospectively reviewed the clinical efficacy and safety of CIs of meropenem in two Australian tertiary hospitals and assessed its stability under simulated OPAT conditions including in elastomeric infusion devices containing 1% (2.4 g) or 2% (4.8 g) concentrations at either 'room temperature' or 'cooled' conditions. Infusate aliquots were assayed at different time-points over 24 hours.
RESULTS: Forty-one (82%) of 50 patients had clinical improvement or were cured. Adverse patient outcomes including hemato-, hepato- and nephrotoxicity were infrequent. Cooled infusers with 1% meropenem had a mean 24-hour recovery of 90.3%. Recoveries of 1% and 2% meropenem at room temperature and 2% under cooled conditions were 88%, 83% and 87%, respectively. Patients receiving 1% meropenem are likely to receive >95% of the maximum deliverable dose (MDD) over a 24-hour period whilst patients receiving 2% meropenem should receive 93% and 87% of the MDD under cooled and room temperature conditions, respectively.
CONCLUSIONS: Meropenem infusers are likely to deliver ~95% MDD and maintain effective plasma concentrations throughout the dosing period. These data reflect our local favourable clinical experience with meropenem CIs.

External validation of a prognostic model for seizure recurrence following a first unprovoked seizure and implications for driving.
Bonnett LJ, Marson AG, et al.
Department of Biostatistics, University of Liverpool, Liverpool, United Kingdom.
Department of Molecular and Clinical Pharmacology, University of Liverpool, Liverpool, United Kingdom.
Medical Research Council Biostatistics Unit, Cambridge Institute of Public Health, Cambridge, United Kingdom.
OBJECTIVE: In the United Kingdom and other European Union countries guidelines for driving following a first unprovoked seizure require the risk of another seizure in the next year to be less than 20%. Using data from one clinical trial, we previously developed a prognostic model to inform driving guidelines. The objective of this work is to externally validate our published model and demonstrate its generalisability.

METHODS: A cohort of 620 people with a first unprovoked seizure was used to develop the original model which included variables for aetiology, first degree relative with epilepsy, seizures only while asleep, electroencephalogram, computed tomography or magnetic resonance scan result, and treatment policy. The validation cohorts consisted of 274 (United Kingdom), 305 (Italy), and 847 (Australia) people. The model was evaluated using discrimination and calibration methods. A covariate, missing from the Italian dataset, was handled via five imputation methods. Following external validation, the model was fitted to a pooled population comprising all validation datasets and the development dataset. The model was stratified by dataset.

RESULTS: The model generalised relatively well. All methods of imputation performed fairly similarly. At six months, the risk of a seizure recurrence following a first ever seizure, based on the pooled datasets, is 15% (95% CI: (12% to 18%)) for patients who are treated immediately and 18% (95% CI: (15 to 21%)) otherwise. Individuals can be reliably stratified into risk groups according to the clinical factors included in the model.

SIGNIFICANCE: Our prognostic model, used to inform driving regulations, has been validated and consequently has been proven as a valuable tool for predicting risk of seizure recurrence following a first seizure in people with various combinations of risk factors. Additionally, there is evidence to support one worldwide overall prognostic model for risk of second seizure following a first.

PMID:24919184


Quality of antimalarial drugs and antibiotics in papua new Guinea: a survey of the health facility supply chain.
Papua New Guinea Institute of Medical Research, Goroka, EHP, Papua New Guinea; Swiss Tropical and Public Health Institute, Basel, Switzerland; University of Basel, Basel, Switzerland.
Curtin University, School of Pharmacy, Perth, WA, Australia.
Central Public Health Laboratory, Boroko, NCD, Papua New Guinea.
Papua New Guinea Institute of Medical Research, Goroka, EHP, Papua New Guinea; The University of Queensland, School of Population Health, Herston, QLD, Australia.
Papua New Guinea Institute of Medical Research, Madang, MDG, Papua New Guinea.
University of Western Australia, School of Medicine and Pharmacology, Fremantle, WA, Australia.
BACKGROUND: Poor-quality life-saving medicines are a major public health threat, particularly in settings with a weak regulatory environment. Insufficient amounts of active pharmaceutical ingredients (API) endanger patient safety and may contribute to the development of drug resistance. In the case of malaria, concerns relate to implications for the efficacy of artemisinin-based combination therapies (ACT). In Papua New Guinea (PNG), Plasmodium falciparum and P. vivax are both endemic and health facilities are the main source of treatment. ACT has been introduced as first-line treatment but
other drugs, such as primaquine for the treatment of P. vivax hypnozoites, are widely available. This study investigated the quality of antimalarial drugs and selected antibiotics at all levels of the health facility supply chain in PNG.

METHODS AND FINDINGS: Medicines were obtained from randomly sampled health facilities and selected warehouses and hospitals across PNG and analysed for API content using validated high performance liquid chromatography (HPLC). Of 360 tablet/capsule samples from 60 providers, 9.7% (95% CI 6.9, 13.3) contained less, and 0.6% more, API than pharmacopoeial reference ranges, including 29/37 (78.4%) primaquine, 3/70 (4.3%) amodiaquine, and one sample each of quinine, artemether, sulphadoxine-pyrimethamine and amoxicillin. According to the package label, 86.5% of poor-quality samples originated from India. Poor-quality medicines were found in 48.3% of providers at all levels of the supply chain. Drug quality was unrelated to storage conditions.

CONCLUSIONS: This study documents the presence of poor-quality medicines, particularly primaquine, throughout PNG. Primaquine is the only available transmission-blocking antimalarial, likely to become important to prevent the spread of artemisinin-resistant P. falciparum and eliminating P. vivax hypnozoites. The availability of poor-quality medicines reflects the lack of adequate quality control and regulatory mechanisms. Measures to stop the availability of poor-quality medicines should include limiting procurement to WHO prequalified products and implementing routine quality testing. PMID:24828338


Clinical Features and Outcome in Children with Severe Plasmodium falciparum Malaria: A Meta-Analysis.
Manning L, Laman M, et al.
School of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, Western Australia, Australia.

