Melbourne Health Research Week
12 – 18 June 2009

This publication contains the Research Week 2009 program and list of abstracts accepted for publication, submitted by members of Melbourne Health and affiliated institutes.

I am indebted to the Research Week Committee, which included the following members in 2009:

- Associate Professor Geoffrey Hebbard
- Professor Stephen Jane
- Ms Carol Jewell
- Ms Angela Kreso
- Professor Andrew Kaye
- Ms Catherine Landers
- Ms Morag Morrison
- Dr Angela Watt

In addition, the efforts of those involved in selecting suitable abstracts and in the adjudication of the Awards during Research Week are greatly appreciated. Research Week is successful because of the generous contributions of time, energy and expertise by so many people – thank you.

Professor Ingrid Winship
Executive Director of Research
**Melbourne Health Research Week Symposium**  
**Friday 12 June 2009**

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**OPENING PLENARY**  
Chair: Professor Ingrid Winship

Welcome and Opening of Melbourne Health Research Week

- Opening Address  
  Emeritus Professor David Penington AC, Chairman Bio21 Board and former Dean of Medicine and Vice Chancellor of the University of Melbourne

- Research Papers  
  Dr David Curtis  *Getting to the heart of the matter – using mouse models to find better therapies*  
  Associate Professor Geoffrey Lindeman  *Breast stem cells – getting abreast of breast cancer*

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### 10.15 am – 11.15 am CONCURRENT SESSIONS

#### Lovell Lecture Theatre

- **Blood Research**

  **Chair:** Prof Stephen M Jane

  1. Simon He  
     A phase 1 and correlative biological study of CSL360 (anti-CD123 mAb) in acute myeloid leukaemia (AML)

  2. Carolyn de Graaf  
     Identification of a gene network regulating megakaryocyte commitment from multipotential hemopoietic stem cells

  3. Charbel Darido  
     The Grainy head-like 3 gene functions as a major tumor suppressor in SCC of the skin through regulation of epidermal P13K/Akt/mTOR signalling

  4. Lina Happo  
     c-Myc-derived murine lymphomas lacking BH3-only proteins, Noxa, Puma and Bim are profoundly resistant to p53-mediated DNA-damaging chemotherapeutic drugs in vitro and in vivo.

#### Seminar Room 1

- **Mental Health Research**

  **Chair:** Mr Greg Miller

  5. Avril Pereira  
     Antipsychotic drug modulation of EGF-ERK cell signalling in cortex and striatum: a novel antipsychotic drug mechanism

  6. Maya Reddy  
     Antipsychotics reduce baseline cortical gamma oscillations but do not inhibit aberrant gamma oscillations induced by NMDA-receptor antagonists.

  7. Meng Yang  
     Environmental enrichment delays the onset of limbic epilepsy and improves anxiety-like and neurocognitive behaviours

  8. Christos Pantelis  
     Structural brain changes during transition-to-illness in individuals at risk for schizophrenia: findings from the Melbourne ultra-high risk studies

#### Seminar Room 2

- **Infection, Immunity and Inflammation Research**

  **Chair:** Prof Leonard Harrison

  9. John Wentworth  
     Pro-inflammatory CD11c+CD206+ adipose tissue macrophages are increased in women with metabolic syndrome

  10. Andrew Cook  
      Urokinase-plasminogen activator derived from a bone marrow cell is required for the development of immune complex-mediated arthritis models

  11. Glen Scholz  
      The innate immune response to infection: a tricky balancing act

  12. Marion Robertson  
      Gentamicin management – improvement following deployment of electronic decision support
### 11.45 am – 12.45 pm CONCURRENT SESSIONS

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13. Lena Ly
Segmental distribution of multiple naevi associated with malignant melanoma

14. Benjamin Namdarian
Circulating endothelial cells: Prognostic markers in urological malignancies.

15. Wei-Ren Pan
The lymphatic drainage of the nasal fossae and nasopharynx: A preliminary anatomical and radiological study with clinical implications.

16. Amir Zayegh
Does widening the criteria for needle biopsy in the assessment of microcalcifications in a breast screening program lead to increased detection of ductal carcinoma in situ (DCIS) and small invasive cancers?

17. Paul Tescher
Surveillance of FAP: A prospective blinded comparison of capsule endoscopy and other GI imaging to detect small bowel polyps.

18. Nigel Jones
Repeted restraint stress accelerates the development of limbic epilepsy in rats

19. Sandra Petty
Bone health and age of commencement of anti-epileptic medication: An AED-discordant twin and sibling pair study

20. Megan Oliva
EEG dipole source localisation in non-lesional TLE with and without hippocampal sclerosis

21. Slave Petrovski
Predicting AED response: Combining a pre-treatment neurocognitive score with a multigenic model to provide predictive value for seizure recurrence in newly treated epilepsy.

22. Rimma Goldberg
Outcomes of surgical treatment for trigeminal neuralgia

23. Michelle Ananda-Rajah
Active screening & isolation is not required to control methicillin resistant Staphylococcus aureus (MRSA) in an endemic high-risk setting: an 8-year time series analysis from an Australian tertiary hospital intensive care unit.

24. Joe Sasadeusz
Pegylated interferon alfa-2a (peg-2a) plus ribavirin (rbv) for patients with chronic hepatitis c virus (hcv) on opioid pharmacotherapy: virological outcomes, psychological impact and safety

25. Benjamin Cowie
Trend analysis for hepatitis B infection in Australia: the correlation between seroprevalence, notifications and migration and predictions from a simple regression model

26. Peter Revill
The role of pregemomic RNA splicing in productive HBV replication

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**LUNCH, POSTER VIEWING, TRADE DISPLAY**

Over 120 posters showcasing research from the Parkville Precinct in Aged Care, Infectious Diseases, Cardio-Respiratory, Neurosciences, Endocrinology, Quality of Care, Mental Health, Musculoskeletal, Emergency and Critical Care, Rehabilitation, Genetics, Anaesthesia, Cancer and more.
### 1.45 pm – 2.45 pm CONCURRENT SESSIONS

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<td>Quality of Care Research and Rehabilitation Research</td>
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| 27. Kathryn Ellis  
Baseline data from a multi-centre, prospective longitudinal study of ageing in 1100 volunteers | 32. Trevor Kilpatrick  
Genome-wide association scan identifies novel multiple sclerosis susceptibility loci on chromosomes 12 and 20. | 37. Elizabeth Aitken  
IPTp and antibody dynamics and protection to malaria in pregnancy |
| 28. James Watt  
Who’s missing out on specialist palliative care at Australia’s busiest hospital and why? | 33. Melissa Gresle  
Validation of a novel serum marker of neurodegeneration in Multiple Sclerosis patients | 38. Katherine Gibney  
Vitamin D deficiency is associated with tuberculosis (TB) and latent TB infection among immigrants from sub-Saharan Africa |
| 29. Francis Connan  
Do routinely repeated CT scans in traumatic brain injury influence management? A prospective study in a level 1 trauma center. | 34. Helmet Butzkueven  
Seasonal variation of onset of relapses in multiple sclerosis in the northern and southern hemispheres: results from the MSBase Registry | 39. Georard Casey  
The effectiveness of 4 monthly albendazole treatment for the reduction of soil-transmitted helminth infections in women of reproductive age in Viet Nam |
| 30. Mingwei Joe Ye  
Comparison of the accuracy of digital with analog preoperative x-ray templating for total hip arthroplasty | 35. Christen Barras  
Quantitative CT densitometry predicts intracerebral hemorrhage growth | |
| 31. Jonathan Knott  
What factors determine the time to arrival at the emergency department following the onset of cerebrovascular accidents? | 36. Bruce Campbell  
Very Low Cerebral Blood Volume (VLCBV) – a new predictor of haemorrhagic transformation after thrombolysis for acute ischaemic stroke | |

### 2.45 pm – 4.00 pm Charles La Trobe Lecture Theatre

**CLOSING PLENARY**

**BioGrid Australia – Oncology Research 2009**

Chair: Associate Professor Peter Gibbs

BioGrid Australia is a record-linkage platform enabling privacy protected research across multiple institutions. Oncology Research has been a focus of BioGrid Australia across a number of tumour streams with Colorectal Cancer being the most mature. This session highlights the research by the BioGrid research fellows Kathryn Field, Maggie Moore and Sumitra Ananda.

Research Papers:

- **Dr Kathryn Field** *Establishing a brain tumour database*
- **Dr Sumitra Ananda** *Impact of the National Bowel Screening Program in Australia (NBCSP) utilising faecal occult blood test (FOBT) screening on the diagnosis of colorectal cancer (CRC)*
- **Dr Maggie Moore** *Rare Tumours: A new way of engaging with consumers and progressing research*
Saturday 13 June 2009
8.30 am – 10.00 am
Ewing Lecture Theatre

Surgical Research Forum
Chair: Prof Andrew Kaye

165 Jeanette Ting
The in-vivo anatomy of the deep circumflex iliac artery (DCIA) perforators: Defining the role for the DCIA perforator flap

166 Nicole Tham
The pudendal thigh flap for vaginal reconstruction: optimising flap survival

167 Benjamin Namdarian
Circulating endothelial cells: Prognostic markers in urological malignancies

168 Anna Taylor
Experimental analysis of the effectiveness of retrograde nerve tracers in vitro and in vivo in male Wistar rats for the potential use in human nerve-sparing radical prostatectomy

169 Wei-Han Tay
Outcomes of delayed union and nonunion of femoral and tibial shaft fractures

170 Francis Connon
Do routinely repeated CT scans in traumatic brain injury influence management? A prospective study in a level 1 trauma center

171 Tanya Yuen
Glutamate and other risk factors for tumor associated seizures

Monday 15 June 2009
1.00 pm to 2.00 pm
Lovell Lecture Theatre

Cruising Research

This informative session aims to assist researchers in all aspects of research from sourcing funds through the grant application process, through to streamlining ethics reviews and Melbourne Health guidelines in research.

- Mr Michael Wright, CEO Victorian Cancer Agency, will talk about applying for funding through the grant application process.
- Dr Angela Watt will discuss the Streamlined Ethics Review Processes which will be introduced in Victoria in late 2009.
- Ms Angela Gray will guide researchers through some of Melbourne Health’s Guidelines in Research.
Tuesday 16 June 2009
1.00 pm to 2.00 pm
Charles La Trobe Lecture Theatre

The chicken or the egg? In research, the bench top is more worthy than the bedside

Master of Ceremonies (MC)
- **Professor Ingrid Winship**, Executive Director of Research, Melbourne Health.

The proceedings will be presided over by:
- **Professor Alex Cockram**, Executive Director NorthWestern Mental Health
  *Eutopia’s Attorney General, Professor “Judge Judy” Alex Cockram*
- **Mr David Ford**, Director of Pharmacy, Melbourne Health
  *Eutopia’s Minister for Lotteries and Gaming (a major contributor to the government purse), The Honorable David Ford*
- **Professor Rodney Judson**, Divisional Director of Surgery and Perioperative Services, Director Of Trauma, Melbourne Health
  *Emeritus Professor of Everything Medical, Lord Rodney Judson*
- **Ms Diane Gill**, Executive Director Royal Melbourne Hospital
  *The president of the Royal Eutopia Yacht Club and CEO of “Philanthropy Eutopia” (now bankrupt), Dame Diane Gill, DBE*

Team for the Affirmative
- **Professor Mark Rosenthal**, Director of Medical Oncology, Royal Melbourne Hospital
- **Ms Felicity Topp**, Interim Director of Operations, Royal Melbourne Hospital
  *Professor No Fiscalidea*
- **Associate Professor David Russell**, Director, Department of General Medicine, Royal Melbourne Hospital.

Team for the Negative
- **Professor Doug Hilton**, Director Designate and Head, Division of Molecular Medicine, The Walter and Eliza Hall Institute of Medical Research, the University of Melbourne, NHMRC Australia Fellow (Inaugural).
- **Ms Emma O’Brien**, Manager and Senior Clinician, Music Therapy - Allied Health, Royal Melbourne Hospital
  *Lady Dame Dr Petriana Singah OBE UFT PC*
- **Professor Terry O’Brien**, James Stewart Professor of Medicine and Head of Department, Department of Medicine, The Royal Melbourne Hospital, The University of Melbourne, Head of Epilepsy Unit, Department of Neurology, Royal Melbourne Hospital
  *Professor Val U. Formoney*
Wednesday 17 June 2009
12.30 pm to 2.00 pm
Charles La Trobe Lecture Theatre

Quality in, quality out
Making the most of hospital data for clinical research and quality improvement

The Clinical Epidemiology and Health Service Evaluation Unit will present this informative and highly relevant educational session which aims to provide a better understanding of content and processes involved from selected departments in order to access data.

- Welcome
  Dr Peter Bradford, Executive Director, Clinical Governance/Medical Services
- Planning your data extraction
  Associate Professor Caroline Brand, Director, Clinical Epidemiology and Health Service Evaluation Unit
- Melbourne Health Data Sources
  Performance Measurement Unit – Mrs Sherie Knight, Manager; Mrs Sok-Wee Yew, Business Analyst
  Health Information Services – Ms Jane Widdison, Director Information and Performance
  Pharmacy – Mr Nick Jones, Deputy Director of Pharmacy
  Nursing Workforce – Ms Joy Turner
  BioGrid Australia – Dr Marienne Hibbert, Project Director, BioGrid Australia
- Data Management
  Ms Alexandra Gorelik, Senior Statistician, Clinical Epidemiology and Health Service Evaluation Unit

Wednesday 17 June 2009
6.00 pm – 7.30 pm
Charles La Trobe Lecture Theatre

PUBLIC LECTURE
How do you mend a broken heart?
Chair: Dr Leanne Grigg

This public lecture will take the audience on a patient's journey through the many stages of cardiac care, from a cardiac event, through to recovery, rehabilitation and changing lifestyle. Three clinical staff - a cardiologist, a surgeon and a cardiac rehabilitation specialist - will speak about the work they do and the research advances being made in treating patients and improving their long-term outcomes.

The final word will come from a cardiac patient who has received treatment at The Royal Melbourne Hospital, successfully completed the cardiac rehabilitation program and has gone on to live a healthy life.

Presenters are:
- Dr Leeanne Grigg, Director, Cardiology
- Associate Professor Rod Warren, Director of Interventional Cardiology
- Mr John Goldblatt, Senior Cardiothoracic Surgeon
- Ms Kath Kelly, Cardiac Rehabilitation Coordinator
diagnosis or even serve as new therapeutic targets for treating or preventing breast cancer. Progenitor and mature luminal cells. Unexpectedly, pre-neoplastic breast tissue from BRCA1 mutation carriers has been found in mastectomy specimens from BRCA1 mutation carriers, we have identified basal stem/progenitor, committed luminal and BRCA2-associated breast cancers. Using breast tissue obtained from reduction mammoplasty and prophylactic breast tissue. A priority is to understand whether stem or progenitor cells are directly linked to the development of BRCA1-predisposing gene, BRCA1. These findings have fuelled speculation that a stem cell, or an early descendant cell, can give rise to BRCA1-associated breast cancers. We have now turned our efforts to identifying stem and progenitor cells in human breast stem cells in mice. Remarkably, even a single stem cell was able to give rise to a complete functional mammary gland. The stem cell was found to resemble a clinically aggressive subtype of breast cancer known as the ‘basal-like’ subtype. This subtype is commonly seen in tumours arising in women with mutations in the hereditary breast cancer predisposing gene, BRCA1. These findings have fuelled speculation that a stem cell, or an early descendant cell, can give rise to BRCA1-associated breast cancers. We have now turned our efforts to identifying stem and progenitor cells in human breast tissue. A priority is to understand whether stem or progenitor cells are directly linked to the development of BRCA1- and BRCA2-associated breast cancers. Using breast tissue obtained from reduction mammoplasty and prophylactic mastectomy specimens from BRCA1 mutation carriers, we have identified basal stem/progenitor, committed luminal progenitor and mature luminal cells. Unexpectedly, pre-neoplastic breast tissue from BRCA1 mutation carriers has been found to contain an expanded luminal progenitor (rather than stem cell) population. In the longer-term, we hope that this research will pave the way for the identification of specific breast cancer markers. These could potentially be used in cancer diagnosis or even serve as new therapeutic targets for treating or preventing breast cancer.

Thursday 18 June 2009
1.00 pm to 2.00 pm
Charles La Trobe Lecture Theatre

Closing Ceremony
Chair: Professor Ingrid Winship

Presentation of Research Week prizes: The Lord Mayor of Melbourne and Chair of Melbourne Health, the Right Hon Lord Mayor Robert Doyle will present the Research Week prizes for best presentations which includes the Cleveland Young Investigator’s Award.

