<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chairman's Report</td>
<td>2</td>
</tr>
<tr>
<td>Directors' Report</td>
<td>3</td>
</tr>
<tr>
<td><strong>ANZAC Research Institute Research Reports</strong></td>
<td></td>
</tr>
<tr>
<td>Public Health &amp; Epidemiology</td>
<td>6</td>
</tr>
<tr>
<td>Andrology</td>
<td>8</td>
</tr>
<tr>
<td>Biogerontology</td>
<td>14</td>
</tr>
<tr>
<td>Bone Biology</td>
<td>16</td>
</tr>
<tr>
<td>Neurobiology</td>
<td>20</td>
</tr>
<tr>
<td>Respiratory Medicine</td>
<td>23</td>
</tr>
<tr>
<td>Vascular Biology</td>
<td>24</td>
</tr>
<tr>
<td>Staff &amp; Students</td>
<td>26</td>
</tr>
<tr>
<td>Grants &amp; Contracts</td>
<td>28</td>
</tr>
<tr>
<td>Publications</td>
<td>30</td>
</tr>
<tr>
<td><strong>ANZAC Health and Medical Research Foundation</strong></td>
<td></td>
</tr>
<tr>
<td>Governance</td>
<td>35</td>
</tr>
<tr>
<td>Financial Performance</td>
<td>37</td>
</tr>
<tr>
<td>Fundraising</td>
<td>38</td>
</tr>
<tr>
<td>Donor Honour Roll</td>
<td>39</td>
</tr>
<tr>
<td>Opportunities To Donate</td>
<td>40</td>
</tr>
</tbody>
</table>
I am deeply honoured to have succeeded the late Professor John Young AO FAA as Chairman of the ANZAC Health and Medical Research Foundation. Professor Young was an inspiring and visionary leader, to whose dedication and commitment the Foundation and the ANZAC Research Institute owe their existence. The new Board plans to honour his memory by continuing to build the research strength and international reputation of the Institute and to fulfil its vision of providing leadership and excellence in research activities.

The Board of the Foundation underwent significant restructuring during the year, to reflect the change in its role, now that the Institute has been established and fully staffed. A new Constitution was adopted in June 2003 to guide this change, improving the Constitution’s alignment with current corporate law and clarifying Directors’ responsibilities in acting as a Board of Management for a modern medical research institute. The twelve-member Board now includes eight representatives of key stakeholder organisations and four from the general community, with all Directors chosen for their expertise in science, health, corporate governance, finance or law. The new Board has approached its work with enthusiasm, and has held extensive discussions on strategic directions for the Institute and on establishing clear objectives for fundraising.

The issues of lifestyle and ageing, on which the work of the Institute is focussed, have received greater national and international attention during the year. Within its National Research Priorities, the Commonwealth Government has established a priority goal of Ageing Well, Ageing Productively. The work of the Institute is already making a major contribution on several fronts under this theme, as demonstrated by the success rate of our research teams both in winning NHMRC and ARC funding and in peer-reviewed publications. The Institute is very well placed to assist the New South Wales Government in achieving its stated objective “to position and promote NSW as a leader in science, innovation and medical research”.

Whilst the research teams have been very successful in attracting grants for individual projects and ongoing research programs, the funding of the Institute’s basic infrastructure and administration remains a concern. The Board has decided to address this issue as its major funding priority and looks forward to attracting the support of governments, the business community and individuals in its endeavours to put the Institute’s operating finances on a sound footing.

The Board and I congratulate the Director, Professor David Handelsman, the research teams associated with the Institute and all the support staff on their achievements in 2003-04 and look forward to further success in the coming year.

Felicity Barr
Chairman
Welcome to the ANZAC Research Institute’s report for its fourth year of operation. The Institute continues to grow and consolidate its scientific directions and achievements. Over the last year the ANZAC Research Institute has provided a research home to now over 70 scientists with many more working in closely affiliated hospital departments. In this year the Institute attracted $2.7 million of peer-reviewed grant funds including $1.4 million from NHMRC. During this time Institute scientists produced 138 peer-reviewed papers. Beyond these are relatively coarse measures of success, you are invited to read in more detail the many and varied projects our scientists are working on in the pages of this Annual Report.

The Institute was pleased this year to have attracted Dr Paul Witting, the only Australian Research Council (ARC) Fellow in the University’s Faculty of Medicine, to be the senior scientist in the Vascular Biology laboratory. Over this year, the Institute has seen four new PhD degrees completed based in its facilities and we continue to attract new PhD students.

A regular difficulty for any medical research institute located off the main University campus is to attract the best students as new PhD candidates. Those who spend time at the Institute often are keen to share the outstanding opportunities and excellent science offered in training here as graduate students supervised by the Institute’s scientists. Yet, the distance from main campus and unfamiliarity with the Institute remain significant hurdles in attracting the best and brightest young science and medical graduates. To help overcome this, we undertook a pilot scheme in this year in offering Summer Scholarships in our research laboratories. Five excellent summer scholars were hosted and all completed very fruitful projects. Based on the success of this pilot, we will continue to offer Summer Scholarships with the view to familiarising the most enthusiastic and committed undergraduate students before they settle on their PhD training options. Following the success of the Institute’s pilot scheme, the University’s Faculty of Medicine is undertaking its own Faculty wide scheme in 2004-05 modelled our initiative.

A key issue for the Institute is to have available the high-tech specialist research equipment required by our scientists to compete effectively at the cutting edge of science. During the last few years, with help from the University’s Equipment Grants, we have acquired a flow cytometer, a mass spectrometer, a micro-X-ray machine, a scanning electron microscope and, soon, a multi-plate reader. In addition one of our high priorities is the Institute’s Transgenic Unit, which is in aiming to become a production facility creating complex in vivo genetic models for human physiology and disease research where these cannot be studied directly in humans. This leading edge work requires substantial infrastructural support for equipment and skilled staff.

Our commercialisation focus has led to a strong association with a new biotechnology R&D company, Avastra, which leases space for its Tissue Welding laboratory within the Institute. Inspired by innovative ideas from the burns and plastic surgeon, Dr Peter Maitz AM, this commercially focused laboratory is developing a suture-free way of joining blood vessels that could revolutionise microvascular surgery. This pioneering work led to the top-ranking Biotechnology Innovation Fund grant being awarded to Avastra’s Tissue Welding laboratory by the Minister for Industry, Ian McFarlane, at a ceremony held in November 2003 at the Institute.

The Institute is a key partner in the Concord Hospital based consortium that is undertaking the Concord Health and Male Ageing Project (CHAMP). This NHMRC funded study will assemble from men living in the Concord area, the world’s largest study of the health and outlook of men over 70 years of age. Most studies of older populations throughout the world have focused on women mainly because they survive longer. The reasons for men’s shorter life expectancy in this and other communities remains unexplained but requires explanation and represents a challenge to improve health and medical care for men. In this context, the CHAMP study will chart the major predictor of health and disability and help identify the most important predictors of healthy, independent ageing for men. This study is emblematic of the Institute as a focus of collaborative research since it brings together all the research groups on the Concord campus and coalesces around our outstanding expertise and facilities. Based on our wide range of research strengths, this study will not only advance knowledge on male ageing and how to promote it, but it will also secure a memorable place for Concord Hospital in the future for improving public health and advancing medical care.

We are also host to a variety of major studies initiated by our own investigators including collaborating with a French-American company to evaluate a hormonal treatment that may prevent prostate growth, a follow-up study of Vietnam Veterans’ health and studies funded by the World Anti-Doping Agency as part of its campaign to detect and eradicate sports doping.
Whilst our scientists have been extraordinarily successful in obtaining competitive grants and commercial contracts, a key determinant of the Institute's overall future success is its fundraising. We need expensive, high technology research equipment as well as funding for scholarships and fellowships to stay at the cutting edge of research. These are crucial for us to maintain our competitive edge both in training the new generation of scientists and in attracting and retaining top class scientists. Tax-free scholarship stipends are a highly cost effective way to support research for scientific training of the next generation of scientists. Postdoctoral fellowships help create the critical mass of diverse scientific skills and so recruit and retain valuable scientific expertise. Scientific trainees and scientists form the core of future medical research in this country and our focus on ageing is an important way to ensure that vital research into healthy ageing in Australia is encouraged. Our fundraising efforts must try to match the successes of our scientists in grant funding and scientific discoveries. This issue of fundraising support will be decisive for our future.

During this last year, towards the end of its first decade filled with major achievements, the Foundation underwent a necessary update of its Constitution. Having been founded as a charitable fundraising organisation aiming to create dedicated research infrastructure on the Concord Hospital campus, the Foundation has very rapidly become responsible for the operations of a modern medical research institute. This rapid transformation flowing from its success in establishing the Institute necessitated a more streamlined, efficient and focused governance structure. Hence its constitutional reform has featured the introduction of a new smaller Board structure retaining all the key stakeholders but with more focus on its challenges and primary role in operating our Institute.

This year the Foundation and Institute lost its great founder and inaugural Chairman, Professor John Young, AO. The products of his strategic guidance are evident everywhere and his peerless wisdom is sorely missed. The goodwill and practical support from Dr Diana Horvath, CEO of Central Sydney Area Health Service together with the continued support from Concord Hospital’s executive managers, Danny O’Connor, Matthew Daley and Dr Margaret Sanger remains a vital pillar of our ongoing success.

We are fortunate indeed to have such fine, accomplished and highly motivated scientific staff. It is my privilege to acknowledge the pleasure of working with them. They provide the very best of scientific collegiality and continue to achieve great things for their laboratories and our Institute. The Institute is more than the sum of its parts because of their productive interactions and collaborations.

My thanks also go to our hard-working management team; Christine Harrison, our General Manager, our office staff and Mamdouh Khalil, Manager of the Molecular Physiology Unit and his staff. It is a privilege to recognise their hard work and dedication, which is vital to such an effective start for the Institute. We are fortunate indeed to have such strong organisational support of our goals. Finally, I thank the Board and our friends and supporters whose continuing efforts will determine how well the ANZAC Research Institute continues to succeed.

The ANZAC Research Institute has now established itself as major independent medical research institute recognised by NHMRC and the NSW Government with a national and international profile. Our proud record of growing achievements in grants, publications and scientific training is outlined in the following pages. I hope you will agree that this progress has been remarkably fast and extraordinarily successful.

David Handelsman
Professor of Reproduction and Andrology
Public Health & Epidemiology 6
Andrology 8
Biogerontology 14
Bone Biology 16
Neurobiology 20
Respiratory Medicine 23
Vascular Biology 24
Concord Health and Ageing in Men Project (CHAMP)

Robert Cumming, David Handelsman, Markus Seibel, Helen Creasey (CERA), Phillip Sambrook (Royal North Shore Hospital), Louise Waite (CERA), Melisa Litchfield, Anita Sharma

CHAMP is designed to be the world’s most comprehensive study of the health of older men, with nearly 3000 participants. This NHMRC-funded project will provide important new information on the role of reproductive hormones in male ageing; risk factors for several major age-related diseases, including osteoporotic fractures and Alzheimer’s disease; and prevalence, incidence and consequences of the major health problems affecting older men.

Nearly 3000 men aged 70 years and over, living in the vicinity of Concord Hospital will be recruited into the study. The Electoral Roll will be the main method of recruitment, supplemented by local publicity.

Prior to attending the study centre at Concord Hospital, participants will complete a series of questionnaires. They will be given a series of tests, including dual energy X-ray densitometry (DEXA) to measure bone, fat and lean mass; detailed assessment of memory and problem solving; tests of muscle strength and gait and balance; a bladder ultrasound and a test of urine flow rates; and spirometry to assess respiratory function. Blood will be taken for reproductive hormones, vitamin D, parathyroid hormone, DNA, and markers of bone turnover.

Most of the baseline interview and examinations will be repeated after two years. Ongoing review every four months will ascertain incidence of falls, fractures and hospital admissions.

The main focus of the CHAMP study will be osteoporosis, muscle weakness, dementia and urinary problems. The role of testosterone and other reproductive hormones in the origin of these conditions will be particularly examined in this study.

Fractures are common in older men with 29% of 60-year-old men experiencing a fracture of some type during the remainder of their lifetime. CHAMP will be one of the first studies in the world to investigate risk factors for fractures in men, second only in size to the Mr Os Study in the USA.

There is some evidence that men lose muscle at a faster rate than women, as they grow older. However, most studies of muscle loss have been small, cross-sectional studies involving few old people. CHAMP will use sophisticated techniques and a longitudinal design to assess muscle mass and function in older men.

Dementia is probably the most disabling condition of old age and yet little research has been done on the specific features of dementia in men. CHAMP will be the world’s largest study of dementia in men and will have a particular focus on testosterone in the origins of Alzheimer’s disease.

Many older men develop lower urinary tract symptoms, such as incontinence, nocturia, weak stream and dribbling, which can mar their quality of life. CHAMP will investigate the causes of urinary problems in older men.

The ANZAC Research Institute is a key partner in the Concord Hospital-based consortium that is undertaking CHAMP.

- Grants:
  NHMRC: $1.8 million, 2004-08
  NHMRC equipment grant: $193,000, 2004.

- Scholarship:
  Anita Sharma
  Northcott Neurosciences Scholarship: $75,000, 2004-06
The Australian Vietnam Veterans’ Health Study

Brian I. O’Toole, Stan Catts (University of Queensland), Jill Cockburn (University of Newcastle), Sue Outram (University of Newcastle)

War has been a part of human history since before there was written records. The devastation brought to man and nature during war is deeply etched in the minds and in the annals of civilisations of those who endured. Where ignorance lies is in the long-term effects of war and combat on the people who fought and survived. The Australian Vietnam Veterans’ Health Study is a long-term epidemiological cohort study that is examining the medium and long-term physical and psychological effects of war on the men who served.

Begun in the late 1980s at the University of Sydney and funded by NHMRC, PHRDC, the Australian War Memorial, Westmead Hospital Research Foundation, with assistance from the Department of Veterans’ Affairs and Ex-Service Communities, the study selected a random sample of 1,000 men who had been posted to Vietnam during 1962-1972, the years of Australia’s involvement. Of those selected, 50 were known to have died, eight in Vietnam, prior to the time of interviews. A total of 641 men were interviewed across Australia using standardised assessment tools to measure physical health, mental health, social and welfare status, and a host of ancillary information on the men who represented their generation in war service. The study results were published in international journals and showed that veterans had a greater health burden than should be expected from Australian national norms. Post Traumatic Stress Disorder (PTSD) was common with over 20% having had this at some time since the war, with over 10% still affected. Analyses of these findings showed that combat exposure was a prime risk factor for PTSD as well as other psychological conditions, and that PTSD itself was linked to a variety of subsequent physical health ailments.

In 2004 the NHMRC funded the second major wave of the study to be set up at the ANZAC Research Institute. This second wave study aims to locate and interview as many of the original cohort of 1,000 as possible. Deaths are being detected via the Australian Institute of Health and Welfare’s National Death Index. The Commonwealth Department of Veterans’ Affairs is assisting with the location and enrolment of the selected sample.

Grants
NHMRC: $575,000, 2004-05

Interviews will commence in the last quarter of 2004 and continue on through 2005. The intensive assessments will include the Australian Bureau of Statistics Health Interview Survey to compare veterans’ health with national norms, psychological tests and a searching interview about Vietnam service, combat exposure, and PTSD. Post-service psychological health is assessed using the Composite International Diagnostic Interview, also used by the ABS in the National Survey of Mental Health and Wellbeing to facilitate further comparison with ABS national norms. Analysis will concentrate on the direct and indirect health effects of war service and enhance our understanding of the intermediate and long-term consequences of participation in war.
Male ageing

PY Liu, DJ Handelsman

Dr Peter Liu is currently completing a two-year NHMRC Neil Hamilton Fairley Overseas Fellowship. Located at the Mayo Clinic in the USA under the supervision of Professor Johannes Veldhuis, where he has continued his studies in male ageing and reproductive health. Peter’s PhD was awarded for clinical research studies of reproductive hormones in young and older men. These studies led to international recognition including keynote presentations at the US Endocrine Society Annual Scientific Meeting two years in a row, highlight publications featured as paper of the month on US Endocrine Society website and in the top clinical research journal, Journal of Clinical Endocrinology and Metabolism. He won the Endocrine Society of Australia’s Servier Young Investigator Award in 2004 in recognition of a study, performed at ANZAC Research Institute with Associate Professor RR Grunstein from the Woolcock Institute, that established the first clear evidence of potential harmful effects of excessive testosterone treatment in older men, an important finding with major safety implications.

A key segment of Peter’s work at the Mayo Clinic is using highly specialised mathematical tools developed by Professor Veldhuis to analyse how and why testosterone secretion falls with age in men. This has potential great importance that may lead to preventative strategies and targeted therapies for low testosterone production, which may also contribute to age-related frailty.

These studies have shown that testosterone production is a network-controlled process governed by specific brain neurons in the hypothalamus that secrete gonadotropin releasing hormone (GnRH), which signals gonadotrope cells in the pituitary gland to produce luteinising hormone (LH). This in turn signals the Leydig cell in the testis to secrete testosterone. Testosterone then signals back to the hypothalamus and pituitary gland to decrease GnRH and LH respectively, thus regulating overall testosterone production. Liu and Veldhuis’s studies have shown that the “network regulation” of GnRH secretion and its consequences, leading ultimately testosterone production, are impaired with ageing and they are dissecting these defects to determine the precise location and nature of these defects in the “network regulation” system. Reduced or irregular GnRH secretion with or without changes in testosterone feedback signaling could explain why older men produce less testosterone. The results of these studies will aid understanding of why less testosterone is produced by older men.

While at the Mayo Clinic, additional studies have focused on how testosterone strengthens bones in older men by altering the balance in bone turnover in favour of bone accumulation. Further studies have been conducted with Dr Sundeep Khosla examining the effect of estradiol on bone, as well as with Dr Lorraine Fitzpatrick examining how testosterone or estradiol, are involved in coronary artery disease. These have been presented at international meetings and submitted for publication.

In 2005 Peter will extend his overseas research with a stay at Harbor-UCLA Medical Center, Los Angeles USA, funded by winning two more fellowships from the US Lalor Foundation and the American Australian Association. In Los Angeles, he will undertake basic research into a mouse model of Klinefelter’s syndrome, a genetic disease that is the most frequent causes of male hypogonadism causing infertility and testosterone deficiency. He is due to return to the ANZAC Research Institute in 2006 to complete his Neil Hamilton Fairley Fellowship.

Genetic models to study the actions of FSH

CM Allan, P Lim, J Spaliviero, M Jimenez, T Borovina, DJ Handelsman

These studies focus on how the two pituitary-derived gonadotrophins, FSH and LH, govern testis development, sperm and testosterone production, male fertility and virilisation. In males, FSH activates a specific receptor found only on Sertoli cells, which support, coordinate and nourish sperm production, spermatogenesis. The total number of Sertoli cells determines the final sperm production capacity of adult testes, so understanding the regulation of Sertoli proliferation and function is critical for testicular development and function, including sperm production and fertility.

We have created genetic mouse lines wherein transgenic expression of human FSH in genetically hypogonadal (hpg) mice can be used to investigate FSH actions on both Sertoli cells and sperm production. These mice lack their own FSH and LH and so expressing human FSH through an introduced transgene allows analysis of FSH actions independently of LH effects, a problem that remains one of the major research challenges in reproductive biology. These studies have shown that FSH alone can induce complete normal Sertoli cell proliferation, and initiate early stages of sperm development but have incomplete effects on later stage sperm development.