BACKGROUND: Although global malaria mortality is declining, estimates may not reflect better inpatient management of severe malaria (SM) where reported case fatality rates (CFRs) vary from 1-25%.

METHODS: A meta-analysis of prospective studies of SM was conducted to examine i) whether hypothesized differences between clinical features and outcome in Melanesian compared with African or Asian children really exist, and ii) to explore temporal changes in overall and complication-specific CFRs. The proportions of different SM complications and, overall and complication-specific CFRs were incorporated into the meta-analysis. Adjustments were made for study-level covariates including geographic region, SM definition, artemisinin treatment, median age of participants and time period.

FINDINGS: Sixty-five studies were included. Substantial heterogeneity (I (2)>80%) was demonstrated for most outcomes. SM definition contributed to between-study heterogeneity in proportions of cerebral malaria (CM), metabolic acidosis (MA), severe anemia and overall CFR, whilst geographic region was a significant moderator in for CM and hypoglycemia (HG) rates. Compared with their African counterparts, Melanesian children had lower rates of HG (10% [CI95 7-13%] versus 1% [0-3%], P<0.05), lower overall CFR (2% [0-4%] versus 7% [6-9%], P<0.05) and lower CM-specific CFR (8% [0-17%] versus 19% [16-21%], P<0.05). There was no temporal trend for overall CFR and CM-specific CFR but declining HG- and MA- specific CFRs were observed.

INTERPRETATION: These data highlight that recent estimates of declining global malaria mortality are not replicated by improved outcomes for children hospitalized with SM. Significant geographic differences in the complication rates and subsequent CFRs exist and provide the first robust confirmation of lower CFRs in Melanesian children, perhaps due to less frequent HG.

PMID:24516538


Iron status and the acute post-exercise hepcidin response in athletes.
This study explored the relationship between serum ferritin and hepcidin in athletes. Baseline serum ferritin levels of 54 athletes from the control trial of five investigations conducted in our laboratory were considered; athletes were grouped according to values <30 mug/L (SF<30), 30-50 mug/L (SF30-50), 50-100 mug/L (SF50-100), or >100 mug/L (SF>100). Data pooling resulted in each athlete completing one of five running sessions: (1) 8x3 min at 85% vVO2peak; (2) 5x4 min at 90% vVO2peak; (3) 90 min continuous at 75% vVO2peak; (4) 40 min continuous at 75% vVO2peak; (5) 40 min continuous at 65% vVO2peak. Athletes from each running session were represented amongst all four groups; hence, the mean exercise duration and intensity were not different (p>0.05). Venous blood samples were collected pre-, post- and 3 h post-exercise, and were analysed for serum ferritin, iron, interleukin-6 (IL-6) and hepcidin-25. Baseline and post-exercise serum ferritin levels were different between groups (p<0.05). There were no group differences for pre- or post-exercise serum iron or IL-6 (p>0.05). Post-exercise IL-6 was significantly elevated compared to baseline within each group (p<0.05). Pre- and 3 h post-exercise hepcidin-25 was sequentially greater as the groups baseline serum ferritin levels increased (p<0.05). However, post-exercise hepcidin levels were only significantly elevated in three groups (SF30-50, SF50-100, and SF>100; p<0.05). An athlete's iron stores may dictate the baseline hepcidin levels and the magnitude of post-exercise hepcidin response. Low iron stores suppressed post-exercise hepcidin, seemingly overriding any inflammatory-driven increases.

PMID:24667393

Hospitalisations for pelvic inflammatory disease temporally related to a diagnosis of Chlamydia or gonorrhoea: a retrospective cohort study.
Reekie J, Donovan B, et al.
The Kirby Institute, UNSW Australia, Sydney, Australia.
The Kirby Institute, UNSW Australia, Sydney, Australia; Sydney Sexual Health Centre, Sydney Hospital, Sydney, Australia.
Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Australia.
Centre for Health Research, University of Western Sydney, Sydney, Australia.
School of Medicine, University of Notre Dame, Fremantle, Australia.
Centre for Health Services and Research, University of Western Australia, Crawley, Australia.
Faculty of Pharmacy and School of Public Health, University of Sydney, Sydney, Australia.
Kolling Institute of Medical Research, University of Sydney, Sydney, Australia.
Centre for Population Health Research, Curtin University, Perth, Australia.
The Kirby Institute, UNSW Australia, Sydney, Australia; Baker IDI, Alice Springs, Northern Territory, Australia.
School of Public Health and Community Medicine, UNSW Australia, Sydney, Australia; The Sax Institute, Sydney, Australia.

OBJECTIVES: The presence and severity of pelvic inflammatory disease (PID) symptoms are thought to vary by microbiological etiology but there is limited empirical evidence. We sought to estimate and compare the rates of hospitalisation for PID temporally related to diagnoses of gonorrhoea and chlamydia.

METHODS: All women, aged 15-45 years in the Australian state of New South Wales (NSW), with a diagnosis of chlamydia or gonorrhoea between 01/07/2000 and 31/12/2008 were followed by record
linkage for up to one year after their chlamydia or gonorrhoea diagnosis for hospitalisations for PID. Standardised incidence ratios compared the incidence of PID hospitalisations to the age-equivalent NSW population.

RESULTS: A total of 38,193 women had a chlamydia diagnosis, of which 483 were hospitalised for PID; incidence rate (IR) 13.9 per 1000 person-years of follow-up (PYFU) (95%CI 12.6-15.1). In contrast, 1015 had a gonorrhoea diagnosis, of which 45 were hospitalised for PID (IR 50.8 per 1000 PYFU, 95%CI 36.0-65.6). The annual incidence of PID hospitalisation temporally related to a chlamydia or gonorrhoea diagnosis was 27.0 (95%CI 24.4-29.8) and 96.6 (95%CI 64.7-138.8) times greater, respectively, than the age-equivalent NSW female population. Younger age, socio-economic disadvantage, having a diagnosis prior to 2005 and having a prior birth were also associated with being hospitalised for PID.