Research Papers

40. Dr Chris French How do anti-epileptic drugs work?
41. Dr Emma McBryde Estimating sensitivity and specificity of the tuberculin skin test and interferon gamma release assay in the absence of a Gold Standard: a statistical approach

Opening Plenary – Research Papers

David Curtis
Getting to the heart of the matter – using mouse models to find better therapies

Peter Kanellakis1, Alex Bobik1 and David J. Curtis2,3
1 Cell Biology Laboratory, Baker Medical Research Institute; 2 BMRL, Royal Melbourne Hospital; 3 Dept. of Medicine, University of Melbourne

In 2001, a study using a mouse model of acute myocardial infarction (AMI), proposed that rare stem cells within the bone marrow could help heal damage to the heart after an AMI. They proposed that these adult bone marrow cells, when placed in the damaged heart, could turn into new heart muscle and blood vessels. These reports quickly led to phase I/II clinical trials in human AMI. Disappointingly, these trials failed to show any clinical benefit, leading to loss of interest by all but the most ardent believers. For the last 5 years, we have been using a mouse model of AMI to explore the underlying mechanism of the initial observations. Our work shows that bone marrow-derived stem cells or their progeny can improve heart repair, not by differentiating into new muscle, but by modulating the inflammatory process and promoting the normal repair process. These findings will lead to new anti-inflammatory therapies for AMI, demonstrating the power of animal models to perform hypothesis-driven translational research.

Geoffrey Lindeman
Breast stem cells – getting abreast of breast cancer.

Elgene Lim1,2, François Vaillant1,2, Di Wu1,2, Natasha C. Forrest1, Bhupinder Pal1, Adam H. Hart1, Marie-Liesse Asselin-Labat1, David E. Gyorki1,2, Teresa Ward1, Audrey Partansen1, Frank Feleppa1, kConFab1, Gordon K. Smyth1, Jane E. Visvader1,2* Geoffrey J. Lindeman1,2,3 *Equal contribution
1 The Walter and Eliza Hall Institute of Medical Research; 2 The University of Melbourne; 3 The Royal Melbourne Hospital; kConFab, The Kathleen Cunningham Foundation Consortium for Research into Familial Breast Cancer.

Our group is trying to understand how breast stem cells or their descendants (called ‘progenitor’ cells) play a role in breast cancer. The breast stem cell is like a seed that gives rise to all the ducts and milk-producing cells in the breast. Stem cells are required for replenishing breast tissue during normal monthly cycles in women and for generating new breast tissue during pregnancy and lactation. It is possible that the stem cell, which is long-lived, may be an important ‘target cell’ in which genetic mishaps progressively accumulate, ultimately leading to breast cancer. A few years ago our team discovered breast stem cells in mice. Remarkably, even a single stem cell was able to give rise to a complete functional mammary gland. The stem cell was found to resemble a clinically aggressive subtype of breast cancer known as the ‘basal-like’ subtype. This subtype is commonly seen in tumours arising in women with mutations in the hereditary breast cancer predisposing gene, BRCA1. These findings have fuelled speculation that a stem cell, or an early descendant cell, can give rise to BRCA1-associated breast cancers. We have now turned our efforts to identifying stem and progenitor cells in human breast tissue. A priority is to understand whether stem or progenitor cells are directly linked to the development of BRCA1- and BRCA2-associated breast cancers. Using breast tissue obtained from reduction mammoplasty and prophylactic mastectomy specimens from BRCA1 mutation carriers, we have identified basal stem/progenitor, committed luminal progenitor and mature luminal cells. Unexpectedly, pre-neoplastic breast tissue from BRCA1 mutation carriers has been found to contain an expanded luminal progenitor (rather than stem cell) population. In the longer-term, we hope that this research will pave the way for the identification of specific breast cancer markers. These could potentially be used in cancer diagnosis or even serve as new therapeutic targets for treating or preventing breast cancer.
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Closing Plenary – Research Papers

Kathryn Field
Establishing a brain tumour database
Kathryn Field1, Kate Drummond1, Mark Rosenthal1
1Biogrid; 2Royal Melbourne Hospital

Brain tumours represent a challenging group of cancers that overall have a poor prognosis. They tend to be treated at specialist centres. This presentation will cover progress in collecting brain tumour data and some of the specific challenges involved. Some of the preliminary data will be discussed and some initial research projects described.

Sumitra Ananda
Impact of the National Bowel Screening Program in Australia (NBCSP) utilising faecal occult blood test (FOBT) screening on the diagnosis of colorectal cancer (CRC).
Sumitra Ananda1,2, McLaughlin S3, Chen F4, Hayes I5, Hunter A6, Skinner I7, Steel M8, Jones I9, Hastie I10, Rieger N11, Shedda S12, Gibbs P13,14.
1 Western Hospital; 2 Box Hill Hospital; 3 Royal Melbourne Hospital; 4 Biogrid Australia, 5 Royal Adelaide Hospital.

Screening for CRC with FOBT is proven to reduce deaths from CRC, but is yet to be widely adopted. The NBCSP was launched in May 2006, with every person turning 55 - 65 years of age offered an FOBT. We aimed to analyse the initial impact of this program on CRC diagnosis. Using data from a prospective, standardised and comprehensive CRC database (ACCORD), at 13 Australian hospitals, 8 public and 5 private, between May 2006 and June 2008, 1268 cases of CRC were identified. Initiation of the NBCSP resulted in 3.2% of CRC being screen detected, including 29% of cancers in the target age. Screen detected cancers were at an earlier stage and there was a trend for less rectal cancers. NBCSP detected cancers were more common in private patients likely reflecting differences in attitudes towards screening test.

Maggie Moore
Rare Tumours: A new way of engaging with consumers and progressing research.
Maggie Moore1, Clare Scott2
1Biogrid; 2Walter and Eliza Hall Institute

Rare tumour have a substantial impact on our community and because of the rarity effective research into potential treatments for these patients have been difficult. Biogrid Australia is developing an international web-based rare tumour database that will allow patients to enter the details of their illness online giving researchers the opportunity to identify larger groups of patients to participate in research projects as well as facilitating enhanced information sharing and support for patients.

Acknowledgement of the Biogrid Oncology Team: Julie John, Ngaia Murigu, Daniel Compston, Sandy Dupuis and Biogrid Australia.

1 Simon He
A phase 1 and correlative biological study of CSL360 (anti-CD123 mAb) in acute myeloid leukaemia (AML)
HE S1,2, Roberts A1,2, Bradstock K3, Hertzberg M4, Durrant S5, Ritchie D5, Lewis I6, Marlton F7, McLachlan A8, Yeardon T9, Busfield S10, Barnden J10, Davis R10, Hosback S10, Mirosa D10, Biondo M10, Bamford S10, DeWitte M10 and Basser R10
1 Division of Cancer and Haematology, The Walter and Eliza Hall Institute of Medical Research; 2 Clinical Haematology and Bone Marrow Transplant Unit, Royal Melbourne Hospital; 3 Department of Haematology, Westmead Hospital; 4 Haematology/BMT Oncology, Royal Brisbane and Women’s Hospital; 5 Dept. of Haematology, Peter MacCallum Cancer Center; 6 Division of Haematology, I.M.V.S., Adelaide; 7 Princess Alexandra Hospital, Brisbane; 8 University of Sydney; 9 Queensland Institute of Medical Research; 10 CSL Ltd, Australia.

CD123 (IL-3Rα) is a phenotypic marker of putative leukemic stem cells (LSC) in AML. CD34+38- cells from AML patients (pts) express high levels of CD123, in contrast to absence of expression on CD34+38- cells in normal individuals. Binding of CD123 by monoclonal antibody (mAb) 7G3 inhibits IL-3 dependent signalling and proliferation in vitro. In a NOD-SCID xenograft model, 7G3 inhibits human AML engraftment, but not normal human hematopoiesis. CSL360 is a recombinant chimeric IgG1 mAb derived from 7G3. CSL360 concentrations ≥ 0.1μg/mL in vitro inhibited 90% AML cell growth in the presence of supraphysiological IL-3 levels. Preclinical toxicology studies showed no CSL360-related adverse effects. AIMS: To evaluate safety, pharmacokinetics (PK) and bioactivity of CSL360 in relapsed, refractory or high-risk AML. Methods: Phase I trial began in March 2007 in Australia with pts receiving 12 weekly (planned) iv infusions unless withdrawn earlier. Additional doses are allowed in pts achieving a response. Bone marrow aspirates/trephine samples are obtained at screening, day 16, and day 29. Results: Over 180 infusions were administered to 26 pts (21M, 5F; 17 de novo, 8 MDS-related, 1 treatment-related) at 5 dose levels: 0.1, 0.3, 1.0, 3.0 and 10 mg/kg. PK parameters over 7 days after doses 1 and 4 were linear with dose-proportional increases in the AUC and Cmax. After first dose, the mean plasma half-life was 83hr with mean systemic clearance of 0.21L/hr and mean volume of distribution of 0.39 L/kg. Anti-CSL360 antibodies were detected post-treatment in 8/12 pts. Flow cytometry studies demonstrated dose-dependent CSL360 coating of both AML blasts and LSC. Saturation of CD123 on marrow and blood leukaemic cells was observed 1 day after dosing at 0.3mg/kg. At higher dose levels saturation of CD123 was maintained 7 days post dosing, associated with reduction in surface CD123 expression. CSL360 has been well tolerated including 7 pts receiving 12 planned doses and 16 pts withdrawn earlier due to progressive disease/investigator’s decision/infections. Three serious adverse events were observed: 1 invasive fungal infection (Gr5), and 2 infusion reactions (Gr2). One complete response (CR) has been observed: a 22-yr old male with relapsed AML (M1) post-2 allografts achieved a morphological AML-free state after 3 doses at 3.0 mg/kg and CR after 12 doses, sustained for > 9 weeks. These preliminary results show anti-CD123 mAb therapy with CSL360 is safe and tolerable with demonstrable biological and clinical effects. The study is ongoing at 10 mg/kg weekly.


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2 Carolyn de Graaf
Identification of a gene network regulating megakaryocyte commitment from multipotential hemopoietic stem cells
DE GRAAF CA, Kauppi M, Baldwin T, Smyth GK, Alexander WS, Hilton DJ.
Walter and Eliza Hall Institute of Medical Research

Megakaryocytes are responsible for the production of platelets; small anuclear cell fragments vital in clotting and wound healing. The chief cytokine responsible for megakaryocyte and platelet production is TPO (thrombopoietin), which acts through the receptor Mpl. Using an ENU (N-ethyl-N-nitosourea) mutagenesis screen on Mpl-/- mice, which have 10-fold less platelets than wild type mice, we have isolated the Plt4 mutation in the transcription factor Myb. Mybplt4/Plt4 mice on both a Mpl-/- and Mpl+/+ background have a platelet level three to five times that of wild type mice, showing that the Plt4 mutation suppresses the Mpl phenotype and Myb is epistatic to Mpl. This megakaryocytosis in the Mybplt4/Plt4 mice is explained by major skewing of lineage commitment toward megakaryocytes, at the expense of erythrocytes, B cells and eosinophils.

Investigation of restricted progenitor populations in Mybplt4/Plt4 mice showed that the Megakaryocyte Erythrocyte Progenitor (Lineage-Sca-Kit+CD34-FcR-) population was missing despite the increase of megakaryocyte production, and colony forming assays revealed Myb Plt4/Plt4 progenitor populations were biased towards megakaryocyte production to the extent that Mybplt4/Plt4 Granulocyte Macrophage Progenitors (Lineage+Sca-Kit+CD34+Fcr+) continue to produce megakaryocytes. This suggested that the defect in megakaryocyte production is established early in hemopoietic development.

In order to better understand the transcriptional changes underlying the early Mybplt4/Plt4 megakaryocyte defect, we have investigated gene expression profiles in bone marrow LSK (Lineage- Sca1+ Kit+) cells, a population that contains stem cells and multi potential progenitors. While many genes were differentially expressed between Myb+/- and Mybplt4/Plt4 LSKs, we were able to focus in on megakaryocyte lineage genes using LSK cells from Mpl-/- mice which have an opposing phenotype of megakaryocyte production compared to Mybplt4/Plt4 mice. This revealed a set of genes that are downregulated in LSK cells in Mpl-/- mice, and upregulated in the Mybplt4/Plt4 mice and have megakaryocyte specific expression. These genes include megakaryocyte transcription factors GATA2 and Meis1, which could be responsible for driving the over production of megakaryocytes in the Mybplt4/Plt4 mice, suggesting a pathway to megakaryocyte commitment.

3 Charbel Darido
The Grainy head-like 3 gene functions as a major tumor suppressor in SCC of the skin through regulation of epidermal PI3K/Akt/mTOR signalling
Darido C, Auden A, Wilanowski T, Caddy C, Papenfuss T, Jane SM
The Royal Melbourne Hospital, Walter and Eliza Hall Institute of Medical Research, University of Melbourne.

Grainy head-like 3 (Grhl3) is a member of a large gene family, which encodes highly conserved transcription factors that regulate the formation and maintenance of the integument in diverse species. Grhl3-null mice die at birth with neural tube defects, and a failure of skin barrier formation. The epidermis of these mice displays cellular hyperproliferation and failed terminal differentiation, with an expanded basal layer. Keratinocytes cultured from Grhl3-null embryos express high levels of proliferative markers, and display lack of cell-cell contact inhibition forming heaped up “pseudo-tumours” in the culture dish.

To examine the role of Grhl3 in tumorigenesis in adult skin, we have utilized a model of chemical-induced skin carcinogenesis in conditional mice lacking Grhl3 expression in the epidermis (Grhl3Flox/-/K14 Cre+). A single application of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butane (NNK) at 8 weeks of age resulted in high-grade squamous intraepithelial lesions (SIL) within 8 weeks in all Grhl3Flox/- mice, which progressed to invasive squamous cell carcinomas (SCC) within 7 weeks. At 30 weeks, no wild type control animals have developed any skin lesions. Using a combination of bioinformatics and molecular biology, we identified two critical negative regulators of the phosphatidylinositol-3-kinase (PI3K)/Akt signalling pathway, PTEN and GSK3β, as direct Grhl3 target genes in the epidermis. Expression of these genes is markedly reduced in embryonic Grhl3-deficient epidermis resulting in increased activity of PI3K/Akt/mTORC1 signalling, disrupting the balance between proliferation and differentiation. Together, our results define the transcription factor Grhl3 as a novel and critical tumor suppressor in the setting of SCC of the skin and pave the way for pre-clinical studies of inhibitors of PI3K/Akt/mTORC1 signalling in this disease.

4 Lina Hapro
C-Myc-derived murine lymphomas lacking BH3-only proteins, Noxa, Puma and Bim are profoundly resistant to p53-mediated DNA-damaging chemotherapeutic drugs in vitro and in vivo.
HAPPO L, Craig M, Jansen E, Michalak E, Cory S, Strasser A, Scott CL
Walter and Eliza Hall Institute of Medical Research

Although DNA damage-inducing chemotherapy is a mainstay of cancer treatment, it frequently fails, at least in part due to impairment of apoptosis. Two pro-apoptotic BH3-only genes, Puma and Noxa, are transcriptional targets for p53 and are known to trigger the apoptotic DNA damage response. In Eµ-myc lymphomas, targeted deletion of puma resulted in increased resistance of most Pre-B lymphomas to DNA damage, but loss of noxa alone did not. Unexpectedly, compared with loss of puma alone, targeted deletion of both puma and noxa conferred marked sensitivity in vivo. A third BH3-only gene, bim, was up-regulated after DNA damage and targeted deletion increased resistance of B cell lymphomas. Knock-down of bim resulted in increased resistance to DNA damaging drugs both in vitro and in vivo most impressively when both puma and noxa were deleted, suggesting a combinatorial role for these genes. Lymphomas derived from Fetal Liver Cells, generated using retroviral induction of c-myc, revealed that triple deletion of noxa, puma and bim, caused resistance as severe as that associated with loss of p53.