Together with previous findings, these experiments have shown that completion of spermatogenesis requires FSH in combination with LH, or testosterone, which is the main product of LH activity. Now the focus will be on the role of...
FSH and steroids during the critical early postnatal period of Sertoli cell development, where these cells complete proliferation and reach the final numbers found in adult life.

Again using the hpg mouse, with its null hormonal background, experiments have been designed to evaluate the effects of a mutant human FSH receptor (FSHR+), a naturally occurring mutation in which a single protein modification (Asp567Gly) changes the receptor so that it becomes autonomous. That is remains active even in the absence of the normal hormone that stimulates this receptor. This FSHR+ mutation was originally identified in a man with complete gonadotrophin deficiency, which normally leads to cessation of sperm production, but who had unexpectedly retained sperm production and fertility. This clinical finding suggested FSHR+ supports full spermatogenesis in the absence of FSH but proof was not possible without verification in controlled experiments in an intact animal. Our previous research using a transgenic mouse model verified that this mutation exerted FSH-like activity. Further work to verify that these effects are specific to the Asp567Gly mutation has been completed. This showed that while transgenic FSHRwt or mutant FSHR+ both increased testicular binding of FSH similarly, only FSHR+ mice exhibited increased development of hpg testes, providing strong evidence that the FSHR+ activity is a specific feature of the Asp567Gly mutation.

Further research on the effects of transgenic FSH on the fertility of normal, non-hpg, mice that have their own FSH production, showed that the addition of transgenic FSH had no additional effect on testis development, sperm production or male fertility. However, in females, transgenic FSH expression did have striking effects to initially increased fertility and litter size, followed by a reduction in litter size and premature infertility. This transgenic mouse line provides novel models of both FSH-driven ovarian hyperstimulation and multiple ovulation as well as unexpected deleterious effects of raised FSH for premature ovarian failure in female reproductive ageing.

**Comparison of androgen and LH actions on spermatogenesis**

J Spaliviero, M Jimenez, CM Allan, DJ Handelsman

In previous experiments, our laboratory first showed that testosterone alone could initiate qualitatively complete spermatogenesis in gonadotrophin-deficient hpg mice. This bypassed completely LH mediated maturation of Leydig cells and steroidogenesis and indicated that at least some sperm production does not require FSH or non-steroidal Leydig cell secretions, such as growth factors, cytokines and vasoactive peptides. However, the testis in these mice remained smaller than normal suggesting that these additional factors may play some role in restoring normal testis size and full sperm production capacity.

To further evaluate this discrepancy and whether the lack of LH action might explain the smaller testes, we studied long-term treatment with an LH analogue, hCG, which is known to rectify Leydig cell development and steroidogenic function. We used stereology to count the testicular germ cell populations and found similar effects with hCG and testosterone on these populations. Since testosterone alone replicates virtually all effects of hCG, this proved that Leydig cell maturation and steroidogenesis are not required for the induction of murine spermatogenesis nor does LH action rectify the gap in testis development and size. This indicates that other non-Leydig cell factors, presumably FSH, are critical for quantitative normalisation of spermatogenesis.

**The role of the androgen receptor in spermatogenesis**

CM Allan, P Lim, K McTavish, J Spaliviero, DJ Handelsman

Having previously showed that androgens alone, without FSH, could initiate and maintain sperm production and fertility in hpg males, the cellular mechanism of action of testosterone is clearly of interest. It is widely accepted that androgen actions are mediated via a specific androgen receptor (AR) that acts to regulate gene expression. Despite having a crucial role in spermatogenesis, AR is not found in any developing sperm cells but is instead located in the supporting Sertoli cells. This suggests that intermediary signals are relayed for the androgen-response to the developing germ cells. This arrangement is striking because the spermatogenic epithelium is the most intensely proliferative epithelium in the body. Yet, despite such intense cellular replication, cancerous cells virtually never develop there. The cellular and signalling mechanisms by which the Sertoli cells regulate such remarkably intense proliferation without loss of control have important implications for understanding the control of the replication of normal and cancerous cells elsewhere in the body.

Patrick Lim, a PhD student in Andrology, is developing a series of new transgenic models to examine the role of AR expression in Sertoli and other cells in the testis that express this steroid receptor. By this means, understanding the cellular and biological process of how androgens are necessary for completion of spermatogenesis will be studied.

Parallel work is underway using AR-specific antibodies to detect AR protein during testis development in normal and hpg mice. Although AR is readily detected at birth in peritubular cells, it only appears significantly in Sertoli cells during postnatal development. In hpg males, AR exhibited a similar developmental, albeit reduced, level of expression in Sertoli cells, which retained immature-like characteristics in mature hpg testes. Further studies will examine the hormonal regulation of AR expression in developing Sertoli cells.
Related research is continuing to investigate the specific genes or pathways regulated by androgens in the testis. We are currently characterising the global transcription profile of genes, expressed in the testis during the initial wave of spermatogenesis, induced by testosterone. This strategy uses micro-assay technology to examine the expression of over 10,000 genes during the testosterone response in hpg testes. Our aim is to identify the candidate pathways and key factors regulated by androgens, which may ultimately provide new targets for more effective treatments for male infertility or new strategies in male contraception.

The role of the androgen receptor in female physiology

DJ Handelsman, CM Allan, P Lim, P Illingworth (Westmead Hospital), J Zajac (University of Melbourne)

About 95% of all androgens, or classical male sex hormones, are produced after sexual maturation by the testis of male mammals, including men. Small amounts of testosterone are also produced from the ovaries and adrenals in women and children but there is little understanding whether this has any physiological role. Yet in recent years there has been increasing prescription of testosterone for menopausal women on the speculative basis of rectifying a presumed testosterone deficiency.

This collaborative project is studying the role of androgens in female mammals by using transgenic tools to remove the androgen receptor (AR), through which androgens exert their physiological effects, from female animals. This research cannot be achieved by natural breeding because the fathers required for such matings are sterile. Hence this project required modern transgenic engineering to produce a novel AR-null female mouse. Currently, analysis of these AR-null females is directed to study potential AR-mediated androgen effects on the ovary, bone, muscle, breast and brain. These studies have importance in understanding the potential physiological, pathological and therapeutic role of androgens in women especially after menopause.

Reproductive hormone assays and methods for physiology, pharmacology and toxicology

M Jimenez, JA Spaliviero, CM Allan, DJ Handelsman

To provide for a wide range of reproductive biology, pharmacology and toxicology studies in rodents, we have become an expert technical centre for mouse and rat hormone assays. Commercial reproductive hormone immunoassay kits, designed for human testing, are usually unsuitable for use with rodent samples, giving misleading or unreliable results. Having identified significant problems for steroid, gonadotrophin; LH and FSH, and inhibin assays for rodents, our laboratory now provides species-specific assays for rodent studies needing much smaller blood samples for accurate results in mice, increasingly the most widely used species for its wider range of genetic models.

This year, in conjunction with colleagues at NV Organon in the Netherlands, we have fully evaluated a new two-site, dimer-specific mouse FSH immunoassay that is more than 30 times more sensitive, more specific and more convenient than the previous standard NIH mouse FSH immunoassay. Further work is ongoing to validate an analogous mouse LH assay along with the modification of commercial assays for inhibin A and B for use in mice. We have also become a reference centre for rodent steroid immunoassays.

To improve the delivery of reproductive hormones in deficient mice, we have also developed a range of hormone implants for rodents that deliver steadily low physiological doses, thus avoiding the problems of existing delivery systems associated with excess dose fluctuations. These new implants will provide new opportunities to study genuine effects of low dose estradiol and testosterone without these underlying confusions.

Novel yeast androgen bioassay to detect sports doping by designer androgens

A Death (Heart Research Institute), K McGrath (Heart Research Institute), R Kazlauskas (ASDTL), DJ Handelsman

Since the first ban on sports doping three decades ago, the most widely practised, effective and persistent form has been the illicit use of androgens or anabolic steroids in power sports. Although the ban on all known synthetic androgens is enforced by use of highly sensitive urine mass spectrometry methods, in recent years two novel, non-marketed designer androgens, norbolethone and tetrahydrogestrinone (THG), were created to avoid detection and have been found in use by elite athletes. THG was a derivative of a seldom used but marketed progestin, gestrinone, and was identified in confidential pharmaceutical company proprietary studies in the 1960s but never made public. THG had never been tested in
Androgens and atherogenesis

A Death (Heart Research Institute), K McGrath (Heart Research Institute), DS Celermajer (Royal Prince Alfred Hospital), DJ Handelsman

In a long-term collaboration with Drs Death and Celermajer, basic and clinical studies continue to identify the role of androgens in the initiation of atherogenic cardiovascular disease, which is still the largest single cause of death in our community. Men are two to three times more likely to have cardiovascular disease than women. Yet the cause of their earlier onset and greater severity, the first real clue to the cause of cardiovascular disease, is not understood. A series of studies have led the field in identifying steps whereby exposure to androgens initiates the process of atherogenesis, the underlying pathological process leading to arterial blockages, heart attacks, angina, stroke, and peripheral vascular disease. This research may lead to clues into how to separate the beneficial from the harmful effects of androgens to provide novel therapeutic targets for cardiovascular disease prevention and treatment.

The short-term effects of androgens on cardiac function

S Kelleher, T Chung, L Turner, AJ Conway, A Sindone (Cardiology, Concord Hospital), L Kritharides, DJ Handelsman

Testosterone has an important role in the development and function of muscles. In high doses, testosterone and the synthetic androgen, nandrolone, can cause increase in muscle size and strength. Androgen abuse for enhancement of muscle mass and strength has been largely confined to cheating by elite athletes. Given that increases in muscle size and strength are now shown to be genuine and dose-dependent, it is possible that such increases in muscle structure and function may be useful in circumstances where muscle loss is a feature, such as in ageing or chronic illnesses.

One medical context where the anabolic effects of androgens on muscle might be beneficial is in chronic cardiac failure. So far there is little evidence of androgen effects on cardiac function. Our research aims to determine any effect that androgens, given weekly over a one-month period, have on cardiac muscle function. We will involve healthy young non-athletic men who will either receive testosterone, nandrolone or placebo. Extensive testing on myocardial contractility and relaxation will be undertaken using cardiac echo ultrasound. If there are consistent benefits from androgen administration, longer-term studies examining rehabilitational outcomes in men with chronic cardiac failure will be considered.

Circulating testosterone threshold for androgen deficiency symptoms

S Kelleher, A J Conway, D J Handelsman

Testosterone deficiency leads to a variety of effects involving most tissues, reflecting the fact that androgen receptors are present and mediate physiological effects in most male tissues. While much attention has been focused on objective evaluation of androgen effects on somatic and reproductive tissues, a major source of disability and impoverished quality of life among androgen deficient men is a range of characteristic but non-specific symptoms.

Most testosterone preparations are relatively short acting. Rapid changes in blood testosterone concentrations make it difficult to define any testosterone threshold. In contrast, subdermal testosterone implants provide stable blood testosterone concentrations over time, whilst gradually declining to baseline over several months. By observing androgen-deficient men as their familiar androgen deficiency symptoms return as testosterone pellets slowly dissolve, it its possible to establish a testosterone threshold for their androgen deficiency. From studies of a group of 52 androgen-deficient men over five years, the average blood testosterone level at which the symptoms became apparent corresponds to the lower limit of the healthy adult reference range for testosterone. Strikingly these thresholds were very consistent within any individual but differed widely between men. This new information that men have differing thresholds for androgen-deficiency although very consistent for any one person, may have important implications for customising treatment to individuals. Further study is planned to assess the contribution of genetic polymorphism to these individual thresholds.

Randomised controlled clinical trial of testosterone for symptoms of borderline androgen deficiency in older men

S Kelleher, AJ Conway, DJ Handelsman

It is now widely accepted that male ageing is accompanied by a gradual decline in circulating testosterone levels. This modest decline, up to 10% per decade, may be neither
severe enough nor treatment effective enough, to warrant testosterone replacement treatment. In other research involving young men with organic androgen deficiency, we identified symptoms of declining testosterone levels including lack of energy, loss of libido, diminished muscle and bone mass, and depression. These non-specific symptoms are also frequently found in otherwise healthy older men, suggesting that male ageing may be a form of functional androgen deficiency. Treatment of such symptoms might improve quality of life.

Increasingly, the evaluation of this concept has focused on objective benefits from testosterone treatment for older men on somatic tissues, such as bone and muscle. Few studies, however, have looked specifically at the potential symptomatic benefit of testosterone on symptoms in common to ageing and androgen deficiency. These symptoms are often the main motivation for middle-aged or older men to seek such treatment. We are aiming to assess the symptomatic effect of testosterone replacement in this group who have borderline androgen deficiency. This study will monitor the participants’ symptoms and quality of life. The use of both a placebo control and a crossover design is vital to reduce subjectivity bias. This means that every participant will receive both testosterone and placebo in a disguised sequence. It is most important to avoid preconceived ideas that may influence expectations of possible benefits by both investigators and participants. This study will help determine whether testosterone treatment does genuinely improve the usual non-specific symptoms reported by ageing men.

**The origins of human prostate disease**

K Griffiths, S Wishart, LP Ly, DJ Handelsman

Human prostate disease is remarkably common, affecting virtually all men who live a full life expectancy. Little is known of its origin and evolution with most clinical research focussed on treatment of end-stage disease. The prostate is highly dependent on androgens for growth and development and requires decades of exposure to adult androgen levels before benign prostate hyperplasia, the most frequent reason for surgery in older men, or prostate cancer, the most frequent fatal internal cancer of men, becomes clinically evident.

Human clinical research studies need to use prostate ultrasound to measure prostate size and growth. Traditionally, the prostate is visualised by a transrectal ultrasound examination that requires insertion of a rectal probe. While this is highly accurate, it is unappealing to most men except in medical necessity. To conduct clinical research involving healthy, younger men in whom prostate disease has not yet become clinically evident, it is necessary to create a simpler, less invasive approach to visualise the prostate, which is more acceptable to this healthy younger population. Our expert sonographers have developed and are validating a new less invasive prostate ultrasound method using transperineal approach. This avoids requirement for a rectal probe and should prove more acceptable to healthy men and allow us to extend our studies to the healthy younger men.

This new prostate ultrasound method is designed to facilitate a project assembling a birth cohort of young men. We aim to determine whether prenatal and perinatal factors influence prostate and testis development. It is expected that participation in this study will improve with implementation of this refined prostate assessment.

In conjunction with the French-American company, Besins/Ascend, we are undertaking a prospective randomised placebo controlled clinical trial to determine whether transdermal gel application of dihydroxytestosterone (DHT) prevents prostate growth in middle-aged and older men without known prostate disease. It is based on our finding that an unexpected slowing of prostate growth occurs in men treated with DHT compared with placebo. This observation will be explored more fully over the next two years and seeks to confirm the medium term bone and cardiovascular safety of DHT treatment. Successful results will represent a novel means in prevention and treatment of prostate growth disorders.

**Role of androgen action and target genes in prostate development and disease**

J Singh, Q Dong (Sydney Cancer Centre), DJ Handelsman

Prostate growth, development and disease are highly dependent on androgens. In the absence of androgens the prostate may not develop at all or, if it does, does not develop late-life diseases particularly prostate hyperplasia and cancer. While androgen withdrawal has for decades been the mainstay of treatment for incurable prostate cancer, this radical treatment has undesirable side-effects making it unsuitable for earlier, curable stage of prostate diseases. Further refinement of such effective treatment to narrow down its mechanism of action would allow wider development of hormonal treatment to retard progression, and reverse or even cure prostate diseases.

Although androgen withdrawal produces a clinical response in the majority of patients with incurable prostate cancer, inevitably the cancer relapses over time as it becomes conditioned to survival in an androgen-deficient environment. This form of androgen-independent cancer (AIC) of the prostate is incurable and is the terminal stage of fatal prostate cancer. The precise cellular and molecular mechanisms responsible for the progress of prostate cancer following removal of androgens is not well understood.

Earlier studies have shown that the androgen signaling pathway can remain active in AIC during androgen ablation therapy. Since androgen action is mediated through its target genes, identification of these genes is important to
gain insight into the growth and progression of AIC. Using a new experimental approach that compares genes active in the prostate of mice under different hormonal conditions, we have identified several target genes that are regulated by androgens. One of the identified genes is a protease inhibitor that has been implicated in the growth of several cancers and we have shown it to be over-expressed in prostate cancer. Further studies on the effects of inhibiting the gene and its protein on cell proliferation and cell invasion are underway. These findings will provide a new marker not only for diagnosis but also more importantly for potential therapeutic interventions.

More basic studies are also being commenced to identify the cellular and developmental mechanism of action of androgens on the prostate. Using transgenic biotechnology in studies aiming to remove AR from specific prostate cell lines, we will examine the cellular interactions within the prostate that underlie the long-term responses to androgens and translate life-long androgen exposure to the development of late-life prostate disease. This will also provide novel insights into approaches that may modify the natural history of androgen-dependent prostate diseases.

Male reproductive health in men with Parkinson’s disease

M Schipper (Free University of Amsterdam), L Turner, AJ Conway, LP Ly, C Meier, MJ Seibel, S Mercer, M Hayes, DJ Handelsman

Parkinson’s disease (PD) is a chronic progressive neurodegenerative disorder featuring tremor, rigidity and akinesia, leading to a profound movement disorder in older people. As a chronic disease, it is expected to impair androgen production but the magnitude and determinants of such effects are not clear. Recent small and uncontrolled studies suggest non-motor symptoms of PD, as well as testosterone deficiency, are improved by testosterone therapy.

To evaluate the feasibility of an interventional study, in conjunction with the Concord Hospital’s Parkinson’s disease clinic, a visiting Dutch elective medical student studied 50 men with PD, aged 42-89 yrs, to evaluate their androgen status, bone density and relationship to markers of disease stage, severity and clinical features. As expected, PD worsened progressively with age and this corresponded to deterioration in functional status, quality of life and muscular strength. Testicular volume and consistency deteriorated with PD stage but was not related to any change in reproductive hormone status except an increase in sex hormone binding globulin. Bone mineral density (BMD) was significantly reduced in only a few men with no significant difference in spinal or hip BMD, body fat composition or lower urinary tract symptoms with PD stage. We concluded that for this population of ambulant men with relatively early stage PD, neither stage nor severity was predictive of reproductive hormone status, bone density or body composition in men with PD. Other aspects of disease appeared to be more predictive and further analysis of these findings is underway.

Epidemiology of male reproductive health in Australia

In conjunction with Andrology Australia, the national Centre of Excellence in Male Reproductive Health, we have contributed to the development and design of the Men in Australia Telephone Survey (MATES), the first population-based, phone survey of male reproductive health in Australia. This study will provide a unique snapshot of male reproductive health and concerns of middle-aged and older Australian men. This will form the basis for further analytical and interventional studies to enhance male health and medical care and narrow the gender gap in life expectancy.

Grants

NHMRC: $770,000, 2001-03; $225,000, 2002-04; $360,000, 2003-05
University of Sydney Cancer Research Fund: $100,000, 2002-03
National Heart Foundation: $100,000, 2003-04

Fellowships

Peter Liu
NHMRC Neil Hamilton Fairley Fellowship: $ 350,000, 2003-2006
Biogerontology studies the biology of ageing and age-related diseases and is an integral component of the Centre for Education and Research on Ageing (CERA) at Concord Hospital. Currently, we are exploring age-related structural changes in the liver and the implications these changes may have for the development of vascular disease and drug metabolism in the elderly. Of particular interest to our group are the endothelial cells of the liver sinusoids where exchange occurs between blood components and the liver.

