



The Baker Institute is a block funded Institute of the National Health and Medical Research Council of Australia, and is also supported by the Victorian Government and the Baker Benefaction. The Institute is affiliated with Monash University and the Alfred Hospital, and Baker staff hold appointments in both of these institutions. In addition, it is a World Health Organisation collaborating centre for research and training in cardiovascular diseases, the only one in Australia.

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In Australia, 50% of all deaths and illnesses are due to diseases of the heart and blood vessels.

Most of them are due to Hypertension (High Blood Pressure) and Atherosclerosis (clogging of the arteries with fatty cholesterol-laden plaques) which cause

The aims of our research are to increase understanding of the basic causes of hypertension and atherosclerosis, to use this kind of knowledge to help reduce the burden of these diseases in the community, and to improve medical and surgical treatment.

FOREWORD

The stereotype of a Research Institute is often impersonal - shiny equipment, benches and test tubes, anonymous figures in white coats to one side. Nothing could be farther from the truth. Research Institutes need equipment, benches and test tubes - true; but more than anything they need people.

They need people in a post-industrial sense, not as cannon fodder or widget producers but as genial, creative, interactive colleagues. Within an Institute their roles may differ; for an institute to be successful they need to share a common resolve. Historically the stereotype of the scientist was often as a loner; today the reality is of team effort, within the institute laboratories in particular, between the various components of the Institute in general.

The people who are the Institute need support not only from their colleagues, but also from the wider community. For this community, support of medical research sometimes reflects philanthropic or charitable concerns, and on other occasions a need-to-know, for instance, by pharmaceutical companies. Whatever the wellsprings, this support should be viewed as an investment, by the philanthropic or corporate or taxpaying community, in the people who undertake medical research on their behalf.

This report thus gives an account of some of the work we do, and more importantly of the people who do it. If we are to continue to receive your support, we need to give such an account of ourselves. If we want more it's not just a matter of banging our spoons and thinking of Oliver Twist: we have to be not only accountable, but to show a level of engagement and productivity that ensures a high return on your investment.

I believe that the Baker currently more than fulfils these criteria, reflecting the dedication and creativity of the people who work here, and invite you to share this conviction by reading about what they do and why they do it.

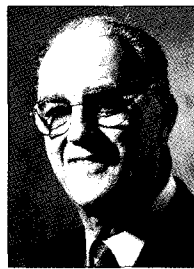


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President of the Baker Board of
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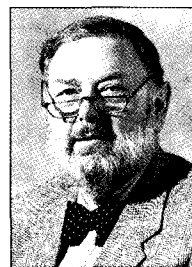
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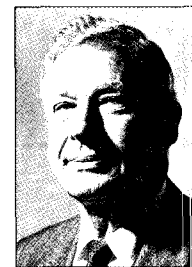
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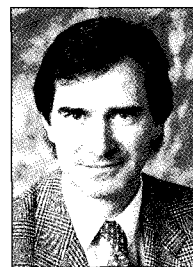
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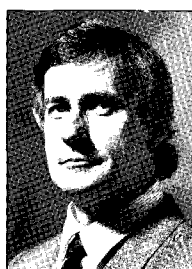
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PRESIDENTS REPORT

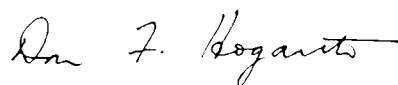
1994 was a very good year for the Baker in a number of ways. First, the scientific staff seemed to have surpassed themselves, with a total of 214 publications for the year, with a very high proportion in front-line international journals. Second, the Institute played a major role in the staging of the Congress of the International Society of Hypertension in March at the Melbourne World Trade Centre, with Warwick Anderson as secretary of the Local Organizing Committee and Garry Jennings as Treasurer: in addition the Institute hosted two satellite meetings, one at Lorne organized by John Funder, and the other at Coolum organized by Alex Bobik and Peter Little. Third, the Baker began a Capital Appeal Campaign in August, and at the year's end had 40% of the target \$6m from the philanthropic and corporate sector, to add to the total of \$8m from the Commonwealth and Victorian Governments.

