

AUSTRALASIAN RESEARCH INSTITUTE

ARI-NEWS

Newsletter

Dec 08 / Jan 09

FINDING EVIDENCE... TAKING ACTION...

Welcome to the Dec 2008 / Jan 2009 edition of the Australasian Research Institute (ARI) newsletter. We have experienced a real whirl of activity this past year. With the addition of new projects and staff in the clinical trials unit and development and progress of our major adolescent health research series, the ARI can add 'innovative use of time' to its list of achievements. Having further consolidated our research framework we look forward to even greater achievements in the coming year.



Research achievements.

It has been a productive year for research at the ARI with the presentation of nine conference abstracts by members at various scientific meetings and the publication of three full scientific papers. As we are in the process of analysing data collected for two of our large adolescent projects we are looking forward to presenting more exciting data throughout 2009.

Staff overview.

Our success in 2008 has only been made possible through the contribution of our staff and talented collaborators who share our passion for health research. We are thankful to all of the members of our various research teams and research advisory and management committees for their dedication to the goals of the institute this past year. It has been a pleasure working with people of such collective talent and enthusiasm. I look forward to continuing our mutually beneficial partnerships.

To maintain the high level of expertise within its research teams the ARI has collaborated widely to fulfill its research agenda. A special thankyou goes to our collaborating institutions (UNSW, Macquarie University, University of Newcastle) for contributing staff-time and resources, leading to success in our key research areas of adolescent health and nutritional medicine.

Our donors.

Once again a very big thankyou to the Novus Foundation who have, for the second year running, remained the chief funding contributor to the ARI with a \$100,000 donation supporting research into the first-of-its-kind study into neurobiological correlates of depression in adolescents. As a not-for-profit research organisation the ARI relies on the financial support of the community to conduct this kind of cutting edge research. It is our highest priority that every donation, small or large be used to further our knowledge of health and disease in ways that will make a practical difference.

Dr Ross Grant
CEO

Australasian Research Institute

In this Issue:

-Feature Article - Omega 3

-In the media

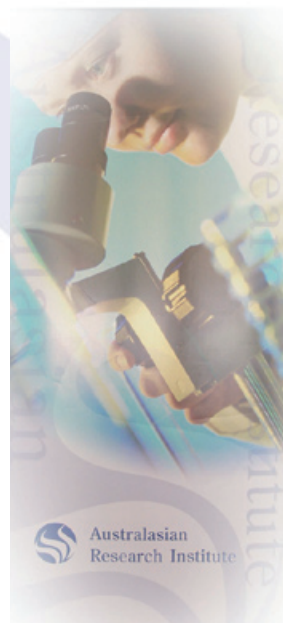
-Staff news

-Research Project Report

-Clinical Trials Report

-ARI Grants

**-Research committee -
Associate Professor
Eric Magnusson**



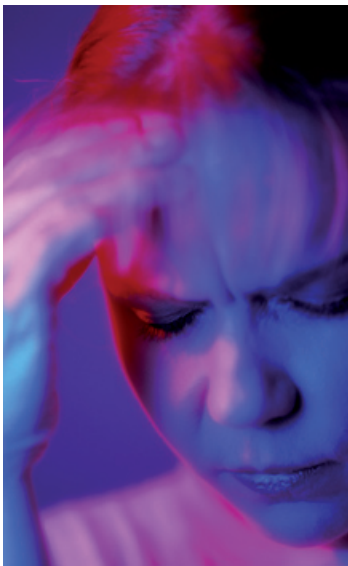
FEATURE ARTICLE:

OMEGA 3



Corilda L. Grant is a wound care specialist and research nurse with the ARI.

The value of fish consumption on general health has stimulated considerable interest in the community due to the large amount of omega 3 contained in certain oily fish. Increasingly, the Omega-3 fatty acids have been linked to numerous health benefits for the heart, joints and skin and an interesting link with reduced depression and suicidal behaviour. Both omega-3 & omega-6 oils are essential for good health but the ratio in recent decades has become significantly imbalanced with excessive amounts of omega-6 being consumed.