10
5 Avril Pereira

Antipsychotic drug modulation of EGF-ERK cell signalling in cortex and striatum: a novel antipsychotic drug mechanism

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Mental Health Research Institute of Victoria; Centre for Neuroscience and Department of Psychiatry, The University of Melbourne; Northern Psychiatry Research Centre, The Northern Hospital

Antipsychotic drugs (APD) are the principal treatment for schizophrenia however, for many patients they are of marginal benefit in improving positive psychiatric symptoms. For these patients, the alternative is the atypical APD clozapine which is superior to other agents in treatment resistant schizophrenia. The mechanism by which clozapine exerts this antipsychotic effect is unknown but may involve alternate cell signalling systems. A potential candidate is the mitogen activated protein kinase-extracellular signal regulated kinase (MAPK-ERK) cascade that links G-protein coupled receptors and ErbB growth factor signalling systems. We have previously reported in vitro that clozapine and other APD acutely inhibited ERK activation but only clozapine stimulated ERK with sustained treatment. This stimulation was mediated by the epidermal growth factor (EGF) receptor (ErbB1). Here we extend our findings in vivo to determine if clozapine, haloperidol, quetiapine and aripiprazole differentially modulate the EGF-ERK1/2 pathway in prefrontal cortex (PFC) and striatum of C57Bl/6 mice following acute treatment. Phosphorylation of the predominant neuronal ERK isoforms, ERK1 and ERK2 and the putative downstream targets p90RSK and c-fos was measured by immunoelectrophoresis. ERK phosphorylation was inhibited by clozapine at 20 and 60 min followed by subsequent activation at 8 hrs and normalization of the pERK1 response at 24 hrs. This in vivo clozapine-induced ERK activation was significantly reduced by the EGF receptor inhibitor, AG1478, in both brain regions (PFC clozapine 8 hrs: 144.7±4% vs clozapine+AG1478 8 hrs: 46.7±10.7%, p<0.001). At 8 hrs, no parallel change in p90RSK or c-fos expression levels in PFC was observed following clozapine treatment in the absence or presence of AG1478. In contrast, aripiprazole triggered biphasic ERK phosphorylation in PFC but had no significant effect in the striatum, whilst haloperidol significantly stimulated pERK1 in striatum for up to 8 hrs. ERK activation seen with aripiprazole and haloperidol in PFC and striatum, respectively, was not EGF receptor mediated. Since perturbations of the EGF system have been reported in schizophrenia, clozapine recruitment of ErbB1 signalling to activate ERK1/2 may present as a novel antipsychotic drug target for treatment resistant patients.

6 Maya Reddy

Antipsychotics reduce baseline cortical gamma oscillations but do not inhibit aberrant gamma oscillations induced by NMDA-receptor antagonists.

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Purpose: A single non-anaesthetic injection of ketamine, a non-competitive NMDA receptor (NMDAr) antagonist with hallucinogenic properties, induces cognitive impairment and psychosis and aggravates schizophrenia symptoms. In conscious rats, an equivalent dose of ketamine increases the power of ongoing γ oscillations in the neocortex and concomitantly induces abnormal behaviour, including ataxia and hyperlocomotion, a key feature of animal models of acute psychosis. This study investigated whether NMDAr antagonist-induced aberrant γ oscillations were reversible with antipsychotic treatment.

Methods: Rats were placed in an open arena for 30 minutes (baseline recording). They were then administered either Clozapine (1.5 mg/kg sc, n=7) or Haloperidol (0.025 – 0.25 mg/kg sc; n=6), and 30 minutes later received an injection of the NMDAr antagonist Ketamine (5mg/kg sc) or vehicle. Quantitative measures of γ power and locomotion were assessed throughout the experiment for all rats. Results: Both antipsychotics significantly reduced the power of ongoing γ oscillations by 30%. As previously demonstrated by us, Ketamine induced hyperlocomotion and aberrant γ oscillations in all rats. This hyperlocomotor response was dose-dependently inhibited by both antipsychotics, but these drugs had no effect on the concurrent increase in γ power induced by ketamine. Conclusion: The present study suggests that antipsychotics reduce the power of ongoing cortical γ oscillations, but do not block the aberrant increase in this measure induced by psychotic drugs, such as ketamine. The observed reductions in γ power observed following antipsychotic treatment may explain why cortical recordings in (medicated) schizophrenia patients reveal reduced γ power compared with control subjects.

7 Meng Yang

Environmental enrichment delays the onset of limbic epilepsy and improves anxiety-like and neurocognitive behaviours

YANG M, Rees SM, Salzberg MR, O’Brien TJ, Jones NJ.
The Royal Melbourne Hospital, University of Melbourne, St Vincent’s Hospital

Purpose: Temporal lobe epilepsy (TLE) is the most common adult epilepsy syndrome with one-third of patients remaining refractory to current pharmacological treatment. In addition, TLE is commonly accompanied by neuropsychiatric and neurocognitive comorbidities including anxiety, depression and learning deficits. Given recent animal studies highlighting enhanced seizure susceptibility following stress, it was of interest to examine the neuroprotective capacity of ‘positive experiences’ created using enrichment, such as ketamine. The observed reductions in γ power induced by ketamine. Conclusion: The present study suggests that antipsychotics reduce the power of ongoing cortical γ oscillations, but do not block the aberrant increase in this measure induced by psychotic drugs, such as ketamine. The observed reductions in γ power observed following antipsychotic treatment may explain why cortical recordings in (medicated) schizophrenia patients reveal reduced γ power compared with control subjects.

8 Christos Pantelis

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YANG M, Rees SM, Salzberg MR, O’Brien TJ, Jones NJ.
The Royal Melbourne Hospital, University of Melbourne, St Vincent’s Hospital

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Structural brain changes during transition-to-illness in individuals at risk for schizophrenia: findings from the Melbourne ultra-high risk studies

Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne & Melbourne Health; ORYGEN Research Centre; Department of Psychology, The University of Melbourne; Department of Neuropsychiatry, University of Toyama, Toyama, Japan.

Background: Structural neuroimaging in schizophrenia consistently identifies ventricular enlargement, and frontal and temporal lobe abnormalities. Recent studies demonstrate that these changes evolve over time following illness onset. We have scanned individuals at ultra-high risk of developing psychosis (criteria developed by Yung & McGorry) and examined brain changes before and during transition to illness, to assess brain changes as illness develops.

Methods: Subjects scanned on a 1.5 Tesla GE Scanner. 135 individuals at ultra-high risk (UHR) for psychosis (39 converters to psychosis) scanned at baseline. Longitudinal scans available on 35 UHR (12 converters), 16 FE schizophrenia and 14 controls (CTLS). In a series of studies we examined cross-sectional and longitudinal changes in prefrontal and temporal cortices (hippocampus, amygdala, superior temporal gyrus (STG) and insular (INS)), anterior cingulate grey matter thickness (ACC), corpus callosum (CC), and ventricular volume (VV). Findings: Cross-sectionally, abnormalities were seen in converters to psychosis in prefrontal regions, STG, ACC, INS and CC; medial temporal structures and VV were normal. Compared with non-converters, those converting to psychosis showed longitudinal changes in temporal and orbital frontal regions, medial temporal, ACC, STG, INS. VV increased post-psychosis onset. Conclusions: Longitudinal MRI findings in UHR reveal excessive structural changes in those converting to psychosis, especially in temporal and prefrontal cortical regions. Further changes may occur post-illness onset. Whilst the pathological processes underlying such changes remain unclear, they may reflect anomalies in genetic and/or other endogenous mechanisms responsible for brain maturation, and/or the adverse effects of stress and other environmental factors.

John Wentworth
Pro-inflammatory CD11c+CD206+ adipose tissue macrophages are increased in women with metabolic syndrome

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Objective: Studies in mice with induced obesity show that adipose tissue macrophages (ATMs) promote adipose tissue inflammation and insulin resistance. We sought to characterize macrophage populations in human subcutaneous and omental adipose tissue and determine their relationship to metabolic abnormalities in obesity. Research Design and Methods: Adipose tissue was obtained from lean and obese women undergoing bariatric surgery. Metabolic markers were measured in fasting serum and ATMs characterized by histology, flow cytometry and tissue culture studies.

Results: ATMs comprised CD11c+CD206+ cells in ‘crown’ aggregates and solitary CD11c- CD206+ cells at adipocyte junctions. In obese women, CD11c+ ATM density was greater in subcutaneous than omental adipose tissue and, in contrast to CD11c- ATM density, correlated with indices of insulin resistance. CD11c+ ATMs expressed higher levels of integrins and antigen presentation molecules than CD11c- ATMs, indicative of an activated, pro-inflammatory phenotype. Furthermore, after isolation and culture, CD11c+ ATMs were distinguished by higher secretion of interleukin (IL)-1β, IL-6, IL-8, IL-10, tumor necrosis factor-α and CC chemokine ligand-3. CD11c+ ATMs were enriched for mitochondria and for RNA transcripts encoding mitochondrial, proteasomal and lysosomal proteins, fatty acid metabolism enzymes and T-cell chemoattractants, whereas CD11c- ATMs were enriched for transcripts involved in tissue maintenance and repair. Conclusions: These findings identify pro-inflammatory CD11c+ ATMs as markers and potential mediators of insulin resistance in human obesity. In addition, the machinery of CD11c+ ATMs suggests that they process lipolipid and could initiate adaptive immune responses.

Andrew Cook
Urokinase-plasminogen activator derived from a bone marrow cell is required for the development of immune complex-mediated arthritis models

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Arthritis and Inflammation Research Centre, Department of Medicine, Royal Melbourne Hospital, University of Melbourne.

Purpose: To determine the requirement for urokinase-plasminogen activator (u-PA) in immune complex-mediated arthritis models and the cellular source of u-PA required for disease development.

Methods: The K/BxN serum transfer model of arthritis was induced in u-PA−/− and C57BL/6 (C57) mice and arthritis development assessed by clinical score and histology. To determine the cellular source of u-PA required for the development of collagen-induced arthritis (CIA), bone marrow (BM) from C57 or u-PA−/− donor mice was transferred to irradiated u-PA−/− or C57 recipient mice, and, following reconstitution of the BM, the chimeric mice were immunized for CIA and disease monitored. Gene expression of inflammatory and destructive mediators was measured in joint tissue by quantitative PCR.

Results: u-PA−/− mice were resistant to K/BxN serum transfer arthritis development. By histology, the joints looked normal with no significant cellular infiltration, cartilage damage or bone erosions. u-PA−/− mice also develop very mild CIA (1), which, similar to the K/BxN serum transfer model, is immune complex mediated. u-PA−/− mice reconstituted with C57 BM (C57→u-PA−/−) developed CIA with an increased clinical severity of disease compared with u-PA−/−→u-PA−/− sham chimeras, whereas C57 mice reconstituted with u-PA−/−→BM (u-PA−/−→C57) developed mild CIA compared with C57→C57 sham chimeras. By histology, C57→u-PA−/−→C57 chimeras were indistinguishable in terms of cell infiltration, cartilage destruction, proteoglycan depletion, and bone erosions to C57→C57 chimeras, while the u-PA−/−→C57 chimeras showed minimal inflammation, cartilage damage or bone erosion similar to u-PA−/− mice. TNF, IL-1 and IL-6 gene expression was increased in the joint tissue of arthritic C57→u-PA−/−→C57 chimeras compared with u-PA−/−→C57 mice. Likewise, MMP-3, -9, and -13 gene expression was also increased in the joint tissue of C57→u-PA−/−→C57 chimeras compared with u-PA−/−→C57 mice.

Conclusions: u-PA is required for the development of immune complex-mediated arthritis, including both the K/BxN serum
Macrophages are key mediators of the immune response to infection by virtue of, amongst other things, their ability to secrete inflammatory cytokines (e.g., TNF). The activation of macrophages by pathogens is largely mediated by Toll-like receptors (TLRs). TLRs recognise specific pathogen-associated molecular patterns (PAMPs), such as bacterial LPS. Because macrophages are likely to encounter multiple PAMPs during an infection, a number of TLR signalling pathways could become activated. The order and timing of TLR activation, together with signalling crosstalk between TLR pathways, may therefore dictate the nature of the inflammatory response. Indeed, signalling crosstalk between TLRs can result in different outcomes including tolerance and the priming of inflammatory reactions. Tolerance is an adaptive mechanism that prevents macrophages from becoming reactivated. Conversely, priming results in an amplified inflammatory response when macrophages subsequently encounter a different PAMP. The balance between tolerance and priming is crucial as the excessive systemic release of inflammatory cytokines can result in septic shock, whereas a blunted inflammatory response may be insufficient to eliminate the pathogen. Members of the IRAK family of protein kinases are key components of TLR signalling pathways. The rapid degradation of IRAK-1 following its PAMP-induced activation has been proposed to represent a major mechanism for tolerance. However, we have established that IRAK-1 degradation is insufficient to cause tolerance towards bacterial DNA or LPS, most likely because IRAK-2 can mediate TLR signalling in its absence. Significantly, tolerance coincided with IRAK-4 down-regulation, which occurred at the protein level via proteolytic degradation as well as at the mRNA level. Differences in the kinetics and extent of IRAK-4 down-regulation by PAMPs may allow macrophages to temporally modulate their inflammatory response. In the setting of sequential TLR activation by different PAMPs, LPS primed the subsequent inflammatory response of macrophages to bacterial DNA. The priming effects of LPS appear to be explained in part by LPS antagonising signalling by the macrophage growth factor, M-CSF, and by potentiating the activation of the stress kinase, JNK. Given that JNK can regulate cell survival through its activation of pro-apoptotic pathways, the priming of JNK activation may also be important in determining if activated macrophages subsequently undergo apoptosis, particularly in the context of infection by intracellular pathogens.

11  Marion Robertson

Gentamicin management – improvement following deployment of electronic decision support


The Royal Melbourne Hospital

Aim: To evaluate the impact of implementation of an electronic prescribing guideline and first dose calculator on management of gentamicin. Methods: We carried out a 6-week audit of gentamicin prescribing in 2007 following implementation of the guideline and first dose calculator in January 2005. We compared results with a pre-implementation audit from 2004. We collected data on demographics, details of the gentamicin prescription, indication and contraindications for use, past adverse drug reactions, renal function, and recent microbiology. We assessed concordance for first dose, duration of course and therapeutic drug monitoring (TDM).

Results

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>132</td>
<td>107</td>
</tr>
<tr>
<td>Female</td>
<td>55 (42%)</td>
<td>54 (50%)</td>
</tr>
<tr>
<td>Age &gt;65 years</td>
<td>48 (36%)</td>
<td>48 (45%)</td>
</tr>
<tr>
<td>Treating unit = surgical</td>
<td>104 (79%)</td>
<td>67 (63%)</td>
</tr>
<tr>
<td>Indication = prophylaxis</td>
<td>41 (31%)</td>
<td>53 (50%)</td>
</tr>
<tr>
<td>Concordant for first dose</td>
<td>40 (30%)</td>
<td>62 (58%)</td>
</tr>
<tr>
<td>Age &gt;65 and first dose too high</td>
<td>28 (58% of 48)</td>
<td>14 (29% of 48)</td>
</tr>
<tr>
<td>Renal impairment and dose too high</td>
<td>22 (61% of 36)</td>
<td>13 (33% of 39)</td>
</tr>
<tr>
<td>Age &gt;65 and duration &gt;48 hours</td>
<td>8 (17% of 48)</td>
<td>6 (13% of 48)</td>
</tr>
<tr>
<td>Therapeutic drug monitoring (TDM) recommended</td>
<td>74</td>
<td>30</td>
</tr>
<tr>
<td>Any TDM done</td>
<td>57 (77% of 74)</td>
<td>27 (90% of 30)</td>
</tr>
<tr>
<td>TDM started on second dose as advised</td>
<td>16 (28% of 57)</td>
<td>18 (67% of 27)</td>
</tr>
<tr>
<td>Concordance for TDM overall</td>
<td>5 (7% of 74)</td>
<td>8 (27% of 30)</td>
</tr>
<tr>
<td>Electronic first dose calculator used#</td>
<td>Not implemented</td>
<td>6 (6%)</td>
</tr>
</tbody>
</table>

*p<0.05;  **p<0.002, †p<0.03, ‡p<0.01

# episodes where patient identifier (ID) entered, but note that ID not required to use calculator or view guidelines

Conclusion: We found statistically significant improvements in concordance with guidelines for gentamicin use after deployment of the electronic system. This could not, however, be attributed to the use of the first dose calculator alone.
Melbourne Health Research Week 12 – 18 June 2009

Segmental distribution of multiple naevi associated with malignant melanoma

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Segmental distribution of skin lesions has been recorded in many genodermatoses. This presentation is unusual in malignant melanoma. We report a segmental distribution of melanoma, naevi and pigmentary change in 5 unrelated individuals. This case series describes a new and distinctive phenotype, precursory to melanoma – a segmental distribution of increased susceptibility to both benign and malignant melanocytic tumours. This predisposition to melanoma may be mediated via increased susceptibility to UV light, suggested by the presence of increased solar lentigines within the segmental area. The phenotype presented here would not fit with Mendelian inheritance, and somatic mosaicism or epigenetic silencing of a tumour suppressor gene is more likely to explain the limited distribution of both the primary and secondary lesions. Individuals encountered with similar patterns of pigmentation and naevi should undergo regular dermatologist review as well as complete sun avoidance of this area of skin, in an attempt to minimise the risk of malignant melanoma. Furthermore, there appears to be a clear phenotype which provides an opportunity to search for the underlying genotype.

14 Benjamin Namdarian

Circulating endothelial cells: Prognostic markers in urological malignancies.