These achievements represent the combined efforts of many people - Board Members, scientific staff and support staff. In particular I owe a debt of thanks to Mrs. Margaret Ross, who served as Vice-President for the first year of my term of office, and subsequently as Chair of the Activities Committee; to my legal friend Norman O'Bryan, whose Presidency very clearly marks the advent of a new generation; to Board Treasurers David Butler and Bill Philip; and to all the other Board members - representing the NHMRC, Alfred and Monash, or in a private capacity - for their input, guidance and support.

These achievements also reflect the leadership afforded the Institute by the Director, John Funder, and the senior scientific staff, who combine their on-ground research responsibilities with a host of national and international activities, including even occasional television appearances. Of particular note in this regard is Warwick Anderson's appointment as Deputy Chair of the Medical Research Committee of NHMRC, plus his appointment to Honorary Professorship in the Monash Department of Physiology, and Michael Berndt's promotion to Senior Principal Research Fellow.

These achievements are in a sense the more remarkable given the current constraints on space and facilities at the Institute. To remedy this we have launched a Capital Appeal Campaign, towards an additional four storey, 4000 sq metre building parallel to the existing Institute building, on the other side of Baker Lane. We have acquired the back third of the RVIB block running down to Mowbray Street, and - with Bill Gurry as Appeal Chairman, and Margaret Jackson his deputy - we anticipate a 'new' Baker, with a Mowbray Street frontage, by the end of 1996.

Mr. John Habersberger, who retired after 17 years as Chairman of the Baker Benefactions in September, has made an extraordinary range of contributions - to the Institute, the Alfred Hospital, Monash and Melbourne Universities inter alia. To commemorate and celebrate these contributions the Benefaction has dedicated a sum of \$1m over three years to the Institute's Capital Appeal, towards a staff amenity and lecture theatre to unite the 'old' and 'new' Baker. Though this is the last report I will write as President of the Baker Medical Research Institute, as John Habersberger's successor on the Baker Benefaction I will clearly remain very much in touch with the Institute, and look forward to the levels of scientific achievement that should be possible in the Baker of the twenty first century.



Don Hogarth

President, Board of Management

DIRECTORS REPORT

1994 marked a period of expansion in some ways, and of consolidation in others. In terms of science it was a vintage year, as reference to the Institute publication list will attest; given the consolidation in terms of staff and student numbers, this reflects a notable increase in productivity. In terms of capital fundraising it marked the launch of a major effort, which saw \$2.5 million from the philanthropic and corporate sector (of a goal \$6 million) to add to the \$4 million each from the Commonwealth and State Governments. In contrast, our running expenses increased, with income (other than the capital appeal, and bequests) relatively static, leading to a significant deficit in our operating account.

1994 also marks a period of change in terms of the Institute Board. At the end of the year the President, Don Hogarth, retires after many years of dedicated, unobtrusive but very effective leadership, and Norman O'Bryan assumes the chair. Don has been a superb chairman, at once stimulating discussion and seeking consensus; to me, as Director, he has acted as guide, counsellor and friend, and for his contributions at a personal and Institute level we are all very much in his debt. In his new role as Chairman of the Baker Benefactions he will continue to keep a keen eye on the activities of the Institute: it is my very sincere hope that we can continue along the path he has set, and justify the confidence he has so often expressed in the staff of the Institute.

1994 similarly saw Ross Barker, of J.B. Were, join the Board and Finance Committee, and in addition changes in the NHMRC representation. Both Professor Graeme Ryan (Dean of Medicine, Melbourne University) and Dr. John Loy, as Secretary of NHMRC, have extraordinary demands on their time; it is the Institute's good fortune that as NHMRC representatives they contributed widely and wisely to the operations of the Board, and thus to the operations of the Institute. During the year we welcomed Professor Stephen Holdsworth (Department of Medicine, Monash University) as a MRC representative on the Board, as well as the acting (Mr. Bob Wells) followed by the present (Ms Fiona Howarth) Secretary of NHMRC as NHMRC representatives. To all the above, and to our other Board members - Dr. Peter Habersberger, Mr. Bill Kricker, Dr. Gerry Johnston, Mr. Bill Philip and Mrs. Margaret Ross - I would like to offer my sincere thanks for their contributions, their friendship and their support. One very telling index of their commitment to the Institute is that the personal contributions from Board members to the Capital Appeal amount to almost a quarter of a million dollars.