After adipose (fat) tissue, the brain is the organ containing the highest lipid (fat) content in the body. These lipids play an important role in maintaining membrane structure. A deficiency of essential fatty acids such as omega-3 has been shown to alter the structure and function of membranes and induce measurable cerebral dysfunction (Young & Conquer, 2005, Hibbeln et al., 2006). As the brain requires high omega-3 levels for normal brain

activity it is not surprising that a decrease in omega-3 content has been associated with some neuropsychiatric disorders including depression, autism and dyslexia and a decline in mental function with aging (Bourre, 2004). The Australian Institute of Health and Welfare (AIHW) suggested nearly a decade ago that the mental health of adolescents should be of major concern (Moon et al., 1999).

With depression being the strongest single risk factor for attempted or completed suicide and substance abuse, strategies to reduce the experience of depression among young people is essential.

Cell signalling is dependent upon membrane fluidity, which is affected by omega-3 concentrations in the membrane. During the last few years, epidemiological studies as well as clinical trials have suggested a significant role for omega-3 fatty acids in the development of depression. While the link between depressed mood in adults is well established, only recently has a link between omega-3-fatty acid content and depression in adolescents been reported (Mamalakis et al., 2006). Since omega-3 fatty acids are obtained only from the diet, it may be highly detrimental to the mental health of Australian adolescents if this dietary intake is not being met. Moreover, the current Australian omega-3 to omega-6 ratio is reported to be 1:8 (Meyer et al., 2003; Howe et al., 2006), with nutrition research suggesting that a ratio of 1:3-4 is desirable (Gebauer et al., 2006; Sugano, 1996).

What are omega 3 and omega 6 fatty acids?

The omega oils are part of the polyunsaturated fatty acid group. Being unsaturated, these fats are short, curved chains rather than rigid straight chains, making them able to move more freely through the system.

EPA and DHA (formed from omega-3) make flexible and pliable cell membranes, allowing them to become more open for transport and activity. They are considered essential because they cannot be made in the body and therefore must be present in the diet.

Essential fatty acids (EFA's) consist of Omega-3, 6, and 9. EFA's are important components of cell membranes and are the building blocks used to make other fats as well as inflammatory and anti-inflammatory chemicals. The Omega-3 EFA's also make chemicals that act like hormones to direct cell activities supporting defence and healing. These fats have a range of important functions in the body and are less likely to be used for energy or storage. The body disposes of any unused omega-3 while the opposite is true for omega-6. Any unused omega-6 is stored in the body as fat. The position of the double bond determines what type of omega fat it is. The omega-3 family has the first double bond after the third carbon in the chain, and the omega-6 family after the sixth carbon. Double bonds can easily be damaged by oxygen, forming free radicals, therefore, polyunsaturated fats are fragile and more sensitive to exposure from heat, light and air than other fats. Vitamin E is the major protector of polyunsaturated fats.

The right balance.

Achieving the correct ratio between omega-3 and 6 is important for keeping inflammation under control. Provided the omega-3's and omega-6's are in balance, they complement each other. However, an omega-6 imbalance promotes inflammatory activity that may contribute to increases in diseases such as cancer, heart disease, stroke, diabetes etc. The correct mix of omega-3 & 6 fatty acids keeps cell membranes fluid enough for effective transport of substances into the cell and the removal of wastes.

Unfortunately our current western diets generally have reduced intakes of Omega-3 FA's, but increased intake of omega 6 FA's.

This negative effect can be compounded as Omega-3 and Omega-6 fats compete for the same enzymes that break them down into usable forms.

Why has the balance changed?

Omega-3 FA consumption has decreased over the last fifty years due to changes in food choices and food processing.

The omega 6 fat (Linoleic acid(LA)), is present in large quantities in most oils such as corn oil, safflower, sunflower and cottonseed, vegetable based fatty foods, processed foods and farm animal products (if they have been fed a grain based diet such as corn, rather than pasture).

The imbalance has occurred largely because of recommendations to replace unhealthy saturated fats with these economical unsaturated (omega-6) oils. Corn oil has a ratio of Omega-6/Omega-3 of 60:1, and safflower oil 77:1. The most easily metabolised omega 3 EFA is fish oil. However, few people like to eat the 100gms of oily fish like sardines, mackerel and herring that was a common diet staple for past generations. There are also legitimate concerns with various toxin levels in fish available in the marketplace today.

Where are good sources of Omega-3 FA's?

- Fish Oil from oily fish such as salmon. While fish oil is currently considered to have the more bioavailable source of DHA omega 3, not all fish are equal. Most Australian fish are relatively low in omega-3 FA's. The top 4 Australian fish yielding the highest amounts of Omega-3 are Swordfish, Atlantic Salmon, Gem Fish and Ocean Trout. Farmed fish may not be of a consistently high quality and the amount of omega 3 may vary depending on their feed.