CONCLUSIONS: Chlamydia and gonorrhoea are both associated with large increases in the risk of PID hospitalisation. Our data suggest the risk of PID hospitalisation is much higher for gonorrhoea than chlamydia; however, further research is needed to confirm this finding.

CONCLUSION: Lower levels of vitamin D may reduce prostate cancer risk in older men. By contrast,
levels of vitamin D did not predict incidence of colorectal or lung cancers. Further studies are needed to determine whether a causal relationship exists between vitamin D and prostate cancer in ageing men.

PMID:24949795


**Lung function, diabetes and the metabolic syndrome.**
Davis TME.
(Davis) University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, WA, Australia
T.M.E. Davis, University of Western Australia, School of Medicine and Pharmacology, Fremantle Hospital, Fremantle, WA, Australia

Diabetes, impaired glucose tolerance and the metabolic syndrome are all associated with a modest restrictive lung defect. There appears to be a dose-response relationship between increasing numbers of components of the metabolic syndrome and the degree of impairment of pulmonary function. Possible underlying mechanisms include glycation of structural proteins within the thorax, the mechanical effects of visceral adiposity, and chronic inflammation. Spirometry as part of usual care may be an inexpensive and efficient way of identifying patients at increased cardiopulmonary risk and as a prognostic marker of all-cause mortality. 2014 JOHN WILEY & SONS.

PMID:2014406722


**Apathy following traumatic brain injury.**
Starkstein SE, Pahissa J.
School of Psychiatry and Clinical Neurosciences, University of Western Australia, Fremantle Hospital T-7, Fremantle, Western Australia 6959, Australia. Electronic address: sergio.starkstein@uwa.edu.au.
Department of Psychiatry, CEMIC University, Valdenegro 4337, Buenos Aires 1430, Argentina.

Traumatic brain injury (TBI) may result in significant emotional and behavioral changes, such as depression, impulsivity, anxiety, aggressive behavior, and posttraumatic stress disorder. Apathy has been increasingly recognized as a relevant sequela of TBI, with a negative impact on the patients' quality of life as well as their participation in rehabilitation activities. This article reviews the nosologic and phenomenological aspects of apathy in TBI, diagnostic issues, frequency and prevalence, relevant comorbid conditions, potential mechanisms, and treatment. Crown Copyright 2014. Published by Elsevier Inc. All rights reserved.

PMID:24529426


**Nurse screening for delirium in older patients attending the emergency department.**
Hare M, Arendts G, et al.
Fremantle Hospital, Fremantle, Australia.
University of Western Australia, Nedlands, Australia. Electronic address: glenn.arendts@uwa.edu.au.
Curtin University, Bentley, Australia.

BACKGROUND: Delirium in older emergency department (ED) patients is common, associated with many adverse outcomes, and costly to manage. Delirium detection in the ED is almost universally poor.

OBJECTIVES: The authors aimed to develop a simple clinical risk screening tool that could be used by ED nurses as part of their initial assessment to identify patients at risk of delirium.

METHODS: A prospective cross-sectional study of patients 65 years and older attending a single ED.

RESULTS: Of 320 enrolled patients, 23 (7.2%) had delirium. Logistic regression analysis revealed 3 risk factors strongly associated with delirium risk: cognitive impairment, depression, and an abnormal
Weighting these variables based on the strength of their association with delirium yielded a risk score from 0-4 inclusive. A cutoff of 2 or more in that score would have given a sensitivity of 87%, specificity of 70%, and NPV of 99%, while avoiding further diagnostic workup for delirium in approximately two-thirds of all patients, when used as an initial screen.

CONCLUSIONS: A simple risk screening tool using factors evident on initial nurse assessment can be used to identify patients at risk of delirium. Further trials are needed to test whether the tool improves patient outcomes. Copyright 2014 Academy of Psychosomatic Medicine. Published by Elsevier Inc. All rights reserved.

PMID:24314593


The outcome of a multi-centre feasibility study of online adaptive radiotherapy for muscle-invasive bladder cancer TROG 10.01 BOLART.

Foroudi F, Pham D, et al.

Peter MacCallum Cancer Centre, Melbourne, Australia; Sir Peter MacCallum Department of Oncology, University of Melbourne, Australia. Electronic address: farshad.foroudi@petermac.org.

Peter MacCallum Cancer Centre, Melbourne, Australia.

Calvary Mater Newcastle, Newcastle, Australia.

Townsville Cancer Centre, Townsville, Australia.

Westmead Hospital, Sydney, Australia.

Royal Prince Alfred Hospital, Sydney, Australia.

Christchurch Hospital, Christchurch, New Zealand.

Fremantle Hospital, Perth, Australia.

Princess Alexandra Hospital, Brisbane, Australia.

Royal Hobart Hospital, Hobart, Australia.

Auckland Hospital, Auckland, New Zealand.

Mater Centre, Brisbane, Australia.

Peter MacCallum Cancer Centre, Melbourne, Australia; Sir Peter MacCallum Department of Oncology, University of Melbourne, Australia.

PURPOSE: To assess whether online adaptive radiotherapy for bladder cancer is feasible across multiple Radiation Oncology departments using different imaging, delivery and recording technology.

MATERIALS AND METHODS: A multi-centre feasibility study of online adaptive radiotherapy, using a choice of three "plan of the day", was conducted at 12 departments. Patients with muscle-invasive bladder cancer were included. Departments were activated if part of the pilot study or after a site-credentialing visit. There was real time review of the first two cases from each department.

RESULTS: 54 patients were recruited, with 50 proceeding to radiotherapy. There were 43 males and 7 females with a mean age of 78 years. The tumour stages treated included T1 (1 patient), T2 (35), T3 (10) and T4 (4). One patient died of an unrelated cause during radiotherapy. The three adaptive plans were created before the 10th fraction in all cases. In 8 (16%) of the patients, a conventional plan using a 'standard' CTV to PTV margin of 1.5cm was used for one or more fractions where the pre-treatment bladder CTV was larger than any of the three adaptive plans. The bladder CTV extended beyond the PTV on post treatment imaging in 9 (18%) of the 49 patients.