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Introduction: Clinical management of patients with prostate cancer is punctuated by critical decision points, spread across the entire course and spectrum of the disease. Over the past few decades, a substantive work has generated various prognostic factors for individual outcomes, which have developed into sophisticated predictive methods in widespread clinical use today. However, individual patients do not always behave as anticipated, which can lead to erroneous undertreatment or overtreatment. Consequently, a continual need exists to identify improved predictors of disease outcome to aid clinical decision-making. Vascularity in the primary, prostate tumor has been established as a predictor of poor outcomes and recent evidence suggests that circulating endothelial cells (CECs) and progenitors (CEPs) are promising surrogate markers of vascularity in the cancer setting. We seek to investigate the relevance of CECs and CEPs as prognostic markers in prostate cancer. Materials and Methods: CEC and CEP levels were enumerated by FACS Analysis, weekly, in SCID mouse xenograft models including: (1) Controls, (2) LNCaP and (2) PC3 prostate cancer, (3) MDA-MB-231 breast cancer and (4) Lewis Lung carcinoma positive control cell lines. Mean comparisons were made between cohorts with correlations noted between CEC levels and tumour variables. Results: CEC levels were significantly elevated in the (1) LNCaP prostate model, 176.7 / μL (p = 0.004); (2) PC3 prostate model, 66.37 / μL (p = 0.009); (3) MDA breast model, 62.22 / μL (p = 0.017) and (4) Lewis Lung model, 131.0 / μL (p = 0.001) as compared to control mice 37.64 / μL at experimental endstage. In addition, CEP levels were significantly elevated in the (1) LNCaP prostate model, 1.90 / μL (p = 0.004) and the (2) Lewis Lung model, 2.48 / μL (p = 0.002) as compared to control mice 0.78 (0.62 – 0.83). Importantly, significant correlations were noted between CEC levels and tumour weight and volume as well as microvessel density (p < 0.05). Preliminary clinical data (n=21) suggests a similar trend in human disease. Conclusion: CEC levels are increased in prostate cancer and the levels are influenced by tumour vascularity in the cancer setting. We seek to investigate the relevance of CECs and CEPs as prognostic markers in prostate cancer.

15 Wei-Ren Pan

The lymphatic drainage of the nasal fossae and nasopharynx: A preliminary anatomical and radiological study with clinical implications.

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Background: The lymphatic pathways of the nasal cavity are of enormous clinical importance. To date there has been no accurate radiographic record of these pathways. Methods: Four halves of the head and neck from two fresh human cadavers were studied. Using the 6% hydrogen peroxide to find the inflated initial lymph vessels. A suitable vessel was injected with a radiopaque solution. Results: The capillary network arises from the mucous membrane of the atrium, the turbinates, the floor of the nasal cavity and the nasopharynx. They drain to the lateral pharyngeal and retropharyngeal lymph nodes. One lymphatic communication is at the junction of the lateral wall of the turbinates and nasopharynx. Another communication was found between two groups of lymph nodes situated between the origin of the facial artery and the bifurcation of the carotid artery. Multiple first tier lymph nodes were found in the lateral pharyngeal and retropharyngeal groups. Conclusions: A rich avascular lymph capillary network exists in the mucous membrane and two major lymph collecting vessels course through the parapharyngeal space to multiple first tier lymph nodes. These results, previously not described, may help with the treatment of patients with cancer of the nasal fossa and nasopharynx.
16  Amir Zayegh
Does widening the criteria for needle biopsy in the assessment of microcalcifications in a breast screening program lead to increased detection of ductal carcinoma in situ (DCIS) and small invasive cancers?
Rose AK, Mou A, Yang N, ZAYEGH A.
North Western BreastScreen (NWBS); Department of Radiology, Royal Melbourne Hospital.

Aim: To determine whether there has been an increase in DCIS and small invasive cancer detection after the change in biopsy criteria, and whether any lesion characteristics are associated with the new criteria. Background and Methods: The indication for biopsy of microcalcifications in population based mammographic screening programs has been traditionally based on morphology allowing the differentiation of benign from suspicious lesions. Criteria included size, shape, distribution and new development. However at NWBS, on a background of steadily falling DCIS detection rates over a six year period, it was decided a more aggressive approach was required in the assessment of microcalcifications, these lesions being the most frequent associated with DCIS. Consequently, all microcalcifications were biopsied unless they displayed obvious layering, were scattered or had no detectable change over a 5 year period. Assessment outcomes were compared in the 12 months before and after implementation of this new policy (February 2005-06 vs February 2007-08). Results: 112 core biopsies for microcalcification were performed between ½/05 – 31/1/06, compared with 233 between ½/07 – 31/1/08. In 2005, the DCIS and small invasive cancer detection rate was 40/34069 (11.7 lesions/10000 screened women). After the change of policy, the number of cases of DCIS and small invasive cancers doubled to 88/35927 (24.5 lesions/10000 women screened). There was no significant difference in the proportion of benign and malignant outcomes between 2005 and 2007 (a benign:malignant ratio of 1.9:1 in 2005, compared to 1.7:1 in 2007). Had the change in practice not been warranted it could be expected that the proportion of benign outcomes would have increased i.e. more unnecessary biopsies. Many lesions were extremely small and difficult to detect at screening. However, this did not correlate with a large increase in benign or low grade lesions. Conclusion: Changing the indications for biopsy, with a more aggressive approach in the assessment of microcalcifications by needle biopsy, resulted in a 2 fold increase in the detection of DCIS and small invasive cancers, with no significant change in the benign: malignant biopsy ratio. We have also found that traditional criteria such as size are unreliable predictors of benign or malignant disease. The change in practice represented a significant departure from traditionally held approaches to the management of microcalcifications in a screening program. If the hypothesis is true, there are statewide implications for training, staffing and funding to support the change in biopsy activity.

17  Paul Tescher
Surveillance of FAP: A prospective blinded comparison of capsule endoscopy and other GI imaging to detect small bowel polyps.
TESCHER P, Macrae FA, Speer T, Stella D, Gibson R, Tye-Din JA, Srivatsa G, Jones IT, Marion K.
The Royal Melbourne Hospital, University of Melbourne

Background: Familial adenomatous polyposis (FAP) is a hereditary disorder characterized by polyposis along the gastrointestinal tract. Information on adenoma status below the duodenum has previously been restricted due to its inaccessibility in vivo. Capsule Endoscopy (CE) may provide a useful adjunct in screening for polyposis in the small bowel in FAP patients. Objective: To evaluate the effectiveness of CE in the assessment of patients with FAP, compared to other imaging modalities for the detection of small bowel polyps. Design: Comparative, prospective, blinded. Setting: Patients with FAP and polyps previously identified in the duodenum. Patients: 20 consecutive patients presenting for routine surveillance of polyps at The Royal Melbourne Hospital. Interventions: Magnetic resonance image of the abdomen, barium small bowel follow-through (SBFT) study, CE and upper gastrointestinal side-viewing endoscopy. Main Outcome: Location, number and size of polyps detected by each imaging modality. Measurements: Size of polyps in mm, number of polyps, location. Results: Within the stomach, upper gastrointestinal endoscopy found more polyps than other forms of imaging. SBFT and MRI generally performed poorly, identifying fewer polyps than both upper gastrointestinal and capsule endoscopy. CE was the only form of imaging that identified polyps in all segments of the small bowel as well as the only form of imaging able to provide multiple findings outside the stomach/duodenum. Limitations: Small, single centre cohort study. Conclusion: CE provides important information on possible poly development distal to the duodenum, which may lead to surgical intervention. The place of CE as an adjunct in surveillance of FAP needs consideration and confirmation in replication studies.

18  Nigel Jones
Repeated restraint stress accelerates the development of limbic epilepsy in rats
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1 Department of Medicine, University of Melbourne; 2 Department of Psychiatry, Fitzroy; 3Department of Pharmacology, University of New South Wales; 4 Department of Anatomy and Cell Biology, University of Melbourne.

RATIONALE: We have previously demonstrated that corticosterone supplementation, used as a model of chronic stress/depression, accelerates epileptogenesis in the amygdala kindling rat model of temporal lobe epilepsy (TLE). This study extended this to examine whether an actual stressor, physical restraint, could influence the development of experimental epilepsy. METHODS: Female Non-Epileptic Control rats 10-13 weeks of age were implanted with a bipolar electrode into the left amygdala, and, following recovery, were randomly assigned into stressed (n=13) or non-stressed (n=13) groups. All rats underwent conventional amygdala kindling (2 electrical stimulations per day) until 5 Class V seizures had been experienced (‘fully kindled’). Stressed rats were exposed to 30 minutes restraint immediately prior to kindling stimulations, and blood samples taken at appropriate intervals to assess stress responsivity. Non-stressed rats received control handling prior to stimulation. RESULTS: Restraint stress increased circulating corticosterone levels (pre-stress: 122±17 ng/ml; post-stress: 632±33 ng/ml), and no habituation to repeated episodes of restraint was observed over the experiment. Stressed rats reached the fully kindled state in significantly fewer stimulations than non-stressed rats (20±1 vs 30±3 stimulations; p<0.015; ANOVA). Further, length of each electrographic seizure was significantly longer in stressed rats (p=0.001; ANOVA). CONCLUSION: The current data suggest that chronic stress accelerates the development of limbic epilepsy, an effect which may be related to elevated corticosterone levels. This may have implications for understanding the effects of chronic stress and depression in initiating and/or exacerbating TLE.
19  Sandra Petty  
Bone health and age of commencement of anti-epileptic medication: An AED-discordant twin and sibling pair study  

PETTY S 1, Paton L 1, Sakellariades M 1, Lawrence K 2, Berkovic S 2, Fedorova T 3, Sambrook P 3, O’Brien T 1,4, Wark, JD 1,5.
1 Department of Medicine RMH, The University of Melbourne; 2 Epilepsy Research Centre, Austin Health, The University of Melbourne; 3 The Kolling Institute of Medical Research, Sydney; 4 Department of Neurosciences, The Royal Melbourne Hospital; 5 Bone and Mineral Research, The Royal Melbourne Hospital.

BACKGROUND: Patients taking anti-epileptic drugs (AEDs) have increased fracture risk. Data is limited regarding effects of age of commencement of AEDs, particularly with respect to AED-use at younger ages and achievement of peak bone mass. AIM: To investigate: (1) bone health in gender-matched, AED-discordant twin/sibling pairs; (2) associations of age of onset of epilepsy with bone mineral density (BMD), stratifying pairs where AED-user commenced AED before or after 18 years, when majority of bone mass is attained. METHOD: Fifty AED (and epilepsy)-discordant pairs were studied. DXA scans were acquired (Hologic 4500A/1000W), measuring BMD at lumbar spine (LS), total hip (TH), femoral neck (FN), total forearm (FA) and total body bone mineral content (TB BMC). Data was adjusted for age, height, weight. Paired t-tests calculated mean within-pair differences (MWPD). Independent t-tests compared within-pair differences of pairs where the AED-user commenced AED under versus over 18 years. RESULTS: 40 female, 10 male pairs (17 monzygous, 15 dizygous twins and 18 sib pairs), mean (SD) age 44.5 (15.8) years were studied. For the 27 pairs where the AED-user commenced AED before 18 years of age, there was a significant MWPD in height (-0.02m, p=0.021). There were no significant MWPDs in age, height, BMI, calcium intake, total fat mass or total lean mass. For 23 pairs where the AED-user commenced AED ≥18 years of age, there was a significant MWPD in calcium intake (+278mg, p=0.021). There were significant differences in the MWPDs between the groups at the TH, FN and in TB BMC, where AED-users who commenced therapy aged less than 18 years had lower scores compared to pairs where the AED-user commenced after 18 years of age. There was no significant difference in AED duration [Mean (SD) AED use: <18y: 20.5 (14.6)y; ≥18y: 15.2 (12.1)y, p=0.170.] CONCLUSION: Commencement of AED therapy at a younger age is associated with shorter stature, reduced BMD at total hip, femoral neck and reduced TB BMC. Whether this is primarily attributable to an AED-associated reduction in peak bone mass or is influenced by duration of the epileptic disorder requires further, longitudinal studies.

20  Megan Oliva  
EEG dipole source localisation in non-lesional TLE with and without hippocampal sclerosis  

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Aim: A subgroup of patients with non-lesional temporal lobe epilepsy (NLTLE) have no evidence of hippocampal sclerosis (HS) on MRI. It is controversial whether they represent a different clinicopathological syndrome from that of mesial temporal lobe epilepsy with HS. In this study EEG dipole source localisation was used to compare underlying dipoles for interictal spikes between NLTLE patients with HS (HS+) and those without HS (HS-). The study also compared patients who had a good versus poor outcome following epilepsy surgery. Method: EEG dipole source localisation of interictal epileptiform spikes recorded during routine prolonged video-EEG monitoring was performed from 22 consecutive HS+ and 12 HS–NLTLE patients utilising NEUROSCAN and Curry software. EEG was acquired using 29 scalp electrodes, including an inferior temporal row. Up to 13 spikes per patient were averaged and sources localised using a boundary element model based on the patients volumetric MRI. Results: 21/34 patients (62%) had dipoles localised to the epileptogenic temporal lobe. The grouped average spikes for the HS+ and HS- groups differed in their localization, as did the good and poor surgical outcome groups. Conclusion: The dipole for interictal spikes differs between HS+ and HS- patients, suggesting that the cerebral generators do differ between these subgroups of patients. The difference in the dipoles between patients with a good vs. poor outcome following temporal lobectomy also suggests that source localization of interictal EEG spikes may be helpful in patient selection for surgery.

21  Slave Petrovski  
Predicting AED response: Combining a pre-treatment neurocognitive score with a multigenic model to provide predictive value for seizure recurrence in newly treated epilepsy  

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Background: We have recently reported the development of a multigenic classifier to predict pharmacoresponsive outcome in a cohort of Australian newly-treated epilepsy patients. However, it is clear that genomic variation will not explain all inter-individual variability in response to AEDs, with disease, environmental and other co-variates likely to play a role. As there is an increasing recognition of the role that psychological stress may play in provoking seizures or aggravating epileptogenic processes we have examined the use of the A-B Neuropsychological Assessment Scale (ABNAS), a validated cognitive and behavioural function scale, as a predictor of seizure control success in a prospective cohort of patients. Greater neurocognitive symptomatology may reflect more widespread brain dysfunction and/or greater stress levels, and therefore potentially a higher chance of seizure recurrence. Methods: 138 newly treated epilepsy patients completed an ABNAS questionnaire prior to anti-epileptic drug (AED) therapy and were then prospectively followed for 12 months. Patients were classified as medication responsive or non-responsive based on whether they had one or more recurrent seizures despite treatment, not explained by medication non-compliance or other significant provoking factors. The pre-treatment ABNAS scores and additional covariates were compared between AED responsive and non-responsive patients. Furthermore, the multigenic model was incorporated into a combined logistic regression model. Findings: AED non-responsive patients (n=45)
had a significantly higher pre-treatment ABNAS score (i.e. worse neurocognitive symptomatology) than patients in whom seizures were controlled (n=93) (median, 10 vs. 5, P=0.005, Mann-Whitney U test). MRI lesion (p=0.003) was also correlated with seizure recurrence. Logistic regression analysis demonstrated that the ABNAS score and the presence of an MRI lesion were predictive of treatment outcome independent of each other, and of the multigenic classifier that our group recently described from this cohort. Logistic model predictive performance: sensitivity 91%; specificity 64%; PPV 84% and NPV 78% for pharmacoresponsiveness. Interpretation: The ABNAS neurocognitive questionnaire administered pre-treatment has prognostic value regarding successful seizure control in patients with newly treated epilepsy. Further work is required to determine the contribution of mood versus underlying brain dysfunction in explaining this association. Importantly this study also shows that multiple types of information should be incorporated into model development in order to develop the most sensitive and specific predictive models for treatment outcomes. This is consistent with the concept that the determinants of pharmacoresistance to AED in patients with epilepsy are multifactorial, and therefore no one data type is likely to provide optimal prediction across multiple individual patients.

