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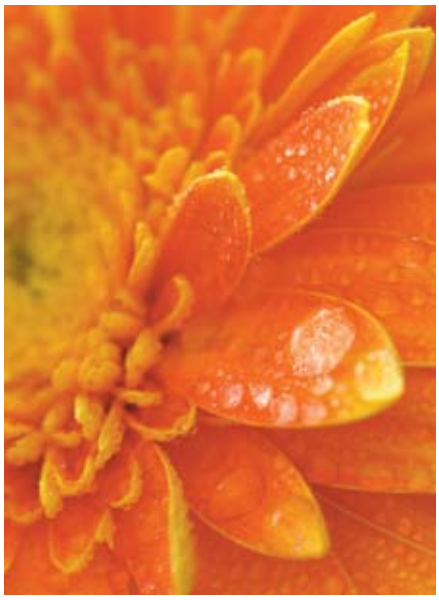
AUTUMN bulletin 50



Dr Jane Zochling has joined Menzies as the Dick Buttfield Research Fellow

International researcher attracted back home to Tasmania

A young Tasmanian doctor has returned home from working in Germany to take up a prestigious State Government medical award at the Menzies Research Institute.

Dr Jane Zochling, who trained at the University of Tasmania and the Royal Hobart Hospital, has been awarded the latest Dick Buttfield Research Fellowship to research a crippling rheumatic disease.

The Fellowship – worth $380,000 over five years – was established by the Department of Health and Human Services in honour of the late Dr Buttfield, who was one of Tasmania's best known and most respected health officials.

Health and Human Services Minister Lara Giddings said that Dr Zochling was an outstanding young researcher who was already building an impressive international research profile in the study of the rheumatic disease, ankylosing spondylitis.

"Ankylosing spondylitis affects as many as 1 in 200 Australians – that's around 2,500 Tasmanians," Ms Giddings said. "Its cause remains unknown, though there appears to be a strong genetic link."

Dr Zochling said that ankylosing spondylitis caused arthritis of the spine and joints of the lower back, as well as inflammation of the eyes, lungs and heart valves.

"It occurs in twice as many men as women, and usually has its onset between the ages of 16 to 35," she said.

"It can vary from intermittent episodes of back pain that occur throughout life, to a severe chronic disease that attacks the spine, peripheral joints and other body organs, resulting in severe joint and back stiffness, loss of motion and progressive deformity."

Dr Zochling said the Fellowship would allow her to study ankylosing spondylitis cases in Tasmania to investigate diagnostic markers of the disease, its activity and the way it affects patients.

Director of the Menzies Research Institute, Professor Simon Foote, said that Menzies is the ideal place to conduct this type of research.

"Menzies has comprehensive population-based disease registries and well developed genealogical resources," Professor Foote said.

"We also have an excellent reputation and links with the community, as well as highly experienced researchers and first-class laboratory facilities.

"We welcome Dr Zochling's appointment as the Buttfield Research Fellow as another example of the important relationship between the Menzies Institute and the State Government."

More than flowers

How often have you read funeral notices in the newspaper and seen the request for 'donations in lieu of flowers'? The family of the late Darrell 'Dasher' Eaton understands the value of such a gesture.

When their beloved Dasher passed away suddenly as the result of a heart attack, his wife Dawn Eaton and daughter Karen Weitnauer requested that friends and family make a donation to Menzies instead of purchasing flowers for the funeral.

When planning the ceremony, Dawn and Karen talked about how best to respect Darrell's wishes. After consultation with other family members, everyone agreed that supporting Menzies' medical research was the ideal way to honour Dasher's life."Menzies represents what Dad stood for – new life, challenge and success", said Karen.

Dasher's family also wanted to make a contribution to an organisation which is working to improve the lives of children. "In our extended family we have two children who suffer childhood illnesses, so the notion of research to make children's lives better is very significant to us," she said. With this in mind, Dawn and Karen nominated Menzies' Childhood Determinants of Adult Health (CDAH) project as the recipient of donations made in Dasher's memory.