CONCLUSIONS: From a technical perspective an online adaptive radiotherapy technique can be instituted in a multi-centre setting. However, without further bladder filling control or imaging, a CTV to PTV margin of 7mm is insufficient. Copyright 2014 Elsevier Ireland Ltd. All rights reserved.

PMID:24746580


Empiric NSU treatment needs updating.

Murray S, Marshall L.

Infectious Disease Department, B2 Clinic, Fremantle Hospital, Perth, Western Australia, Australia.

Early discontinuation of endocrine therapy for breast cancer: who is at risk in clinical practice?
Kemp A, Preen DB, et al.
PMID:24936397


Plasma angiopoietin-1 is lower after ischemic stroke and associated with major disability but not stroke incidence.
(Golledge, Clancy) Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville 4811, Australia (Golledge) Department of Vascular and Endovascular Surgery, Townsville Hospital, Townsville, Australia (Maguire) Faculty of Health and Medicine, School of Nursing and Midwifery, University of Newcastle, Newcastle, Australia (Levi, Sturm) Faculty of Health, School of Health Sciences, University of Newcastle, Newcastle, Australia (Lincz, McEvoy, Attia) Hunter Medical Research Institute, Newcastle, NSW, Australia (Lincz) Hunter Haematology Research Group, Calvary Mater Newcastle, Waratah, NSW, Australia (Golledge) Queensland Research Centre for Peripheral Vascular Disease, School of Medicine and Dentistry, James Cook University, Townsville 4811, Australia. E-mail: jonathan.golledge@jcu.edu.au

BACKGROUND AND PURPOSE - Studies in rodent models suggest that upregulating angiopoietin-1 (Angpt1) improves stroke outcomes. The aims of this study were to assess the association of plasma Angpt1 with stroke occurrence and outcome. METHODS - Plasma Angpt1 was measured in 336 patients who had experienced a recent stroke and 321 healthy controls with no stroke history. Patients with stroke (n=285) were reassessed at 3 months and plasma Angpt1 concentration on admission compared between those with severe and minor disability as assessed by the modified Rankin scale. In a separate cohort of 4032 community-acquired older men prospectively followed for a minimum of 6 years, the association of plasma Angpt1 with stroke incidence was examined. RESULTS - Median plasma Angpt1 was 3-fold lower in patients who had experienced a recent stroke (6.42, interquartile range, 4.26-9.53 compared with 17.36; interquartile range, 14.01-22.46 ng/mL; P<0.001) and remained associated with stroke after adjustment for other risk factors. Plasma Angpt1 concentrations on admission were lower in patients who had severe disability or died at 3 months (median, 5.52; interquartile range, 3.81-8.75 ng/mL for modified Rankin scale 3-6; n=91) compared with those with minor disability (median, 7.04; interquartile range, 4.75-9.92 ng/mL for modified Rankin scale 0-2; n=194), P=0.012, and remained negatively associated with severe disability or death after adjusting for other risk factors. Plasma Angpt1 was not predictive of stroke incidence in community-dwelling older men. CONCLUSIONS - Plasma Angpt1 concentrations are low after ischemic stroke particularly in patients with poor stroke outcomes at 3 months. Interventions effective at upregulating Angpt1 could potentially improve stroke outcomes. 2014 American Heart Association, Inc.
PMID:2014222823
5-fluorouracil-induced mucositis leads to spinal GFAP expression changes in rats.


(Bajic, Hutchinson) School of Medical Sciences, University of Adelaide, Adelaide, Australia (Howarth, Eden, Lampton) School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, Australia (Mashtoub) School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia

J.E. Bajic, School of Medical Sciences, University of Adelaide, Adelaide, Australia

Background and Aims 5-Fluorouracil (5-FU) is a widely utilised chemotherapy agent that induces side-effects, termed mucositis in the gastrointestinal tract (GIT) and glial dysregulation in the central nervous system (CNS). Glia, particularly astrocytes, are vital in neuronal and CNS homeostasis; increased expression of their marker, glial fibrillary-associated protein (GFAP), implies neuroinflammation, linked with neuropathic pain and memory impairment. We determined whether 5-FU-induced neuroinflammation via mucositis by immuneto- CNS signalling pathways (neuronal vs humoral) and secondly, examined if astrocyte reactivity persisted beyond the mucositis-driven GIT injury. Methods Female Dark Agouti rats (n=8) were randomly allocated to saline control or 5-FU (i.p. 150 mg/kg) groups and tissues collected at either injury peak (day 3) or recovery (day 5). Western Blot analysed hippocampal and thoracic sections for GFAP and Interleukin-1 beta (IL-1beta) expression. Myeloperoxidase (MPO) assay quantified intestinal inflammation. Statistical comparisons conducted using a linear model in R studio. Results 5-FU reduced bodyweight (p<0.01) and increased MPO activity at day 3 compared to vehicle controls (p<0.01). Although hippocampal GFAP expression showed little variance (p>0.05), interestingly thoracic GFAP expression was significantly reduced by 28% in 5-FU treated rats - compared to vehicle controls at injury peak (p<0.05) but normalised during the recovery phase (day 5; p>0.05). IL-1beta expression levels remained unchanged at both time-points. Conclusions Down-regulation of thoracic GFAP expression reflects astrocyte dysregulation in rats with 5-FU-induced mucositis. This may have further implications for CNS homeostasis and neuronal signalling. Future studies should clarify the role of glial dysregulation in 5-FU-related cognitive impairment and neuropathic pain.

Publication Types: Conference Abstract

Aqueous rhubarb extract improves mucosal integrity and reduces acute inflammation in the ileum in a rat model of chemotherapy-induced intestinal mucositis.