There are numerous fish oil supplements on the market -always check for purity of the oil as heavy metals and pesticides can accumulate to significant amounts in some fish.



Some people are concerned that harvesting for fish oil is not a viable option given lack of future sustainability particularly of the wild variety. The way some fish oil is harvested and the amount of time that passes before it is processed may result in inferior quality oil.

Fish oil also contains vitamin D and vitamin A, particularly if it was obtained from the liver. (Due to its very high levels of vitamin A and vitamin D, women who are or who could become pregnant should not take cod liver oil before consulting their doctor. All others should consult with a doctor before taking any supplements containing more than 25,000IU (7,500 mcg) of vitamin A per day or 800 IU of vitamin D per day.)

Vitamin E is often added to fish oil to prevent the formation of free radicals due to oxidation (rancidity).

- Krill oil. Krill is a tiny crustacean that lives in cold bodies of water and are the main dietary source of most whales. Although fish oil has a higher percentage of EPA and DHA fatty acids, krill oil has the advantage of having astaxanthin (an important

anti oxidant), vitamins A and D, and possibly other nutrients such as small amounts of phospholipids. However, as phospholipids can be easily obtained from other food, such as eggs, or lecithin (phosphatidylcholine is found in lecithin), krill oil supplements may not have a significant advantage over fish oil. Significantly, some people have environmental concerns regarding the harvesting of krill oil for the purposes of supplementation. According to the journal Nature (Marris E, (2004)), populations of krill have fallen by 80% in the past 30 years so the viability of such a commercial enterprise is in question.

- Seal oil. There is recent interest in seal oil as a more compatible source of Omega-3 fatty acids as it contains 3 types of omega-3 FA's: EPA, DHA, and DPA. However the beneficial effect of DPA to humans is not yet known.



- Vegetarian options.

Omega-3 oil is found in a variety of vegetable sources. In fact the reason that fish is high in omega-3 is because they feed on micro algae in the oceans. Hens with eggs high in amounts of Omega-3 have had their diet enhanced with flax seeds and other supplements such as micro algae. The algae and plant omega-3 differ in composition. Plant sources such as flax (linseed),

walnuts, canola, soy, pumpkin seeds and green leaf vegies (particularly wild varieties such as purslane), all contain the alpha linoleic acid (ALA) variety as well as some omega-6.



ALA is the 'parent' Omega-3 which the body can convert to EPA and DHA, and is an important dietary nutrient itself. However, it may be harder to process into the longer chain FA's of EPA and DHA in those whose health is compromised and in the elderly where absorption and conversion may not be as efficient.

It is important to remember that the higher the diet is in omega-6, the lower the conversion rate of ALA to EPA and DHA. Some studies have shown ALA is converted to DHA in the brain, but not in the rest of the body. Further studies need to be undertaken to observe the effect this may have and answer questions such as 'Is allowing the body to adjust for it's own conversion needs adequate and is this beneficial or detrimental?' For the purpose of cognitive function, flax seed and other plant originated Omega-3's are effective alternatives to animal sources provided there are adequate amounts consumed.

Importantly the omega-3 contained in micro algae is in the DHA form and should be available as a supplement in health food stores.

It should be remembered that all oils are vulnerable to damage via light and heat, so whatever form of omega 3 supplement you chose, ensure it is stored in a cold environment (fridge), out of light and is well sealed. Flaxseed oil and walnuts are known for rapidly oxidizing and therefore prone to causing free-radical damage.

Conclusion.

While the general health benefits of Omega 3 are numerous, recent evidence suggests that the essential Omega 3 FA's play an important role in healthy brain development throughout the different stages of life. Importantly, depression and anxiety in childhood are likely to persist with age if not effectively treated.

In the context of other biological factors, we look forward to sharing with you further insights into the link between omega-3, brain biochemistry and adolescent depression in our current study: The Neurobiology of Depression in Adolescents (see ARI - Research Activities).