Hepatic sinusoidal endothelial cells differ from vascular endothelial cells in that they are perforated by 50-100 nm holes, termed fenestrations. These fenestrations are located in groups forming porous structures known as sieve plates, the function of which is to allow the passage of particles below a certain size into and out of the liver. Our research has demonstrated that with advancing age the number and diameter of fenestrations decreases. This decrease in porosity may result in impeded transfer of blood components across the liver sinusoids. Members of our group have been exploring how these changes may impact on aspects of ageing.

We actively encourage younger scientists to undertake studies in advanced research. Mimi Saba joined the group in 2003 as a PhD student co-supervised between Biogerontology and Vascular Biology. Mimi is pursuing research on the effects of age and oxidative stress as a model of accelerated ageing on intracellular trafficking of apolipoprotein E in primary cultured hepatocytes. This work will contribute to our understanding of the causes of hyperlipidaemia in the elderly.

Jameel Khan commenced work with us in December 2003 as a Summer Research Scholar sponsored by the ANZAC Research Institute. Following the successful completion of this project, he elected to continue his investigations on hepatic sinusoidal endothelial cells by undertaking an honours degree in Medicine. His work contributed to a recent manuscript that has been accepted for publication in the Journal of Hepatology.

**The ageing liver and hyperlipidaemia**

S Hilmer, V Cogger, D Sullivan (Royal Prince Alfred Hospital), D Le Couteur

This year Dr Sarah Hilmer has continued her research towards a PhD on the impact of ageing changes in the liver on lipoprotein and drug metabolism. She investigated the hepatic disposition of lipoproteins in young and old rats and the expression of lipoprotein receptors in young and old rat livers. She also studied the role of the hepatic sinusoidal endothelium, which undergoes significant structural changes with age, in the pharmacokinetics of liposomal formulations of drugs. Her research findings suggest that age-related changes in the liver may impair lipoprotein and drug metabolism, identifying the liver as a potential therapeutic target to modulate these processes in older people.

Sarah presented her research at the Australian Association of Gerontology Annual Scientific Meeting in November 2003 as a recipient of the RM Gibson Award. She also presented her work at the Australian Society of Clinical and Experimental Pharmacologists and Toxicologists Annual Scientific Meeting in December 2003 and at the Australian Society of Geriatric Medicine Annual Scientific Meeting in May 2004.

She continues to be supported by an NHMRC Medical Postgraduate Scholarship and has been awarded an NHMRC travel grant to continue her research on pharmacokinetics in older people at the National Institute of Ageing, National Institute of Health, USA from October 2004.

**The ageing liver**

V Cogger, D Le Couteur

Dr Victoria Cogger completed her PhD in 2003 and is continuing her research on age-related morphological changes in the liver sieve and how these changes affect liver function. In particular, she has been studying the link between defenestration of the liver sinusoidal endothelium and hyperlipidaemia.

Recent research has been focused on the poloxamer 407 hyperlipidemic rodent model. It has been shown that a single injection of poloxamer 407 causes profound increases in cholesterol and triglycerides. We have been investigating the role of the liver sieve in this process.

Examination of the liver sieve in these hyperlipidemic animals has shown that the endothelium is almost completely defenestrated. That is, there is a total loss of endothelial pores. Moreover, the administration of poloxamer 407 directly into the portal vein is associated with immediate defenestration associated with apparent coating of the endothelial cell and plugging of the fenestrae with poloxamer 407 leading to increased thickness of the endothelium.

We are currently investigating the time course of these events, whether these changes impair hepatic oxygenation and finally, how these changes affect the liver uptake of lipids and drugs.
The genetics of cholestatic liver disease and the ageing liver

M Harris

Cholestasis or bile secretory failure is a frequent and serious consequence of hepatitis viral infection, various drug exposure, metals, diet, development and chemicals. Work carried out by Dr. Matthew Harris focuses primarily on genetic liver diseases that lead to cholestasis. This year he has centred on understanding the basic function of the genes involved in genetic cholestasis and has identified and cloned a number of related genes. Through analysis of these genetic mechanisms, an understanding of basic liver metabolism can be established, which can then be transposed to acquired liver diseases during ageing.

Matthew has had a very productive year, publishing four papers and two extensive reviews. He also supervised Mimi Saba, a PhD student in Biogerontology and Vascular Biology. He has maintained a strong collaboration with a laboratory at the American National Institute of Health on the fundamentals of acquired cholestasis and also established collaboration with the Centre for Vascular Research at the University of NSW on novel proteins involved in cholesterol metabolism and atherosclerosis.

Oxidative stress and the sinusoidal endothelium

M Muller, J Khan, V Cogger, D Le Couteur

Oxygen can be metabolised to free radicals and other active forms, termed reactive oxygen species (ROS). When the production of ROS exceeds the host antioxidant defence capacity oxidative stress ensues, resulting in indiscriminate damage to biomolecules, including proteins, genetic material and lipids. The liver is recognised as a major site of ROS formation due to its metabolic role in homeostasis and detoxification of ingested xenobiotics, such as alcohol and pharmaceuticals. It is also known that with advancing age the formation of ROS increases. Previously we used a tissue culture model to demonstrate that disruption of mitochondrial function leads to depletion of ATP, an energy rich molecule required to maintain the cytoskeleton of the cell and the structure of fenestrae, resulting in rapid defenestration. As ROS are known to rapidly deplete cellular ATP levels we have been investigating ROS formation as a possible mechanism for defenestration. We have established that exposure of isolated sinusoidal endothelial cells to low levels of hydrogen peroxide, a known ROS, causes pronounced defenestration. Moreover, these studies showed similar structural changes to cells as to those obtained from whole livers exposed to oxidative stress. Our studies will now focus more closely on age-related changes in endothelial mitochondria in order to understand better the relationship between mitochondrial dysfunction, ATP production and defenestration.

Drug evaluation and toxicology

M Harris, M Muller

The expertise of members of our Biogerontology group has been recognised both nationally and internationally. Dr Matthew Harris was appointed in 2003 for a five-year term to the Pharmaceutical Subcommittee of the Australian Drug Evaluation Committee at the Therapeutic Goods Administration, Canberra. In 2004 Dr Michael Muller was appointed as a member of the toxicology peer-review panel for the Environmental Protection Agency (EPA) of the United States of America. At a recent meeting of the EPA in Cincinnati he discussed the requirements for a weight-of-evidence approach in assessing the relevance of chemically induced rodent liver tumours to human risk assessment. These discussions and ongoing work will lead to the setting of new national environmental exposure standards for several chlorinated aromatic compounds.

Grants

NHMRC: $360,000, 2003-05
NHMRC/DVA: $240,000, 2002-05
NHMRC Equipment Grant: $73,000, 2004

Fellowships

Matthew Harris
NHMRC CJ Martin Fellowship: $320,000, 2001-05

Scholarships

Sarah Hilmer
NHMRC Postgraduate Medical Scholarship: $85,296, 2002-04
Allesandra Warren
NHMRC Dora Lush Postgraduate Scholarship: $65,559, 2002-04
Karen Brennan, James de Winter, Colin Dunstan, Christian Meier, Markus Seibel, Hong Zhou

Our Bone Research Program pursues research in basic bone biology, applied bone metabolism and clinical research in metabolic bone disease. In addition, our laboratory has a strong interest in the development of transgenic models of bone disease.

Since opening our laboratory in 2002 we have grown rapidly. Dr Hong Zhou joined the Bone Research Program at the beginning of 2004, moving from the bone research group at St. Vincent's Institute for Medical Research in Melbourne. She has extensive experience in bone cell biology and molecular biology, and a record of high scientific achievement.

A number of exciting and competitive projects are presently underway or near completion. These have been supported through achievement of funding from within Australia and overseas. We have also established industry links through research partnerships with Amgen, Aventis Pharma in USA and Australia, Merck, Sharp & Dohme from Switzerland, Roche Pharmaceuticals from Switzerland and Novo Nordisk from Switzerland.

Our plan is to develop further a comprehensive research program that makes use of the many opportunities provided by a multidisciplinary institution such as the ANZAC Research Institute. Our goal is to intensify collaborations with both basic and clinical research groups here and on the Concord Hospital campus, and to extend our research efforts to other areas relevant to bone biology and disease.

Hormonal determinants of age-related changes in bone turnover and predictors of fracture risk in elderly men
C Meier, J de Winter, MJ Seibel, JA Eisman (Garvan Institute, Sydney)

Fractures resulting from osteoporosis are a major cause of hospital admission, loss of independence, and reduced life expectancy in the elderly. Osteoporosis affects not only women, but also men. It is estimated that approximately one third of osteoporotic fractures occur in men. Several independent risk factors for fracture have been identified, such as bone mineral density, bone turnover rate, family history, and presence of other diseases. However, not all men, and especially not all men with age-related hormone deficiency, exhibit a decrease of bone mass leading to osteoporosis. In this study we aim to identify the forces behind age-related changes in bone metabolism and bone strength, and identify best predictors of fracture risk. Through collaboration with Professor John Eisman, Bone and Mineral Research Program, Garvan Institute of Medical Research, we have access to the large population of elderly men contained in the Dubbo Osteoporosis Epidemiology Study.

Recently we have demonstrated that in men, high bone resorption is associated with an increased risk of osteoporotic fractures. This relationship is independent from other risk factors such as bone mineral density, and is comparable to the risk that has been observed for postmenopausal women. Further studies are underway to unravel the determinants of bone turnover rate in elderly men.

Studies of the relative contributions of estrogen and androgens to bone turnover in men
C Meier, P Liu, J de Winter, DJ Handelsman, MJ Seibel

Sex hormones are of major importance for the accrual and the maintenance of bone mass. While the role of estrogen in regulating bone metabolism in women is well established, the relative contributions of estrogen and androgens in regulating bone turnover in men remain unclear. We have evaluated the effect of dihydrotestosterone (DHT), the most potent naturally occurring androgen, and recombinant human chorionic gonadotropin (rhCG) in comparison with placebo on bone turnover in healthy, elderly men over 60 years. Our results confirm earlier studies that estradiol, secreted in rhCG treated men, has a prominent effect on bone in older men, while no direct effect of DHT on bone turnover was found. However, the direct effects of DHT to maintain bone metabolism could not be excluded by our study.

Bone structure and turnover in hypogonadal (hpg) mice
N Sims (St Vincent’s Institute, Sydney), K Brennan, J Spaliviero, T Borovina, DJ Handelsman, MJ Seibel

In a collaborative effort with Bone Biology and Andrology and Dr Natalie Sims at St Vincent’s Institute for Medical Research, we are studying the effects of male sex hormones on the structure and turnover of bone. The effects of female sex hormones on bone density, specifically the withdrawal of estrogen after menopause, are already well known. Osteoporosis in elderly men is now a recognised problem, as are the effects of testosterone deficiency on bone. We aim, in this project, to contribute to the understanding of how androgens influence bone strength in males. Using the testosterone deficient hpg mouse to examine the bone structure and turnover, we have demonstrated significant differences in bone turnover in testosterone deficiency. We also have shown that androgen replacement using either testosterone or its non-aromatisable pure androgen metabolite DHT was able to normalise bone turnover in these male mice. These experimental studies are helping dissect the relative contributions of androgens and estrogens to maintenance of mature male bone.
The genetics of Paget’s disease of bone

C Meier, N Kormas*, F Lang*, MJ Seibel, MJ Hooper* (*Endocrinology, Concord Hospital), SH Ralston (University of Aberdeen)

Paget’s disease of the bone (PDB) is the second most common form of metabolic bone disease after osteoporosis. The aetiology of Paget’s disease of the bone is unknown, although it is often seen in multiple family members and seems to exhibit autosomal dominant inheritance. Various genetic mutations affecting the ubiquitin associated (UBA) domain of Sequestosome 1 (SQSTM1) have recently been shown to be a common cause of familial and sporadic Paget’s disease of bone. In collaboration with Professor Ralston, Department of Medicine and Therapeutics, University of Aberdeen, UK we have investigated the frequency of SQSTM1 mutations in different populations of mainly British descent, since marked geographical differences exist in the prevalence of Paget’s disease. Our results provide strong evidence to suggest that most Paget’s patients of British descent, including patients living in Australia who carry the SQSTM1 P392L mutation, share a common ancestor. This indicates that the true rate of de novo mutations may be lower than previously suspected.

Inhibition of bone repair during breast cancer metastasis to bone.

C Dunstan, H Zhou, MJ Seibel

The Bone Research Program has been awarded a University of Sydney Cancer Research Fund Grant to evaluate the low level of repair associated with breast cancer metastases. Lytic effects of breast cancer metastases predominate and despite extensive bone destruction there is often little evidence of coupled bone formation or other compensating bone formation activity, despite marked changes in the strength of remaining bone. In this study, we will assess the ability of cancer cells to inhibit osteoblast function in vitro with co-culture techniques, and in vivo through dynamic assessment of the effects of bone metastases on local and systemic bone formation.

Preventing the spread of malignant tumours to bone


Breast cancer and prostate cancer have a particular preference to form cancer metastases in bone. Breast cancer in bone is associated with bone destruction that frequently results in significant pain and disability. Whilst prostate cancer in bone induces high rates of bone formation and bone resorption resulting in disorganisation of bone structure and severe pain. Bone provides a “fertile soil” for breast and prostate cancer cells that have moved from the original cancer site. Tumour cells grow in bone and induce normal bone resoring and bone forming cells of the bone marrow to destroy the surrounding hard bone. The destruction of bone releases factors that help cancer cells grow faster thus creating a vicious cycle that contributes to the serious consequences of bone metastases. We are studying mice with transplanted breast cancer cells to understand what makes the bone marrow a receptive site for breast cancer metastasis. We are manipulating bone-remodelling rates in mice to see how this impacts on the ability of circulating cancer cells to target bone and to establish destructive tumours there. The response of the tumour to these changes in bone cell activity is being assessed at cellular and molecular levels.

In collaboration with Dr Julie Blair of the Oncology Research Laboratory at Prince of Wales Hospital, we are conducting studies with prostate cancer derived cell lines, assessing relationships between bone resorption and tumour growth in mice.

Glucocorticoid-induced changes in bone metabolism

H Zhou, MJ Seibel, C Dunstan, K Brennan

Glucocorticoids (GC) have proven benefit to numerous patients suffering from diseases such as rheumatoid arthritis, asthma, inflammatory bowel disease and malignancies, or who have undergone organ transplantation. It is well known that glucocorticoids may exert deleterious effects on bone causing osteoporosis. We are using a novel transgenic mouse model to study the effects of GC treatment on bone. The transgene carried by these mice causes a local inactivation of GC in the bone forming cells, the osteoblasts, by directing these cells to produce an enzyme known as 11β hydroxysteroid dehydrogenase, which is normally found in the kidney. This
model allows us to separate effects on bone that are due to direct action of GC on the osteoblasts, from indirect effects such as reduced absorption of calcium in the gut. We intend to study the contribution of factors such as gender, age and diet to GC induced bone loss and to examine the role of endogenous GC in bone damage caused by inflammation and arthritis. In the long term, these studies may point to strategies to reverse or even prevent of the detrimental effects of cortisone on the skeleton.

**Effects of bisphosphonates on serum OPG and RANKL levels in patients with postmenopausal osteoporosis and Paget’s disease of bone**

C Meier, C Dunstan, F Lang (Concord Hospital), MJ Hooper (Concord Hospital), MJ Seibel

Differentiation and activity of bone resorbing cells, osteoclasts, are regulated by osteoprotegerin (OPG) and RANK ligand (RANKL). Bisphosphonates have been used successfully to treat metabolic bone diseases characterised by bone resorption as in postmenopausal osteoporosis. It has been shown in cell culture that bisphosphonates modulate OPG production in human osteoblasts. There is, however, no data on the effects of bisphosphonates on OPG and soluble RANKL levels in people with metabolic bone diseases.

We aim to investigate the change in serum levels of OPG and RANKL and correlate these with different biochemical bone marker levels whilst on bisphosphonate treatment. Participants with postmenopausal osteoporosis and Paget’s disease are being assessed before and during the first 6 months of their bisphosphonate treatment. The results of this trial will give us a better understanding of the mechanisms by which bisphosphonates reduce bone resorption.

**Study into the genetic determinants of bone loss and osteoporosis in an affected family**

C Meier, ML Kennerson, GA Nicholson, MJ Seibel

Whilst multiple environmental factors are involved in the pathogenesis of osteoporosis, a common multifactorial disorder of reduced bone mass, genes play a major role, as reflected by the heritability of many components of bone strength. Treatment is currently limited both in efficacy and by the drug classes available. Therefore identification of new therapeutic targets is of highest priority.

The usual form of osteoporosis is thought to be a polygenic disorder arising from the interaction of common polymorphic alleles at quantitative trait loci. Recent publications have reported a major gene pattern of bone mineral density inheritance in several ethnic populations. Identification of major genes contributing to osteoporosis would be of value for assessment of risk in individual patients.

To this end, we are studying a large family with an autosomal dominant inheritance pattern of low bone mineral density. Simulation studies have revealed that statistically this family seems to map disease locus on a single chromosome. We are using total genomic screen to map the gene mutation to its chromosomal locus.

**Studies on biochemical markers of bone metabolism**

C Meier, J de Winter, M Seibel, D Handelsman, P Liu, P Sambrook (Royal North Shore Hospital), K Ho (Garvan Institute), J Wark (University of Melbourne).

Bone formation and bone resorption keep bone alive, healthy and strong and are both compromised in metabolic bone disease. Recently specific bone markers in urine and blood have been discovered. Many clinicians are now using bone markers to assess the severity of most common bone diseases such as osteoporosis and to monitor their treatment. Given this success, we are seeking to refine and identify new and improved markers of bone turnover.

We are collaborating with a several research groups to evaluate bone turnover in a variety of settings. These include in the very elderly, associated with androgens in men, in association with growth hormone and androgens in elite athletes, with anti-epileptic drugs, smoking and other factors.
Longitudinal studies of testosterone levels on androgen target tissues

C Meier, M Jimenez, J de Winter, JA Eisman (Garvan Institute), DJ Handelsman, MJ Seibel

In men, serum testosterone levels decrease progressively with age. Physiological changes, such as decreased bone mass and decreased muscle strength, are also seen in individuals with hypogonadism. Diminished testosterone levels have been associated with a variety of chronic conditions in elderly men, and have formed the basis for trials investigating the effects of androgen replacement therapy in elderly men with partial androgen deficiency.

The impact of different degrees of androgen deficiency on age-related conditions remains unclear. The influence of longitudinal changes in serum testosterone on the occurrence of androgen-related diseases is also unknown. We are particularly interested in the effect of partial androgen deficiency on musculoskeletal measures, such as fractures, rate of bone loss, muscle strength, quality of life and overall mortality. Again, using the population of elderly men contained in the Dubbo Osteoporosis Epidemiology Study, we will assess the impact of androgens on the physiological role of sex hormones in elderly men and explore more effective therapy for osteoporosis in men.