(Eden, Lampton, Lynn, Howarth) School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, Australia (Cheah) Gastroenterology Department, Women's and Children's Hospital, North Adelaide, Australia (Yool) School of Medical Sciences, University of Adelaide, Adelaide, Australia (Mashtoub) School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia

G.L. Eden, School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, Australia

Background and Aims Mucositis, a common side-effect of chemotherapy, is characterised by acute intestinal inflammation and impaired mucosal integrity. Currently, no effective treatment has been established for this debilitating disorder. In the present study, aqueous rhubarb extract (RE) was investigated as a therapeutic modality for intestinal mucositis due to its anti-inflammatory properties and its potential to protect against mucosal damage. Methods Female dark agouti rats (n=8/group) received a daily gavage (1 mL) of water, high-dose RE (HDR; 200 mg/kg) or low-dose RE (LDR; 20 mg/kg) for 8 days. Mucositis was induced on day five following an intraperitoneal injection of 5-Fluorouracil (5-FU; 150 mg/kg). Rats were euthanized on day eight and intestinal tissue samples were collected for quantitative assessment of myeloperoxidase (MPO) activity and histological structure. Statistical significance was assumed at P<0.05 by oneway ANOVA. Results 5-FU significantly reduced intestinal mucosal thickness (>29%; P<0.001) compared to healthy controls. However, LDR
significantly increased ileal mucosal thickness in 5-FU treated rats (19% ; P<0.05), back towards normal values, relative to 5-FU controls. Although 5-FU significantly increased MPO levels (>307% ; P<0.001) in all intestinal regions, compared to healthy controls, LDR in 5-FU treated rats was able to significantly decrease ileal MPO activity (45% ; P<0.05), compared to 5-FU controls; suggesting a reduction of acute inflammation in the ileum. Conclusions In conclusion, LDR improved ileal mucosal integrity and reduced inflammation manifested as a result of 5-FU cytotoxicity. RE has the potential to act as an adjunct to chemotherapy regimens by reducing inflammation and protecting against mucosal damage associated with intestinal mucositis.

Publication Types: Conference Abstract
PMID:71501807

Supportive Care in Cancer. 2014; 1): S93.

A formulation of EMU oil and Lyprinol reduces acute small intestinal inflammation in a rat model of 5-fluorouracil-induced mucositis.
(Lampton, Eden, Lynn, Howarth) School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, Australia (Cheah) Gastroenterology Department, Women's and Children's Hospital, North Adelaide, Australia (Mashtoub) School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia
L.L. Lampton, School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, Australia
Background and Aims Mucositis is typified by ulceration and inflammation of the alimentary tract following chemotherapy. Emu Oil (EO) and Lyprinol have individually demonstrated anti-inflammatory properties in gastrointestinal ailments, including intestinal mucositis. We investigated EO and Lyprinol in combination for their potential to further reduce the severity of chemotherapy (5-Fluorouracil; 5-FU)-induced mucositis in rats. Methods Female Dark Agouti rats (n=8/group) were oro-gastrically gavaged (1ml) with Water, Olive Oil (OO), EO+OO, Lyprinol+OO or EO+Lyprinol from days 0-7 and injected with saline (control) or 5-FU (150 mg/kg) on day 5. Intestinal tissues were collected on day 8 for quantitative histological analysis and myeloperoxidase activity (MPO). p<0.05 was considered significant. Results 5-FU administration significantly elevated ileal MPO levels by 4.1-fold relative to saline controls (p<0.001). Amongst 5-FU-injected groups, only EO+Lyprinol reduced ileal MPO activity by 1.7-fold compared to 5-FU controls (p=0.012). Moreover, OO and EO+Lyprinol administration to 5-FU-treated rats resulted in decreased ileal MPO levels (1.2-fold and 1.4-fold respectively; p<0.05) compared with EO+OO treatment. Furthermore, all oil treatments decreased histological severity scores in the jejunum and ileum, and normalised crypt depth in the mid small intestine (>24%), relative to 5-FU controls (p<0.05). Additionally, OO maintained ileal villus height (21%) and crypt depth (24%) relative to 5-FU controls (p<0.05). Conclusions Emu Oil in combination with Lyprinol reduced damage associated with intestinal mucositis; however, Olive Oil demonstrated similar effects. Further studies are warranted to isolate the bioactive constituents of these naturally sourced oils for their potential utility in protection against mucositis.

Publication Types: Conference Abstract
PMID:71501807

Supportive Care in Cancer. 2014; 1): S94.
Oral nucleotides partially attenuate 5-fluorouracil-induced mucositis in rats.
Mashtoub S, Feo B, et al.
(Mashtoub) School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia (Feo, Whittaker, Lynn, Howarth) School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, Australia (Martinez-Puig) Bioiberica, S.A., Barcelona, Spain
S. Mashtoub, School of Medicine and Pharmacology, University of Western Australia, Fremantle, Australia
Background and Aims Chemotherapy-induced mucositis is characterized by inflammation and ulceration of the intestinal mucosa, compromising intestinal function. Exogenous nucleotides have been reported to repair the mucosa. The nucleotide preparation, Nucleoforce F0328 (Nucleoforce), was investigated for its potential to ameliorate intestinal mucositis in rats. Methods Female Dark Agouti rats (110-130 g; n=8/group) were oro-gastrically gavaged daily with Nucleoforce (175 mg/kg) or water from days 0 to 8 and injected (i.p.) with 5-Fluorouracil (5-FU:150 mg/kg) or saline on day 5. Sucrase activity was quantified in vivo by the sucrose breath test. Tissue sections were collected on day 8 for histological (disease severity, crypt depth and villus height measurements) and myeloperoxidase activity (indicative of acute inflammation) analyses. Results 5-FU significantly decreased (81%) the cumulative dose of 13C (% CD), compared to normal controls, indicative of decreased sucrase activity (p<0.05). Intestinal myeloperoxidase activity was significantly elevated by 5-FU (8.8-fold), compared to normal controls (p<0.05). Conclusions Nucleoforce only partially improved parameters associated with experimentally-induced mucositis. Future studies could investigate increased concentrations, more frequent administration, or protective microencapsulation delivery methods, to increase bioavailability.