CDAH Project Manager, Marita Dalton, says that the study aims to investigate how much lifestyle and biological factors in childhood affect the risk of developing diseases like heart disease and diabetes in adulthood.

"The donations made in Mr Eaton's memory are very valuable. They will assist us to translate and communicate the findings of the CDAH study so that we can improve the health and wellbeing of Tasmanians, other Australians and beyond," Marita said.

Dasher was a man who understood the benefit of daily exercise. Wearing his favourite beanie, he took daily walks in the early morning around his home suburb of Old Beach. Dasher took delight in getting his morning exercise before most of Hobart had even thought about getting out of bed!

From the age of 19, when he joined the North Hobart Football Club, Dasher pushed himself to do well. He played 179 games for the club, including two premierships in 1947 and 1957. He went on to coach the club from 1960 to 1964, and led them to back to back premierships in 1961 and 1962.

Darrell 'Dasher' Eaton

His tenacity also served him well in his career as a bookmaker that spanned 26 years. Retiring at the age of 64 in 1991, Dasher was able to spend more time with Dawn, their children and their ever growing families.

With Dasher's passing, Hobart has lost one of its great characters, fondly remembered by his family, friends, team-mates and colleges. His family's decision to ask for donations in lieu of flowers also means he will be remembered by Menzies.

If you would like to make a donation in lieu of flowers, or if you would like to make an 'in memorium' donation, please phone Melita Griffin on 6226 7700.

Lasting Legacy

Gifts of remembrance have been made in honour of:
Mr Darrell "Dasher" Eaton
Mrs Hazel Limbrick
Mrs Fran McKendrick
Mr Roger Stephen Penny
Mrs Daphne Louisa Philpott
Mr Sydney Ploughman
Mrs Helena Tapson
Mrs Diane Woodward
Mr Graeme David Woolley

Jolly good fellows...

Three young researchers have been awarded prestigious fellowships to enable them to continue their innovative research programs at the Menzies Research Institute.

Dr Ingrid van der Mei will continue her internationally recognised work on multiple sclerosis (MS) with a National Health and Medical Research Council (NHMRC) Training Fellowship. Recent work by Menzies has shown that low personal exposure to ultraviolet radiation, history of Epstein-Barr infection, and low sibling exposure might increase the risk of MS. Dr van der Mei will analyse data from case-control studies and clinical cohort studies to examine the role of genes related to these immunological pathways in the development and progression of the disease.

Seana Paul was awarded an NHMRC Public Health Fellowship to undertake research into how social and environmental factors in childhood lead to the development of damaging vascular risk factors in adulthood, such as low physical activity or smoking. By better understanding of the origins of such behaviours, researchers may be able to develop interventions that can prevent them, thereby reducing the risk of future disease.

Dr Mike Schmidt will investigate whether physical activity and fitness can modify the effects of childhood obesity on adult heart and diabetes disease risk with a fellowship from the National Heart Foundation. His research will investigate if being overweight in childhood increases risk of developing heart disease or diabetes as an adult, and if it does, whether being physically active or fit can lower the risk.

The NHMRC fellowships last for four years each, and the National Heart Foundation fellowship is of two years duration. Fellowships such as these are extremely competitive and demonstrate the high quality of our Menzies researchers.

Lights, camera... action! A new TV advertising campaign for Menzies started this month. The advertisement features the leukaemia project and highlights how every person can support medical research.

Shining light on Leukaemia

Thanks to the generous support of people like yourself, Menzies has made significant progress with their research to identify some of the genes which influence the development of diseases like multiple sclerosis and prostate cancer.

Researchers have started work on Menzies' project to find the origins of leukaemia. They are aiming to uncover the genetic causes of blood cancers and improve the tools for diagnosis, treatment and prevention of the disease.

Pathologist Dr Elizabeth Tegg has recently joined the study team as a PhD student. She is currently examining the types of leukaemia that occur in study participants and comparing them to cases which do not appear to have a familial link.