In terms of science, in many senses the high point of the year was the biennial Congress of the International Society for Hypertension (ISH), held at the World Trade Centre in Melbourne in March 1994. Institute scientists presented over 30 'free communications', both oral and as posters, in addition to a variety of invited presentations by the senior staff. The Baker hosted two satellite symposia - one at Lorne, on the salt retaining hormone aldosterone and hypertension, before the Congress, and the other, post Congress, in Coolum (Qld) on vascular reactivity. In addition, we hosted a reception at the Institute for our colleagues and collaborators, national and international, who had come to Melbourne for the meeting - plus our far flung alumni. Watching over all this - and breathing a sigh of relief when Melbourne turned on great weather, and the whole scientific and social program was widely adjudged the best yet - were Warwick Anderson and Garry Jennings, respectively secretary and treasurer of the Congress local organizing committee. It's relatively easy to say, but the amount of work - days, nights, weekends - that the LOC put in to ensure the success of the meeting was truly prodigious, testimony to the dedication and collegiality of those involved.

1994 also saw a very disappointing financial result in terms of the Budgetary allocation for medical research, particularly in the context of the bipartisan 1993 pre-election pledge to raise medical research funding to 2% of the total health budget by the year 2000. The strains that insufficient funding levels have placed on the NHMRC system have become increasingly obvious over the past 2-3 years, with success levels for project grants around the 25% level; while this may sound a relatively modest fall from previous levels of 35-40% funding, they have radically altered the funding patterns for the second quintile of applications, which often come from people with leadership roles in other areas (clinical/teaching/administration), and who thereby are only able to devote part of their time and energies to research. For essentially the first time the spirit is abroad that those in full-time research are favoured, in that they can prepare more persuasive grant applications, and that those in full-time research within the Institutes are even more privileged. The grass is always greener, and there are a number of countervailing considerations that can be, and have been, pointed out to those making such

DIRECTORS REPORT

claims; but the reality of the situation is that we are in danger of a divided medical research constituency, with potentially negative implications for all involved. One of the principal agenda items for the present (1994-6) NHMRC Medical Research Committee, of which Warwick Anderson is Deputy Chair, is how to address, balance and reconcile these claims; at base, what is required is for Australia to invest more, along the 2% lines foreshadowed. In political terms, spare us the circuses, and give us the bread.

The Institute's relationships with Monash University have never been better. Currently we have over 30 students enrolled for honours or postgraduate degrees; four of the senior staff have been made honorary Professors, and two Associate Professors. Across the board, the staff have attachment to/academic status in seven different departments within the University, and teach in a wide variety of courses at a Departmental level. Within the Alfred Hospital, with which the Institute is also affiliated, the spectrum of cardiovascular services was reviewed in mid 1994, with the recommendations that the ABMU and Cardiology be not only colocated but coalesced. This is a development in which the Baker, as an equal stakeholder in the ABMU, is obviously keenly interested; in a 'first' for us all, Monash, the Alfred and the Baker will be equally represented on the selection committee for the new Professor/Director of Cardiovascular Medicine, to head the new amalgamated department, a position advertised shortly before the year's end.

As previously foreshadowed, in 1994 we started our Capital Appeal Campaign, to build additional laboratory and animal facilities to take the Baker into the twenty first century. A Task Force of twenty prominent Australians was assembled, with Bill Gurry of Potter Warburg as chairman and Margaret Jackson of the TAC as deputy chair, and the services of Everaldo Compton International, in the person of Glen Kruger, retained as fundraisers. Through the combined good offices and strenuous efforts of those involved, by the year's end \$2.5 million had been raised or pledged, with outstanding requests totalling another \$6.5 million - towards an ultimate target of \$6 million from the philanthropic and corporate sectors. As Director, I have become involved in the process at a level and with an intensity which while not unanticipated was something entirely new. Bill Gurry and Norman O'Bryan, as President elect, have been both tireless workers and a constant inspiration, and to them in particular I would like to place my thanks on record.