22 Rimma Goldberg
Outcomes of surgical treatment for trigeminal neuralgia
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This retrospective, descriptive, clinical study compares the outcome of microvascular decompression (MVD) and radiofrequency rhizotomy (RF) performed for trigeminal neuralgia (TN) over 10 years at The Royal Melbourne Hospital and Melbourne Private Hospital. We compare our results with the literature, with a particular focus on outcomes in older patients. We analysed the records of 100 patients identified from the departmental database, who underwent surgical treatment for TN between 1994 and 2004. A telephone interview was used wherever possible to extend follow-up. Patients undergoing RF were significantly older than those undergoing MVD (p<0.0001). MVD provided a significantly longer pain free interval than RF

23 Michella Ananda-Rajah
Active screening & isolation is not required to control methicillin resistant Staphylococcus aureus (MRSA) in an endemic high-risk setting: an 8-year time series analysis from an Australian tertiary hospital intensive care unit

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Objectives: Intensive efforts to control nosocomial MRSA remain controversial. We report a decline in MRSA blood stream and other clinical isolates from our ICU in the absence of specific interventions against MRSA. Methods: Retrospective time series analysis of Staphylococcus aureus (SA) isolates from the Royal Melbourne Hospital ICU 2000-2007. Clinical isolates were electronically extracted from the microbiology database. Screening swabs and duplicate isolates collected within 7 days from sterile and 30 days from non-sterile sites respectively were excluded. Results: The number of MRSA clinical isolates/1000 occupied ICU bed days within consecutive 6 month periods from 2000-2007 is reported in table 1. The number of MRSA blood culture isolates (unadjusted for occupancy) per year from 2000-2007 is also presented in table 1. Trauma, cardiothoracic & other surgical patients comprised 70% of ICU admissions/year (mean). No MRSA specific infection control program involving active screening, targeted patient decolonisation or isolation was implemented in the ICU. General measures introduced included an antibiotic stewardship program using a computerized tool to guide antibiotic selection (Jan 2001) regular ICU ward rounds by the infectious diseases service (from April 2004), temporary screening and barrier nursing of Acinetobacter colonised patients to control an outbreak of non-multiresistant Acinetobacter in the ICU (Nov 2004-Dec 2005) and hospital wide hand hygiene education (from April 2005). Conclusion: Sustained control of endemic MRSA was achieved by general quality improvement measures and limited infection control interventions. Intensive and expensive MRSA control measures may not always be necessary.

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<th>6 monthly time period ending</th>
<th>MRSA clinical isolates/1000 ICU bed days</th>
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Background and Aims: HCV treatment uptake has been limited in people on drug dependency treatment due to concerns regarding efficacy, adherence and adverse effects, especially psychological effects such as depression and the inherent increased suicide risk. This study aimed to evaluate these parameters in patients receiving opioid pharmacotherapy.

Methods: Fifty-three patients at four Australian sites received Peg-2a 180 ug/week and RBV 800-1200 mg/day for 48 weeks (22 genotype 1(G1) or 24 weeks (31 G non1). HCV RNA was assessed at week 12 (EVR), end-of-treatment (ETR) and 24 weeks post-treatment (SVR). Depression was assessed using the Beck Depression Index (BDI II). Adherence was defined as taking 80% of both drugs for 80% of the planned duration. Results: Seventy-nine percent of patients were male, with a mean age of 37.9 years. 75% were receiving methadone and 25% buprenorphine, and 36 % had injected in the previous 6 months. Fifty one percent of patients had high viral load (>400,000 IU/ml) and 27% had F3/4 fibrosis. Sixty-eight percent of G1 patients achieved EVR. SVR by ITT analysis was 36% for G1 and 71% for G non1 patients respectively. Twenty-five percent of patients injected during the treatment or post-treatment follow-up, with SVR of 63% among injectors and 53% among non-injectors, respectively. Only two patients relapsed, both G1, of which one was an active injector while the other was not. Sixteen patients (12 G1 and 4 G non1) withdrew prematurely from treatment: 5 due to safety and 11 due to non-safety reasons. Adherence to therapy was 59% for G1 patients and 84% for G non1 patients. There were no significant differences in mean BDI scores between or within groups at either beginning of treatment or at week 24. Conclusions: HCV treatment of patients undergoing opioid pharmacotherapy has comparable efficacy to non-pharmacotherapy patients. There was good treatment adherence, no significant increase in depression and similar levels of withdrawals due to adverse events. Adherence was better in patients receiving 24-week therapy and post-treatment reinfection rates were low. HCV treatment should be considered suitable for patients on opioid pharmacotherapy including selected active injectors.

Patterns of hepatitis B surface antigen (HBsAg) prevalence by birth cohort in the Victorian Hepatitis B Serosurvey 1995 – 2005 are suggestive of underlying population trends related to changing patterns of migration into Australia. We have analysed these trends and compared them with migration records since 1945 by source country HBsAg seroprevalence and with national notifiable diseases surveillance system data. Once time lags between birth, age at migration and age at notification are incorporated, striking correlations between these different data sources are observed. To more rigorously assess the nexus between migration and notifications, we undertook simple univariate linear regression modelling and established strong statistical correlation between estimated numbers of HBsAg positive settlers and notifications of unspecified (chronic) HBV infection ten years later. Using this linear model, we present projections of notifications until 2016 and discuss recent changes to migration policy that may result in inaccuracies in the model presented. Notwithstanding these, our model suggests more than 50,000 Australians who settled in the last decade have not yet been notified as chronically infected with HBV. Failure to diagnose these infections will lead to adverse outcomes for individual patients, and ongoing transmission of infection.
Abrogation of the major splice acceptor site reduced HBV replication and co-transfection with spliced DNA increased HBV replication. These findings are significant as increased HBV DNA replication is the single-greatest risk factor for developing progressive liver disease and HCC. As splicing also results in increased production of linear HBV DNA, future studies will focus on the association of splicing, DNA integration and HCC.

27  Kathryn Ellis

The AIBL study: baseline data from a multi-centre, prospective: Longitudinal study of ageing in 1100 volunteers

Ames D (1), Rowe C (2), Masters C(3), Martins R (4), Szeke C (5), Hudson P (6), Milner A (6), ELLIS KA (7), AIBL study group (8).

The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing (AIBL) is a three-year prospective longitudinal study of over 1100 volunteers from a cross-section of Australia’s elderly population. The cohort comprises 1112 volunteers aged over 60 years [211 patients with AD (mean age 78.0 + 8.6 years), 133 patients with MCI (mean age 75.7 + 7.8 years), and 768 healthy volunteers (HV: 70.0 + 7.0 years)]. At baseline, volunteers completed lifestyle questionnaires and underwent comprehensive clinical and neuropsychology assessment. An 80ml blood sample was provided for clinical pathology, biomarker analysis, and storage in liquid nitrogen. 286 participants received a [C-11] PIB-PET scan (a measure of in vivo amyloid) and a MRI scan. In addition, 100 received scans of body composition (DEXA) and 91 participated in actigraph monitoring of activity levels. AD patients performed worse on all neuropsychological measures compared to both HV and MCI groups, and MCI patients showed greater impairment than HVs (all p< 0.05). Neuroimaging subgroup results revealed a significant difference between groups in the PiB +ve volunteers (98% of AD patients, 64% of MCI patients and 29% of HVs). HVs with an apolipoprotein-E (ApoE) ε4 allele were significantly more likely to be PiB+ve than ApoE ε4 negative HVs (49% compared to 21%, respectively). Cross sectional analysis of baseline data will reveal links between cognition, brain amyloid burden, structural brain changes, biomarkers, and lifestyle. An 18-month follow-up will reveal risk factors associated with cognitive decline and identify early diagnostic indicators of AD. These findings will assist development of techniques to identify factors which may delay onset of AD, and provide a cohort suitable for future intervention studies.

28  James Watt

Who’s missing out on specialist palliative care at Australia’s busiest hospital and why?

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Background: The Royal Melbourne Hospital (RMH) services a metropolitan area of nearly one million residents and the hospital-based palliative care consultative service receives over 1000 referrals per year. Currently, this expanding service is made up of medical and nursing staff and can assist with pain and other symptom management, setting appropriate goals of care, referral to community or inpatient palliative care units and provision of support to patients and their caregivers. In 2007 funding was obtained from the Victorian Department of Human Services’ Turning Policy into Practice Grant Scheme to conduct a year long quality improvement project. The aim of this project was to improve access for patients with advanced illness at the end-of-life to specialist palliative care within the RMH. Methods: A multi-methods approach was taken incorporating: a literature review investigating issues of referral and access to palliative care; a retrospective chart-audit using the Liverpool Care Pathway to assess quality of end-of-life care; and semi-structured interviews with clinicians to collect data regarding their understanding about palliative care and how referral decisions are made. Results: The literature review identified tools that could be used in the development of referral guidelines and identified barriers to referral. The chart audit demonstrated a wide variation in referral practices among treating teams, with overall, only 42% of dying patients referred. The audit also highlighted a number of deficiencies in the care of dying patients within the hospital, however, referral for palliative care consultation was associated with improvements in: implementation of appropriate end of life medication orders, cessation of futile treatment/interventions, and communication with patients and families. Several key themes emerged from the interviews with clinicians, including uncertainty as to the role of palliative care, and discrepancy between medical and nursing views of the utility and timing for palliative care. Conclusions: The findings demonstrate both the need for more frequent and/or earlier referral of dying patients and the need for generalist staff to become more skilled in the delivery of palliative care. Referral guidelines were developed as an outcome of the project but require further evaluation. The project findings have provided insights into how palliative care education and the introduction of referral guidelines can be effectively approached.

29  Francis Connolly

Do routinely repeated CT scans in traumatic brain injury influence management? A prospective study in a level 1 trauma center.


Royal Melbourne Hospital

Background: Previous research using serial computed tomography (CT) scans has demonstrated that following head trauma, intracranial injuries can progress without change in clinical condition. On this basis, several authors have advocated the routine repetition of CT brain scans in head-injured patients to monitor for clinically undetectable progression of an intracranial injury. Several retrospective analyses in major trauma centres worldwide have suggested that only those patients with clinical deterioration require surgical or medical intervention, but only one group of authors has prospectively examined this hypothesis in a small cohort of patients. Methods: We prospectively observed 640 patients who were admitted to the Royal Melbourne Hospital for at least 24 hours following an initial CT brain scan ordered due to blunt head trauma. If a patient underwent subsequent CT brain scans, we noted whether the scan was ordered following a clinical deterioration or performed routinely. Post-operative scans were noted but they are not included in our analysis. Results: In total 190 repeat CT brain scans were ordered without any clinical deterioration, of which 114 were the initial repeat scan. None of routine scans demonstrated a radiological deterioration requiring acute alteration of the patient’s management either medically or surgically. Conclusion: Performing repeat CT scans routinely carries a significant burden in terms of radiation to the patient,
resource use and medical risks to severely unwell patients whilst in transit to and from the CT scanner. In a major tertiary hospital with staff trained in performing regular neurological observations and the facilities to perform urgent craniotomy rapidly should the need arise, the routine use of repeat CT brain scans without clinical indication for head trauma patients may not be necessary.

**30** Mingwei Joe Ye

Comparison of the accuracy of digital with analog preoperative x-ray templating for total hip arthroplasty

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University of Melbourne *, Department of Orthopaedics The Royal Melbourne Hospital **

Introduction: With the advent of digital radiology, the Department of Orthopaedics at Royal Melbourne Hospital (RMH) has introduced digital templating for preoperative planning of total hip arthroplasty (THA). However, it is not clear if digital preoperative templating for THA is safe and accurate. Prior studies comparing the accuracy of digital templating with conventional analog templating had contradictory results. Therefore, this study was done to compare the accuracy of digital and analog templating in planning THA. Methods: An ethics approval was obtained from the Human Research Ethics Committee as a quality assurance project. A total of 90 patients were recruited for this study. 68 patients had analog templating while 22 patients had digital templating performed. In the analog plans, patients recruited underwent THA during the period of January 2006 to October 2007. In the digital plans, patients recruited underwent THA during the period of April 2008 to February 2009. The templated hip sizes were compared with the actual hip implants inserted. A retrospective review of medical records was made to obtain the sizes of hip implants inserted during THA. Accuracies of both templating methods were compared in four outcomes: 1. prediction of acetabular cup size 2. prediction of femoral stem size 3. prediction of femoral offset 4. prediction of femoral neck length. Results: Digital templating was more accurate than analog templating in all the outcomes assessed except predicting neck length. In predicting the exact acetabular cup size, the accuracy of digital templating was 45.5% while that of analog templating was 30.8%. Digital templating (45.5%) was also more accurate than analog templating (39.7%) in predicting the exact stem size. Of the four outcomes, statistical significance was obtained only for prediction of offset (p-value = 0.049). Conclusion: Although not statistically significant, there was a trend to increased accuracy with digital templating in all outcomes except predicting neck length. We conclude that digital templating is at least as safe and accurate as analog templating in planning THA. Currently, digital templating improvements and functionality are in development. It is likely that in time digital templating will become the mainstay of preoperative planning in most hospitals.

**31** Jonathan Knott

What factors determine the time to arrival at the emergency department following the onset of cerebrovascular accidents?

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INTRODUCTION: Stroke is a leading cause of adult death and disability worldwide. Approximately 50,000 events occur annually in Australia. Early hospital arrival is important for optimal management of stroke patients but there has been limited assessment of patient variables affecting time to presentation. METHODS: An observational study conducted over a non-consecutive four-month period at RMH. Of 295 stroke patients presenting to the ED, 172 were studied using information from patient interview and review of medical records. The primary endpoint was time to arrival (TTA) at the ED; the secondary endpoint was TTA greater than two hours. Factors found to be significant in the univariate analyses were put through multivariate regression models. RESULTS: The median TTA was 119 min. Factors significantly associated with increased TTA and TTA greater than two hours included diagnosis of ischaemic stroke, night-time onset, being alone at symptom onset, indefinite knowledge of stroke, nausea or vomiting, visiting family or friends, and visiting the local medical officer (LMO). Unconscious collapse calling the ambulance and coming into the hospital directly were associated with both decreased TTA and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. After independent association, only three factors remained significant: a partial knowledge of symptoms, and TTA of less than two hours. Conclusion: Although not statistically significant, there was a trend to increased accuracy with digital templating in all outcomes except predicting neck length. We conclude that digital templating is at least as safe and accurate as analog templating in planning THA. Currently, digital templating improvements and functionality are in development. It is likely that in time digital templating will become the mainstay of preoperative planning in most hospitals.

**32** Trevor Kilpatrick

Genome-wide association scan identifies novel multiple sclerosis susceptibility loci on chromosomes 12 and 20


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Non-HLA genetic risk factors have recently been identified for multiple sclerosis (MS). To identify additional MS susceptibility loci we conducted a genome-wide association scan (GWAS) in 1.618 MS cases from Australia and New Zealand (ANZ) and used control data from the United Kingdom and the United States of America (n=3,413). Replication was conducted in an independent set of 2,256 ANZ MS cases and 2310 ANZ controls, making a total sample of 3,874 cases and 5,723 controls. We identified novel MS risk-associated SNPs on chromosome 12 p=2.2x10^-10, p=2.7x10^-10, and 1.4x10^-7 for the 3 most associated SNPs. We also found associations between SNPs on chromosome 20 p=1.7x10^-7 and p=4.0x10^-7. Several previously reported MS associations were also replicated (HLA-DR15, p=6.8x10^-193; CD58, p=3.4x10^-7; EV15/RPL5, p=1.7x10^-6; IL2RA, p=7.4x10^-6; CLEC16A, p=1.5x10^-5; IL7R, p=2.8x10^-4). Evidence of statistical interaction was identified between SNPs in EV15/RPL5 and HLA-DR15 (p=0.001). Both novel chromosome locations identified have been previously associated with other organ-specific autoimmune diseases. Therefore, this current study of MS confirms an aetiopathogenic overlap between different immune-mediated complex diseases.
In multiple sclerosis (MS), progressive axonal loss occurs from disease onset and is thought to be the main pathological determinant of permanent disability. Importantly, several immuno-modulatory and immuno-suppressive drugs are approved for the treatment of MS, and these have been shown to reduce relapse rate and delay disability progression in relapsing-remitting (RR) MS. However, disability progression still occurs in treated patients, suggesting that these drugs cannot sufficiently reduce axonal injury. Although it is clear that novel neuroprotective therapies are required for the treatment of MS, their development has been hindered by a lack of specific and sensitive measures of axonal injury in humans, which are needed to monitor disease activity and to compare the efficacy of putative neuroprotective therapies. In this study we aim to validate a novel serum biomarker of neurodegeneration, phosphorylated neurofilament heavy chain (pNF-H) in a mouse model of MS, and subsequently, in MS patients. Initially, we used an enzyme-linked immunosorbant assay (ELISA) to assess the validity of serum pNF-H as a marker of axonal injury in a mouse model of neuro-inflammatory disease, experimental autoimmune encephalomyelitis (EAE). At the time of maximum disease severity, the average serum pNF-H level reached 5.7 ng/ml, and levels were correlated significantly with paraplegia scores (R=0.74, P<0.001), inflammation (R=0.75, P<0.05) and the extent of axonal loss in the dorsal column of the lumbar spinal cord (R=0.80, P<0.001). Preliminary analyses of serum pNF-H levels in 78 patients with clinically definite MS and 10 healthy volunteers showed elevated serum pNF-H levels in 10 patients with first demyelinating event (FDE) or RR-MS (range of 0.03 to 0.26 ng/ml when normalized to healthy background levels). As we have shown that the detection of pNF-H in the serum of MS patients is feasible, we now aim to recruit 220 patients with established RR-MS and 216 FDE patients to establish the rate of detection and dynamics of serum pNF-H release, and then, to assess whether serum pNF-H positivity is associated with clinical or para-clinical correlates of CNS axonal injury. For these patients we will utilize likely clinical and para-clinical measures of axonal injury, namely lesion activity as measured by conventional cerebral MRI scans, disability outcome measures, and cerebral volume loss over time to validate serum pNF-H as a biomarker of acute axonal injury. This study could facilitate clinical neuroprotective trials for MS, and provide important prognostic information that could be used to potentially triage patients to different treatment regimes.