"Sometimes many cases of leukaemia occur in a person's extended family. These families can help us to find the genes that may influence the development of the disease.

"It's an exciting time to join the team working on this project. I am hoping that my skills in haematology and genetics will help us to make the breakthrough we are all hoping for," Elizabeth said.

New program to study physical activity:

Thanks to you

We all know that physical activity is important for maintaining good health. Despite this simple fact, only a minority of Australians perform the amount of physical activity recommended for optimum health.

In June last year we asked our committed donors to financially support a new study designed to address gaps in knowledge about how doctors assess and improve their patients' levels of physical activity.

Thanks to your generous support, work has started on the pilot stage of the study. The pilot will test the feasibility of a large-scale project, and it is hoped that the data collected will assist researchers to secure funding for a comprehensive project in the near future.

Special thanks to the Masonic Centenary Medical Research Foundation for their generous major gift to this study. Their donation funded the purchase of 20 accelerometers, small electronic devices that can tell us how much physical activity a person has done.

research | thanks to you

Andy's wrongs are right by Menzies

In his first week of hosting the breakfast show on local radio station 936 ABC Hobart, comedian Andy Muirhead decided to put his inevitable fumbles to good use by declaring he would donate 50 cents for each of his on-air mistakes to a local charity nominated by listeners.

By the end of the week he had collected $55 for the Menzies Research Institute which was gratefully accepted by Melita Griffin, Development Manager (right). Great work Andy – a week's worth of mistakes can go a long way!

Menzie's Melita Griffin grabs the cash from 936 ABC Hobart's Andy Muirhead.

2007 golf Classic

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Thanks also to celebrity caddies and special guests:

• Jane Bestwick • Blair Brownless • Jo Cornish • Simon Foote • Peter Gee • Commissioner Richard McCreadie • Christian Rainey • Craig Wellington • John Xintavelonis

Golfers dig deep to support researchers of the future

More than $23,000 was raised to fund scholarships in medical research at the Menzies Research Institute's fourteenth annual Golf Classic on 2 March. The event was a great success, with one hundred and twenty golfers braving the drizzly weather to network and develop new relationships, participate in some physical activity by walking around the scenic golf course, and raise valuable funds to support the work of the Institute.

The Corporate Express IT & Office Equipment Golf Classic Cup was won by the Total Freight Solutions team, made up of Neil Roberts, Peter Barnett, Brett Johns and Brett Orr. The team from Direction by Design took out the Veolia Environmental Services Runners-up prize.

Nine celebrity caddies participated in the day and were silently auctioned off to teams in the lead up to the event. Plenty of fun was had by these prominent Tasmanian personalities who generously donated their time to support the Institute.

The Fosters Bradman Award for the second highest team score was once again 'won' by Team Menzies II. A team from Eyelines also took out the Best Mixed Team Award for the second year running.

Tasmanian actor and comedian John X, recently returned from Melbourne and Shanghai, gave a very interesting account of his experiences playing Pumbaa the warthog in the musical production of The Lion King. Television personality Jo Cornish was the Master of Ceremonies.

The 2007 Golf Classic raised funds to support education and training for the medical researchers of the future. Funds will be directed into scholarships for Tasmania's brightest young science and medical graduates to embark on research careers with the Institute.

Golf Classic attendees enjoyed healthy and delicious food thanks to 4 Lunch, and premium beverages from Fosters. Thanks must go to all of the sponsors, caddies, supporters, volunteers and participants who contributed to the success of the day.

The 2008 event is looking to be even bigger and better – ensuring that the Menzies Research Institute Golf Classic remains one of Hobart's premier corporate fundraising events!

Corporate Express Team II with their celebrity caddy, John X

Aspirin on trial

Aspirin is a commonly available drug that many of us take to relieve minor pains and aches. Many people are aware that low-dose aspirin has been proven to prevent blood clotting and therefore heart attacks and strokes. Less commonly known is the fact that there is increasing evidence of its potential to reduce the rate of intellectual decline in older people.