**The efficacy of selective arterial embolization in the management of colonic bleeding.**
Adusumilli S, Gosselink MP, et al.
(Adusumilli, Ctercteko, Pathmanathan, El-Khoury, Dutton) Westmead Hospital, Sydney, NSW, Australia (Adusumilli, Makin, Wallace) Fremantle Hospital, Perth, WA, Australia (Gosselink) Oxford University Hospitals, Oxford, United Kingdom
S. Adusumilli, 23 Hope Street, Blaxland, NSW 2774, Australia. E-mail: sadu1@hotmail.com

Background: The aim of the present study was to determine the efficacy of mesenteric embolization in the management of acute haemorrhage from the colon. Methods: A retrospective review was performed of a consecutive series of patients who underwent selective arterial embolization between 2002 and 2010 at two Australian institutions. An analysis was performed of each patient's present and past medical history, procedural details and subsequent post-procedural recovery. Results: Seventy-one patients were reviewed in the study. Sixty-one patients (86%) had immediate cessation of bleeding following embolization. In total, 20% had some form of morbidity due to mesenteric embolization being performed, the three most common being worsening renal function, groin haematoma and contrast allergy (11, 9 and 7%, respectively). Only one patient developed superficial bowel ischaemia. Overall, 11 patients (18%) had recurrent bleeding. Of these patients, five had repeat embolization. Of the patients who underwent re-embolization, three stopped bleeding. Surgery was required in 5 patients 2 of whom died postoperatively of systemic complications. Conclusions: Colonic bleeding can be treated successfully in most patients by embolization, without causing ischaemia. Eighteen per cent of patients rebleed during the first hospital admission, and 20% patients experienced a procedure-related complication. In those patients that proceed to surgery, the morbidity, mortality and length of hospital stay increase dramatically. Springer-Verlag 2013.

PMID:2014486961


**The implementation of long range PCR and ion torrent sequencing into the routine diagnostic HLA laboratory.**
De Santis D, Vukovic I, et al.
(De Santis, Vukovic, Doran, Gorea, Campbell, Martinez) PathWest, Royal Perth Hospital, Perth, Australia (Sayer, Goodridge) Conexio Genomics, Fremantle, Australia (Shi, Dinauer) Life Technologies, Brown Deer, United States
D. De Santis, PathWest, Royal Perth Hospital, Perth, Australia. E-mail:
The high resolution genotyping of human leukocyte antigen (HLA) class I and II alleles is important for successful organ transplantation and genetic association studies. The high degree of polymorphism at the HLA loci and the inability to sequence each allele independently by current Sanger Sequencing Based Typing (SBT) at a low cost has led to the increase in HLA genotyping ambiguities. The challenge for registries and clinical laboratories is to provide the highest resolution typing results using efficient low-cost workflows. Next Generation Sequencing (NGS) on the Ion Torrent Personnel Genome Machine (PGM) provides a low cost alternative to current Sanger SBT overcoming the HLA genotype ambiguity through the combination of i) clonal amplification, which resolves the cis-trans ambiguities, and ii) massively parallel, which enables an expansion of the HLA regions sequenced. We have developed an in-house long range PCR method which amplifies the full gene length of HLA-A, -B and -C and exon 2 through to exon 3 of DRB1/3/4/5, DQB1 and DPB1 in 6 separate PCR reactions. Long range gene-specific amplicons for each individual are then pooled for a single library preparation using a modified version of the Ion Torrent PGM library preparation and 400bp sequencing chemistry protocol. All data generated was analysed with software provided by Conexio Genomics and Life Technologies. There was good concordance with our current Sanger SBT methods and in the majority of cases the typing resolution exceeded that of our first pass Sanger SBT. The implementation of Ion Torrent NGS into the routine laboratory not only relies on accurate genotyping and ambiguity resolution but also the ability to provide an efficient workflow at a low cost. We have achieved this by automation on robotic liquid handling systems at amplicon pooling and library preparation steps, and the development of an in-house sample management database which allows sample tracking through the entire NGS process. Ion Torrent sequencing of long range PCR amplicons together with implementation of automation and a sample management database provides an efficient, low cost, high resolution typing alternative to our current Sanger SBT method.


Impact of MHC gamma block (Gamma type) mismatching in the outcome of unrelated hematopoetic stem cell transplantation.

Getz J, Sayer DC, et al.

Matching for HLA is not enough to prevent life-threatening complications in unrelated hematopoetic stem cell transplants (HSCT). MHC has blocks of genetic diversity associated as haplotypes that can encode unidentified transplantation antigens. Previous HLA-A,B,DRB1 linkage study showed that MHC haplotype matching in HSCT lowered risk of aGVHD and increased relapse. A recent study identified single nucleotide polymorphisms (SNPs) in C4A/C4B genes (gamma block) which lie between HLA-B/C and DRB/DQB blocks, and showed that mismatching at these SNPs may occur in HLA matched unrelated individuals suggesting they are markers for partial MHC haplotype matching. This study investigated the effect of C4A/C4B SNPs mismatching on the outcome of HSCT. Cohort included 225 patients (pts) transplanted with HLA10/10 (66%) and 9/10 (34%) unrelated donors, in 3 Brazilian centers between 1996 and 2013. Pts/donors were typed by PCR-SSP using Gamma Type (GT) assay (Conexio Genomics, Australia) that detects 23 SNPs in C4A/C4B genes. Probability of GVHD occurrence and overall survival were estimated from time of Tx by Kaplan Meier, and group differences compared by Log-rank. In HLA10/10 group 77 (52%) pairs were GT Matched (GT-M) and 71 (48%) GT Mismatched (GT-MM) (1-7 SNPs); in the HLA9/10 group 16 (21%) were GT-M and 61 (79%) GT-MM (1-11 SNPs). Univariate analysis showed in HLA 10/10 matched pts that 19.7% (14/71) of GT-MM pts developed grade III-IV aGVHD in comparison to only 3.9% (3/77) of GT-M patients (p=0.008), they were also more likely to develop chronic GVHD (p=0.047) despite no significant
difference was seen in survival. In the 9/10 HLA transplants the likelihood of survival at 5 years is higher when pt and donor were GT-M (65.6%) compared with GT-MM (37.1%) (p=0.074). There were no significant differences in GVHD between GT-M and GT-MM probably due to the small sample size. This study shows that GT mismatching identifies patients at risk of adverse events following unrelated HSCT. This is likely to be because GT is a haplotype marker and GT-MM results in additional incompatibilities in non-HLA MHC sequences, which may be important in unrelated HSCT immunobiology. The differences seen between the 9/10 and the 10/10 HLA matched groups may reflect the interplay between HLA matching and non-HLA MHC sequence matching in unrelated HSCT.