Regulation of osteoblast and adipocyte differentiation from common precursors

H Zhou, K Brennan, C Dunstan, MJ Seibel

Osteoblasts and adipocytes develop from a common mesenchymal precursor. Clinical observation suggests an inverse relationship between these two cell types. Marrow adipocyte numbers increase while osteoblast numbers decrease during age-related bone loss or after treatment with glucocorticoids. In this study, we aim to identify the factors that control commitment at the branching point between osteoblast and adipocyte differentiation. Knowing that steroid hormones play an important role in regulating osteoblast and adipocyte differentiation, we are treating a common precursor cell line with steroid hormones and have been able to inhibit adipocyte differentiation and promote osteoblast differentiation. Further studies are planned to determine the gene expression profile in this system.
Our Neurobiology group attracts recognition for its expertise in neurogenetics. Its research focuses on finding genes for various neurodegenerative diseases of peripheral nerve, and motor neuron disease in particular. As one of the leading authorities in this field, our group has made important contributions to the characterisation of neuropathy phenotypes, the identification of new disease entities and the mapping and identification of the mutant genes causing nerve disease. Mapping and identification of these genes contribute to understanding the underlying mechanisms causing neurone degeneration and the late onset degenerative disorders of nerve.

**Finding the gene for dominant intermediate Charcot-Marie-Tooth Neuropathy**
ML Kennerson, G Walizada, D Zhu, GA Nicholson

Charcot-Marie-Tooth (CMT) neuropathy is a clinically and genetically heterogenous disorder of peripheral nerves affecting both the motor and sensory neurons. Clinically CMT is characterised by progressive weakness and loss of the distal muscles and of deep tendon reflexes. An increasing number of chromosomal loci are being identified illustrating the large number of genes that can cause CMT.

Initially we described dominant intermediate Charcot-Marie-Tooth type B (DI-CMTB) neuropathy as a new form of CMT. Its defining clinical features suggest that this gene may be involved in the development of nerve and other tissues. The gene was mapped to chromosome 19 and the region harbouring the gene has been refined to a 1.32 megabase interval containing 27 transcripts. Refinement has made our search for the gene amenable to positional cloning and bioinformatic strategies for identifying candidate genes and subsequent mutation analysis.

When the mutation is identified, further research to understand how the mutation leads to defects in cell function and ultimately to causing the disease will be necessary. DI-CMTB has both axonal and demyelinating features where the gene mutation may be involved with axonal/myelin interactions. Understanding these molecular pathways will suggest possible treatments to prevent axonal degeneration, which actually causes the disability and disease in all spinal cord and peripheral neuropathies.

**Finding the gene for X-linked recessive Charcot-Marie-Tooth neuropathy (CMTX)**
IG Huttner, ML Kennerson, GA Nicholson

Charcot-Marie-Tooth (CMT) disease is one of the most common inherited neurological disorders affecting approximately 1 in 2,500 people. Around 15% of all CMT is inherited on the X-chromosome (CMTX). Most cases are caused by mutations in the connexin32 (Cx32) gene, which codes for a gap junction protein. When analysing our database of 700 families, we found only 50% of our CMTX patients show a mutation in the Cx32 gene. Hence, we suspect that the other 50% represent new forms of CMTX that are genetically and phenotypically different from the classic Cx32-positive form.

From 37 families with non-Cx32 positive CMTX, we selected the largest for clinical characterisation and linkage analysis to map the disease-causing gene. In this family, affected males present in childhood or early adolescence with variably degree of foot drop, weakness and atrophy of distal leg and hand muscles, and mild loss of sensation in the limbs. In contrast, female carriers of the disease are themselves asymptomatic showing only subtle clinical signs.

Performing X-chromosome screening has shown linkage to a region on the distal long arm of the chromosome Xq27.1, a region of DNA containing about 20 genes. The next steps towards the identification of the disease gene involve determining the neural expression profiles of transcripts and mutation screening of candidate genes.

The outcome of this study will lead to the development of a genetic test to enable proper diagnosis of Cx32-negative X-linked CMT and may lead to the development of a new treatment.

**Understanding the molecular and cellular mechanisms of Hereditary Sensory Neuropathy type 1 (HSN1)**
SJ Myers, V Dedov, I Dedova, ML Kennerson, GA Nicholson

HSN1 is the most common and best characterised of the degenerations of sensory neurones, although very little is known about its pathogenesis. It is an autosomal dominant disorder of peripheral sensory neurons that presents with clinical symptoms in the second and third decade of life due to progressive degeneration of dorsal root ganglia. The longest nerves are involved first, presenting as sensory loss in the feet, followed by distal muscle wasting and weakness. The loss of pain sensation leads to painless injuries and chronic skin ulcers and eventually the possibility of distal amputations for osteomyelitis.
Our group found the gene and its mutations encoding to subunit 1 of serine palmitoyltransferase (SPTLC1), the enzyme that catalyses the first step in sphingolipid synthesis, which is important for cell survival. By understanding the impaired function in relation to the neuropathology of peripheral nerve and dorsal root ganglia, we will be able to test compounds to prevent or slow the disease.

We aim to investigate the functional cell and molecular aspects of this disease using a two-pronged approach. Firstly, we are making a transgenic mouse model to examine impaired function of this mutant gene to look at altered protein expression, activity and membrane localisation of SPTLC1. Secondly, we are developing of a cell culture model using neuronal cells, which over-express the mutant gene, to explore whether the mutations in SPTLC1 cause a gain in toxic function in HSN1 either by self-protein aggregation or by secondary protein interactions. This will allow us to identify the cellular and molecular mechanisms causing neuronal cell death and eventually to target drugs to treat the disease.

Localising the gene for Hereditary Motor and Sensory Neuropathy with pyramidal Signs

C Kok, ML Kennerson, GA Nicholson

Hereditary sensory neuropathy type I (HSNI) is a group of dominantly inherited degenerative disorders predominantly affecting sensory nerves. We have mapped the chromosomal location of the gene mutation causing a new form of HSNI with chronic cough and gastroesophageal reflux (GOR), to chromosome 3p, in a single large Australian family. The predominant clinical feature is a severe adult-onset paroxysmal cough, often exacerbated by inhalation of noxious stimuli such as perfume and cigarette smoke. GER symptoms are usually mild, with minimal heartburn. Oesophageal pH monitoring has shown multiple episodes of severe reflux, temporarily related to coughing attacks. A clinically pure sensory axonal neuropathy develops later, presenting with sensory loss or lancinating pains.

We have investigated two families with similar clinical symptoms and found linkage to the same locus. Through bioinformatic analysis, this region has been completely sequenced and estimated to contain 19 genes. Nine genes, including the candidate genes TOP2B and SLC4A7 were investigated for a pathogenic role in HSNI with cough and GER. The results of this analysis excluded all of these genes from involvement in the pathogenesis of the disease phenotype. Finding the gene mutation will provide
information about a possible pathogenic mechanism of this
disorder. Results and the construction of the physical map
of this study will be published in Neurogenetics.

Identifying new gene mutations for motor
neurone disorders

S Gopinath, ML Kennerson, S Christodoulou, GA Nicholson

Motor neurones control muscle function and can be
affected by a variety of environmental and genetic causes.
The genetic forms of disorders of motor neurones range
from rapidly progressive disorders such as familial
amyotrophic lateral sclerosis (FALS) to slowly progressive
conditions such as hereditary motor neuropathies (HMN).
These two ends of the spectrum of familial disorders differ
from one another based on the age of onset of disease, rate
of progress and survival after disease onset. In spite of these
differences, there may be an overlap of clinical features
between the rapidly and slowly progressive conditions.
Several different gene mutations have been described as
causing FALS and HMN, occasionally different mutations in
the same gene are known to cause both ALS and HMN.
The familial forms of ALS constitute about 10 to 20 percent of
all cases. It is possible that genes known to cause disease in
familial families may constitute risk factor genes in the more
common sporadic forms of ALS. Identification of gene
mutations of the familial disorders will increase
understanding of the biology of motor neurones, reveal
mechanisms underlying motor neurone disorders and
provide insight into familial and sporadic forms of the disease.

We are aiming to identify new gene mutations causing
familial ALS and hereditary motor neuropathies. Since ALS
is a late onset disorder, the identification of new families and
banking of DNA samples from affected individuals is
important for the future success of this project. We are
actively recruiting families for our database and banking
DNA samples from both affected and nonaffected
individuals. The database has been expanded from 96 families
in January 2003 to 166 by June 2004 and currently
we have banked 133 samples of DNA.

In our largest ALS family, we have excluded all known genes
and loci associated with familial ALS. Therefore in this
family, ALS is caused by a new unknown genetic defect.
Whilst the family’s evidence is not sufficiently powerful for
an independent genome screen to locate new loci, it is
useful for extended haplotype studies to known loci. This
family and other smaller families will be used in
international collaborations to assist the search for other
new loci.

In our largest hereditary motor neuropathy family, we
excluded all known loci for autosomal dominant hereditary
motor neuropathy. The next phase of our project consists of
whole genome screening for this family to identify the
chromosomal locus to look for the causative gene mutation.

Grants

NHMRC: $615,000, 2001-03; $225,000, 2003-05
Muscular Dystrophy Association (USA):
$241,320, 2002-05
Amyotrophic Lateral Sclerosis Association (USA):
$87,500, 2002-05
NHMRC Equipment: $10,000, 2003
University of Sydney Sesqui Near Miss Grant:
$60,000, 2004
Motor Neurone Disease Research Institute of Australia:
$29,000, 2004

Scholarships

Sumana Gopinath
Motor Neurone Association Research Institute of Australia:
$24,000, 2003, $24,000, 2004
Shahab Lajevardi
Northcott Neuroscience Scholarship: $75,000, 2004-04

Prizes

Cindy Kok
Princes Beatrice Fonds (Netherlands): $18,000, 2003-04
Macrophages are cells found within the lungs that can limit infections by both bacteria and viruses. We have found that rhinoviruses are able to infect these cells, but the macrophage is capable of limiting the viral infection. However, once infected, the macrophage has a reduced ability to respond to bacteria. This may help to explain why there is an increased bacterial colonisation of the airways during exacerbations of both COPD and asthma.

Rhinovirus can also infect the airways’ smooth muscle cells. These cells control the diameter of the airways, and as such are very important in regulating how easily a person can breathe. We have found that cells that originate from asthmatics release different amounts of cytokines when compared to cells that are from a non-asthmatic origin. This is possibly a contributing factor in rhinovirus-induced exacerbation of asthma. By examining these mechanisms, we hope that our knowledge will reduce the burden placed upon the health system by rhinovirus.

Regulation of inflammation in Chronic Obstructive Airways Disease (COPD)

LJ Seeto

At both the Thoracic Society of Australia and New Zealand Annual Scientific Meeting held in Sydney and the American Thoracic Society International Conference held in Orlando, Florida this year, Dr Linda Seeto presented a paper detailing the findings of her two year clinical study. This study in ex-smokers with chronic obstructive pulmonary disease documented the anti-inflammatory effects of low-dose theophylline, a drug previously used predominantly in patients with asthma for its bronchodilating effects. The latter effects require higher doses of theophylline, which unfortunately also increase the possibility of unpleasant side effects. In this study, the low-dose theophylline was found to improve the quality of life in some ex-smokers and to reduce the sensitivity of their airways to an inhaled chemical that normally narrows the airways. These novel findings in patients with smoking-related lung disease shed new light on the therapeutic actions of theophylline, which was first used over 80 years ago. The results of the study were well received at the international conferences with offers of further research collaborations and requests for journal publications.

Linda will be submitting her PhD thesis this year and resuming full-time clinical practice as a respiratory physician both in private suites and as a hospital consultant.

Grants
NHMRC: $390,000, 2002-04

Scholarships
Melissa Baraket
Australian Postgraduate Award, PhD Scholarship: $58,977, 2002-04
Ravinay Bhindi, David Brieger, Tommy Chung, Ben Freedman, Len Kritharides, Harry Lowe, Ben Rayner, Mimi Saba, Ying Shen, Chiangjie Song, Alice Tiong, Paul Witting

This group is new this year to the ANZAC Research Institute and now has eight people working in the laboratory, and another five with clinical and laboratory responsibilities. Mixing basic and clinical science allows us to conduct research into clinically important disorders of the heart and blood vessels using both experimental models and patients with coronary heart disease. We were fortunate in recruiting an accomplished ARC career researcher, Dr Paul Witting, to be the senior scientist, and he has already established collaborations with all members of the Vascular Biology group. As an example of this, he has analysed blood from heart attack patients treated by our clinician scientists and demonstrated the presence of the abnormal heart protein he predicted would be formed following balloon and stent placement for heart attack. The group has a range of research interests and focuses in three areas: vascular and heart muscle injury by oxidation or intervention, inflammation and thrombosis, and atherosclerosis.

Can heart proteins harm the heart during treatment for heart attack to open the blocked artery?

P Witting, B Rayner

We are attempting to answer this question because mortality and morbidity from heart attack remains a significant problem despite advances in therapy that restore coronary blood flow. The oxidation stress from restoration of blood flow can damage heart muscle proteins, such as myoglobin, to form an abnormal protein that may damage the small blood vessels in the heart and the heart muscle itself. This may impede the full restoration of blood flow to the damaged region, as well as reducing the pumping capacity of the partially injured heart muscle. We have developed a novel synthetic antioxidant that inhibits the abnormal myoglobin derived protein. Our studies aim to determine whether this anti-oxidant can ameliorate the damaging effects of restoration of blood flow to both the blood vessel lining and the heart muscle itself during a heart attack. Currently, there are no available therapies to minimise the severity of this oxidative stress following heart attack.

Cellular and clinical aspects of vascular disease

L Kritharides, G Lau (Cardiology, Concord Hospital), M Saba, T Chung, L Ridley (Radiology, Concord Hospital).

Members of this group are investigating cellular and clinical aspects of coronary heart disease. With the joint supervision of Dr Ridley from the Concord Hospital’s Radiology Department, George Lau is investigating the potential of calcium scoring and CT angiography to identify blocked arteries and to assess the condition of coronary artery bypass grafts after surgery. He has found that the absence of calcium on CT scan does not guarantee the absence of coronary disease and that blockages of bypass grafts can occur quite soon after surgery.

A new and important finding was that early blockage of arterial bypass grafts appears to be related to abnormally high levels of triglyceride in the blood. Previous studies from our Biogerontology group have shown that aged liver tissues contain an increased intracellular distribution of apolipoprotein E, a protein that is essential for the clearance of cholesterol from the blood stream. With the joint supervision of Professor Le Couteur, Mimi Saba is investigating how ageing liver cells secrete proteins and how this process may be disturbed as we age. This may help us understand how atherosclerosis increases with age.

Cardiovascular injury

H Lowe, R Bhindi, C Song

Our research focuses on cardiovascular injury, encompassing both injury to blood vessels and heart muscle. Blood vessels can be injured during balloon angioplasty with stenting, resulting in recurrent narrowing of the artery, and vein grafts used for coronary bypass surgery can also be injured during surgery, reducing their longevity. Additionally, heart muscle is injured when blood flow is stopped and then restored, as happens during heart attack and its therapy. We are developing animal models of all these processes to allow us to investigate which genes and which signalling mechanisms are involved. This allows us to study novel gene-targeting approaches to modify the deleterious responses to cardiovascular injury.
Inflammation and fibrinolysis

D Brieger, A Tiong, B Zeng

Our studies have focused on the broad themes of inflammation and fibrinolysis, the dissolving of blood clots, in acute coronary disease such as angina and heart attacks. Pilot studies in our department identified elevated circulating enzymes, matrix metalloproteinases or MMP, in patients with sudden onset of chest pain. The levels of these enzymes were related to markers of inflammation, and we are currently investigating this relationship. We are measuring these enzymes using a variety of techniques in a range of patients with coronary artery disease, including those with heart attacks, stable angina and before and after balloon angioplasty for severe coronary narrowing. We are relating these measurements to the degree of activation of circulating inflammatory cells to determine if these cells are responsible for the elevation of the enzymes. We believe these MMP and the inflammatory cells may play a role in precipitating heart attacks, by weakening the fibrous cap of coronary artery narrowings, but then may help break down the blood clots that form during the heart attack. In a separate series of experiments, involving genetically engineered mice, we are characterising the enzymes contained in the neutrophil, a specific inflammatory cell. In addition to MMP, we believe these cells contain other enzymes that may contribute to heart attack evolution and resolution, and we are attempting to identify these novel proteins.

Inflammation and thrombosis

B Freedman, C Song, Y Shen

There is increasing recognition that heart attack and other acute coronary syndromes are brought on by an inflammatory process in the coronary arteries. Inflammation can lead to the rupture of cholesterol-laden plaques, and then to obstruction of the artery by thrombosis or blood clots. Our group is researching the mechanisms that underlie how inflammation can interact with blood clotting in patients with coronary artery disease that predicts death and heart attack in populations at risk for coronary events. We have observed that blood monocytes can be stimulated to produce a powerful substance that promotes thrombosis in arteries. Our studies in cells taken from patients with and without heart disease as well as experimental animals will be directed at better understanding the mechanism of the interaction between inflammation and thrombosis, which may identify new targets for treatment.