However, part of the benefit of aspirin may be offset by a variety of negative side-effects. Thinning the blood can lead to strokes and bleeding from the stomach. In order to safely make the best use of aspirin's therapeutic effects, we need to properly understand the balance of risks and benefits when prescribing a program of low-dose aspirin for older patients.

The Menzies Research Institute is involved in a new collaborative study that is investigating whether the benefit of aspirin in reducing clotting events outweighs the side-effects of bleeding in people aged 70 and over.

The Aspirin in Reducing Events in the Elderly (ASPREE) study is a large-scale double-blind controlled trial involving up to 20,500 participants around Australia.

In addition to examining the effects of low-dose aspirin on heart disease and stroke, the study will also see if it helps to prevent a decline in brain function associated with ageing. Other outcomes that will be

Grants

The following grants have been awarded to the Menzies Research Institute have since the last issue of the Bulletin.

Royal Hobart Hospital Research Foundation. *Bettiol, SS; *Sanderson, K; *Reid, DW. Neutrophil function in patients with cystic fibrosis. **$12,150**

National Heart Foundation. *Clark, MG; *Rattigan, S; *Richards, SM; Kolka, CM. Endothelin-1, type2 diabetes and hypertension. **$112,680**

Clive & Vera Ramaciotti Foundation. *Chung, RS. Can Metallothionein protect against Axonal Degeneration following traumatic brain injury? **$30,000**

Royal Hobart Hospital Research Foundation. *Chuah, MI; *West, AK; *Muller, HK. Protection of the brain from infection: Immune properties of olfactory ensheathing cells. **$10,000**

Cancer Council of Tasmania. *Dickinson, JL; *Stankovich, J; Lowenthal, RM; Marsden, KA; *Patterson, B; *Quinn, SJ. Investigating the genetics of familial haematological cancers in Tasmania. **$60,000**

Australian Cancer Research Foundation. *Foote, SJ; *Venn, A; Lowenthal, RM; *Vickers, JC; *Dickinson, JL; *Blizzard, CL; *Stankovich, J; Bahlo, M. The ACRF Tasmanian Inherited Cancer Centre (ATICC). **$1,100,000**

David Collins Leukaemia Foundation. *Holloway, AF. Deregulation of Gene Expression by RUNX1 Fusion Proteins in Leukaemia. **$25,000**

Royal Hobart Hospital Research Foundation. *Holloway, AF; Shannon, MF; *Walters, EH. Switching genes on in immune cells: how does basal chromatin structure predict cytokine gene responses? **$20,000**

National Health & Medical Research Council. *Nelson, MR. Aspirin in reducing events in the elderly (ASPREE). **$85,000**

High Blood Pressure Research Council of Australia. *Nelson, MR; *Winzenberg, TM. A Cluster Randomised controlled trial of an Automated versus manual device for Blood pressure management (CRAB). **$59,086**

National Health & Medical Research Council - Fellowship. *Paul, SL. Cardiovascular disease risk behaviours: understanding childhood origins. **$274,000**

National Heart Foundation - Fellowship. *Schmidt, MD. Fatness and fitness: effects on heart disease, diabetes and metabolic syndrome risk from childhood to adulthood. **$122,686**

Royal Hobart Hospital Research Foundation. *Stewart, NJ. The role of Vitamin D and its receptor in the action of T regulatory cells, a set of cells important in the prevention of autoimmune diseases. **$4,979**

National Health & Medical Research Council - Fellowship. *Van der Mei, IAF. Gene-environment interaction in MS risk and progression: focus on ultraviolet radiation and Epstein-Barr virus pathways. **$137,000**

Royal Hobart Hospital Research Foundation. *Vickers, JC; *Dickson, TC. Axon regeneration in the mature CNS. **$20,000**