34 Helmut Butzkueven

Seasonal variation of onset of relapses in multiple sclerosis in the northern and southern hemispheres: results from the MSBase Registry

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Background: Previous studies into time of onset of relapses in Multiple Sclerosis have suggested that relapses are seasonal, with more relapses in spring and summer and fewer in winter. The proposed mechanism is that reduced Vitamin D levels at spring onset precipitate relapses. However these studies have been limited by small numbers, differing diagnostic criteria and the involvement of single regions. Objective: To determine if there is a temporal variation in onset of relapses using the MSBase registry, a large, multi-centre cohort study of MS outcomes. Methods: Data was extracted on 8th April 2009. The dataset comprised 10,082 cases with all forms of MS from 35 centres in 16 countries, including 34,481 documented relapses. Relapses with 1st or 15th of any month recorded as day of onset were excluded, as these were common default dates. Statistical analysis was performed using log-linear regression analysis. Results: 14,947 relapses were included (12,836 northern, 2,111 southern). Relapse onset followed a cyclical pattern with peaks in early spring and troughs in autumn in both hemispheres. Conclusions: A seasonal variation in onset of relapses is present with a spring peak and an autumn trough in both northern and southern hemispheres.

35 Christen Barras

Quantitative CT densitometry predicts intracerebral hemorrhage growth

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Background: Intracerebral hemorrhage (ICH) growth independently predicts disability and death. We have previously demonstrated that visually rated density heterogeneity independently predicts ICH growth, but employing operator-dependent methodology. There is a need to identify new, reliable imaging predictors of ICH expansion. We hypothesized that automated, quantitative CT densitometry of ICH on non-contrast CT brain (NCCCT) would improve predictive models of ICH growth, beyond known predictors, baseline volume (BV) and time-to-scan (TTS), with a view to creating a novel prognostic tool. Methods: We analysed 81/96 baseline sub-3 hour CT brain scans of the placebo arm of the phase IIb trial of recombinant Factor VIIa in ICH. 15 scans could not be analysed for technical reasons, but with no significant difference in baseline characteristics. ICH growth was examined using a continuous scale and three binary definitions: i) any growth, ii)33% or ≥12.5mL ICH growth and iii) >1mm radial expansion between baseline and 24 hour follow-up CT. Hounsfield unit (HU) density distributions were expressed as probability density functions. Mathematical descriptors (moments, or their derivatives) of these distributions (mean, standard deviation (SD), coefficient of variation (CV), skewness (measure of distribution asymmetry) and kurtosis (measure of distribution peakedness vs. flatness)) were incorporated into stepwise multiple linear regression models for the continuous growth scale, and binary logistic regression models for binary definitions and were compared with models limited to known growth predictors. Results: Average (+/-SD) mean density was 56.4HU (+/-6.16), range 35.51 (37.74 to 73.24), Average SD was 59.61 (+/-16.43), range 90.74 (28.29 to 119.03). Mean CV was 1.05 (+/-0.25), range 1.11 (0.56 to 1.67). Mean skewness was −0.21 (+/-0.25), range 1.17 (-0.837 to 0.334). Mean kurtosis was 2.21 (+/-0.387), range 2.02 (1.654 to 3.675). Multiple linear regression revealed superiority of a model incorporating CT densitometry (adjusted R-squared=0.202, P<0.001) over known predictors (adjusted R-squared=0.115, P=0.003), with similar results using a >1mm radial expansion binary growth definition. Conclusions: ICH CT densitometrics improved a
predictive model of ICH growth, accounting for up to 76% more data variability than BV/TTS alone. Densitometric-based models can potentially replace TTS information, as in cases of "wake-up stroke." The most powerful metrics were SD and CV. A novel, easily calculated, NCCT-derived, operator-independent predictive model of ICH growth has been created and awaits validation.

36  Bruce Campbell

Very Low Cerebral Blood Volume (VLCBV) – a new predictor of haemorrhagic transformation after thrombolysis for acute ischaemic stroke

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Background Haemorrhagic transformation (HT) after thrombolysis is rare but potentially devastating. Severe ischaemia damages blood vessel integrity and with reperfusion can lead to HT. Very low cerebral blood volume (VLCBV) is an indicator of severe ischaemia on MRI perfusion imaging. We tested VLCBV against the current best predictor of HT (diffusion-weighted-imaging (DWI) lesion volume ie stroke core) using data from the EPITHET study. Methods Normal percentile values of CBV were calculated from segmented CBV maps of the non-stroke hemisphere. Whole brain masks with CBV thresholds of < 0, 2.5th, 5th and 10th percentiles were created. The volume of VLCBV was calculated within the ischaemic lesion on acute DWI studies. HT was graded as per ECASS-II where haemorrhagic infarction (HI) indicates petechial blood in the region of infarction and parenchymal haematoma (PH) indicates blood clot with mass effect. Results HT occurred in 44 of 91 patients. PH occurred in 14 (4 symptomatic), asymptomatic HI in 32. All VLCBV thresholds predicted HT with optimal ROC characteristics at the < 2.5th percentile (AUC 0.73 for HT Vs no HT and 0.78 for PH Vs no PH) compared to DWI (AUC any HT 0.71, PH 0.73). Median volume of VLCBV (mL) was significantly higher in HT compared with non-HT (5.22 Vs 0.35 p=0.0002), in PH compared with non-PH patients (12.6 Vs 1.51 p=0.001) and in PH compared to HI (12.6 Vs 3.45 p=0.038). In multivariate logistic regression analysis VLCBV remained a significant predictor of HT (p=0.002) and PH (p=0.014) after inclusion of known clinical predictors as co-variates. DWI volume also remained significant in multivariate analysis with clinical factors (for HT p=0.005, for PH p=0.035) but was not significant in combination with VLCBV. A cut-point at 2mL VLCBV had sensitivity 100% for PH and in patients treated with tPA was associated with a 43% rate of PH (95% CI 22-66%, Likelihood Ratio (LR)=16, p=0.0003). The combination of VLCBV>2mL and recanalization had 50% PH (CI 0.19-0.81, LR 10, p=0.007). The topographic location of VLCBV overlapped with the PH location in 10/10 assessable cases. Conclusions VLCBV is a strong predictor of HT following thrombolysis and outperforms DWI volume in this large patient cohort. The effect holds true at a range of CBV thresholds and prediction is better in patients who recanalize or receive IPA. Specificity may be improved by incorporating other predictive factors. The addition of VLCBV to pre-thrombolysis decision making could reduce the incidence of HT.

37  Elizabeth Aitken

IPTP and antibody dynamics and protection to malaria in pregnancy

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Plasmodium falciparum parasites that cause Pregnancy Associated Malaria (PAM) express unique variant surface antigens (VSA-PAM). IgG levels to VSA-PAM are parity dependent and at delivery are associated with protection from disease. Using flow cytometry we measured IgG levels to the surface of chondroitin sulfate A (CSA) binding parasitized red blood cells (PRBC), to examine IgG levels to VSA-PAM in women receiving Intermittent Preventive Treatment (IPTp). IgG levels were measured throughout pregnancy, post partum and over successive pregnancies. Patterns of IgG acquisition were examined as well as the protective relationship between IgG to VSA-PAM in multigravidae at the beginning of pregnancy and clinical outcomes at the end of pregnancy. Among women receiving IPTp who were at low to moderate risk of parasitemia, development of IgG to VSA-PAM is dynamic. Many primigravidae do not develop an IgG response, however there is no evidence that this leads to low IgG levels in successive pregnancies. Also, it was found that IgG levels in early pregnancy were associated with protection against low birth weight in secundigravidae but were not a good measure for protection against clinical outcomes in multigravidae. This study was able to describe IgG dynamics in the cohort and also suggests that evaluating the protective efficiency of VAR2CSA specific vaccines may be difficult in the contexts of routine IPTp administration and falling malaria prevalences.

38  Katherine Gibney

Vitamin D deficiency is associated with tuberculosis (TB) and latent TB infection among immigrants from sub-Saharan Africa

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Objective: Vitamin D deficiency and Mycobacterium tuberculosis (MTB) infection are common among African immigrants to Western countries. While an association between vitamin D deficiency and tuberculosis (TB) has been reported in other populations, little is known about the association between low vitamin D levels and latent TB infection (LTBI) and TB in this population. Methods: A retrospective clinical audit was conducted of sub-Saharan African patients attending the infectious diseases outpatient clinics of the Royal Melbourne Hospital between January 1, 2003 and June 30, 2006. Results: Of 375
Soil-transmitted helminth (STH) infections are endemic in northern Viet Nam where the climate and agricultural practices, such as the use of human excreta as fertiliser and the use of wastewater for irrigation, favour transmission. An intervention was conducted in Yen Bai Province, north-west Viet Nam, to measure the effectiveness of single dose albendazole (400 mg) administered every 4 months for reducing the prevalence of STH infections in women of reproductive age. Stool samples were collected from women before the intervention and 3 and 12 months post-intervention. Information on a range of demographic and socioeconomic variables was also collected to measure the major risk factors for high STH burden in this area. The prevalence of hookworm, Ascaris lumbricoides and Trichuris trichiura infection in the baseline sample of 366 women were 76.2%, 19.2% and 29.1%, respectively. In the women who were surveyed at baseline and again at 3 and 12 months after the intervention (n = 118) cure rates were 71.3% for hookworm, 87.0% for A. lumbricoides and 81.4% for T. trichiura by the end of the 12 month study period (i.e. after three doses of albendazole). The main risk factor for hookworm infection was if women worked outside (OR [odds ratio] = 3.2 (95% CI [confidence interval] 1.6-6.2), P = 0.001) and the major risk factor for A. lumbricoides and T. trichiura infection was a lack of education. Low educational attainment was also the strongest risk factor for co-infection with all three species of STH (OR= 7.5 (95% CI 3.4-16.4), P < 0.001). The high rates of hookworm infection in this area of Viet Nam and the high cure rates for all three species of STH with 4 monthly albendazole treatment suggest that this program should be expanded to all endemic areas in Viet Nam. The study also highlights the important contribution of education to women’s health.
disease prevalence of each population being studied. Findings: Estimates of the parameters were in keeping with expectations regarding disease prevalence in the groups. QFT was found to have superior positive likelihood ratio and specificity, with possibly inferior negative likelihood ratio and sensitivity. Interpretation: This latent variable approach is a useful method for determining sensitivity and specificity in the absence of a Gold Standard and could be applied to other novel tests.

42 Karen Borschman
Challenging barriers to undertaking physical activity amongst older Macedonian and Polish people
BORSCHMANN K I, Ledgerwood KJ, Brown C2, Sison J2, Moore K1, Fearnley-Sander W1, Renehan E1, Lin XI.
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44 Jean Tinney
Staff resident communication practices: strategies for enhancement
TINNEY J, Haralambous B, Dowson L, Hempton C.
National Ageing Research Institute

45 Freda Vrantsidis
Living Longer Living Stronger™ (community strength training for older people): an evaluation
National Ageing Research Institute, Preventive and Public Health; Council on the Ageing

46 Alison Dwyer
Helping doctors help themselves: Healthcare management to support poorly-performing and ‘at-risk’ junior medical staff
Dwyer A.
Melbourne Health

47 Alison Dwyer
Medical administrators in contemporary healthcare organisations: A consideration of the literature
Dwyer A.
Melbourne Health

48 Alison Dwyer
Roles, attributes and career paths of medical administrators in public hospitals: survey of Victorian metropolitan directors of medical services
Dwyer A.
Melbourne Health

49 Sue Hookey
Structured outpatient letters pilot report
Hookey SJ, Gilchrist J.
Royal Melbourne Hospital

50 Susan Luu
When is a hospital ready to introduce electronic antimicrobial stewardship? The use of a readiness assessment tool.
LUU S, Thursky K, Busing K, Robertson M, Hage B.
The Royal Melbourne Hospital, Victorian Infectious Diseases Service, University of Melbourne.

51 Lena Ly
An overview of the dressings used in epidermolysis bullosa blister wounds
LY L1, Su JC2.
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52 Marion Robertson
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ROBERTSON M, Ibrahim J, Kevorkian L, Smith T, Wan V, Hayward K
The Royal Melbourne Hospital

53 Cassandra Sharrock
Junior medical staff recruitment program
SHARROCK C
The Royal Melbourne Hospital

54 Jason Chen
The prospective trial of dexmedetomidine sedation for awake fibreoptic bronchoscopy
Chen J, Lee K, Segal R, Orme R, Williams D.
Royal Melbourne Hospital

55 Cristian Udovicich
Does Continuous Interscalene Nerve Block Infusion affect hospital length of stay for patients undergoing minimally invasive shoulder surgery?
Udovicich C
The Royal Melbourne Hospital, The University of Melbourne, The Epworth Hospital
| 57 | Richard Bignell  
Guillain-Barré Syndrome in Australia: a retrospective audit  
BIGNELL R, Amatya B, Ng L, Khan F  
Royal Melbourne Hospital |
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| 58 | Fary Khan  
Multiple sclerosis rehabilitation outcomes: analysis of a national casemix dataset  
KHAN F, Turner-Stokes L, Stevermer T, Simmonds F.  
The Royal Melbourne Hospital, Northwick Park Hospital, Australasian Rehabilitation Outcomes Centre |
| 59 | Fary Khan  
Multiple Sclerosis rehabilitation: a pilot study for clinical practice improvement approach  
KHAN F, Zhang N, Ng L.  
The Royal Melbourne Hospital |
| 60 | Ng Louisa  
Multidisciplinary care for Motor Neurone Disease  
Ng L, Khan F, Mathers S.  
The Royal Melbourne Hospital, Bethlehem Hospital |
| 61 | Tania Romano  
Mothers with pregnancies complicated by uteroplacental insufficiency do not have impaired bone mineral content, density or strength during and after lactation  
ROMANO T, Wark JD, Wlodek ME.  
Department of Medicine, The University of Melbourne; Bone and Mineral Service, Royal Melbourne Hospital; Department of Physiology, The University of Melbourne. |
| 62 | Derek Lacey  
Pro-inflammatory cytokines inhibit osteogenic differentiation from stem cells: implications for bone repair during inflammation  
LACEY D, Simmons PJ, Graves SE, Hamilton JA.  
The University of Melbourne, Department of Medicine, Arthritis and Inflammation Research Centre, Royal Melbourne Hospital |
| 63 | Derek Lacey  
Low dose metal particles can induce monocyte/macrophage survival  
Lacey DC1, De Kok B1, Clanchy FI1, Bailey MI1, Speed K1, Haynes D3, Graves SE1, Hamilton JA1,2.  
1The University of Melbourne, Cooperative Research Centre for Chronic Inflammatory Disease, Royal Melbourne Hospital; 2The University of Melbourne, Arthritis and Inflammation Research Centre, Royal Melbourne Hospital; 3University of Adelaide, Rheumatology |
| 64 | Saeed Asadollahi  
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Richardson M, de Steiger R, ASADOLLAHI S  
Royal Melbourne Hospital |
| 65 | Ilana Ackerman  
Exploring factors associated with longer-term quality of life after joint replacement surgery: A mixed methods approach  
ACKERMAN IN, Osborne RH.  
Centre for Rheumatic Diseases, Department of Medicine (RMH), The University of Melbourne |
| 66 | Maritsa Papakonstantinou  
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PAPAKONSTANTINOUK M, Pan W-R, Richardson MD.  
The Jack Brockhoff Reconstructive Plastic Surgery Research Unit, The Royal Melbourne Hospital, Department of Anatomy and Cell Biology, The University of Melbourne |
| 67 | Sajna Shoukath  
A modified ink cadaveric injection technique for embalmed forearms  
SHOUKATH S, Pan WR, Richardson M.  
Jack Brockhoff Reconstructive Plastic Surgery Research Unit, University of Melbourne. |
| 68 | Benjamin Namdarian  
Circulating endothelial cells: A new prognostic marker in prostate cancer.  
Namdarian B, Georgiou HD, Corcoran NM, Costello AJ, Hovens CM.  
Department of Surgery (RMH/WH), University of Melbourne |
| 69 | Kevin Tan  
Renal cell carcinoma: circulating endothelial cells as a new biomarker  
Tan KVS, Namdarian B, Georgiou HD, Corcoran NM, Costello AJ, Hovens CM.  
Department of Surgery (RMH/WH), University of Melbourne |
70 Nicholas Cheng
The arterial supply of the long head of biceps tendon: an anatomical study
CHENG NM, Pan WR, Vally F, Richardson M
The Jack Brockhoff Reconstructive Plastic Surgery Research Unit, Royal Melbourne Hospital. Department of Anatomy and Cell Biology, University of Melbourne.