Grants

- ARC Discovery Grant: $145,000, 2003-07
- Ramaciotti Foundation: $11,300, 2004
- NHMRC Equipment Grant: $73,200, 2004
- Welcome Trust Large Equipment grant: $44,000, 2004
- University of Sydney Start-up Grant: $37,500, 2004

Contracts

- Pfizer CVL: $97,300, 2003-04

Fellowships

Harry Lowe
NHMRC Post Graduate Medical Scholarship: $258,000, 2000-04

Scholarships

Tommy Chung
APA Scholarship: $55,000, 2004-06
Alice Tiong
APA Scholarship: $55,000, 2003-05
Ravinay Bhindi
National Heart Foundation Post Graduate Medical Scholarship: $85,296, 2004-06

Prizes and Awards

Paul Witting
Contributing to Australian Scholarship and Science Travel Award: $1,600, 2004
Chiangjie Song
Ralph Reader Clinical Science Prize: Cardiac Society of Australia and New Zealand: $3,000, 2004
Scientific Staff

Scientific Program Leaders
Professor Bob Cumming MB BS, MPH, PhD, FAFPHM
Professor Ben Freedman MB BS, FRACP, FACC, FESC, PhD
Professor David Handelsman MB BS, PhD, FRACP
Professor David Le Couteur MB BS, PhD, FRACP
Dr Sam Lim MB BS, PhD, FRACP
Professor Garth Nicholson MB BS, PhD
Dr Brian O’Toole PhD, MPH
Professor Markus Seibel MD, PhD, FRACP

Clinical Research Associates
Associate Professor David Brieger MB BS, FRACP, PhD
Associate Professor Ann Conway MB BS, FRACP
Associate Professor Len Kritharides, MB BS, FRACP, FAHA, PhD

Research Fellowships
Dr Matthew Harris PhD
Dr Harry Lowe MB BS, FRACP, FACC, PhD
Dr Peter Liu MB BS, FRACP PhD
Dr Christian Meier MD (Switzerland)
Dr Paul Witting PhD

Principal Research Fellow
Dr Colin Dunstan PhD

Senior Research Fellow
Dr Charles Allan PhD
Dr Vadim Dedov MD (Russia), PhD
Dr Jillian Kriil PhD
Dr Marina Kennerson PhD
Dr Michael Muller MA, PhD
Dr Simon Myers Dip Ed, PhD
Dr Jaskarit Singh PhD
Dr Hong Zhou MD (China), PhD
Dr Danqing Zhu PhD

Project Managers
Karen Brennan MSc
Melisa Litchfield BAppSc, MPH

Research Scientists
Dr Victoria Cogger PhD
Dr Irina Dedova MD (Russia), PhD
Kaye Griffiths AM, AMS, DMU, RN
Dr Inken Huttner MD (Germany)
Mark Jimenez BSc (Hons)
Dr Chiangjie Song MD (China), MSc
Jenny Spaliviero MSc
Dr Greg Sutherland BSc, PhD

Clinical Research Nurses
Dr Sharyn Kelleher RN, BA, PhD
Leo Turner RN
Susan Wishart RN, BA, Grad Dip Counselling

Project Officers
Stella Christodoulou BSc
Dr Lam Ly MD (Vietnam), PhD

Research Assistants
Tina Borovina Dip Ap Sci
James de Winter BSc, Ass Dip Chem, Cert Art Direction & Copywriting
Patrick Lim BSc (Hons)
Kirsten McTavish BSc (Hons)
Ben Rayner BBioSc (Hons)
Ben Marshan BSc (Hons)
Gina Walizada BSc (Hons)

Technical Support
Fay Bacha BSc
Irene Di Pierro Dip Path Tech
Sabina Horky
Arturo Samcam-Ruiz BAgSc (Nicaragua)
Ljudica Vrga BSc (Slovenia)

Graduate students
Dr Arun Aggarwal MB BS
Dr Melissa Baraket MB BS
Dr Ravinay Bhindi MB BS, FRACP
Dr Tommy Chung MB BS
Dr Sumana Gopinath MB BS, FRACP
Sharyn Kelleher RN, BA
Drs Cindy Kok MD (Netherlands)
Shahab Lajevardi BSc (Hons)
Patrick Lim BSc (Hons)
Brian Oliver MSc
Dr Alex Phoon MB BS, BSc
Mimi Saba BSc (Hons)
Dr Linda Seeto MB BS
Dr Anita Sharma DSM, AMC, FRACP
Ying Shen MD (China)
Dr Alice Tiong BSc (Hons), MB BS, FRACP
Leo Turner RN
Alessandra Warren MSc

Undergraduate Students
Jameel Khan
Magreet Schipper (Netherlands)
Marieke Teeuw (Netherlands)
## Administrative Staff

**Director**  
Professor David Handelsman MB BS, PhD, FRACP  

**General Manager**  
Christine Harrison BSc (Hons), FIBMS, Grad Dip Bus, AFACHSE, AIMM  

**Manager, Molecular Physiology Unit**  
Mamdouh Khalil BSc, Ass Dip Animal Technology  

**Manager, Transgenic Services**  
Karen Brennan MSc  

**Accounts**  
Annet Doss Dip Acc, Dip Comp Prog  

**Computer Support**  
Marco Fabiani BMath, Dip Comp Prog  

**Office Managers**  
Lydia Andreas BNS  
Dianne Quinn JP  

**Receptionist**  
Colleen Fitzgibbons Dip Sec

### Growth at ANZAC Research Institute

<table>
<thead>
<tr>
<th>Staff/students</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program Directors</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Post Doctoral Scientists</td>
<td>-</td>
<td>6</td>
<td>9</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Graduate Students</td>
<td>4</td>
<td>9</td>
<td>17</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Scientific &amp; Technical</td>
<td>-</td>
<td>7</td>
<td>11.5</td>
<td>14.5</td>
<td>21</td>
</tr>
<tr>
<td>Administration</td>
<td>1</td>
<td>3.5</td>
<td>4</td>
<td>3.2</td>
<td>3.2</td>
</tr>
<tr>
<td>Total Full Time Equivalent</td>
<td>6</td>
<td>28.5</td>
<td>46.5</td>
<td>51.7</td>
<td>70.2</td>
</tr>
<tr>
<td>Source</td>
<td>Title</td>
<td>Investigators</td>
<td>Annual $</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------------------------------------------------------------------</td>
<td>------------------------------------------------------</td>
<td>-----------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Andrology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Mechanisms of pro-atherogenic effects of androgens in human vascular</td>
<td>Death, Celermajer, Handelsman</td>
<td>70,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cells</td>
<td>cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Studies of the paracrine role of Inhibin A/activin A in ovulation</td>
<td>Illingworth, Handelsman</td>
<td>75,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Hormonal regulation of Sertoli cell function</td>
<td>Allan, Handelsman</td>
<td>150,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>The role of FSH in spermatogenesis</td>
<td>Handelsman, Allan</td>
<td>95,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Neil Hamilton Fairley Fellowship</td>
<td>Liu</td>
<td>100,182</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Prenatal factors in male reproductive health</td>
<td>Handelsman</td>
<td>45,830</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>The role of androgens in female physiology</td>
<td>Handelsman, Zajac, Illingworth, Allan, McManus</td>
<td>125,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ramaciotti Foundation</td>
<td>Automatic tissue-processing workstation</td>
<td>Allan</td>
<td>30,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ramaciotti Foundation</td>
<td>Mass spectrometry upgrade of HPLC</td>
<td>Handelsman</td>
<td>30,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>University of Sydney</td>
<td>Cellular and molecular mechanisms of neonatal hormonal imprinting</td>
<td>Handelsman</td>
<td>25,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer Research Fund of the prostate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Collaborations</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASA Program</td>
<td>Defining interactions between anabolic and peptide hormones: requirements for a robust test for growth hormone doping (with Garvan Institute)</td>
<td>Ho, Kazalaukas, Handelsman, Irie</td>
<td>220,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grant, DCITA</td>
<td>Identification of potentially undetected androgens derived from marketed</td>
<td>Death, Handelsman</td>
<td>67,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grant, DCITA</td>
<td>Non androgenic steroids: implications for sports doping (with Heart Research Institute)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National Heart Foundation</td>
<td>Androgen exposure and its effects on cardio vascular disease in men</td>
<td>Death, Celermajer, Handelsman</td>
<td>33,333</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(with Heart Research Institute)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>World Anti-Doping Agency</td>
<td>Australian Japanese Consortium - Defining interactions between anabolic and peptide hormones: requirements for a robust test for growth hormone doping (with Garvan &amp; Kolling Institutes &amp; ASDTL)</td>
<td>Ho, Kazalaukas, Baxter, Handelsman, Irie</td>
<td>US $400,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Contracts</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lawley Pharmaceuticals</td>
<td>Long term pharmacokinetics and clinical efficacy of Andromen Forte 5% cream for androgenreplacement therapy in hypogonadal men</td>
<td>Handelsman</td>
<td>4,100</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Biogerontology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC/DVA</td>
<td>Pharmacological, metabolic and therapeutic implications of the oxygen diffusion carrier hypothesis of ageing in the liver</td>
<td>McLean, Le Couteur</td>
<td>20,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>The effect of hepatic pseudocapillarisation of old age on the disposition of chylomicron</td>
<td>Le Couteur, Fraser, Sullivan, McLean</td>
<td>65,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Geriatric pharmacology</td>
<td>Le Couteur, McLean</td>
<td>55,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Postgraduate Medical Scholarship</td>
<td>Hilmer</td>
<td>28,432</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Dora Lush Postgraduate Scholarship</td>
<td>Warren</td>
<td>21,853</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>CJ Martin Fellowship</td>
<td>Harris</td>
<td>60,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bone Biology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSW Health</td>
<td>BioFirst award</td>
<td>Dunstan</td>
<td>100,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swiss National Foundation</td>
<td>Postdoctoral Fellowship</td>
<td>Meier</td>
<td>65,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>University of Sydney Cancer Research Fund</td>
<td>Bone metastases and inhibition of skeletal repair</td>
<td>Seibel, Dunstan</td>
<td>42,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Contracts</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aventis Pharma</td>
<td>OPG and RANKL in bisphosphonate therapy &amp; Jobson family genetic study</td>
<td>Seibel, Meier, Dunstan</td>
<td>56,551</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merck Sharp And Dohme</td>
<td>Determinants in bone turnover in man</td>
<td>Meier</td>
<td>10,192</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novo Nordisk</td>
<td>Determinants in bone turnover in man</td>
<td>Meier</td>
<td>30,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roche Pharma</td>
<td>Ibandronate in bone metastases</td>
<td>Seibel, Dunstan</td>
<td>33,565</td>
<td></td>
<td></td>
</tr>
<tr>
<td>World Anti-Doping Agency</td>
<td>Australian Japanese Consortium - Defining interactions between anabolic and peptide hormones: requirements for a robust test for growth hormone doping</td>
<td>Ho, Kazalaukas, Baxter, Handelsman, Irie</td>
<td>73,120</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Public Health &amp; Epidemiology</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Concord Health and Ageing Men Project (CHAMP)</td>
<td>Cumming, Handelsman, Seibel, Creasey, Sambrook, Waite</td>
<td>360,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source</td>
<td>Title</td>
<td>Investigators</td>
<td>Annual $</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>----------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC</td>
<td>Australian Vietnam Veterans’ health study: Cohort wave 2</td>
<td>O’Toole, Catts, Cockburn, Outram</td>
<td>120,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHMRC Equipment Grant</td>
<td>Bone densitometer for CHAMP study</td>
<td>Cumming, Handelsman, Seibel, Creasey, Sambrook, Waite</td>
<td>193,000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Neurobiology

**Grants**

<table>
<thead>
<tr>
<th>Source</th>
<th>Title</th>
<th>Investigators</th>
<th>Annual $</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHMRC</td>
<td>Molecular genetics of Hereditary Motor and Sensory Neuropathy with Pyramidal Signs</td>
<td>Nicholson, Kennerson</td>
<td>75,000</td>
</tr>
<tr>
<td>NHMRC</td>
<td>Molecular genetics of Intermediate Charcot-Marie-Tooth Neuropathy</td>
<td>Nicholson, Kennerson</td>
<td>30,000</td>
</tr>
<tr>
<td>MDA RIA</td>
<td>Possible shortcut to finding a new drug for therapy in MND</td>
<td>Dedov, Nicholson</td>
<td>14,500</td>
</tr>
<tr>
<td>MDA RIA</td>
<td>Genetic markers in neural diseases (PhD Scholarship)</td>
<td>Gopinath, Nicholson, Kennerson</td>
<td>23,000</td>
</tr>
<tr>
<td>MDA RIA</td>
<td>Finding new pathogenic genes effecting motor neurones (PhD Scholarship)</td>
<td>Gopinath, Nicholson, Kennerson</td>
<td>12,000</td>
</tr>
<tr>
<td>Muscular Dystrophy Association USA</td>
<td>Construction and characterisation of a Hereditary Sensory Neuropathy</td>
<td>Nicholson, Allan, Kennerson, Pollard</td>
<td>61,850</td>
</tr>
<tr>
<td>Amyotrophic Lateral Sclerosis Association USA</td>
<td>Identifying new gene mutations for Motor Neuron Disease</td>
<td>Nicholson</td>
<td>23,600</td>
</tr>
<tr>
<td>University of Sydney Near Miss Grant</td>
<td>CMT with pyramidal signs</td>
<td>Nicholson, Kennerson</td>
<td>30,000</td>
</tr>
<tr>
<td>DEST/University of Sydney APA Scholarship</td>
<td></td>
<td>Gopinath</td>
<td>9,223</td>
</tr>
</tbody>
</table>

### Respiratory Medicine

**Grants**

<table>
<thead>
<tr>
<th>Source</th>
<th>Title</th>
<th>Investigators</th>
<th>Annual $</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHMRC</td>
<td>The role of the alveolar macrophage in the regulation of inflammation and matrix destruction of COPD</td>
<td>Lim</td>
<td>125,000</td>
</tr>
<tr>
<td>DEST/University of Sydney APA Scholarship</td>
<td></td>
<td>Baraket</td>
<td>19,659</td>
</tr>
</tbody>
</table>

### Vascular Biology

**Grants**

<table>
<thead>
<tr>
<th>Source</th>
<th>Title</th>
<th>Investigators</th>
<th>Annual $</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARC Discovery Grant</td>
<td>Biochemical properties of S-nitrosomyoglobin and its role in regulating nitric oxide bioavailability</td>
<td>Witting</td>
<td>145,000</td>
</tr>
<tr>
<td>ARC Discovery Grant Cardiac Society of Australia and New Zealand</td>
<td>Novel vitamin E analogues with enhanced specificity for malignant cells</td>
<td>Neuzil, Witting and Salvatore</td>
<td>5,000</td>
</tr>
<tr>
<td>National Heart Foundation</td>
<td>Travel Award</td>
<td>Witting</td>
<td>1,600</td>
</tr>
<tr>
<td>National Heart Foundation</td>
<td>Post Graduate Medical Scholarship</td>
<td>Bhindi</td>
<td>28,000</td>
</tr>
<tr>
<td>NHMRC</td>
<td>Clinical fellowship</td>
<td>Lau</td>
<td>28,000</td>
</tr>
<tr>
<td>Pfizer CVL</td>
<td>Characterisation of plaque instability in patients with symptomatic vein graft atherosclerosis</td>
<td>Lowe, Brieger</td>
<td>94,600</td>
</tr>
<tr>
<td>Pfizer CVL</td>
<td>Upgrade ESP 300 EPR Spectrometer</td>
<td>Tiong, Brieger</td>
<td>16,667</td>
</tr>
<tr>
<td>Ramaciotti Foundation</td>
<td>Nitric oxide electrode</td>
<td>Witting</td>
<td>11,300</td>
</tr>
<tr>
<td>Welcome Trust Large Equipment Grant</td>
<td>MMP after primary coronary intervention</td>
<td>Lay, Kennedy, Davies, Witting</td>
<td>44,000</td>
</tr>
<tr>
<td>DEST/University of Sydney APA Scholarship</td>
<td></td>
<td>Chung</td>
<td>9,223</td>
</tr>
<tr>
<td>DEST/University of Sydney APA Scholarship</td>
<td></td>
<td>Tiong</td>
<td>9,223</td>
</tr>
<tr>
<td>University of Sydney Startup grant Paul Witting</td>
<td>Startup grant</td>
<td>Saba</td>
<td>18,446</td>
</tr>
<tr>
<td>University of Sydney Startup grant Paul Witting</td>
<td>Startup grant</td>
<td>Witting</td>
<td>37,500</td>
</tr>
</tbody>
</table>

### Institute-wide Grants

<table>
<thead>
<tr>
<th>Source</th>
<th>Title</th>
<th>Investigators</th>
<th>Annual $</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHMRC</td>
<td>Cell culture facility</td>
<td>Le Couteur, Harris, Kril, Allan, Handelsman</td>
<td>65,000</td>
</tr>
<tr>
<td>NHMRC Equipment grant</td>
<td>Digital stereology system</td>
<td>Handelsman, Allan, Le Couteur, Nicholson, Illingworth, Kril</td>
<td>54,500</td>
</tr>
<tr>
<td>NHMRC Equipment Grant</td>
<td>Bench-top ultracentrifuge</td>
<td>Witting, Handelsman, Muller et al</td>
<td>73,200</td>
</tr>
<tr>
<td>University of Sydney Scanning electron microscope</td>
<td></td>
<td>Le Couteur, Muller, Harris, Handelsman, Seibel, Nicholson</td>
<td>67,300</td>
</tr>
</tbody>
</table>

---


Seibel MJ. Available pharmacotherapies for bone loss. Long Term Health Care Strategies 2003 (published and available on CD only).


Waldman L, Kritharides L. Non-


* Equal first author

Vascular Biology


Felicity Barr

Felicity Barr is Chairman of the ANZAC Health and Medical Research Foundation. Her interest in the issues of ageing developed during her service with the Commonwealth Department of Veterans' Affairs, including five years as Deputy Commissioner in NSW. She has completed master's studies in gerontology and is now working towards her doctorate in the Faculty of Health Sciences, University of Sydney. She is Chair of the Board of the War Widows’ Guild (NSW), Honorary Governor of the Ageing & Alzheimer’s Research Foundation, a member of the NSW Ministerial Advisory Committee on Ageing and NSW President of the Australian Association of Gerontology.

Professor David Handelsman

Professor Handelsman has been Director of the ANZAC Research Institute since its inception in 1998. He is an international expert in Andrology, the study of male reproductive health, medicine and biology. While studying for his PhD, he established the first clinical Andrology centre in Australia that has eventually become the first hospital Andrology department in the country. He has served as adviser to the WHO Human Reproduction Programme, Secretary of the International Society of Andrology and President of the Endocrine Society of Australia. He was awarded the Susman Prize from the Royal Australasian College of Physicians in 1994 and the inaugural AMA Men’s Health Award in 2003. He was promoted to a Personal Chair at the University of Sydney in 1996 to become the first Professor in Andrology in Australia.

Professor Andrew Coats

Professor Andrew Coats is Dean of the Faculty of Medicine at the University of Sydney. Prior to this appointment in 2003, he was the Viscount Royston Professor of Clinical Cardiology at the National Heart and Lung Institute, Imperial College of Science, Technology and Medicine, London and formerly Director of Cardiology at the Royal Brompton Hospital, London. Though born in Melbourne, he completed his tertiary studies in the UK graduating in Medicine from Cambridge, awarded DM (Oxon) in 1992 and obtained an MBA from the London Business School in 2001. His research interests lie in the area of heart failure and high blood pressure. He serves on the editorial boards of a number of international scientific journals in the area of cardiology and on working parties of British and European organizations related to his research interests. He brings a wealth of experience of clinical and academic medicine as well as health management to the Board.

Professor David Cook

Professor David Cook currently holds the Chair of Cellular Physiology at the University of Sydney. He was awarded an MD in 1995, the Gottschalk Medal of the Australian Academy of Science in 1996 and became University of Sydney Medical Foundation Fellow of the Faculty of Medicine in 1997 when he was also promoted to professor. His research interests are in the role of ion channels and other transporters in the cell membrane and how control membrane transport activity. In addition to his research and teaching within the Department of Physiology, he serves as Deputy Chair of the Central Sydney Area Health Service Human Ethics Committee and chairs the Clinical Trials Subcommittee at Royal Prince Alfred Hospital.

Matthew Daly

For the last twenty years Mr Daly has been involved in health management in a variety of settings including teaching, district, and private hospitals, and community health services. He has been Executive Director of two University of Sydney teaching hospitals, Concord Repatriation General and Canterbury. At present, he is seconded to South Western Area Health Service as Deputy CEO. He holds tertiary qualifications in health administration and business and has been surveyor for the Australian Council of Healthcare Standards and NSW State Branch Councillor with the Australian College of Health Service Executives.

Professor David Handelsman
Dr Diana Horvath AO

Dr Horvath was appointed Chief Executive Officer of the Central Sydney Area Health Service in 1992. She has chaired the National Health and Medical Research Council, been President of the Australian Hospital Association, and served a five-year term as a Commissioner with the Health Insurance Commission. She is an active member of the Trade Policy Advisory Commission. She was recognised for her work in Australian public health when she was made an Officer of Australia in 1995.

Brian Lee

Brian Lee spent his career in the medical supply industry and recently retired as Area Managing Director (Australia and New Zealand) for Baxter Healthcare. He is the serving National President of the Leukemia Foundation of Australia as well as being a long-time advocate and supporter of ANZAC Health and Medical Research Foundation. He is currently a director of Medical Specialities Australia. He has accepted the position to chair the Fundraising Subcommittee on the current Board.

David MacGowan

David MacGowan brings a wealth of financial management experience to the Board. Since his retirement from BHP Steel, where he held the position of General Manager Finance, he has been active in the community and served as Finance Director and consultant to Opera Australia. On the Foundation’s Board he has recently accepted the position to chair the Board’s Finance Subcommittee.

Paul McClintock

Paul McClintock is Deputy Chair of the ANZAC Health and Medical Research Foundation. He is Chairman of Affinity Health Limited, a Commissioner of the Health Insurance Commission, and has previously been Chairman of the Woolcock Institute of Medical Research and Director of the Health Services Association of New South Wales. He is the former Secretary to Cabinet and Head of the Cabinet Policy Unit for the Australian Government.