Masonic Centenary Medical Research Foundation. Vickers, JC. PhD Scholarship: Cathy Blizzard. **$60,000**

Cancer Council of Tasmania. *Woods, GM; *Muller, HK. Effects of UV radiation and vitamin D deficiency on the development of the skin immune system. **$35,000**

GlaxoSmithKline Australia - Fellowship. *Wood-Baker, R; *Walters, EH; *Reid, DW. Investigation of airway inflammation in COPD. **$80,000**

Royal Hobart Hospital Research Foundation. *Walters, EH; Dharmage, S. Risk factors for BHR in middle age: a prospective study from childhood to middle age among northern Tasmanians. **$20,000**

Clifford Craig Medical Research Trust. *Roddam, LF; *Sanderson, K; *Wood-Baker, R; Tristram, SG; Haug, G. The acquisition of new strains of non-typeable Haemophilus Influenzae is the leading cause of acute exacerbations in Tasmanian COPD patients. **$43,467**

*Menzies researchers.

examined include dementia, cancer, disability, depression and quality of life.

Half of the participants in ASPREE will receive low dose aspirin and the other half a dummy tablet. The two groups will then be observed over a five year period, checking in with a research nurse every twelve months so that information can be gathered about their medical history, mental function, mood and general activities. The nurse will also take a blood pressure measurement and a small sample of blood for analysis.

A feasibility study has been completed and final data analysis is underway with a manuscript in preparation. The main ASPREE study began in Tasmania in September 2006 and recruitment in other Australian states depends on the availability of further funding. The trial is supported by the NHMRC, the National Heart Foundation, the National Stroke Foundation, Alzheimer's Australia and the Australian Divisions of General Practice.

Publications

The following papers from the Menzies Research Institute have been published since the last issue of the Bulletin.

Collins N, Litt J, Moore M, *Winzenberg T, *Shaw K. General practice: professional preparation for a pandemic. Medical Journal of Australia 2006;185:S66-9.

General practice will play a key role in both prevention and management of an influenza pandemic. There are few published data addressing the issues that general practitioners and their practices will face in dealing with such a crisis. The outcome will revolve around preparation in three key areas: Definition of the role of general practice within a broad primary care pandemic response, adequate preparation within general practices, and resource provision.

*Ding C, Cicuttini FM, *Blizzard L, Scott F, *Jones G. A longitudinal study of the effect of sex and age on rate of change in knee cartilage volume in adults. Rheumatology 2007;46:273-9.

Within the age range we studied, knee cartilage volume declines at a faster rate with increasing age. Furthermore, women have substantially higher knee cartilage loss than men, and these sex differences first appear at age 40 and become more marked with increasing age, which has implications for prevention of cartilage loss from middle age.

*Haas MA, *Vickers JC, *Dickson TC. Rho kinase activates ezrin-radixin-moesin (ERM) proteins and mediates their function in cortical neuron growth, morphology and motility, in vitro. Journal of Neuroscience Research 2007;85(1): 34-46.

The ezrin-radixin-moesin (ERM) family of proteins contribute to cytoskeletal processes underlying many vital cellular functions. In these experiments the potential role of Rho kinase mediated ERM activation in cortical neurons was investigated utilizing a new pharmacologic inhibitor of Rho kinase and quantitative analysis of aspects of neuronal functions potentially mediated by ERM proteins. It was found that Rho kinase is an important activator of ERMs in mediating specific neuronal functions.

Janakiramanan N, *Ding C, *Jones G, Cicuttini F. Osteoarthritis Cartilage defects: Does size matter? Current Rheumatology Reviews 2006;2:311-7.

There has been evidence of early cartilage changes consisting of 'splits' or 'cracks' which have not received much attention or research in the literature. Further research is needed to determine if these 'cracks' do progress, whether they lead to pain, whether it is possible to accurately diagnose them, whether it is possible or necessary to treat them and whether current grading systems of articular cartilage lesions should include these 'crack's in their classification systems.