When this report is being drafted next year the scene should be one of bulldozers and brickdust; by the time the 1995 Annual Report is being read the new Baker should be rising on the other side of Baker Lane, parallel to the existing building, and looking down to a street frontage opposite Wesley on Moubray Street. Over the intervening year there is money to be raised and plans to be drawn up. Most importantly, there are a myriad of scientific questions to be asked, and answered. To our many supporters, whose faith and generosity enables us to ask and hopefully answer some of these questions, I commend the Institute's Annual Report.



John Funder



Neil Potter, who took these pictures, is to photography what Graeme Murphy is to modern ballet. From left to right Elena Lukochovska, Yoko Fujiwara, Rosie Idrus (top); Barb Roland, Paolo Ferrari and Atsuhisu Sato (centre); and Fumihiko Tomoda, Mario Vaz and Akiyo Matsumoto (bottom).

Australia is a big country with a small population. Through accidents of history, and a fair amount of hard work, Australia is a rich country. As a small country we have much to learn; as a rich country we have much to offer.

At the Baker one way we do both is to encourage people from overseas to spend time at the Institute. In 1994 we welcomed 25 visiting scientists from 11 different countries - from Ph.D. students doing a segment of their thesis work to Professors on sabbatical leave.

Most of our visitors, like the nine shown opposite, are postdoctoral Fellows, young people on the threshold of their careers as independent investigators. They bring with them boundless energy and enthusiasm, and take home the message that Australian medical research is at world's best standard.

Yoko Fujiwara (centre top) is from Chiba in Japan, and Akiyo Matsumoto (bottom right) from Tokyo. Both are working with Noel Fidge in the Lipoprotein/ Atherosclerosis laboratory. Akiyo's research is directed to putting the finishing touches on a longterm project for Noel and Alana Mitchell, the cloning and characterization of the cell uptake mechanisms for high density lipoproteins (HDL) in the blood.

HDL is 'good' cholesterol, in that high levels appear to be protective. One of the apoproteins (apo A1) which coat fat (lipid) droplets in the blood to form lipoproteins is also protective against heart disease, and Yoko will spend the next two years trying to work out how, by molecular biology studies on bacteria transformed to produce apo A1.

Mario Vaz (centre bottom) is from Bangalore in India, supported by Murray Esler's grant from the U.S. National Institutes of Health - further evidence for the internationalism of medical research, and the high regard Murray is held by his overseas colleagues. Mario works, in the human autonomic function laboratory, on how adrenaline and exercise and obesity are all interrelated in terms of blood pressure levels.

Elena Lukochovska (top left), one of six visitors in 1994 from Moscow, is also interested in hypertension. She works day and night ("because I cannot do these experiments at home") in Geoff Head's Neuropharmacology laboratory, on how the hormones renin and angiotensin affect nerve cells in the brain to regulate blood pressure.

Two more of our Japanese contingent are Fumihiro Tomoda (bottom left), from Toyama, and Atsuhisu Sato (centre right), who works with John Funder. Atsuhisu, from Tokyo, has shown how a particular 'bad' lipoprotein called Lp(a) alters the way in which steroid hormones from the adrenal gland affect blood vessel walls leading to atherosclerosis.

Fumihiro, with Roger Evans and Warwick Anderson, is doing experiments on the role of a particular enzyme (called, for short, 24.15) in blood pressure control. Many of the hormones and local factors that affect blood pressure are small proteins, that can either be activated or destroyed by enzymes. Knowing about enzymes is thus crucial for a number of reasons, not the least in terms of designing new and better drugs.

Enzymes also have a role in activating or destroying steroid as well as protein hormones. In Zig Krozowski's laboratory Ruszymah ("call me Rosie") Idrus from Kuala Lumpur (top right) did a six month sabbatical on the enzyme 11-HSD2 in the pituitary gland: 11-HSD2 keeps the glucocorticoid (cortisone-like) hormones out of receptors (keyholes) for salt- retaining steroids.