Publication Types: Conference Abstract
PMID:71540637


**Why does gamma-type matching in unrelated hematopoietic stem cell transplants (HSCT) result in a greater likelihood of survival and reduced risk of severe acute graft-versus-host-disease?**

Hogan H, Banister LE, et al.
(Hogan, Banister, Dimovski, Sayer) Conexio Genomics, Fremantle, Australia
D.C. Sayer, Conexio Genomics, Fremantle, Australia. E-mail: david@conexio-genomics.com

A recent study from Brasil showed that 9/10 HLA matched HSCT patients were almost twice as likely to die before 5 years if they were also Gamma-Type mismatched (GT-MM), compared with patients who were GT matched (GT-M). Furthermore patients who were 10/10 HLA matched and GT-M were unlikely to develop severe aGVHD (n=4%), compared with those who were GT-MM (n=20%). The MHC is usually inherited as a single locus. Recombination occurs in specific regions, creating a 4 x genomic block structure of the MHC. HLA-A is located in the alpha block, HLA-B and HLA-C in the beta block, the C4 genes are in the gamma block and the DRB and DQB genes are in the delta block. The region between the Gamma and Beta blocks contain inflammatory and immune regulatory genes. The HLA genes are the most polymorphic genes within their blocks and serve as block "markers" but the HLA alleles are not always haplotype specific and so haplotype matching cannot always be predicted. Furthermore, a recombination event cannot be identified. It has also been shown that outcomes following HSCT from HLA matched / haplotype matched donors differ from HLA matched / haplotype mismatched donors, implicating non-HLA MHC sequences in HSCT outcome. The Gamma block is a key locus when predicting haplotype matching in unrelated HSCT but is never typed. GT types for SNPs in the Gamma block, enabling Gamma block typing. GT / HLA-B / C matching indicates complete sequence matching across the beta block-central MHC-gamma block region, whereas GT-MM indicates a recombinant between the beta block and the gamma block resulting in haplotype mismatching across this region. Given that the central MHC contains pro-inflammatory cytokine and immune response genes and has been implicated in many MHC disease associations it can be speculated that this region may also be key to outcome in unrelated HSCT. GT is a simple PCR SSP for 27 SNPs but a powerful addition to the HSCT matching arsenal. GT provides critical matching information and impacts HSCT outcome in HLA matched and mismatched transplants but in different ways. Poor survival following HLA mismatching and GT-MM HSCT may reflect additional haplotype mismatching which is additive to the HLA mismatch effect, whereas HLA mismatching and GT-M maybe sufficient to prevent severe aGVHD and minimize disease relapse. GT may be key in enabling HLA mismatched HSCT.

Publication Types: Conference Abstract
PMID:71540629


**Accuracy of initial clinical diagnosis of acute bacterial meningitis in children from a malaria-endemic area of Papua New Guinea.**

Aipit J, Laman M, et al.
A pragmatic approach to embedding patient blood management in a tertiary hospital.
Leahy MF, Roberts H, et al.
Hematology Department, Fremantle Hospital, Fremantle, Western Australia, Australia; University of Western Australia, Perth, Western Australia, Australia.
BACKGROUND: We describe the implementation and impact of a patient blood management program (PBMP) in an Australian teaching hospital.
STUDY DESIGN AND METHODS: A PBMP was introduced at a single tertiary care hospital in 2009 as a pilot for the Western Australian Health Department statewide PBMP. The first 3 years of interventions aimed to make effective use of preoperative clinics, manage perioperative anemia, improve perioperative hemostasis, reduce blood sample volumes, and implement restrictive transfusion triggers and a single-unit transfusion policy.
RESULTS: Between 2008 and 2011, admissions to Fremantle Hospital and Health Services increased by 22%. Using 2008 as a reference year, the mean number of red blood cell (RBC) units per admission declined 26% by 2011. Use of fresh-frozen plasma and platelets showed 38 and 16% declines, respectively. Cryoprecipitate increased 7% over the 4-year period. For elective admissions between 2008 and 2011, the leading decline in RBC transfusion rate was seen in cardiothoracic surgery (27.5% to 12.8%). The proportion of single RBC unit use increased from 13% to 28% (p<0.001), and the proportion of double units decreased from 48% to 37% (p<0.001).
CONCLUSION: This is the first tertiary hospital in Australia to establish a multidisciplinary multimodal PBMP. Interventions across disciplines resulted in decreased use of RBC units especially in orthopedic and cardiothoracic surgery. Continuing education and feedback to specialties will maintain the program, improve patient outcomes, and decrease the transfusion rate. 2013 American Association of Blood Banks.
Publication Types: Research Support, Non-U.S. Gov't
PMID:23927725