In the Media



The Sun-Herald newspaper 30/12/07



West Australian Newspaper 18.03.2008



Private Hospital Publication Dec, 2007



'Research Thank-You Day' in Martin Place, Sydney



NOVAS Fundraising Dinner, 2008
(from left to right: Prof Margaret Morris, Dr Ross Grant, Caroline Pemberton (Miss World, Australia, 2007), Barry O'Farrell MP, Honourable Dr Brendan Nelson MP)



A very big thankyou to Ms Caroline Pemberton (2007 Miss World Australia) for her support as Novus Ambassador in the Fund raising effort of the Novus Foundation (the major sponsor for our adolescent depression study). Ms Pemberton also visited schools with the ARI research team to help inform students about depression. Ms Pemberton is an excellent presenter, managing to hold the attention of large groups of teenagers while explaining the media distortion of body-image and its link to feelings of self-worth and depression.'

ARI Research Projects Update

Project Title: Uterine Prolapse: The Self-reported knowledge and impacts of a uterine prolapse and hysterectomy on underprivileged Nepali women and families.

Investigator(s): B. Watson, Tonia Crawford, S. Heise.

It is estimated that between 10% -37% of Nepali women suffer from uterine prolapse. Such women often endure significant social, health and economic hardships as a result. The Asian Aid NGO has so far funded ~ 3000 operations to correct this problem anecdotally resulting in health, economic, psychological and social benefits. However no study has formally evaluated the impact of this important surgery. This study is investigating the incidence of uterine prolapse, the level of knowledge among poor Nepali men and women of the cause and prevention of uterine prolapse, the social impact of hysterectomy and the potential for the use of hysterectomy recipients as prolapse awareness community educators to raise community understanding. Preliminary results were presented at the Asia-Pacific ICSD Conference, 2008.



Project Title: The New Leaves Writing Project.

Investigator(s): A/Prof J. Gordon, J. Beveridge, C. Rickett, A. Campbell, Dr C. Grieve

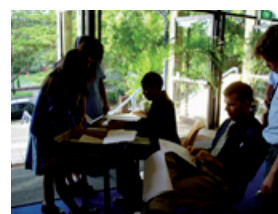
This project is an initial investigation of the potential benefits of writing poetry for participants who have experienced, or are experiencing, life threatening illness and who have, or who are receiving treatment at Sydney Adventist Hospital. Judith Beveridge, a distinguished Australian poet, lead a ten week poetry writing program which allowed participants to express their feelings about their experience of illness. The program is being evaluated with a pre and post test measure of well being and pre and post test interviews. This project is a pilot study to test the method for potential use with a larger number of participants.



Project Title: Characterisation of Picolinic acid levels and related metabolites in human cerebro spinal fluid.

Investigator(s): S. Coggan, Dr R. Grant, A/Prof. G. Smythe

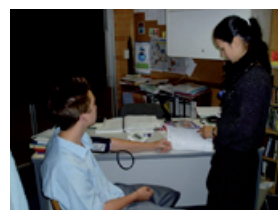
Picolinic acid is a metabolic product of tryptophan catabolism via the kynurenine pathway (KP). This pathway has become the centre of significant research activity among neuroscientists in recent years due to the neuroactive properties of some of the metabolites. Picolinic acid (PIC) is present in significant levels in the brain, however no one currently knows what its function is. This study was designed to help us understand some of the characteristics of PIC and how it might be related to health and/or disease. We identified that PIC levels are significantly increased in the brain as a person ages. We also found that PIC levels in the brain change throughout the day being highest around midnight and lowest at midday. This data adds to our limited knowledge of PIC and will help researchers design experiments that identify what important roles it plays within our brains. These results were recently published in the Journal of Neurochemistry, (2009).



Project Title: Neuroprotective effects of natural polyphenol antioxidants on human neurons treated with quinolinic acid. Relevance for ageing.

Investigator(s): Dr R. Grant, Dr G. Guillemin, N. Braidly.

Increased free radical activity and quinolinic acid induced excitotoxicity is a feature of the aging brain and a major contributor to the pathological changes in neurodegenerative diseases such as Alzheimer's. There are a number of molecules contained in ordinary food with demonstrated



antioxidant activity. However the action of these antioxidants has generally not been tested. This study tested the ability of key, food derived, antioxidants to preserve the health of brain cells in the presence of excitotoxic insult. Preliminary data showing significant protection of neuronal cells by some polyphenols via a novel mechanism was observed. This data was presented at the Australian Neuroscience Society conference and the Australian Health and Medical Research Congress in 2008.