Barbara Roland (centre left) from San Diego works with John Funder on the same enzyme, using sophisticated microscopy to determine in exactly which cells the enzyme operates. Finally, Paolo Ferrari (centre middle), from Switzerland, spends his time with Zig Krozowski searching (in the rat colon, of all places) for 11-HSD3, the next member of this family of enzymes crucial for salt-handling.

Our visiting scientists make a major contribution to the work of the Institute, and historically have formed a very collegial network of Baker alumni back home. When you think that Australia does 2% of the world's medical research, and that we need to know and factor in the remaining 98%, networking and collegiality become very important words.



Jeannie Campbell and Warwick Anderson read a proof copy of 'Animals and Us', the two volume NHMRC sponsored school resource book they edited and produced.

If you want to block development of blood vessels in tumors, you start with studies on rats and mice, not women with breast cancer or children with leukaemia. If you are going to transplant human hearts, most people would think it both foolish and unethical to start without preliminary studies in dogs.

On the other hand, there are people who believe that it is unethical to use animals at all in medical research. In the UK, US and to a lesser extent in Australia this viewpoint has attracted a committed, and at times vociferous, group of supporters. As is the case for a range of disputed issues in a pluralist society, what we need to seek is accommodation, even if it is unlikely that we will achieve agreement.

To do this we need dialogue rather than declamatory statements, plus willingness to learn and change. In Australia, there is clear evidence that this is more advanced than in some other places. An important recent initiative in this area was the publication of 'Animals, Scientists and You', a two volume introduction to the subject by Jeannie Campbell and Warwick Anderson, supported by a grant from the NHMRC.

What the books do is to talk about animals in general - their biology, their relationship with human society (food sources, zoos, companions), and their particular roles in veterinary and medical research. The teacher's volume is a lot more detailed and closely-textured than the students'; both are fascinating, beautifully illustrated and non-adversarial. In this latter regard, it is significant that they were officially launched by Dr. Hugh Wirth, President of the RSPCA of Victoria.

Why do Warwick, and Jeannie, and the NHMRC go to all this trouble? The answer is complex, but might be broken down into two main reasons. First, we do medical research to maximize health and prevent disease on the basis of knowledge rather than fashion or prejudice: we thus think that knowledge is enormously important, and the best place for people to learn is the schools. Second is self-interest: if people know how we regard animals - and the care and respect they receive - then we are confident that the vast majority of the community will support the continued, properly overseen use of animals in research. Ultimately, of course, it is the community that determines how big its investment in research will be.

Until 20 years ago, the bulk of medical research involved experiments on animals. We thus developed a certain level of understanding of how mice and man develop, maintain themselves, reproduce and die. Over the past two decades the focus has increasingly shifted to within the cell, as the tools of cellular and molecular biology have enabled us to look at differentiation, regulation, division and death of individual cells, previously uncharted waters.

Paradoxically, this has accentuated the need for parallel studies in whole, normal - or almost normal - animals. Gaining access to the genes that code for proteins made in various cells - enzymes, hormones, structural proteins, contractile proteins - means that their contribution to the animal as a whole can be established. Most cells make only a small selection of the total protein portfolio, so that the overall contribution - to development, maintenance, reproduction and death, in man or mouse - cannot be established from isolated cell studies.

What can now be done is to 'knock out' a particular gene in a mouse, to find the effect on a whole-organism basis. We can also make 'transgenics', transplanting a gene into the mouse, so that it makes more of a particular protein, or something that completely blocks the effect of a protein.

Transgenic and knockouts are a long way from today's classrooms, but that's where tomorrow's scientists are. If they can get a feel for biology, and a sense of wonder at the patterns that are beginning to reveal themselves, we have a real chance of continuing to contribute to this knowledge explosion in the 21st century, and of applying that knowledge to health and disease. Among all the exciting publications from the Institute in 1994, it may well be that a pair of school text books may have the most long-term impact.



In the foreground holding a hand lens is Sue Luff, flanked in the foreground holding a hand lens is Sue Luff, flanked to the left by a magnifying lamp and the right by a light microscope. In the background is Simone Young at the electron microscope.

Sue Luff and Rod Dilley are morphologists, people who study biological structures. Their tools are the microscope and the camera, and they make what many people - scientists and non-scientists alike - think are very beautiful pictures.