Dr Charles Pawsey

After Charles Pawsey graduated from the University of Adelaide in 1967, he spent three years at Queen Elizabeth Hospital in Adelaide. Later at Greenslopes Hospital in Brisbane he worked as a National Heart Foundation Research Assistant undertaking research into the Renin-Angiotensin system and hypertension. He undertook his physician traineeship at Sydney Hospital in 1972-73 and his Cardiology training at Royal Prince Alfred Hospital in 1974-75 and at Johns Hopkins Hospital in 1976. Since 1977, he has been a Staff Cardiologist at Concord Repatriation General Hospital.

Godfrey (Rusty) Priest AM

Rusty Priest was an inaugural member of the ANZAC Health & Medical Research Foundation serving as its Deputy Chair from 1995 to 2003. Rusty enlisted in the 2nd AIF in June 1945, serving in Japan with British Commonwealth Occupation Forces from April 1946 to December 1948, the Australian Regular Army from 1946 to 1967 and the Emergency Reserve until 1975. Then he undertook a management position at the University of Sydney, retiring in 1990. He is a Past President of the Returned and Services League of Australia (NSW Branch), having held office between 1993 and 2002. He is extensively involved in all matters affecting the welfare of veterans and their dependants. He serves currently as Chairman of the Board of Directors of the Kokoda Track Memorial Walkway Ltd.
## Synopsis of Financial Performance

<table>
<thead>
<tr>
<th>Income Streams</th>
<th>2000-01</th>
<th>2001-02</th>
<th>2002-03</th>
<th>2003-04</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peer reviewed Funding</td>
<td>$314,959</td>
<td>$1,288,014</td>
<td>$1,508,389</td>
<td>$2,329,584</td>
</tr>
<tr>
<td>Clinical Trials</td>
<td></td>
<td>$84,806</td>
<td></td>
<td>$441,435</td>
</tr>
<tr>
<td>State Government Grants</td>
<td>$442,400</td>
<td>$442,400</td>
<td>$492,400</td>
<td>$532,044</td>
</tr>
<tr>
<td>Donations</td>
<td>$186,911</td>
<td>$195,278</td>
<td>$676,161</td>
<td>$203,405</td>
</tr>
<tr>
<td>Fundraising</td>
<td>$89,042</td>
<td>$64,842</td>
<td>$94,953</td>
<td>$60,800</td>
</tr>
<tr>
<td>Interest</td>
<td>$122,319</td>
<td>$110,072</td>
<td>$157,709</td>
<td>$224,973</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td>$287,770</td>
</tr>
<tr>
<td><strong>Total Income</strong></td>
<td><strong>$1,155,631</strong></td>
<td><strong>$2,100,606</strong></td>
<td><strong>$3,014,418</strong></td>
<td><strong>$4,080,011</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Expenditure Streams</th>
<th>2000-01</th>
<th>2001-02</th>
<th>2002-03</th>
<th>2003-04</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salary Costs</td>
<td>$203,959</td>
<td>$725,879</td>
<td>$674,508</td>
<td>$852,884</td>
</tr>
<tr>
<td>Administrative Costs</td>
<td>$211,728</td>
<td>$327,728</td>
<td>$490,409</td>
<td>$371,393</td>
</tr>
<tr>
<td>Consumables</td>
<td>$41,341</td>
<td>$141,796</td>
<td>$364,263</td>
<td>$599,811</td>
</tr>
<tr>
<td>Repairs and Maintenance</td>
<td>$313,663</td>
<td>$167,556</td>
<td>$118,436</td>
<td>$146,089</td>
</tr>
<tr>
<td>Depreciation</td>
<td>$148,306</td>
<td>$258,281</td>
<td>$291,125</td>
<td>$498,928</td>
</tr>
<tr>
<td><strong>Total Expenditure</strong></td>
<td><strong>$918,997</strong></td>
<td><strong>$1,621,240</strong></td>
<td><strong>$1,938,741</strong></td>
<td><strong>$2,469,105</strong></td>
</tr>
<tr>
<td><strong>Net increase in funds</strong></td>
<td><strong>$236,634</strong></td>
<td><strong>$479,366</strong></td>
<td><strong>$1,075,677</strong></td>
<td><strong>$1,610,906</strong></td>
</tr>
</tbody>
</table>

The ANZAC Research Institute continues to expand its research interests attracting high quality scientists and students from around the world. Current success of their research projects in attracting funding is largely responsible for the increases seen in our assets.

Expenditure continues to rise reflecting the continuing growth and diversification of the Institute’s research efforts. The purchase, through generous equipment funding, has also increased the facilities for research and the net assets of the organisation.

Detailed, audited financial statements are available in the pocket in the back cover of this report.
This year the Foundation contracted Markson Sparks! to facilitate the Annual Dinner and Auction. As this coincided with the beginning of the 2003 Rugby World Cup, that was adopted as the theme for the evening. The master of ceremonies was well known media personality Peter FitzSimons who provided engaging commentary and ensured a sparkling pace for the evening proceedings. The entertainment included a lively discussion between some past and present greats of rugby - Colin Meads, Ken Catchpole and Jason Little. Each table was hosted by a notable rugby personality. Pianist Simon Tedeschi performed beautifully for the dinner entertainment. A lively auctioneer, Michael Hawkins, made short work of the fifteen lots on auction. An appeal raised $32,000 in donations of which our stalwart supporters Baxter Healthcare gave $25,000. This was followed by a lively time on the dance floor.

The venue was the historic Westin Hotel, in Martin Place, Sydney, whose catering staff excelled themselves with a fine feast. We were fortunate that another generous and constant supporter of the Foundation, Tintilla Estate, donated the wine for the evening.

After the recent period of significant growth experienced by the ANZAC Research Institute, the Foundation will be refocussing its fundraising efforts in the coming year with seminar, dinner and other activities being planned.

We are very fortunate that the Friends of the ANZAC Research Institute, the FOTARI, continue to be a constant source of support, as do the many RSL Sub Branches and Veterans groups. These generous supporters together with NSW Health Grants allow the ANZAC Research Institute the ability to offer excellent facilities to the many researchers who choose to work here.
Veterans and Community Organisations

$40,000
Ageing and Alzheimer’s Research Foundation

Under $10,000
2/104 Australian General Transport AIF Association
Australian Society of Sports History
Charcot-Marie-Tooth Association of Australia Inc
Chester Hill-Carramar RSL Sub-Branch
North Sydney RSL Sub Branch
Pittwater RSL Sub Branch
Prinses Beatrix Fonds (Netherlands)

FOTARI

$1,000 and over
Frank Carioti
Paul Collett
Michael Halliday
Neville Jeffress
David & Helen Jobson
Steven Kalowski
John Linsley
Stephen Lidbury
Richard Osborn
Charles Pawsey
Elizabeth Tracey
Peter Tracey
Paul Waizer
Garry Wayling

$500 and over
Eric Appleton
Ross Bradbury
Ramon Bullock
Eileen Collins
Gregory Falk
M W Hayes
Thomas Karplus
G D Pearce

$100 and over
Keith & Joan Allan
AXA Australia
RW Balfour
JR Belcher
Ken Catchpole
Xavier Collin
Alan Davidson
Graham Dunn
Reg Elliott

George & Helen Ferguson
B E Fitzgerald
William James Forbes
LJ & GJ Ford
Ben Freedman
Catherine Hanley
B J Harrison
Risetag Jacobson
Keith Jobson
Major John P Kelly
David Le Couteur
H Overton
RTA Parkes
Phil L Peters
Andrew G Richardson
Anh Dung Tran
Charles Tonna
Frank & Pam Tracey
I & J Vassett
WB & MJ White
John D Yeo Pty Limited

Corporate Sponsors

$25,000 and above
Aventis Pharma Pty Ltd
Baxter Healthcare Pty Ltd
Pfizer Neuroscience Research Grants

$5,000 to $10,000
Eli Lilly Australia Pty Ltd
Merck Sharp & Dohme (Australia) Pty Ltd
Pharmatel
Roche Diagnostics

Under $5,000
Glaxo Smith Kline Australia
Immuno Diagnostics
Johnson & Johnson Medical
Novartis Pharmaceuticals Australia Pty Ltd

Sponsorship for Annual Dinner and Auction
Baxter Healthcare
Markson Sparks!
Tintilla Estate Vineyard and Olive Grove

Acknowledgements
Professor Bob Lusby
Peter FitzSimons
Bob Lavigne
Max Markson
J&M Promotions
A bequest to ANZAC Health & Medical Research Foundation is a way of helping future generations to enjoy longer and more fulfilling lives.

**Estate Planning**
More and more supporters of ANZAC Health & Medical Research Foundation are ensuring that our vital research continues by including a bequest in their will. This can also be done by codicil to an existing will. There are usually four types of bequests to consider:

**A Specific Bequest**
This specifies the type of gift clearly, whether it is a gift of money, shares, property or life assurance policy.

**A Percentage Bequest**
This is the most flexible method of giving; the gift is automatically determined by the size of the estate and takes inflation into account.

**A Residual Bequest**
This is the amount that remains after the provisions for family and relatives have been made.

**Your Whole Estate**
This usually occurs when there are no living relatives and the benefactor wishes to achieve something significant with their estate.

The suggested wording for a bequest to ANZAC Health and Medical Research Foundation is:

"I give to ANZAC Health & Medical Research Foundation, ABN 48 066 780 005, (the whole), or (a specific sum or piece of property), or (a percentage), or (the residue) of my Estate free of all duties and a receipt from the Treasurer or other authorised person shall be a complete and sufficient discharge for the Executor."

---

**OTHER GIVING OPPORTUNITIES**

- Yes, I would like to help ANZAC Health & Medical Research Foundation.
- I would like to meet a representative from the Foundation to discuss making a bequest.
- I have already remembered ANZAC Health & Medical Research Foundation in my Will.
- Please send me more information about the Foundation’s Bequest Program, including the recognition of benefactors.
- A gift to continue vital scientific research.
- Please send me more information on the FOTARI.

I / We wish to make a donation of $_____________ to ANZAC Health and Medical Research Foundation.

Name: _____________________________
Address: ___________________________
Postcode: __________________________
Telephone: H: _______________ W: _______________
Mobile: ____________________________
Email: _____________________________

Payment is by:
- [ ] Cheque
- [ ] Money Order
- [ ] Visa
- [ ] Bankcard
- [ ] Mastercard

Expire: ____ / _____
Signature: ____________________________________________
Date: _____________

For further information contact:
**ANZAC Health & Medical Research Foundation**
ANZAC Research Institute
Hospital Road CONCORD NSW 2139
Telephone: (02) 9767 9100 or Facsimile: (02) 9767 9101
d www.anzac.edu.au
Email: anzac@anzac.edu.au

All gifts over $2.00 are tax deductible
The directors hereby present their report for the year ended 30 June 2004

**Directors**

The names and details of directors in office at the date of this report are:

**Mrs Felicity Barr** BA FAICD FAAG  
Chairman  
Chairman, War Widows’ Guild of Australia (NSW) Ltd  
Honorary Governor, Ageing and Alzheimer’s Research Foundation  
President, Australian Association of Gerontology (NSW)  
Member, National Institute for Governance

**Mr Paul McClintock** BA LLB  
Deputy Chairman  
Director, McClintock Associates Pty Ltd  
Chairman, Affinity Health Ltd  
Chairman, ADI Ltd and Thales Australia Holdings Pty Ltd  
Director, Perpetual Trustees Australia Ltd  
Director, Macquarie Infrastructure Investment Management Ltd  
Commissioner, Health Insurance Commission

**Mr David MacGowan** BEcom CPA FAICD  
Chair, Finance Subcommittee

**Mr Brian M Lee**  
Chair, Fundraising Subcommittee  
National President, Leukaemia Foundation of Australia  
National President, Medical Industries Association of Australia  
Member, Parramatta Development Board

**Professor David J Handelsman** MB BS FRACP PhD  
Director, ANZAC Research Institute  
Sub-Dean Research (Concord), University of Sydney  
Director, Department of Andrology, Concord Repatriation General Hospital

**Professor Andrew J S Coats** MA DM MB BChir FRACP FRCP FESC FACC FAHA MBA  
Dean, Faculty of Medicine, University of Sydney

**Professor David Cook** MB BS MSc MD FRACP  
Professor, Department of Physiology, University of Sydney

**Mr Matthew Daly** ADipHA BBus AFACHSE  
Acting Deputy CEO, South Western Sydney Area Health Service  
Executive Director, Concord Repatriation General Hospital and Canterbury Hospital

**Mr Diana G Horvath** MB BS (Hons) MHP FRACMA FAFPHM FCHSE  
Chief Executive Officer/Administrator, Central Sydney Area Health Service  
Administrator, South Western Sydney Area Health Service  
Board Member, Centenary Institute for Cancer Medicine and Cell Biology  
Board Member, Sydney Cancer Foundation
2 DIRECTORS’ REPORT

Dr Charles G Pawsey  MB BS FRACP DDU
Member, Concord Repatriation General Hospital Medical Staff Council
Senior Specialist in Cardiology

Mr Godfrey E Priest  AM
Chairman, Kokoda Track Memorial Walkway
Chairman, Lady Davidson Private Hospital Advisory Committee
Executive Member, Australian Red Cross (NSW Division)
Community Member, Graduate Medical Program, University of Sydney
Member, NSW Health Participation Council

At this date no director has any interest in the equity of the Foundation.

Principal Activities
The principal activities of the ANZAC Health and Medical Research Foundation during the year were that of acting as trustee for the ANZAC Health and Medical Research Foundation Trust Fund. There was no significant change in the nature of that activity during the year.

Operating Results
The company did not trade in its own right, and made neither a profit nor a loss.

Significant Changes in the State of Affairs
There were no significant changes in the state of affairs of the ANZAC Health and Medical Research Foundation during the year.

Matters Subsequent to the End of the Financial Period
No matter or circumstances have arisen since the end of the financial period which significantly affected or may significantly affect the operations of the ANZAC Health & Medical Research Foundation, the results of those operations, or the state of affairs of the ANZAC Health & Medical Research Foundation in subsequent years.

Likely Developments
The company will continue to act as trustee of the ANZAC Health and Medical Research Foundation Trust Fund.

Review of Operations
The combined effect of all fund raising campaigns conducted by the trust throughout the financial year has raised $177,245 in cash ($177,045 for 2002/2003) and $800 in pledges ($1,000 for 2002/2003).
Meetings of Directors'

During the financial period, meetings of directors, including committees, were held. Attendances are tabulated below:

### Council Meetings

<table>
<thead>
<tr>
<th>Name</th>
<th>Eligible to Attend</th>
<th>Number Attended</th>
<th>Approved leave</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emeritus Prof J Young AO (Chair)</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mr G Priest AM (Deputy Chair)</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>The Hon Ms K Chikarovski MP</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mr G Collins</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mr M Daly</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mr A Davidson AM MBE</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>The Hon. T. Fischer MP</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Prof D Handelsman</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Dr D Horvath AO</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dr E Kremer OAM</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mrs. E Lane AM MBE</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Dr C Pawsey</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Mr. G Richardson</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Ms K Russell</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ms A Sanders</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dr M Sanger</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Rear Admiral Peter Sinclair AC</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Sir Bruce Williams KBE</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

### Board Meetings

<table>
<thead>
<tr>
<th>Name</th>
<th>Eligible to Attend</th>
<th>Number Attended</th>
<th>Approved leave</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emeritus Prof J A Young AO (Chair)</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Ms F M Barr (Chair)</td>
<td>3</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Mr. M. Daly</td>
<td>4</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Prof D Handelsman</td>
<td>4</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Dr D Horvath AO</td>
<td>4</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Dr C Pawsey</td>
<td>4</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Mr G Priest</td>
<td>3</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Prof D Cook</td>
<td>3</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Prof A Coats</td>
<td>3</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Mr D MacGowan</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Mr P McClintock (Deputy Chair)</td>
<td>3</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Mr B Lee</td>
<td>3</td>
<td>3</td>
<td>-</td>
</tr>
</tbody>
</table>
Directors' Indemnification

The ANZAC Health and Medical Research Foundation during or since the financial year, in respect of any person who is or has been an officer, has not been

- indemnified or made any relevant agreement for indemnifying against a liability incurred as an officer, including costs or expenses in successfully defending legal proceedings; or
- paid or agreed to pay a premium in respect of a contract insuring against a liability incurred as an officer for the costs or expenses to defend legal proceedings.

CGU Professional Risk Insurance, a division of CGU Insurance Limited, insures all directors against liabilities for costs and expenses incurred by them in defending any legal proceedings arising out of their conduct while acting in the capacity of director of the company, other than conduct involving a wilful breach of duty in relation to the company.

Employees

The Foundation employed no employees as at 30 June 2004 (2003: nil employees).

Environmental Regulation and Performance

The Foundation is not subject to any environmental regulation.

Directors' Benefits

Neither since the financial year nor during the financial year has a director received or become entitled to receive a benefit by reason of a contract made by the company, an entity controlled by the Company, or a body corporate that was related to the company when the contract was made or when the director received or became entitled to receive the benefit with the director or with a firm of which the director is a member, or an entity in which the director has a substantial financial interest.

Signed in accordance with a resolution of the Board of Directors.

Felicity Barr
Chair

Dated this thirteenth day of November 2004 at Sydney.
Financial Statements as at 30 June 2004
INDEPENDENT AUDIT REPORT

ANZAC Health and Medical Research Foundation

To Members of the New South Wales Parliament and Members of the ANZAC Health and Medical Research Foundation

Audit Opinion

In my opinion, the financial report of ANZAC Health and Medical Research Foundation is in accordance with:

(a) the Corporations Act 2001, including:
   (i) giving a true and fair view of the ANZAC Health and Medical Research Foundation’s financial position as at 30 June 2004 and financial performance for the year ended on that date, and
   (ii) complying with Accounting Standards in Australia, and the Corporations Regulations 2001,

(b) other mandatory financial reporting requirements in Australia, and

(c) section 41B of the Public Finance and Audit Act 1983.

My opinion should be read in conjunction with the rest of this report.

The Directors’ Role

The financial report is the responsibility of the company’s directors. It consists of the statement of financial position, the statement of financial performance, the statement of cash flows and the accompanying notes, and directors’ declaration.

The Auditor’s Role and the Audit Scope

As required by the Public Finance and Audit Act 1983 and the Corporations Act 2001, I carried out an independent audit to enable me to express an opinion on the financial report. My audit provides reasonable assurance to Members of the New South Wales Parliament and the members of the ANZAC Health and Medical Research Foundation that the financial report is free of material misstatement.

My audit accorded with Australian Auditing and Assurance Standards and statutory requirements, and I:

- evaluated the accounting policies and significant accounting estimates used by the directors in preparing the financial report, and
- examined a sample of the evidence that supports the amounts and other disclosures in the financial report.
An audit does not guarantee that every amount and disclosure in the financial report is error free. The terms 'reasonable assurance' and 'material' recognise that an audit does not examine all evidence and transactions. However, the audit procedures used should identify errors or omissions significant enough to adversely affect decisions made by users of the financial report or indicate that the company's directors had not fulfilled their reporting obligations.

My opinion does not provide assurance:

- about the future viability of the Foundation,
- that it has carried out its activities effectively, efficiently and economically, or
- about the effectiveness of its internal controls.