Project Title: *The effect of diet and lifestyle on serum adipocytokine levels in adolescent females: Implications for insulin resistance and Type 2 diabetes.*

Investigator(s): Prof M. Morris, Dr R. Grant, Dr A. Bilgin, Dr R. Pearce, Dr S. Bains, Carol Zeuschner.

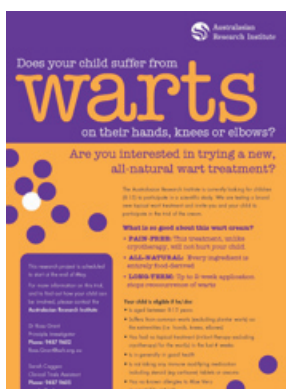
There is an increasing trend in the incidence of type-2 diabetes in children and adolescents in many populations around the world, including Australia. The increase in type-2 diabetes is often paralleled by an increase in body mass in the same population, but this is not predictive. The reason for this association is not yet completely understood but appears to be linked with decreased production of an important molecule called adiponectin by white adipose tissue, i.e. fat cells. Through this research we hope to better understand this association so that foods identified to promote adiponectin production can be promoted. We look forward to communicating our findings in the next issue.

Project Title: *Brain biology food and mood- Neurobiological correlants of depression in adolescents.*

Investigator(s): Prof M. Morris, Dr R. Grant, Dr A. Bilgin, Dr R. Pearce.

An increasing proportion of children and adolescents are being diagnosed with depression, anxiety, eating disorders and obesity. This project seeks to investigate the neurobiological processes that occur as a result of a “depressed” state. Similar research has been conducted in adults but no research has yet been published regarding this issue in adolescents. Our results may reveal some of the reasons why certain adolescents are more prone to depression and/or symptoms of anxiety. Further, we may also identify dietary/ lifestyle patterns (e.g. low Omega-3 fatty acid intake, excessive caffeine, inadequate exercise) that may worsen symptoms of depression. We recently visited two high schools within Sydney to collect data and plan to gather more within the coming year.

Clinical Trials



Project Title: *Phase 1, single centre, randomised, placebo controlled, fixed dose, clinical trial of the safety and efficacy of up to 14 days application of ‘Zb cream in the treatment of subjects with common warts.*

Investigator(s): Dr R. Grant, Dr J. Lewis.

Common warts are skin infections of the human papillomavirus (HPV), and occur in up to 20% of all school-age children. The infection results in a benign disfigurement of the skin surface, which is harmless but can cause social embarrassment. A number of wart-removal treatments are currently on the market, however, some need long term administration and can often be painful, while none can guarantee preventing the reoccurrence of warts over time. The cream under trail is comprised entirely of all-natural sources, and is therefore considered completely non-toxic which is ideal for paediatric medicine. We look forward to inform you of the results in the next issue.

Project Title: *Proof of concept; an open label pilot study to determine the efficacy and tolerability of a treated gliadin-containing product in asymptomatic subjects with coeliac disease.*

Investigator(s): Dr R. Grant, Prof B. Jones, Dr J. Ashton.

Coeliac disease is an inflammatory disorder affecting the upper small intestine and is usually caused by an allergic response to ingestion of gluten found in wheat, rye and barley causing inflammation of the small intestine often preventing efficient absorption of important nutrients from food.

This study is in the process of testing whether a new process for removing toxic gluten proteins is affective. If successful, the treatment process should enable patients with coeliac disease to again eat wheat containing products provided they have been detoxified in this way.

Project Title: Randomised comparative study of FOLFOX6m plus SIR-Spheres versus FOLFOX6m alone as first line treatment in patients with non-resectable liver metastases from primary colorectal carcinoma.

Investigator: Dr G Marx

Colorectal cancer is the 3rd most common cancer in the western worlds. 70% of all patients will develop mtastases in the liver. The outlook for such patients is poor with conventional treatments. Selective internal radiation Therapy (SIRT), using SIR Spheres is a method of delivering therapeutic radiation to hepatic tumours while sparing the normal liver cells. This international study will assess the effect of a single implant of SIR-Spheres to a standard regimen of FOLFOX.

Project Title: An international multi-centre study of Tamoxifen vs Anastrozole in postmenopausal women with hormone sensitive ductal cell carcinoma in situ (DCIS).

Investigator(s): Dr G Marx, Dr TM Hughes, Dr T. Curren, Dr Philip Middleton, Dr D. Sharp, Dr J. Rutovitz.