71 Daniel Chubb
Macrovascular Arteriovenous Shunts (MAS): a newly identified structure in the abdominal wall with implications for thermoregulation and free tissue transfer
CHUBB D, Rozen WM, Ashton MW, Grinsell D.

72 Neiraja Ganeswaran
Radiographic analysis of hip joint anatomy in children with spastic cerebral palsy to determine the effects of soft tissue release surgery on acetabular morphology
Ganeswaran N, Khot A, Selber P, Graham HK.
University of Melbourne

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Preserving the neurovascular supply to the superomedial pedicle for vertical breast reduction.
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Jack Brockhoff Reconstructive Plastic Surgery Research Unit, Royal Melbourne Hospital. Department of Anatomy and Cell Biology, University of Melbourne.

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Radiographic analysis of hip joint anatomy in children with spastic cerebral palsy to determine the effect of proximal femoral osteotomy on acetabular morphology.
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The blood supply to the ulnar nerve as determined by a modified lead oxide cadaveric injection technique
VALLY F, Pan WR, Cheng N, Richardson M.
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76 Domenica Zentner
Tetralogy of Fallot: any correlation between echocardiographic measures, radionuclide angiography and (gold standard) MRI?
D ZENTNER 1, A Ellims 1, D Sivaratnam 1, M Cheung 2, L Grigg 1
1 Cardiology Dept, Royal Melbourne Hospital; 2 Cardiology Dept, Royal Children’s Hospital

77 Ruvan Gurvitch
Long-term clinical outcomes of restricting drug-eluting stent use to patients at highest risk of re-stenosis.
Department of Cardiology, Royal Melbourne and Melbourne Private Hospitals

78 Rosemary Higgins
Cardiac rehabilitation after coronary artery bypass surgery: overcoming the barriers
Heart Research Centre, Melbourne

79 Caroline Medi
Incessant focal atrial tachycardia: Prevalence and outcomes
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The University of Melbourne; The Department of Cardiology. The Royal Melbourne Hospital.

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The University of Melbourne, The Department of Cardiology, The Royal Melbourne Hospital; The Department of Cardiology, The Alfred Hospital

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Repeat circumferential pulmonary vein isolation for recurrent paroxysmal atrial fibrillation: A highly effective strategy
The University of Melbourne; The Department of Cardiology, The Royal Melbourne Hospital.

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Circumferential pulmonary vein isolation for paroxysmal atrial fibrillation. Five year cure comparable to 1 year cure.
The University of Melbourne, The Department of Cardiology, The Royal Melbourne Hospital.
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Vagal paroxysmal atrial fibrillation: prevalence and ablation outcome in patients without structural heart disease
ROSSO R, Sparks PB, Morton JB, Kistler PM, Vohra JK, Halloran K, Medi C, Kalman JM.
The Department of Cardiology, Royal Melbourne Hospital; Department of Medicine, University of Melbourne.

85 Andrew Teh
ECG and electrophysiological characterisation and radiofrequency ablation of atrial arrhythmias late after orthotopic heart transplantation
The Department of Cardiology, Royal Melbourne Hospital and the Department of Medicine, University of Melbourne.

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Atrial fibrillation does not occur long term following successful catheter ablation for focal atrial tachycardia originating from the pulmonary veins.
The Department of Cardiology, Royal Melbourne Hospital and the Department of Medicine, University of Melbourne.

87 Marian Worcester
Overcoming difficulties of long-term follow-up studies in cardiovascular disease
WORCESTER M (1,2), Goble A (1), Elliott P (1,2), Murphy B (1,2), Hare D (2), Chen N (1)
(1) Heart Research Centre; (2) The University of Melbourne, Melbourne

88 William Wilson
Beta-blockers in systemic right ventricular dysfunction post atrial switch repair for transposition of great arteries
Zentner D, WILSON W, Wheeler M, Sivaratnam D, Grigg L
Royal Melbourne Hospital

89 Michael Frank
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Frank M, Rofe O, Galbraith K
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90 Ross Vlahos
The glutathione peroxidase mimetic ebselen suppresses IL-17A, chemokines and blood growth factors to inhibit cigarette smoke-induced lung inflammation
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Department of Pharmacology, The University of Melbourne

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Macrophage production of SAA occurs in response to bacterial LPS and may drive steroid resistant inflammatory processes in COPD.
Bozinovski S(1), Zhang Y(1), Thompson M(3), Hutchinson A(3), Steinfort D(3), Vlahos R(1), Smallwood D(3), Irving LB(3), Anderson GP(1,2)
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92 Sarah Whittle
Brain structure interacts to predict depressive symptoms in adolescence
Allen NB1,2, WHITTLE S 1,2,3, Yap MBH1,2, Yücel M 1,3, Sheeber L 4, Simmons JG 1,2, Pantelis C 3.
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93 Alan Goble
Trajectories of anxiety and depression before and after coronary artery bypass graft surgery
Goble, A (1), Murphy, B. (1,2), Elliott, P. (1,3), Le Grande, M. (1), Higgins, R. (1), Worcester, M. (1,4)
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94 Leanne Hides
Substance use screening in first episode psychosis.
Hides L, Cotton S, Lubman D, Gleeson J, Berger G.
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The influence of early cannabis use on psychotic-like experiences in a community adolescent sample
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The bimodality of healthy ageing: how do the differing profiles of healthy controls compare to patients with mild cognitive impairment?
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Self-disturbance as a phenotypic marker of vulnerability to schizophrenia and other psychotic disorders: Background and study design.
NELSON B
ORYGEN Youth Health Research Centre, Centre for Youth Mental Health, University of Melbourne.

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Clinical observations and the management of risk in the acute psychiatric inpatient setting – is there a better model of care? Sundram S, HARRINGTON A.
Northern Area Mental Health Service, North Western Mental Health.

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The identification of co-morbid substance use disorder in in-patient with psychiatric illness
SUNDARAM S, Matsudaira A, Happell B, Gough K.
Northern Psychiatry Research Centre, Northern Hospital In-patient Unit, University of Melbourne, Mental Health Research Institute.

100 Marie Yap
Maternal responses to positive affect and adolescents’ neural reward circuitry
YAP M1, Whittle S 1,2, Simmons IG 1,3, Yuvel M 1,2, Sheeber L 1,4, Allen NB 1,3
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101 Yang Yun
The relationship among childhood trauma, stress and coping in the first episode psychotic population: preliminary results from SHARP study
Yun Y(1,2), Parslow R(1), Garner B(1,2), Phillips L(1), Phassouliotis C(1), Markulev C(2), Leong C(1), Bendall S(1,2), Berger G(1,3), McGorry P(1,2).
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102 Marc Seal
Quantifying the development of white matter abnormalities in schizophrenia
SEAL M (1), Walterfang M (1), Tang PY (1), Yuvel M (1,2), Wood SJ (1), Berger GE (2,3), McGorry P (2), Pantelis C (1).
(1) Melbourne Neuropsychiatry Centre, The University of Melbourne; (2) ORYGEN Research Centre, The University of Melbourne; (3) Department of Research & Education, The Schloessli Clinic, Oetwil am See, Zuerich, Switzerland.

103 Bruce Campbell
Real time visual assessment of the perfusion-diffusion (PWI/DWI) penumbra has limited agreement with volumetrically calculated mismatch
CAMPBELL B1, Christensen S2, Foster S2, Butcher K3, De Silva D1, Peeters A4, Desmond P2, Parsons M5, Levi C5, Barber PA6, Bladin C7, Donnan G8, Davis S1, EPITHEI Investigators
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104 Lisa Cardamone
Longitudinal diffusion-weighted imaging following traumatic brain injury in the rat
CARDAMONE L, Liu YR, Williams J, Myers DE, O'Brien TJ
Royal Melbourne Hospital, University of Melbourne, Howard Florey Institute

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Brain recovery: The ocular motor system as a surrogate marker of motor and cognitive recovery post ischaemic stroke. (An ongoing study)
Dong W, Yan B, Fielding J, Millist L, Davis S, White O.

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The Grainyhead-like gene family in zebrafish regulates neural development and midbrain-hindbrain boundary formation
DWORKIN S 1, Caddy, J 1, Darido C 1, Lieschke GI 2,4, Jane SM 1,3
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107 Elizabeth Bowman
The antisaccade task and pursuit eye movements in people at ultra-high risk of psychosis.
EA Bowman,1,2 LA Abel,1 C Bartholomeusz,2 B Nelson,3 AR Yung,3 M Yücel,2,3 C Pantelis,2 B Luna,4 PD McGorry,3 SJ Wood.2
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108 Hans Tu
Atrial fibrillation is associated with increased infarct size, hemorrhagic transformation, and worse outcome in patients with ischemic stroke
HANS TU(1), Bruce Campbell(1), Soren Christensen(2), Ken Butcher(3), Marnie Collins(4), Mark Parsons(5), Patricia Desmond(2), Alan Barber(6), Chris Levi(5), Chris Bladin(7), Deidre De Silva(1), Andre Peeters(8), Geoffrey Donnan(9), Stephen Davis(1), for t
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109 Vilija Jokubaitis
Disabled-2 (Dab2) increases the CNS autoimmune pathogenesis of EAE
JOKUBAITIS VG, Kemper D, Kilpatrick TJ, Butzkueven H. Department of Neurology, Royal Melbourne Hospital; University of Muenster, Germany; Howard Florey Institute and Centre for Neuroscience, The University of Melbourne

110 Kumar Gaurav
Postnatal stress, kindling epileptogenesis, corticosterone and hippocampal cell loss
KUMAR G1, Jones NC1, Morris MJ2, Rees SR3, Salzberg MR4, O’Brien TJ5. Department of Medicine1, Anatomy and Cell Biology3 and Psychiatry4, University of Melbourne, Australia; 2Department of Pharmacology, University of New South Wales, Australia

111 Lisa Cardamone
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112 Mark Marriott
Paraclinical correlates of visual acuity loss in multiple sclerosis
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113 Ng Caroline
A Brain and heart links: alterations in cardiac function and HCN channel expression in genetic absence epilepsy rats from Strasbourg.
NG C, Powell K, Jones N, Megatia I, Urmaliya V, Pinault D, White P, O’Brien T. 1. The Departments of Medicine and Neurology, The Royal Melbourne Hospital, The University of Melbourne; 2. Department of Pharmaceutical Biology, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University; 3. INSERM U666, physiopathologie clinique

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B A Cav3.2 T-type calcium channel point mutation has splice variant-specific effects on function and segregates with seizure expression in a polygenic rat model of absence epilepsy

114 Jade Bayly
Time frequency mapping of the rhythmic limb movements during non-epileptic seizures (NES)
O’Brien T, Vinton A, Horne M, Carino J, Smit M, BAYLY J. Royal Melbourne Hospital

115 Michelle Rutherford
Managing the global research project, MSBase, using an innovative web based framework
RUTHERFORD M, Tanner M, Butzkueven H. Royal Melbourne Hospital

116 Marian Todaro
KONQUEST: Keppra versus Older AEDs and Neuropsychiatric, Neurocognitive and QUALity of life outcomes in treatment of Epilepsy as Substitution monoTherapy. Interim Analysis of Baseline to Three Month Data.

117 Anneke van der Walt
The Apolipoprotein genotype does not influence MS severity, cognition or brain atrophy.
VAN DER WALT A(1,2), Stankovich J(4,5), Bahlo M(4), Taylor BV(5), Van der Mei IAF(5), Foote SJ(4), Kilpatrick TJ(3), Rubio JP(2,3), Butzkueven H(1,2). 1. The Royal Melbourne Hospital; 2. Howard Florey Institute, University of Melbourne; 3. Centre for Neuroscience, University of Melbourne; 4. Walter and Eliza Hall Institute of Medical Research, Parkville; 5. Menzies Research Institute, University of Tasm
118 Joshua Ye
Treatment outcomes of intracranial pilocytic astrocytoma in children and adults
YE J*, Lo P**
University of Melbourne*, Department of Neurosurgery The Royal Melbourne Hospital**

119 Zhou Xiaoyu
The clinical efficacy of different dosages of intravenous alteplase in Chinese patients with acute ischemic stroke
Zhou XY, Collins ML, Wang SS, Davis SM, Yan B.

120 Susan Kantor
P3- 382: Differential effects of aromatase inhibition on growth and bone mineralization in peripubertal male rats
Bajpai A, Russo V, Simp M, KANTOR S*, Wark JD*, Werther GA.
Department of Endocrinology and Diabetes, Centre for Hormone Research, Murdoch Childrens Research Institute, Royal Children’s Hospital; Department of Paediatrics and Department of Medicine*, University of Melbourne.

121 Jemma Christie
Detrimental bone effects of smoking and a high fat diet in mice
CHRISTIE JJ, Chen H, Anderson GP, Morris MJ, Wark JD.
University of Melbourne, Department of Medicine, Royal Melbourne Hospital; Department of Pharmacology, School of Medical Sciences, University of New South Wales.

122 Jemma Christie
Determinants of bone density in twins discordant for cigarette smoking
CHRISTIE JJ, Osborne RH, Kantor S, Nowson CA, Seibel MJ, Sambrook P, Wark JD.
Department of Medicine, University of Melbourne. Australia Centre for Rheumatic Diseases, University of Melbourne. Australia School of Exercise and Nutrition Sciences, Deakin University. Australia Bone Research Program, University of Sydney. The Kolling I

123 Elise Coghill
Over-expression of granulocyte macrophage colony stimulating factor (GM-CSF) in T-cells leads to spontaneous tissue inflammation
COGHILL EK, Campbell IK, Van Nieuwenhuijze A, Cornish AL, Blyth J, Lawlor KE, Murphy J, Wicks IP.
The Walter and Eliza Hall Institute of Medical Research

124 Leonard Harrison
Novel CD4+CD52hi regulatory T cells are activated by autoantigen and decreased in autoimmune disease
Dromey JA 1, Lee BH 1, Reinwald S 1, Bandala-Sanchez M-E 1, Young HE 1, Ngui K 1, Jensen KP 1, Thearle DJ 1, Fourlanos S 1,2, Manneering SI 1, HARRISON LC 1,2
1. The Walter & Eliza Hall Institute of Medical Research, Parkville ; 2. Burnet Clinical Research Unit, The Royal Melbourne Hospital

125 Jemma Christie
Associations between smoking cessation and changes in lifestyle and constitutional factors related to bone health and osteoporosis
Janssen SM, CHRISTIE JJ, Segan C, Osborne RH, Nowson C and Wark JD.
University of Melbourne Department of Medicine; Bone and Mineral Service, Royal Melbourne Hospital; QUIT Victoria; Cancer Council Victoria; Centre for Rheumatic Diseases, Royal Melbourne Hospital; Radboud University Nijmegen, Netherlands; Deakin University

126 Mary Sakellarides
Short-term vs long-term duration of AED (anti-epileptic drug) pharmacotherapy: effects on bone health parameters
SAKELLARIDES M, Bright T, Todaro M, Roten A, Day LH, O’Brien TJ, Wark JD.
The University of Melbourne Department of Medicine, Bone & Mineral Service and Department of Neurology, The Royal Melbourne Hospital.

127 John Wark
Bone mineral density (BMD) and associations in postmenopausal Balinese women aged 50-70 years
Suryadi MAH, Gorelik A, Suryadih NT, Brand C, WARK JD.
Department of Medicine, RMH, The University of Melbourne; Clinical Epidemiology and Health Services Evaluation Unit (CEHSEU), Melbourne Health; The Faculty of Medicine, Udayana University, Denpasar, Bali, Indonesia.

128 John Wark
Determinants of long-term persistence in osteoporosis therapy: a large Australian cohort study
WARK JD, Chow S-L, Calcino G, Kemp AG and Gorelik A.
University of Melbourne Department of Medicine and Bone & Mineral Service, Royal Melbourne Hospital; Hi Connections Pty Ltd; Medilims; Clinical Epidemiology & Health Services Evaluation Unit, Melbourne Health.