King AE, *Chung RS, *Vickers JC, *Dickson TC. Localisation of glutamate receptors in developing cortical neurons in culture and relationship to susceptibility to excitotoxicity. Journal of Comparative Neurology 2006; 498:277-294.

This study investigated the cell-type-specific changes in glutamate receptor localization in developing cortical neurons in culture, as well as the relationship between glutamate receptor subunit distribution with synapse formation and susceptibility to excitotoxicity. The relationship between glutamate receptor subunit expression and localization with synaptogenesis and the development of neuronal susceptibility to excitotoxicity were demonstrated. The data also suggests that excitotoxicity can be mediated through extrasynaptic receptor subunit complexes along dendrites.

Kolka CM, *Rattigan S, *Richards SM, *Clark MG. Potential for endothelin-1-mediated impairment of contractile activity in hypertension. Clinical and Experimental Pharmacology and Physiology. 2007 Mar;34(3):217-22.

The present study examined the potential for reduced exercise capacity observed in hypertensive patients as a result of elevated levels of endothelin (ET)-1. It was concluded that although lower concentrations of ET-1 do not affect exercise capacity, higher concentrations that may occur in hypertension are inhibitory to metabolism and aerobic capacity of muscle.

*Rattigan S, Bradley EA, *Richards SM, *Clark MG. Muscle metabolism and control of capillary blood flow: insulin and exercise. Essays in Biochemistry. 2006;42:133-44.

It is clear that exercise and insulin mediate capillary recruitment as part of their actions in vivo. In all insulin-resistant states examined thus far, insulin-mediated capillary recruitment is impaired with little or no change to the exercise response. Control mechanisms for capillary recruitment for exercise and insulin are considered, and the failure of the micro-vasculature to respond to insulin is examined for possible mechanisms that might account for impaired vascular responses to insulin in insulin resistance.

Ross RM, Kolka CM, *Rattigan S, *Clark MG. Acute blockade by endothelin-1 of haemodynamic insulin action in rats. Diabetologia. 2007 Feb;50(2):443-51.

Plasma levels of endothelin-1 are frequently elevated in patients with hypertension, obesity and type 2 diabetes. It was found that endothelin-1 blocks insulin's haemodynamic effects, particularly capillary recruitment, and is associated with decreased muscle glucose uptake and glucose infusion rate. These findings suggest that elevated endothelin-1 levels may contribute to insulin resistance of muscle by increasing vascular resistance and limiting insulin and glucose delivery.

*Stankovic RK, *Chung RS, Penkowa M. Metallothioneins I and II: Neuroprotective significance during CNS pathology. Invited review in International Journal of Biochemistry and Cell Biology. 2004; 39:484-9.

Metallothioneins (MTs) are a superfamily of highly conserved, low molecular weight polypeptides. The major forms of the protein, MT-I and MT-II, are induced by numerous stimuli and pathogens but most importantly their induction by metals is closely linked to the physiological metabolism of zinc and protection from the toxic affects following heavy metal exposure. MT-I and II may provide neurotherapeutic targets offering protection against neuronal injury and degeneration.

*Zhai G, *Ding C, Cicuttini F, *Jones G. A longitudinal study of the association between knee alignment and change in cartilage volume and chondral defects in a largely non-osteoarthritic population. Journal of Rheumatology 2007;34:181-6.

It has been unclear whether malalignment of the knee is a cause of knee osteoarthritis or a marker of disease progression. We investigated whether baseline malalignment of the knee predicts subsequent change in knee cartilage volume and chondral defects in subjects with and without radiographic knee osteoarthritis. Our study shows that baseline knee alignment is not associated with subsequent loss of cartilage volume or progression of chondral defects over 2 years. Further studies with a longterm followup are needed, but these results suggest malalignment is primarily a marker of disease progression.

*Menzies researchers.

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Mr Clive Pearce

The Menzies Research Institute is also deeply indebted to those generous donors who wish to remain anonymous.

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