This study is looking at the possibility of preventing the return of breast cancer in women who have been diagnosed with ductal carcinoma in situ (DCIS) of the breast. The study will involve 4,000 women from around the world, who are postmenopausal and have been diagnosed with DCIS within the last six months. The drugs being tested in the study, tamoxifen and anastrozole, are provided by the pharmaceutical company AstraZeneca at no cost to study participants.

In recent clinical trials women with DCIS have been given tamoxifen, and results show a reduction in the number of women whose DCIS progressed into invasive breast cancer. However, further research is needed to determine the particular group of women with DCIS who will benefit from taking tamoxifen.

The purpose of the IBIS II DCIS study is to find out whether anastrozole is as effective or better than tamoxifen in preventing the development of breast cancer .The study will also compare the effects (good and bad) of tamoxifen and anastrozole.

ARI Grants

ARI GRANTS – 2008

The ARI is pleased to announce the following researchers were successful in being awarded an ARI Grant for research into health and community issues this year.

Mr Brad Watson Uterine Prolapse: The Self-reported knowledge and impacts of a uterine prolapse and hysterectomy on very poor Nepali women and their families.

Staff Happenings



Farewell Angie Low. Angie was an invaluable member of our team as the Research Assistant (2006- 2007). All the best as she takes up her new role in the food technology industry.



Welcome to Jade Guest who replaces Angie as the ARI's Research Assistant. Jade is completing her Masters in Public Health and has a background in Biomedical Science.



Also joining the team is Carolyn Illes. Carolyn joined us in July and is assisting Renee Trotter with Clinical Trails. Carolyn is a registered nurse with previous experience in the conduct of clinical trials.

ARI Corporate Members:

Sydney Adventist Hospital, Avondale College, Adventist Health, Sanitarium.



Meet our Research Committee

Associate Professor Eric Magnusson



The ARI Research Advisory Committee (RAC)

The ARI is privileged to have a very qualified team of 12 Scientists and Clinicians from diverse specialties available to review the quality and relevance of research projects funded by the ARI. So that you can get to know these important members of our executive research team, we will profile on of the RAC members in each issue of ARI News. In this addition, we are pleased to introduce you to Associate Professor Eric Magnusson.

Associate Professor Eric Magnusson has been the ARI's chair of the Research Advisory Committee since its inception in 2004.

Born in 1933, Dr Eric Magnusson brings a wealth of experience to the board, having served in many institutions as lecturer, researcher and administrator.

Eric graduated with a BSC in Chemistry from the University of London and the following year became an Associate with the Royal Australian Institute of Chemistry. In 1957, Eric completed his PhD in Inorganic Chemistry from the University of NSW, followed by a number of international scholarships and national and international research fellowships.

In 1960, Eric completed his second PhD in Theoretical Chemistry from the University of London, becoming a Fellow with the Royal Australian Institute of Chemistry. While in London in 1959, he programmed the enormously expensive 'Mercury', the university's first mainframe computer. His major interest in synthetic chemistry at UNSW was working with the precious metal platinum which after 54 years has now led him to computing the electrical

structures of platinum compounds to help his UNSW colleagues find better ways to bind DNA and kill cancer cells.

For 10 years (1971-80), he was president of Avondale College and after the Chamberlain trial in 1982, he started investigating the way juries interpret scientific evidence in criminal courts. This led him to publish his findings on the Comprehension of Forensic Science by Criminal Court Jurors.

Following his term at Avondale, Eric taught at the Australian National University Research School of Chemistry and later at the Defense Force Academy as Associate Professor and upon retiring following the death of his first wife, is now an appointed Visiting Fellow. Eric's main publications in Chemistry are in the use of quantum theory to investigate chemical bonding in molecules. Other special interests are drug policy and drug education. Eric Magnusson has been honoured in the Peoplescape display on the lawns of Parliament House, Canberra.

Dr Eric Magnusson has been of great support to the Australasian Research Institute.

Your gift of support (over \$2.00) is tax deductible

Name..... Address.....

Phone.....

My cheque of \$.....is enclosed Please debit \$.....from my (please circle)

Bancard Mastercard Visa Diners Amex

Card Number..... Name on Card.....

Signature..... Expiry Date.....

Send your fully tax deductible donation to:
AUSTRALASIAN RESEARCH INSTITUTE
185 Fox Valley Road, Wahroonga, NSW 2076
or fax 02 9487 9626