But even though one picture may be worth a thousand words, Rod and Sue are scientists rather than artists. Their questions are similar to those asked by other research workers at the Baker - for instance, the way in which nerves to the kidney contribute to raising blood pressure, or whether the same hormones that cause blood vessels to constrict also cause them to grow.

Where they are different is the techniques they use to address these questions. Rod is a light microscopist, and Sue an electron microscopist. What Rod's pictures show are cells and tissues magnified some hundreds of times, photographed down a microscope of the sort we are all more or less familiar with. Sue's electron microscope looks not at a tissue section, but at the image it leaves when sprayed with fine particles of uranium or gold - and the magnification able to be achieved is a hundred fold more than with the light microscope.

What the microscope shows is structure - of a tissue, of a cell, of a bacterium or even a virus. From the mid 19th to mid 20th century the microscope was the mainstay of scientific medicine - with changes in function more or less able to be correlated with changes in structure. X-rays in their turn brought some degree of structural information into medical practice, though not with nearly the same precision as the microscope.

Over the past fifty years, on the shoulders of the morphologists, we have developed additional, more direct techniques for measuring how tissues and cells and bacteria and even viruses function. Just as optics took structure to the microscopic level, electrophysiology and biochemistry have done the same for function. Craig Neylon can measure the current that flows across the membrane of a cell when it is stimulated to contract. Murray Esler can show, by infusing radioactive noradrenaline, that the nerves to the kidney fire off at a different rate in high blood pressure and heart failure.

But where one picture really is worth a thousand words is to translate squiggly lines from a polygraph or histograms of isotope spillover into real tissues and cells. Sue can tell Murray where the nerve endings are close to the blood vessels, and where they are not, which in turn will affect which blood vessels are constricted, and which are less likely to be so. In a complicated organ like the kidney, which filters and reabsorbs and makes hormones and controls salt balance, there are very different effects of lowering blood inflow and outflow - so what Sue can tell Murray is also of very great interest to Warwick Anderson and Robyn Woods and John Funder, all of whom work on different aspects of how the kidney regulates blood pressure.

Squiggly lines on a polygraph give an electrical record of stimulus-contraction coupling; to most of us it could represent an array of soldier ants storming across the page. Rod and Craig can induce a living cell to take up a dye which changes colour with the amount of calcium present. When the cell is stimulated, levels of calcium within the cell change rapidly: and over a time frame of milliseconds, they can show the real-time phenomenon of excitation-contraction coupling, as a blue wave that flows and then ebbs throughout the cell.

In the early days of the Baker morphology was the mainstay of medical research; and though there are currently a variety of other very powerful techniques to ask the questions, it is as crucial now as it was then. In the physical world, at least, function - normal or abnormal - depends on structure, normal or abnormal. In the cardiovascular world, what we often see, as heart attacks or strokes, is the acute functional effects of longstanding structural change in blood vessel walls. These underlying structures are the province of the morphologist - and what Rod and Sue do is thus a major contribution to the ongoing work of the Institute.



Two of the attending physicians at the Greek Women's clinic, Euhana Varigos (left) and Georgia Karabatsos, and the patient's bulging, inescapable medical history.....

As a medical research institute, the Baker is in the knowledge business. Part of the knowledge business is discovery, which is what we try and do in our laboratories. The other part is application, which we do in our clinics. In the case of the Baker, the two are married by a common cardiovascular theme, so that our medical staff see patients with hypertension and high blood cholesterol.

We also have a Menopause Clinic, and in 1994 the Hon. Marie Tehan, as Minister for Health, officially opened the Greek Women's Clinic. Those whose image of the menopause is hot flushes and osteoporosis may wonder why the Baker is involved. The answer is that almost 90% of the morbidity and premature mortality following oestrogen withdrawal is cardiovascular, women having heart attacks and strokes before their time.

In terms of discovery, the Baker has had a superb record of clinical investigation, of involving patients in studies on their levels of blood pressure or cholesterol. The menopause clinic, in the three years of its operation, has continued that tradition, with patients enrolled in a number of studies under the direction of Dr. Paul Komesaroff.