Modeling the Benefits and Costs of Integrating an Acceptable HLA Mismatch Allocation Model for Highly Sensitized Patients.
1 School of Medicine and Pharmacology, The University of Western Australia, Crawley, Australia. 2 Department of Renal Medicine, Sir Charles Gairdner Hospital, Nedlands, Australia. 3 Sydney School of Public Health, The University of Sydney, Sydney, Australia. 4 Centre for Kidney Research, The Children's Hospital at Westmead & Centre for Transplant and Renal Research, Westmead Hospital, Westmead, Australia. 5 Eurotransplant Reference Laboratory, Department Immunohematology and Blood Transfusion, Leiden University Medical Centre, Leiden, The Netherlands. 6 School of Pathology and Laboratory Medicine, The University of Western Australia, Crawley, Australia. 7 Department of Clinical Immunology, Royal Perth Hospital, Perth, Australia. 8 Department of Renal Medicine, Royal Perth Hospital, Perth, Australia. 9 Department of Renal Medicine, Fremantle Hospital, Fremantle, Australia. 10 Address correspondence to: Hung Do Nguyen, M.D., School of Medicine and Pharmacology, University of Western Australia, Perth, WA 6009, Australia.
BACKGROUND: The Eurotransplant acceptable mismatch program has improved transplantation access for highly sensitized recipients. However, the benefits and costs of implementing such a program remain unknown.
METHODS: Using decision analytical modeling, we compared the average waiting time for transplantation, overall survival gains (in life-years and quality-adjusted life-years gained), and costs of integrating an acceptable mismatch allocation model compared with the current deceased-donor kidney allocation model in Australia.

PMID:23927725
RESULTS: Acceptable mismatches were identified in 12 of 28 (43%) highly sensitized recipients using HLAMatchmaker. Inclusion of acceptable mismatches in the current allocation model improved the transplantation access for four (14%) highly sensitized recipients, with an average reduction in waiting time of 34 months (from 86 to 52 months). Compared with the current allocation model, incorporating an acceptable mismatch allocation model achieved an overall lifetime gain of 0.034 quality-adjusted life-years and savings of over $4,000 per highly sensitized patient, with a small consequential loss of 0.005 quality-adjusted life-years and extra costs of $800 for every reallocated patient.

CONCLUSIONS: Despite modest overall health gains, application of an acceptable mismatch allocation model is an equitable approach to improve transplantation access for highly sensitized transplant candidates without compromising the overall health benefits among the other patients on the deceased-donor waitlist in Australia.

PMID:24690676


Development of a scale to assess performance following primary total knee arthroplasty.
Lewis S, Price M, et al.
RTI Health Solutions, Research Triangle Park, NC.
DePuy Synthes Joint Reconstruction, Inc. Warsaw, IN.
Belfast Trust, Musgrave Park Hospital, Belfast, Northern Ireland, UK.
Heekin Orthopedic Specialists, Jacksonville, FL.
Fremantle Hospital, Crawley, Australia.
RTI Health Solutions, Ann Arbor, MI. Electronic address: mmordin@rti.org.

BACKGROUND: Quantitative assessment of postsurgical knee motion provides sensitive measurements, but results are technical and may not be meaningful to patients. Although several knee-specific instruments exist, no patient-reported outcome (PRO) measure correlates function with improved stability, motion, satisfaction, and confidence.

OBJECTIVE: To address both the above limitations by developing a PRO measure to assess the phenomenon of a "normal" knee after primary total knee arthroplasty (TKA).

METHODS: A draft conceptual model linking the impact of clinical mechanics to hypothesized functional outcomes was generated after a literature review of available assessment tools. Participants aged 18 to 80 years having undergone TKA within the past 10 to 18 months were identified and screened by clinical sites to participate in phase 1 focus groups or phase 2 in-depth interviews. Participants were asked to describe their TKA experiences, including how their knee feels now, followed by cognitive debriefing of Patient's Knee Implant Performance (PKIP) draft items.

RESULTS: Phase 1 results indicated that concepts of confidence, stability, and satisfaction in patients' replacement knee when performing certain activities were distinct and important in the patients' assessment of their TKA. Phase 2 efforts yielded a final version of the PKIP measure containing nine items assessing the broader concepts of stability, confidence, and satisfaction in association with activities. Presurgical and postsurgical versions of the measure were created.

CONCLUSIONS: Results of this qualitative study support use of the PKIP as a complementary PRO measure to assess performance after primary TKA. Psychometric evaluation of the PKIP is planned.

Copyright 2014 International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc. All rights reserved.

PMID:24968994


What is left when anti-tumour necrosis factor therapy in inflammatory bowel diseases fails?
Lawrance IC.
(Lawrance) Centre for Inflammatory Bowel Diseases, Fremantle Hospital, Fremantle, WA 6059, Australia (Lawrance) Department of Medicine and Pharmacology, University of Western Australia, Fremantle Hospital, Fremantle, WA 6059, Australia
The inflammatory bowel diseases (IBDs) are chronic incurable conditions that primarily present in young patients. Being incurable, the IBDs may be part of the patient's life for many years and these conditions require therapies that will be effective over the long-term. Surgery in Crohn's disease does not cure the disease with endoscopic recurrent in up to 70% of patients 1 year post resection. This means that, the patient will require many years of medications and the goal of the treating physician is to induce and maintain long-term remission without side effects. The development of the antitumour necrosis factor alpha (TNFalpha) agents has been a magnificent clinical advance in IBD, but they are not always effective, with loss of response overtime and, at times, discontinuation is required secondary to side effects. So what options are available if of the anti-TNFalpha agents can no longer be used? This review aims to provide other options for the physician, to remind them of the older established medications like azathioprine/6-mercaptopurine and methotrexate, the less established medications like mycophenolate mofetil and tacrolimus as well as newer therapeutic options like the anti-integins which block the trafficking of leukocytes into the intestinal mucosa. The location of the intestinal inflammation must also be considered, as topical therapeutic agents may also be worthwhile to consider in the longterm management of the more challenging IBD patient. The more options that are available the more likely the patient will be able to have tailored therapy to treat their disease and a better long-term outcome. 2014 Baishideng Publishing Group Co., Limited. All rights reserved. PMID:2014078798