129 Michelle Ananda-Rajah
The economic impact and resource utilisation of invasive fungal infections (IFI) in haematological stem cell recipients (HSCT) and patients with acute leukaemia at a tertiary Australian hospital
ANANDA-RAJAH MR1, Morrissey CO*2,3,4,6 Woodger JS, Neville AM5, Frost M6, Slavin MA1,2,4
1. Victorian Infectious Diseases Service, Royal Melbourne Hospital 2. Infectious Diseases Unit, The Alfred Hospital, Melbourne; 3. Department of Medicine, Monash University, Melbourne; 4. Macfarlane Burnet Institute, Melbourne; 5. Pretium P/L, Sydney; 6.
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<th>Carolyn Chua</th>
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<td>Glucose transporter-1 (GLUT-1) expression in placental malaria</td>
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<td>CHUA CL (1), Umbers AJ (1), Sanders PR (2), Chaluluka E (3), Glazier JD (4), Rogerson SJ (1), Boeuf P (1).</td>
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<td>1 Department of Medicine, University of Melbourne, Parkville; 2 The Walter and Eliza Hall Institute of Medical Research, Melbourne; 3 College of Medicine, University of Malawi, Blantyre, Malawi; 4 Maternal and Fetal Health Research Group, Research School</td>
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<th>131</th>
<th>Benjamin Cowie</th>
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<td>The Victorian hepatitis B serosurvey 1995 – 2005</td>
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<td>COWIE BC (1-3), Karapanagiotidis T (1), Enriquez A (1), Kelly H (1,2)</td>
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<td>(1) Victorian Infectious Diseases Reference Laboratory; (2) Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne; (3) Victorian Infectious Diseases Service, The Royal Melbourne Hospital</td>
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<th>Justin Denholm</th>
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<td>Management of latent TB infection by Australasian physicians and trainees: a survey of current practices and concordance with international guidelines.</td>
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<td>DENHOLM JT, McBryde E.</td>
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<th>133</th>
<th>Damon Eisen</th>
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<td>Polyoma viruses may cause chronic cystitis and respond to intravesical cidofovir.</td>
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<td>EISEN D, Fraser I, Sung L, Finlay M, Bowden S, O'Connell H.</td>
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<td>VIDS, Internal Medicine, Anatomical Pathology, VIDRL, Urology, Melbourne Health</td>
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<td>Infectious diseases recommendations at a Melbourne teaching hospital - are they followed?</td>
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<td>GEORGE C, Neilsen S, Galbraith K, Robertson M</td>
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<th>Caroline Marshall</th>
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<td>Daily hazard of MRSA acquisition in the intensive care unit.</td>
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<td>MARSHALL C(1,2), Spelman D(3), Harrington G(3), McBryde E(2).</td>
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<td>1. Centre for Clinical Research Excellence in Infectious Diseases, University of Melbourne; 2. Victorian Infectious Diseases Service, Royal Melbourne Hospital; 3. Infection Control and Hospital Epidemiology Unit, The Alfred Hospital, Melbourne.</td>
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<th>Michaela Petter</th>
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<td>Membrane association of A-type RIFINs in P. falciparum infected erythrocytes</td>
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<td>Petter M, Schmetz C, Klinkert MQ.</td>
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<td>Department of Medicine, RMH, University of Melbourne, Australia; Bernhard-Nocht-Institute for Tropical Medicine, Hamburg, Germany</td>
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<th>Ann Bull</th>
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<td>Learning from the pathogens in surgical site infection: implications for surgical antibiotic prophylaxis</td>
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<td>Rogers BA (1) BULL AL(2), Brett J (2), Richards MJ (2) and the VICNISS contributing hospitals</td>
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<td>1 Victorian Infectious Diseases Service, Royal Melbourne Hospital; 2 VICNISS, Parkville.</td>
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<td>Fertility is significantly reduced by pelvic tuberculosis</td>
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<td>Schulz T, Eisen D</td>
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<td>The effect of malaria infection on term placental 11bHSD2 expression</td>
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<td>Umbers A, Clapham C, Robertson R.</td>
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<td>Orthopaedic Prophylactic Antibiotic Usage: An audit of prescribing patterns and adherence to local guidelines in THR and TKR.</td>
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<td>ETTY-LEAL M, Galbraith K, Robertson M</td>
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<td>The Royal Melbourne Hospital; Faculty of Pharmacy and Pharmaceutical Sciences, Monash University</td>
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<th>Kate Leslie</th>
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<td>Forced-air warming vs midazolam in preoperative anxiolysis</td>
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<td>Wen R, LESLIE K, Rajendra P.</td>
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<th>Zi Hao Phang</th>
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<td>A prospective, randomised, single blind, controlled trial of the LMA supremeTM disposable laryngeal mask during anaesthesia in spontaneously breathing adult patients.</td>
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<td>William DL, Pemberton E, PHANG ZH.</td>
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<td>Department of Anaesthesia, The Royal Melbourne Hospital</td>
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<td>Demographics of the accident and emergency department at a small Australian rural hospital</td>
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<td>CHEN TM, Tescher Paul  Royal Melbourne Hospital</td>
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Determinants of lymph node yield in colorectal cancer: Analysis of 10,082 patients from prospective Australian databases.

BioGrid Australia, Royal Melbourne Hospital, Western Hospital, St John of God hospital, Royal Adelaide Hospital, Flinders Medical Centre, Box Hill Hospital

Wei-Ren Pan
Senile changes in human lymph nodes
Pan WR, Suami H, Shayan R, Taylor GI.
Jack Brockhoff Reconstructive Plastic Surgery Research Unit, RMH, Department of Anatomy and Cell Biology, University of Melbourne.

Stanley Styli
Nck adaptor proteins link Tks5 to invadopodia actin regulation and extracellular matrix degradation in tumour cells
STYLI S(1,2), Tam ST(1), Courtenidge SA(3), Kaye AH(1,2), Lock P(4)
(1) Department of Surgery, University of Melbourne, Royal Melbourne Hospital; (2) Department of Neurosurgery, Royal Melbourne Hospital; (3) Burnham Institute for Medical Research, La Jolla, CA, United States; (4) Department of Biochemistry, LaTrobe Univer

Edward Wang
Influence of gated blood pool scans on management of oncological patients
WANG E, Lichtenstein M
The Royal Melbourne Hospital

Gerhard Rank
PRMT5-mediated methylation of histone H4R3 recruits DNMT3A coupling histone and DNA methylation in gene silencing
Rank G1, Zhao Q1, Cerruti L1, Tan YT1, Moritz RL2, Simpson RJ2, Allis CD3, Cunningham JM4, Jane SM1,5
1Rotary Bone Marrow Research Laboratories, Royal Melbourne Hospital; 2Joint Protein Structure Laboratory, Ludwig Institute for Cancer Research and Walter and Eliza Hall Institute for Medical Research; 3Laboratory of Chromatin Biology, The Rockefeller Univ

Maira Kentwell
Long-term follow up of carriers of a cancer pre-disposition gene: An alternative model for clinical follow up
Hodgkin LJ1,2, Kentwell M1, Bogwitz M1, Bylstra Y, D’Souza R1, Macrae F1, Lindeman G1
1. Familial Cancer Centre, Royal Melbourne Hospital; 2. Genetic Health Services Victoria, Royal Children’s Hospital.

Jeanette Ting
The in-vivo anatomy of the deep circumflex iliac artery (DCIA) perforators: Defining the role for the DCIA perforator flap
TING J, Rozen WM, Grinsell D, Stella DL, Ashton MW.
Jack Brockhoff Reconstructive Plastic Surgery Research Unit, University of Melbourne, Royal Melbourne Hospital

The deep circumflex iliac artery (DCIA) provides a dependable option for use as an osteo-musculo-cutaneous flap, particularly in mandibular reconstruction. Modifications to flaps based on DCIA perforators have been sought in order to prevent donor site morbidity or to decrease the area of muscle cuff harvest. Previous studies have been inconsistent in their descriptions of perforator anatomy, and means of assessing these preoperatively have not often been widely described. A clinical anatomical study was undertaken, with a cohort of 44 hemiabdominal walls in 22 consecutive patients undergoing preoperative computed tomographic angiography (CTA) prior to free flap surgery. The feasibility of CTA and the regional vascular anatomy were both assessed. The use of CTA was shown to demonstrate DCIA perforators with high resolution and to be able to assess vessel size and location. In 44 hemiabdominal walls, there were 44 perforators of >0.8mm diameter. There were no suitable perforators in 40% of sides, with 32% of sides having 1 perforator >0.8mm diameter, 16% having 2 perforators, <10% had 3 perforators, and only 1 side had over 4 perforators. Perforators emerged from the deep fascia on average 5.1cm cranial and 3.9cm posterior to the anterior superior iliac spine (ASIS). Of 44 perforators identified, 82% of perforators were located within a 4cm by 4cm area, 3cm superior and 2 cm posterior to the ASIS. The current study has demonstrated the utility of preoperative CTA for identifying DCIA perforators, and for selecting patients who may be suitable for a DCIA perforator flap given the variable perforator anatomy.

Nicole Tham
The pudendal thigh flap for vaginal reconstruction: optimising flap survival
THAM N, Pan WR, Rozen WM, Carey MP, Taylor GI, Corlett RJ, Ashton MW
The Jack Brockhoff Reconstructive Plastic Surgery Research Unit, the Royal Melbourne Hospital, Department of Anatomy and Cell Biology, University of Melbourne

Background: The pudendal thigh fasciocutaneous (PTF) flap is a useful flap in perineal reconstruction, that is reliable when small but is frequently unreliable when large flaps are raised. Large flaps in particular, are associated with an increased incidence of apical necrosis. Thorough descriptions of the vascular anatomy of this flap have been lacking from the literature, with the current study evaluating this anatomy, aimed to provide the anatomical basis for the flap's vascular problems and for techniques to maximise its survival. Methods: Five unemmbalmed human cadaveric pelvis specimens were studied. Lead oxide injectant enabled radiographic and dissection analysis of the arterial anatomy of the perineal integument. Results: A consistent pattern of vascular supply was found in all specimens. 1. The blood supply to the pelvic floor was supplied sequentially by the posterior labial/scrotal arteries (terminal branches of the internal pudendal artery), cutaneous branches from the anterior branch of the obturator artery, and branches from the external pudendal arteries. 2. These vessels ran close to the midline, medial to the PTF flap. 3. The posterior labial/scrotal arteries were deep to the Colles' fascia and the branches from the obturator artery and external pudendal arteries were located superficial to the Colles' fascia. Conclusion: This study has demonstrated that: 1. The PTF flap is a three vascular territory flap. Given the third territory of supply to the apex of the
flap, a delay procedure may help to avoid flap necrosis. 2. The pedicle is situated close to the midline. This may explain why regions of the PTF flap have a potentially precarious blood supply and suggests that the PTF flap should be designed more medially. 3. The relationship of the blood supply of the flap to Colles' fascia enables the proximal part of the flap to be de-bulked and not just de-epithelised from the superficial aspect to lessen the risk of pedicle compression. 4. The apical part of the flap can be de-bulked from the deep aspect up to the level of Colles' fascia if a thinner flap is required.

167  Benjamin Namdarian (see abstract no. 14)

168  Anna Taylor

Experimental analysis of the effectiveness of retrograde nerve tracers in vitro and in vivo in male Wistar rats for the potential use in human nerve-sparing radical prostatectomy.

Costello AJ, Hovens CM, Namdarian B, TAYLOR AL.
The Royal Melbourne Hospital

Background: Although techniques have been developed to save the neurovascular bundle crucial for erectile function, impotence remains a major morbidity of radical prostatectomies. Injury to the autonomic nerves is primarily due to the lack of knowledge of the neuronal pathway, and the variability of this pathway. It was the objective of this study to establish an effective in vivo visualisation of the nerves for surgical use to optimise nerve-sparing and morbidity outcomes.

Methodology: Using male Wistar rats, three fluorescent nerve tracers were investigated. These were Fluoro Gold, Fast Blue and Alexa Fluor 488. The tracers were applied, and over different periods of time, the major pelvic ganglion and cavernous nerves were assessed in vivo and in vitro. Through the use of fluorescent microscopy, the effectiveness of cell labelling was compared between selected tracers. Potential neuronal toxicity of the tracers was also established through erectile functional testing. Results: All nerve tracers were visualised in vivo and in vitro at certain time points and all proved to be non-toxic. Fluoro Gold and Fast Blue were best visualised 7 days following their application, while Alexa Fluor 488 fluoresced optimally at 14 days post-application. Comparatively, Alexa Fluor 488 was significantly more effective. It labelled the most nerve cells and clearly delineated neural pathways in vivo. Conclusions: While all tracers were effective and most likely non-toxic, Alexa Fluor 488 was the ultimate in fluorescence, specificity and sensitivity of nerve tracing. The optimal time following application to view the nerves was 14 days. Due these outstanding outcomes, further toxicity tests are being carried out, with potential human application in mind.

169  Wei-Han Tay

Outcomes of delayed union and nonunion of femoral and tibial shaft fractures

TAY WH, Gruen RL, Richardson MR, de Steiger RN
The University of Melbourne, The Royal Melbourne Hospital, The Alfred Hospital

Aim: To compare the effect on self-reported health outcomes of delayed union or nonunion of femoral and tibial shaft fractures treated at two major metropolitan trauma centres in Victoria. Methods: Patients admitted to the Royal Melbourne Hospital and the Alfred with extra-articular femoral and tibial shaft fractures during 2003-2004 and 2005-2006, and followed up by the Victorian Orthopaedic Trauma Outcomes Registry (VOTOR) were included. Hospital medical records were reviewed to identify the outcome of each fracture. Fracture healing was assessed by the need for revision surgery for delayed union or nonunion, and clinical and radiological evidence of union. Prospectively-gathered VOTOR health outcome measurements included the Short Form 12-Item Health Survey (SF-12), and return to work and pain status at 6 and 12 months post injury. Results: 260 femoral and 282 tibial shaft fractures were included. 285 fractures progressed to union, 138 fractures developed delayed union or nonunion and 119 fractures had an unknown outcome. Factors that were significantly different between the union and delayed union or nonunion groups included fund source, mechanism of injury, other injuries, wound and Gustilo type, and fixation method. On linear regression modeling, an inverse relationship was demonstrated between delayed union or nonunion and the Physical and Mental Component Summary scores of the SF-12. This was statistically significant at both 6 and 12 months post injury and adjusted for age, gender and other injuries. On logistic regression modeling, patients with delayed union or nonunion showed a risk ratio of <1 and >1 to return to work and to have pain, respectively. This was statistically significant at 12 months post injury and adjusted for age, gender and other injuries. Conclusions: Patients with delayed union or nonunion of femoral and tibial shaft fractures have poorer physical and mental health at 6 and 12 months post injury. In addition, they are less likely to have returned to work and more likely to still have pain at 12 months post injury.

170  Francis Connan (see abstract no. 29)

171  Tanya Yuen

Glutamate and other risk factors for tumor associated seizures

Background: The pathogenesis of tumor associated seizures (TAS), a common, disabling co-morbidity of brain tumors, remains poorly understood. We examined clinical and molecular factors associated with the development of TAS in patients with glioma. Methods We retrospectively analyzed the medical records and tumor specimens of 190 patients with supratentorial glioma. Molecular factors assayed on tumor specimens were glutamate levels, glial glutamate transporters (EAAT1, EAAT2, system Xc-) and HCN1 and HCN2 ion channels. Results: Of the 190 patients, 84 (44%) had TAS. Clinical features associated with TAS were: younger age, preoperative seizures and temporal lobe location and low grade histology of tumor. Molecular features associated with TAS were: increased glutamate levels, increased system Xc-expression, reduced EAAT2 expression, increased nuclear EAAT1 expression and decreased HCN1 and HCN2 expression. Multivariate regression analysis identified younger age and tumor glutamate levels as independently predictive of TAS. Conclusion: We found that elevated tumor glutamate levels, altered glutamate transport and HCN channel expression were associated with TAS. We also found that age at diagnosis and tumor glutamate levels were independently predictive of TAS. We suggest a mechanistic role for glutamate in TAS pathogenesis, possibly via a secondary change in HCN channel expression in interposed neuronal tissue. This observation may have therapeutic implications for TAS.
Tsutomu Takahashi

Progressive gray matter reduction of the superior temporal gyrus during transition to psychosis

Takahashi T(1,2), Wood SJ(1), Yung AR(3), Soulsby B(1), McGorry PD (3), Suzuki M(2), Phillips LJ(4), Velakoulis D(1,5), Pantelis C(1)

1 Melbourne Neuropsychiatry Centre, Department of Psychiatry, University of Melbourne & Melbourne Health; 2 Department of Neuropsychiatry, University of Toyama; 3 ORYGEN Research Centre, Department of Psychiatry, University of Melbourne & Melbourne Health; 4 Department of Psychology, University of Melbourne; 5 The Royal Melbourne Hospital