Audit Independence

The Audit Office complies with all applicable independence requirements of Australian professional ethical pronouncements and the Corporations Act 2001. The Public Finance and Audit Act 1983 further promotes independence by:

- providing that only Parliament, and not the executive government, can remove an Auditor-General, and
- mandating the Auditor-General as auditor of public sector agencies but precluding the provision of non-audit services, thus ensuring the Auditor-General and the Audit Office are not compromised in their role by the possibility of losing clients or income.

P J Boulous, CA
Director of Audit

SYDNEY
23 December 2004
Statement of Financial Performance
For the Year Ended 30 June 2004

<table>
<thead>
<tr>
<th>Notes</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expenses from ordinary activities</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Revenue from ordinary activities</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Profit from ordinary activities before income tax expense</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Income tax expense relating to ordinary activities</td>
<td>1(C)</td>
<td>-</td>
</tr>
<tr>
<td>Net profit from ordinary activities after related income tax expense</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total changes in equity other than those resulting from transactions with owners as owners</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Statement of Financial Position
For the Year Ended 30 June 2004

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Assets</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total Liabilities</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Net Assets</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Accumulated Funds</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Notes to the Financial Statements

30 June 2004

Note 1: Summary of Significant Accounting Policies

(A) Basis of Accounting
The financial report is a general purpose financial report that complies with the requirements of the Corporations’ Act 2001, including Accounting Standards, Urgent Issues Group Consensus Views and with the requirements of the Public Finance and Audit Act 1983 and the Health Services Act 1999 and its regulations. The accounting policies used are consistent with those adopted in the previous year. The financial statements have been prepared in accordance with the historical cost convention.

(B) Accounting Records
As required by Section 45C of the Public Finance and Audit Act 1983, the Foundation has kept proper accounts and records in relation to all its activities.

(C) Income tax
The Foundation is exempt from income tax under Section 23(j) of the Income Tax Assessment Act.

(D) Trustee
The company acts as trustee for the ANZAC Health and Medical Research Foundation Trust Fund. The accounting policies adopted by the company in the preparation of the financial statements for the year ended 30 June 2004 reflect the fiduciary nature of the company’s responsibility for the assets and liabilities of the ANZAC Health and Medical Research Foundation Trust Fund which are set out in note 4.

Note 2: Revenue From Ordinary Activities
The company did not trade during the past financial year.

Note 3: Statement of Cashflows
No cashflows took place within the Foundation and hence no Statement of Cash Flows has been prepared. The Foundation does not maintain a bank account and has no other source of funding that meets the definition of a cash equivalent.

Note 4: Assets and Liabilities of the Foundation
The company acts as trustee for the ANZAC Health and Medical Research Foundation Trust Fund. The assets and liabilities of the ANZAC Health and Medical Research Foundation Trust Fund as disclosed in the financial statements of the Trust are as follows:

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Assets</td>
<td>5,803,951</td>
<td>4,106,858</td>
</tr>
<tr>
<td>Non-Current Assets</td>
<td>6,010,641</td>
<td>5,899,985</td>
</tr>
<tr>
<td><strong>Total Assets</strong></td>
<td><strong>11,814,592</strong></td>
<td><strong>10,006,843</strong></td>
</tr>
<tr>
<td>Current liabilities</td>
<td>265,945</td>
<td>128,194</td>
</tr>
<tr>
<td>Non-Current liabilities</td>
<td>10,954</td>
<td>4,392</td>
</tr>
<tr>
<td><strong>Total Liabilities</strong></td>
<td><strong>276,899</strong></td>
<td><strong>132,586</strong></td>
</tr>
<tr>
<td><strong>Net Assets</strong></td>
<td><strong>11,537,693</strong></td>
<td><strong>9,874,257</strong></td>
</tr>
<tr>
<td><strong>Represented by Trust Funds</strong></td>
<td><strong>11,537,693</strong></td>
<td><strong>9,874,257</strong></td>
</tr>
</tbody>
</table>
Note 5: Directors’ Remuneration and Retirement Benefits
No directors received, directly or indirectly income paid, payable, or otherwise made available from ANZAC Health and Medical Research Foundation during this financial year.
No amount was paid, on behalf of a director, to a superannuation plan.

Note 6: Related Party Disclosures
The names of Foundation’s directors who have held office during the financial year are:

- Ms F M Barr Appointed 14/10/03
- The Hon Ms K A Chikarovski MP Resigned Sept 2003
- Prof A Coats Appointed 14/10/03
- Mr G Collins Resigned Sept 2003
- Prof D Cook Appointed 14/10/03
- Mr M Daly Appointed 14/12/00
- Mr A K Davidson AM MB Resigned Sept 2003
- The Hon Mr T A Fischer Resigned Sept 2003
- Prof D J Handelsman Appointed 16/06/98
- Dr D J Horvath AO Appointed 21/01/95
- Dr E P Kremer OAM Resigned Sept 2003
- Mrs E M Lane AM MBE Resigned Sept 2003
- Mr B Lee Appointed 14/10/03
- Mr D MacGowan Appointed 03/06/04
- Mr P McClintock Appointed 14/10/03
- Dr C Pawsey Appointed 18/03/97
- Mr G E Priest AM Appointed 30/09/03
- Mr G Richardson Resigned Sept 2003
- Ms K J Russell Resigned Sept 2003
- Dr C Pawsey Appointed 18/03/97
- Mr G E Priest AM Appointed 30/09/03
- Mr G Richardson Resigned Sept 2003
- Ms K J Russell Resigned Sept 2003
- Dr M M Sanger Resigned Sept 2003
- R/Adm Peter Sinclair AC Resigned Sept 2003
- Emeritus Prof J A Young AO Deceased February 2004

Note 7: Auditors’ Remuneration
The auditors’ remuneration was paid by a related party. No amounts were charged to the Foundation by the related party in respect of the auditors’ remuneration.

Note 8: Guarantee
The Foundation is limited by guarantee. In the event that the Foundation is wound up, the Memorandum of Association states that each director is required to contribute $20.00 each towards meeting outstanding obligations of the Foundation.

Note 9: Segment Information
As the trustee for the ANZAC Health and Medical Research Foundation Trust Fund, the principal activity of the Trust during the financial period was to promote and facilitate healthcare delivery and research on illness and disease associated with lifestyle and ageing. The financial results of the Trust reflect the conduct of this activity.
The geographical location of the company is Australia.

Note 10: Financial Instruments
(a) Interest Rate Risk
All financial instruments are non-interest bearing.

(b) Net Fair Values
All financial assets and liabilities have been recognised at the balance date at their net fair values. The carrying amounts of all financial assets and liabilities approximate their fair values due to their short term to maturity.

(c) Credit Risk Exposures
The Foundation’s maximum exposure to credit risk at balance date in relation to each class of recognised financial asset is the carrying amount of those assets as indicated in the balance sheet.
Note 11: Impact of Adopting AASB Equivalents to IASB Standards
Management have reviewed the pending Australian equivalents of International Financial Reporting Standards (IFRS) and do not believe that the adoption of these standards will have a material impact on the financial report of the Foundation.

Directors’ Declaration
In accordance with a resolution of the directors of ANZAC Health and Medical Research Foundation, we state that:
In the opinion of the directors:
(a) the financial statements and notes of the Foundation are in accordance with the Corporations’ Act 2001, including:
(i) giving a true and fair view of the Foundation’s financial position as at 30 June 2004 and of its performance for the year ended on that date; and
(ii) complying with Accounting Standards and Corporations’ Regulations 2001; and
(b) there are reasonable grounds to believe that the Foundation will be able to pay its debts as and when they become due and payable.

On behalf of the Board

Felicity Barr  
Chair

David MacGowan  
Director

Dated this thirteenth day of November 2004 at Sydney.
Financial Statements as at 30 June 2004
INDEPENDENT AUDIT REPORT

ANZAC Health and Medical Research Foundation Trust Fund

To Members of the New South Wales Parliament

Audit Opinion Pursuant to the Public Finance and Audit Act 1983

In my opinion, the financial report of the ANZAC Health and Medical Research Foundation Trust Fund:

(a) presents fairly the ANZAC Health and Medical Research Foundation Trust Fund’s financial position as at 30 June 2004 and its financial performance and cash flows for the year ended on that date, in accordance with applicable Accounting Standards and other mandatory professional reporting requirements in Australia, and

(b) complies with section 41B of the Public Finance and Audit Act 1983 (the PF&A Act).

Audit Opinion Pursuant to the Charitable Fundraising Act 1991

In my opinion:

(a) the accounts of the ANZAC Health and Medical Research Foundation Trust Fund show a true and fair view of the financial result of fundraising appeals for the year ended 30 June 2004

(b) the accounts and associated records of the ANZAC Health and Medical Research Foundation Trust Fund have been properly kept during the year in accordance with the Charitable Fundraising Act 1991 (the CF Act) and the Charitable Fundraising Regulation 2003 (the CF Regulation)

(c) money received as a result of fundraising appeals conducted during the year has been properly accounted for and applied in accordance with the CF Act and the CF Regulation, and

(d) there are reasonable grounds to believe that the ANZAC Health and Medical Research Foundation Trust Fund will be able to pay its debts as and when they fall due.

My opinions should be read in conjunction with the rest of this report.

The Board’s Role

The financial report is the responsibility of the Members of the Board of the ANZAC Health and Medical Research Foundation Trust Fund. It consists of the statement of financial position, the statement of financial performance, the statement of cash flows and the accompanying notes.

The Auditor’s Role and the Audit Scope

As required by the PF&A Act and the CF Act, I carried out an independent audit to enable me to express an opinion on the financial report. My audit provides reasonable assurance to Members of the New South Wales Parliament that the financial report is free of material misstatement.
My audit accorded with Australian Auditing and Assurance Standards and statutory requirements, and I:

- evaluated the accounting policies and significant accounting estimates used by the Board in preparing the financial report,
- examined a sample of the evidence that supports:
  (i) the amounts and other disclosures in the financial report,
  (ii) compliance with accounting and associated record keeping requirements pursuant to the CF Act, and
- obtained an understanding of the internal control structure for fundraising appeal activities.

An audit does not guarantee that every amount and disclosure in the financial report is error free. The terms ‘reasonable assurance’ and ‘material’ recognise that an audit does not examine all evidence and transactions. However, the audit procedures used should identify errors or omissions significant enough to adversely affect decisions made by users of the financial report or indicate that Board had not fulfilled their reporting obligations.

My opinions do not provide assurance:
- about the future viability of the ANZAC Health and Medical Research Foundation Trust Fund,
- that it has carried out its activities effectively, efficiently and economically, or
- about the effectiveness of its internal controls.

Audit Independence

The Audit Office complies with all applicable independence requirements of Australian professional ethical pronouncements. The PF&A Act further promotes independence by:

- providing that only Parliament, and not the executive government, can remove an Auditor-General, and
- mandating the Auditor-General as auditor of public sector agencies but precluding the provision of non-audit services, thus ensuring the Auditor-General and the Audit Office are not compromised in their role by the possibility of losing clients or income.

P J Boulous, CA
Director of Audit

SYDNEY
23 December 2004
# Statement of Financial Performance

For the Year Ended 30 June 2004

<table>
<thead>
<tr>
<th>Notes</th>
<th>2004 $</th>
<th>2003 $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue from ordinary activities</td>
<td>2(b) 3,997,685</td>
<td>3,013,892</td>
</tr>
<tr>
<td>Expenses from ordinary activities</td>
<td>2(a) 2,334,249</td>
<td>1,938,741</td>
</tr>
<tr>
<td>Operating surplus before income tax expense</td>
<td>1,663,436</td>
<td>1,075,151</td>
</tr>
<tr>
<td>Income tax expense relating to ordinary activities</td>
<td>1(D) -</td>
<td>-</td>
</tr>
<tr>
<td>Operating surplus after related income tax expense</td>
<td>1,663,436</td>
<td>1,075,151</td>
</tr>
<tr>
<td>Total changes in equity attributable to beneficiaries of the trust</td>
<td>1,663,436</td>
<td>1,075,151</td>
</tr>
</tbody>
</table>

# Statement of Financial Position

For the Year Ended 30 June 2004

<table>
<thead>
<tr>
<th>Notes</th>
<th>2004 $</th>
<th>2003 $</th>
</tr>
</thead>
<tbody>
<tr>
<td>CURRENT ASSETS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash assets</td>
<td>4 402,538</td>
<td>271,362</td>
</tr>
<tr>
<td>Other financial assets</td>
<td>5 4,792,082</td>
<td>3,706,762</td>
</tr>
<tr>
<td>Receivables</td>
<td>6 609,331</td>
<td>89,123</td>
</tr>
<tr>
<td>Other</td>
<td>-</td>
<td>39,611</td>
</tr>
<tr>
<td>Total Current Assets</td>
<td>5,803,951</td>
<td>4,106,858</td>
</tr>
<tr>
<td>NON-CURRENT ASSETS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Property, plant and equipment</td>
<td>7 6,010,641</td>
<td>5,899,985</td>
</tr>
<tr>
<td>Total Non-Current Assets</td>
<td>6,010,641</td>
<td>5,899,985</td>
</tr>
<tr>
<td>Total Assets</td>
<td>11,814,592</td>
<td>10,006,843</td>
</tr>
<tr>
<td>CURRENT LIABILITIES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Payables</td>
<td>8 186,429</td>
<td>72,861</td>
</tr>
<tr>
<td>Provisions</td>
<td>9 79,516</td>
<td>55,333</td>
</tr>
<tr>
<td>Total Current Liabilities</td>
<td>265,945</td>
<td>128,194</td>
</tr>
<tr>
<td>NON-CURRENT LIABILITIES</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provisions</td>
<td>9 10,954</td>
<td>4,392</td>
</tr>
<tr>
<td>Total Non-Current Liabilities</td>
<td>10,954</td>
<td>4,392</td>
</tr>
<tr>
<td>Total Liabilities</td>
<td>276,899</td>
<td>132,586</td>
</tr>
<tr>
<td>Net Assets</td>
<td>11,537,693</td>
<td>9,874,257</td>
</tr>
<tr>
<td>TRUST FUNDS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Settlement Capital</td>
<td>12 100</td>
<td>100</td>
</tr>
<tr>
<td>Accumulated Surplus</td>
<td>11 11,292,427</td>
<td>9,628,991</td>
</tr>
<tr>
<td>Reserves</td>
<td>13 245,166</td>
<td>245,166</td>
</tr>
<tr>
<td>Total Trust Funds</td>
<td>11,537,693</td>
<td>9,874,257</td>
</tr>
</tbody>
</table>
Statement of Cash Flows
For the Year Ended 30 June 2004

<table>
<thead>
<tr>
<th>Notes</th>
<th>2004 $</th>
<th>2003 $</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CASH FLOWS FROM OPERATING ACTIVITIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receipts - State Government Funding</td>
<td>532,044</td>
<td>492,400</td>
</tr>
<tr>
<td>Receipts - Commonwealth Research Consultancy</td>
<td>67,500</td>
<td>45,000</td>
</tr>
<tr>
<td>Receipts from donations</td>
<td>217,110</td>
<td>795,828</td>
</tr>
<tr>
<td>Receipts from peer reviewed funding</td>
<td>2,211,399</td>
<td>1,558,589</td>
</tr>
<tr>
<td>Payments to suppliers and employees</td>
<td>(1,878,857)</td>
<td>(1,771,374)</td>
</tr>
<tr>
<td>Interest received</td>
<td>205,368</td>
<td>164,179</td>
</tr>
<tr>
<td>Other receipts</td>
<td>297,050</td>
<td>123,789</td>
</tr>
<tr>
<td><strong>Net cash flows from operating activities</strong></td>
<td><strong>3</strong></td>
<td><strong>1,651,614</strong></td>
</tr>
<tr>
<td><strong>CASH FLOWS USED IN INVESTING ACTIVITIES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Payment for property, plant and equipment</td>
<td>(435,118)</td>
<td>(323,090)</td>
</tr>
<tr>
<td>Net cash flows used in investing activities</td>
<td><strong>(435,118)</strong></td>
<td><strong>(323,090)</strong></td>
</tr>
<tr>
<td>Net increase in cash held</td>
<td>1,216,496</td>
<td>1,085,321</td>
</tr>
<tr>
<td>Cash at the beginning of the financial year</td>
<td>3,978,124</td>
<td>2,892,803</td>
</tr>
<tr>
<td><strong>Cash at the end of the financial year</strong></td>
<td><strong>3</strong></td>
<td><strong>5,194,620</strong></td>
</tr>
</tbody>
</table>
Statement of Financial Performance

Note 1: Summary of Significant Accounting Policies

(A) Basis of Accounting
The financial report is a general purpose financial report that complies with Accounting Standards, Urgent Issues Group Consensus Views and with the requirements of the Public Finance and Audit Act 1983 and the Health Services Act 1999 and its regulations in accordance with the Trust Deed (dated 21 February 1995). The accounting policies used are consistent with those adopted in the previous year. The financial report has been prepared in accordance with the historical cost convention, except for leasehold buildings which have been measured at fair value.

(B) Accounting Records
As required by Section 45C of the Public Finance and Audit Act 1983, the Trust Fund has kept proper accounts and records in relation to all its activities.

(C) Depreciation
Depreciation is provided for on a straight-line basis against all depreciable assets so as to write off the depreciable amount of each depreciable asset as it is consumed over its useful life to the ANZAC Health and Medical Research Foundation. Land is not considered a depreciable asset.

Property, plant and equipment have been depreciated from not later than the month following acquisition or operation. Depreciation rates on individual assets are reviewed annually.

Detail of depreciation rates and useful lives for major asset categories, according to NSW Health Accountancy Manual rates, are as follows:

<table>
<thead>
<tr>
<th>Depreciation Rates</th>
<th>Rate (%)</th>
<th>Life (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leasehold Buildings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electro Medical Equipment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costing less than $200,000</td>
<td>10.0</td>
<td>10</td>
</tr>
<tr>
<td>Costing more than $200,000</td>
<td>12.5</td>
<td>8</td>
</tr>
<tr>
<td>Computer Equipment</td>
<td>20.0</td>
<td>5</td>
</tr>
<tr>
<td>Computer Software</td>
<td>20.0</td>
<td>5</td>
</tr>
<tr>
<td>Office Equipment</td>
<td>10.0 - 12.5</td>
<td>8 - 10</td>
</tr>
<tr>
<td>Plant and Machinery</td>
<td>10.0</td>
<td>10</td>
</tr>
<tr>
<td>Furniture, Fittings and Furnishings</td>
<td>10.0</td>
<td>10</td>
</tr>
</tbody>
</table>

(D) Income Tax
The Trust Fund is exempt from income tax under Section 23(j) of the Income Tax Assessment Act.

(E) Property, Plant and Equipment
Plant and equipment are brought to account at cost, less, where applicable, any accumulated depreciation.

The depreciable amount of all fixed assets is depreciated over their useful lives commencing from the time the asset is held ready for use.

Costs incurred in relation to the construction of the ANZAC Health & Medical Research Institute have been capitalised as leasehold buildings. Leasehold buildings are carried at fair value. In the directors’ opinion the written down value is equal to fair value.

Where the assets have been revalued, the potential effect of the capital gains tax on disposal has not been taken into account in the determination of the revalued carrying amount.

The leasehold buildings have been built on land leased from Central Sydney Area Health Service. The lease for the land and buildings is for 25 years, and the New South Wales’ Minister of Health may terminate this lease at any time on reasonable notice.
(F) Cash
For the purpose of the statement of cash flows, cash includes; cash on hand and at call deposits with banks or financial institutions, net of bank overdrafts.

(G) Settlement
The ANZAC Health and Medical Research Foundation Trust Fund was made between Robert Edward McKeown, the settlor, and the ANZAC Health and Medical Research Foundation, the trustee, on 21 February 1995.
The Trust has carried out all trading activities in accordance with the provisions of the trust deed.

(H) Financial Instruments
Financial instruments give rise to positions that are a financial asset of either ANZAC Health & Medical Research Foundation or its counterparty and a financial liability (or equity instrument) of the other party. For ANZAC Health and Medical Research Foundation these include cash at bank, receivables, investments and payables.

In accordance with Australian Accounting Standard AAS33, "Presentation and Disclosure of Financial Instruments", information is disclosed in Note 18 in respect of the interest rate risk and credit risk of financial instruments. All such amounts are carried in the accounts at net fair value. The specific accounting policy in respect of each class of such financial instrument is stated hereunder.

Classes of instruments recorded at cost and their terms and conditions at balance date are as follows:

(i) Cash
Accounting Policies: Cash is carried at nominal values reconcilable to monies on hand and independent bank statements.

Terms and Conditions: Monies on deposit at balance date attract an effective interest rate of between 0.00% and 0.85% (2003: 1.09%) and between 1.09% and 3.85% (2003: 1.09% and 3.20%).

(ii) Receivables
Accounting Policies: Receivables are carried at nominal amounts due less any provision for doubtful debts. A provision for doubtful debts is recognised when collection of the full nominal amount is no longer probable.

Terms and Conditions: Accounts are issued on 30 day terms.

(iii) Investments
Accounting Policies: Investments reported at cost include both short term and fixed term deposits. Interest is recognised in the Statement of Financial Performance when earned.

Terms and Conditions: Fixed term deposits have an average maturity of 33 days (2003: 32 days) and effective interest rates of 4.64% to 5.30% (2003: 4.53% to 4.70%).

(iv) Payables
Accounting Policies: Payables are recognised for amounts to be paid in the future of goods and services received, whether or not billed to the Foundation.

Terms and Conditions: Trade liabilities are settled within any terms specified. If no terms are specified, payments are made by the end of the month following the month in which the invoice is received.

There are no classes of instruments that are recorded at other than cost or market valuation. All financial instruments including revenue, expenses and other cash flows arising from instruments are recognised on an accrual basis.

(I) Research and Development Costs
Research and development costs are charged as an expense in the year in which they are incurred.

(J) Employee Benefits
Provision is made for employee benefits accumulated as a result of employees rendering services up to the reporting date. These benefits include wages and salaries, annual leave and long service leave.

Liabilities arising in respect of wages and salaries, annual leave and any other employee benefits expected to be settled within twelve months of the reporting date are measured at their nominal amounts based on remuneration rates which are expected to be paid when the liability is settled. All other employee benefit liabilities are measured at the present value of
the estimated future cash outflow to be made in respect of services provided by employees up to the reporting date. In determining the present value of future cash outflows, the market yield as at the reporting date on national government bonds, which have terms to maturity approximating the terms of the related liability are used.

Employee benefit expenses and revenues arising in respect of the following categories:

- wages and salaries, non-monetary benefits, annual leave, long service leave and other leave benefits; and
- other types of employee benefits;

are recognised against profits on a net basis in their respective categories.

(K) Revenue Recognition

Revenue arising from the sale of goods, the provision of services and the use of the Trust’s assets is recognised when:

a) the Trust has passed control of the goods or other assets to the buyer;

b) the Trust controls a right to be compensated for services rendered;

c) the Trust controls a right relating to the consideration payable for the provision of investment assets;

d) it is probable that the economic benefits comprising the consideration will flow to the entity;

e) the amount of the revenue can be measured reliably.

The following specific recognition criteria must also be met before revenue is recognised:

Grants
Operating grants received from the Government are allocated as revenue upon receipt.

Donations
Donations are taken to revenue when received.

Interest
Interest is accrued on a daily basis.

(L) Goods and Services Tax (GST)

Revenues, expenses and assets are recognised net of the amount of GST, except:

- the amount of GST incurred by the agency as a purchaser that is not recoverable from the Australian Tax Office is recognised as part of the cost of acquisition of an asset or as part of an item of expense;

- receivables and payables are stated with the amount of GST included.

(M) Provisions

Provisions are recognised when the Trust has a legal, equitable or constructive obligation to make a future sacrifice of economic benefits to other entities as a result of past transactions or other past events, it is probable that a future sacrifice of economic benefits will be required and a reliable estimate can be made of the amount of the obligation.
### Note 2:

#### (a) Expenses from ordinary activities

<table>
<thead>
<tr>
<th>Description</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Employee Benefits</td>
<td>892,495</td>
<td>674,508</td>
</tr>
<tr>
<td>Consumables</td>
<td>541,413</td>
<td>364,263</td>
</tr>
<tr>
<td><strong>Administrative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conference, Training &amp; Travel</td>
<td>75,357</td>
<td>82,356</td>
</tr>
<tr>
<td>Advertising</td>
<td>7,823</td>
<td>5,437</td>
</tr>
<tr>
<td>Functions</td>
<td>3,185</td>
<td>46,455</td>
</tr>
<tr>
<td>Consultants</td>
<td>1,225</td>
<td>3,000</td>
</tr>
<tr>
<td>Accounting &amp; Legal Fees</td>
<td>7,645</td>
<td>16,314</td>
</tr>
<tr>
<td>Audit Fees</td>
<td>10,000</td>
<td>-</td>
</tr>
<tr>
<td>Books &amp; Reference Material</td>
<td>18,962</td>
<td>16,586</td>
</tr>
<tr>
<td>Stationery &amp; Office Supplies</td>
<td>33,138</td>
<td>30,897</td>
</tr>
<tr>
<td>Freight &amp; Courier</td>
<td>6,302</td>
<td>7,929</td>
</tr>
<tr>
<td>Miscellaneous Admin Expenses</td>
<td>266,154</td>
<td>281,435</td>
</tr>
<tr>
<td><strong>Depreciation</strong></td>
<td>429,791</td>
<td>490,409</td>
</tr>
<tr>
<td><strong>Repairs, Maintenance &amp; Renewals</strong></td>
<td>324,462</td>
<td>291,125</td>
</tr>
<tr>
<td>Equipment</td>
<td>109,596</td>
<td>91,276</td>
</tr>
<tr>
<td>Other</td>
<td>36,492</td>
<td>27,160</td>
</tr>
<tr>
<td><strong>Total Expenses</strong></td>
<td>1,234,249</td>
<td>1,938,741</td>
</tr>
</tbody>
</table>

#### (b) Revenue from ordinary activities

<table>
<thead>
<tr>
<th>Description</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corporate Donations</td>
<td>92,455</td>
<td>37,900</td>
</tr>
<tr>
<td>RSL Donations</td>
<td>4,247</td>
<td>23,858</td>
</tr>
<tr>
<td>Other Donations</td>
<td>106,658</td>
<td>614,403</td>
</tr>
<tr>
<td>Fundraising Activities</td>
<td>25,000</td>
<td>94,427</td>
</tr>
<tr>
<td>Commonwealth Research Consultancy</td>
<td>67,500</td>
<td>0</td>
</tr>
<tr>
<td>State Government Funding</td>
<td>665,055</td>
<td>492,400</td>
</tr>
<tr>
<td>Interest Income</td>
<td>224,973</td>
<td>157,709</td>
</tr>
<tr>
<td>Peer Reviewed Funding</td>
<td>2,488,184</td>
<td>1,508,389</td>
</tr>
<tr>
<td>Other Revenue</td>
<td>323,613</td>
<td>84,806</td>
</tr>
<tr>
<td><strong>Total Revenue from ordinary activities</strong></td>
<td>3,997,685</td>
<td>3,013,892</td>
</tr>
</tbody>
</table>
Note 3: Statement of Cash Flows

(a) Reconciliation of the operating surplus after income tax to net cash provided by operating activities

<table>
<thead>
<tr>
<th>Description</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating surplus after income tax</td>
<td>1,663,436</td>
<td>1,075,151</td>
</tr>
<tr>
<td>Adjustments for non-cash income and expense items</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depreciation</td>
<td>324,461</td>
<td>291,125</td>
</tr>
<tr>
<td>Provision for employee entitlement</td>
<td>30,746</td>
<td>22,955</td>
</tr>
<tr>
<td>(Increase)/Decrease in receivables</td>
<td>(520,208)</td>
<td>181,798</td>
</tr>
<tr>
<td>Increase/(Decrease) in creditors</td>
<td>113,568</td>
<td>(123,007)</td>
</tr>
<tr>
<td>(Increase)/Decrease in other</td>
<td>39,611</td>
<td>(39,611)</td>
</tr>
<tr>
<td><strong>Net cash from operating activities</strong></td>
<td><strong>1,651,614</strong></td>
<td><strong>1,408,411</strong></td>
</tr>
</tbody>
</table>

(b) Reconciliation of Cash

Cash at the end of the financial year as shown in the statement of cash flows is reconciled to the related items in the statement of financial position as follows:

<table>
<thead>
<tr>
<th>Description</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash at Bank</td>
<td>402,488</td>
<td>271,312</td>
</tr>
<tr>
<td>Cash on Hand</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Current Investments</td>
<td>4,792,082</td>
<td>3,706,762</td>
</tr>
<tr>
<td><strong>Total Cash</strong></td>
<td><strong>5,194,620</strong></td>
<td><strong>3,978,124</strong></td>
</tr>
</tbody>
</table>

Note 4: Cash Assets

<table>
<thead>
<tr>
<th>Description</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash on hand</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>General Account</td>
<td>3,483</td>
<td>25,275</td>
</tr>
<tr>
<td>Research Account</td>
<td>7,023</td>
<td>20,634</td>
</tr>
<tr>
<td>Donations Cash Management Account</td>
<td>8,329</td>
<td>0</td>
</tr>
<tr>
<td>General Cash Management Account</td>
<td>100,626</td>
<td>31,333</td>
</tr>
<tr>
<td>Research Cash Management Account</td>
<td>283,027</td>
<td>194,070</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>402,538</strong></td>
<td><strong>271,362</strong></td>
</tr>
</tbody>
</table>

Note 5: Other Financial Assets

<table>
<thead>
<tr>
<th>Description</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short Term Cash Deposits</td>
<td>4,792,082</td>
<td>3,706,762</td>
</tr>
</tbody>
</table>

Investments comprise of interest bearing deposits held with financial institutions.

Market values of investments are the same as their book value.
### Note 6: Receivables - Current

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accounts receivable</td>
<td>579,284</td>
<td>78,681</td>
</tr>
<tr>
<td>Interest receivable</td>
<td>30,047</td>
<td>10,442</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>609,331</strong></td>
<td><strong>89,123</strong></td>
</tr>
</tbody>
</table>

### Note 7: Property, Plant and Equipment

#### Leasehold Buildings

<table>
<thead>
<tr>
<th></th>
<th>2004Total</th>
<th>2003Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance 1 July 2003</td>
<td>5,999,999</td>
<td>6,034,687</td>
</tr>
<tr>
<td>Additions</td>
<td>435,118</td>
<td>323,090</td>
</tr>
<tr>
<td>Disposals</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Reclassification/Transfers</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Revaluation increment/decrement</td>
<td>(865,627)</td>
<td>271,735</td>
</tr>
<tr>
<td><strong>Balance at 30 June 2004</strong></td>
<td>5,134,372</td>
<td>6,199,003</td>
</tr>
</tbody>
</table>

#### Plant & Equipment

<table>
<thead>
<tr>
<th></th>
<th>2004Total</th>
<th>2003Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance 1 July 2003</td>
<td>629,513</td>
<td>729,527</td>
</tr>
<tr>
<td>Charge for the year</td>
<td>84,462</td>
<td>291,125</td>
</tr>
<tr>
<td>Adjustments for Disposals</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Revaluation increment/decrement</td>
<td>(865,627)</td>
<td>26,569</td>
</tr>
<tr>
<td><strong>Balance at 30 June 2004</strong></td>
<td>-</td>
<td>729,527</td>
</tr>
</tbody>
</table>

**Written Down Value**

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leasehold Buildings</td>
<td>5,134,372</td>
<td>6,010,641</td>
</tr>
<tr>
<td>Plant &amp; Equipment</td>
<td>876,269</td>
<td>5,899,985</td>
</tr>
</tbody>
</table>

### Note 8: Payables

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creditors and Accruals</td>
<td>97,785</td>
<td>65,894</td>
</tr>
<tr>
<td>GST Payables</td>
<td>88,644</td>
<td>6,967</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>186,429</strong></td>
<td><strong>72,861</strong></td>
</tr>
</tbody>
</table>

### Note 9: Provisions

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Employee Benefits</td>
<td>79,516</td>
<td>55,332</td>
</tr>
<tr>
<td>Non-Current Employee Benefits</td>
<td>10,954</td>
<td>4,392</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>90,470</strong></td>
<td><strong>59,724</strong></td>
</tr>
</tbody>
</table>
Note 10: Commitments
Capital expenditure commitments for plant and equipment that have not been provided for in the accounts

<table>
<thead>
<tr>
<th>Payable not later than one year</th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>236,711</td>
<td>93,578</td>
</tr>
</tbody>
</table>

Note 11: Accumulated Surplus
Balance at beginning of financial year
9,628,991 8,553,840
Operating surplus for the year
1,663,436 1,075,151
Balance at the end of financial year
11,292,427 9,628,991

Included in the operating surplus for the year are contributions received for research purposes, where externally imposed conditions exist. Refer Note 15 and 16 for details of conditions on these contributions.

Note 12: Settlement Account
Payment by the Settlor of the Trust Deed
100 100

Note 13: Reserves
Asset Revaluation Reserve
245,166 245,166

Note 14: Directors’ Remuneration and Retirement Benefits
One director, the Director of ANZAC Research Institute, received vehicular expenses in the amount of $4,193 in 2004. No other Director received, directly or indirectly income paid or payable, or otherwise made available from ANZAC Health and Medical Research Foundation Trust Fund during this financial year.
No amount was paid, on behalf of a director, to a superannuation plan.

Note 15: Conditions on Contributions - Research Purposes

<table>
<thead>
<tr>
<th>Purchase of Assets</th>
<th>Research</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>$</td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>Contributions recognised as revenues for which expenditure in manner specified has not occurred as at balance date</td>
<td>67,300</td>
<td>1,166,745</td>
<td>478,556</td>
</tr>
<tr>
<td>Contributions recognised in previous years that were not expended in the current financial year</td>
<td>-</td>
<td>-</td>
<td>1,032,393</td>
</tr>
<tr>
<td>Total amount of unexpended contributions as at balance date</td>
<td>67,300</td>
<td>1,166,745</td>
<td>1,510,949</td>
</tr>
</tbody>
</table>

Further comments on restricted assets are included in Note 16.
Note 16: Restricted Assets - Research Purposes

These financial statements include the following assets that are restricted by externally imposed conditions e.g. donor requirements. The assets are only available for application in accordance with the terms of the donor restrictions.

**Category**

**Specific Purposes**
- Donations for research specific use
  - 2004: $740,519
  - 2003: $776,628

**Research Grants**
- Specific project grants
  - 2004: $1,166,745
  - 2003: $309,975

**Other**
- Holding Funds
  - 2004: $291,874
  - 2003: $397,806
- Purchase of electron microscope
  - 2004: $67,300
  - 2003: $-
- Contracted studies
  - 2004: $478,556
  - 2003: $138,676
- Establishment and subsequent maintenance of a Medical Research Centre
  - 2004: $323,090
  - 2003: $-

**Total**
- 2004: $2,744,994
- 2003: $1,946,175

Note 17: Fundraising and Appeal Activities

The ANZAC Health and Medical Research Foundation is a certified holder of an authority to raise funds under the provision of Section 16 of the Charitable Fundraising Act, 1991.

Income received and the cost of raising income for specific fundraising has been audited and all revenue and expenses have been recognised in the financial statement of the ANZAC Health and Medical Research Foundation.

<table>
<thead>
<tr>
<th></th>
<th>Income Raised</th>
<th>Direct Expenditure</th>
<th>Indirect Expenditure</th>
<th>2004 Net Proceeds</th>
<th>2003 Net Proceeds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appeals: In house</td>
<td>177,245</td>
<td>16,936</td>
<td>1,800</td>
<td>158,509</td>
<td>78,609</td>
</tr>
<tr>
<td>Functions</td>
<td>30,350</td>
<td>-</td>
<td>-</td>
<td>30,350</td>
<td>33,909</td>
</tr>
<tr>
<td>Total</td>
<td>207,595</td>
<td>16,936</td>
<td>1,800</td>
<td>188,859</td>
<td>112,518</td>
</tr>
</tbody>
</table>

Percentage of Income
- 2004: 100%
- 2003: 8.16%

Direct expenditure includes printing, raffle prizes, postage, food and beverage.

Indirect expenditure includes additional staff time.

The net proceeds were held by ANZAC Health & Medical Research Foundation pending allocation.

The provisions of the Charitable Fundraising Act 1991 and the regulations under the Act have been complied with and internal controls exercised by the ANZAC Health & Medical Research Foundation are considered appropriate and effective in accounting for all the income received in all material respects.
Note 18: Financial Instruments

(a) Interest Rate Risk

The weighted average effective interest rate for cash assets during the year was 2.36% (2003: 2.96%). The weighted average effective interest rate for other deposits and investments was 5.02% (2003: 4.61%). All other financial instruments are non-interest bearing.

(b) Credit Risk Exposures

Credit risk is the risk of financial loss arising from another party to a contract/or financial position failing to discharge a financial obligation thereunder. The ANZAC Health and Medical Research Foundation's maximum exposure to Credit Risk is represented by the carrying amounts of the financial assets included in the Statement of Financial Position.

<table>
<thead>
<tr>
<th>Credit Risk by classification of counterparty.</th>
<th>Banks 2004</th>
<th>Other 2004</th>
<th>Total 2004</th>
<th>Total 2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financial Assets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash</td>
<td>402,488</td>
<td>-</td>
<td>402,488</td>
<td>271,362</td>
</tr>
<tr>
<td>Receivables</td>
<td>30,047</td>
<td>579,284</td>
<td>609,331</td>
<td>89,123</td>
</tr>
<tr>
<td>Other Loans &amp; Deposits</td>
<td>4,792,082</td>
<td>-</td>
<td>4,792,082</td>
<td>3,706,762</td>
</tr>
<tr>
<td>Total Financial Assets</td>
<td>5,224,617</td>
<td>579,284</td>
<td>5,803,901</td>
<td>4,067,247</td>
</tr>
</tbody>
</table>

(c) Net Fair Values

All financial assets and liabilities have been recognised at the balance date at their net fair values. The carrying amounts of all financial assets and liabilities approximates their fair value due to their short term to maturity.

Note 19: Impact of Adopting AASB Equivalents to IASB Standards

Management have reviewed the pending Australian equivalents of International Financial Reporting Standards (IFRS) and do not believe that the adoption of these standards will have a material impact on the financial report of the Trust.
In accordance with a resolution of ANZAC Health and Medical Research Foundation Trust Fund, we state that:

In the opinion of the Trustees:

(a) the financial statements and notes of the Trust:
   i. present fairly the Trust's financial position as at 30 June 2004 and of its performance as represented by the results of its operations and its cash flows for the year ended on that date; and
   ii. comply with Accounting Standards; and

(b) there are reasonable grounds to believe that the Trust will be able to pay its debts as and when they become due and payable.

On behalf of the Trustees

Felicity Barr
Chair

David MacGowan
Director

Dated this thirteenth day of November 2004 at Sydney.