In terms of application, in 1994 we established the Greek Women's Clinic. In Australia we are fortunate to have people from a wide range of countries from all around the world as migrants and new citizens; in the area that the Baker and Alfred serve, the largest population of people with a non-English speaking background are from Greece. Whereas the children of this generation are doing chemical engineering or selling car phones or whatever, their mothers and grandmothers are often very much more isolated in terms of communication.

While the menopause is physiological (natural), it can also be attended by troublesome symptoms (hot flushes, sweats, mood changes), and is often invested with a mixture of folk-wisdom and myth. Until recently, it was also largely ignored or taboo, making communication and where required intervention even more difficult. Whereas such communication may be generally difficult, it is doubly so for someone across a language barrier.

In 1993 Paul Komesaroff sought advice from the Greek members of the Melbourne medical community, and the support of the John T. Reid Trusts, with a view to establishing a parallel service for our largest non-English speaking group of women. In 1994, with the goodwill of the Greek doctors and seed money of \$30,000 for two years from the John T. Reid Trust, the clinic opened its doors.

So what's different about the Greek Women's Clinic? First, it has a Greek woman doctor, Dr. Euhana Varigos. Second, it has a dedicated interpreter - not a daughter, or a cleaner - to help the non-Greek speaking doctors. Finally, and perhaps most importantly given our knowledge remit, it has Betty Kafanelis, a Master's student, as an integral part of the process. What Betty does is to explore with those attending the clinic what they think about the menopause, their areas of concern and fear, to establish where the social and cultural context which has shaped this viewpoint differs from that of women of the same age called Elizabeth or Kathleen or Heather.

It's a different sort of research from test tubes and echocardiograms, but it's very important. The end product will not be a new drug or surgical procedure, but a handbook. The handbook will describe how Greek women see themselves and the menopause, the many ways in which this parallels the still evolving Anglo-Celtic norm, and where there may be important differences. The handbook will, hopefully, go to every general practitioner in Victoria with Greek speaking patients - to enable them to listen with understanding and advise with confidence.

For the Greek Women's Clinic we are thus indebted to the John T. Reid Trust, and to the enthusiastic efforts of the tireless and very dedicated staff. Most of all, we are indebted to the women who attend, for taking part in the study, so that their insights and knowledge can illuminate what in the past has been largely an area of ignorance, silence and prejudice - which, after all, is exactly what research is about.



Zig Krozowski, reading out DNA sequences from the ladders of radioactive nucleotides on a sequencing gel, and feeding them directly into the computer.

Jamshid lives in Forest Hills and works for Telecom. Every few months he visits Dr. Frank Alford at St. Vincent's Hospital, who takes his blood pressure and adjusts his medication. Rather less regularly he is visited before work by John Funder, who takes a blood sample. The reason for all this activity is that Jamshid, without medication, has very high blood pressure, due to a condition called Apparent Mineralocorticoid Excess (for short, AME).

In 1994 at the Baker Anthony Albiston and Zig Krozowski cloned and expressed an enzyme with a crucial role in the body's salt handling, an enzyme called 11 hydroxysteroid dehydrogenase type 2 (for short, 11-HSD2). In Jamshid the enzyme doesn't work at all, giving him salt retention and hypertension. We (and others) believe that more subtle defects in 11-HSD2 activity - particularly in blood vessel walls - could play a major role in Essential Hypertension, which is the medical way of saying that the blood pressure is elevated, but we don't know why.

What happens in AME is that the steroid hormone hydrocortisone, which is secreted in response to stress, fits into and activates the receptors (keyholes) for the salt retaining steroid hormone aldosterone. This leads to salt retention, which normally turns aldosterone secretion off - a classic negative feedback control system - but has no effect on the levels of hydrocortisone. Normally 11-HSD2 sits in the kidney cells where aldosterone acts to retain salt, and keeps hydrocortisone out of the keyholes by converting it into a steroid that won't fit. If you have no 11-HSD2, like Jamshid, you have hydrocortisone in your aldosterone receptors all the time. While we think of it as a stress hormone it's not just bungy-jumping, or Formula 1 driving: for some reason we have 'stress' levels just before we wake up, and quite reasonable increases with meals.

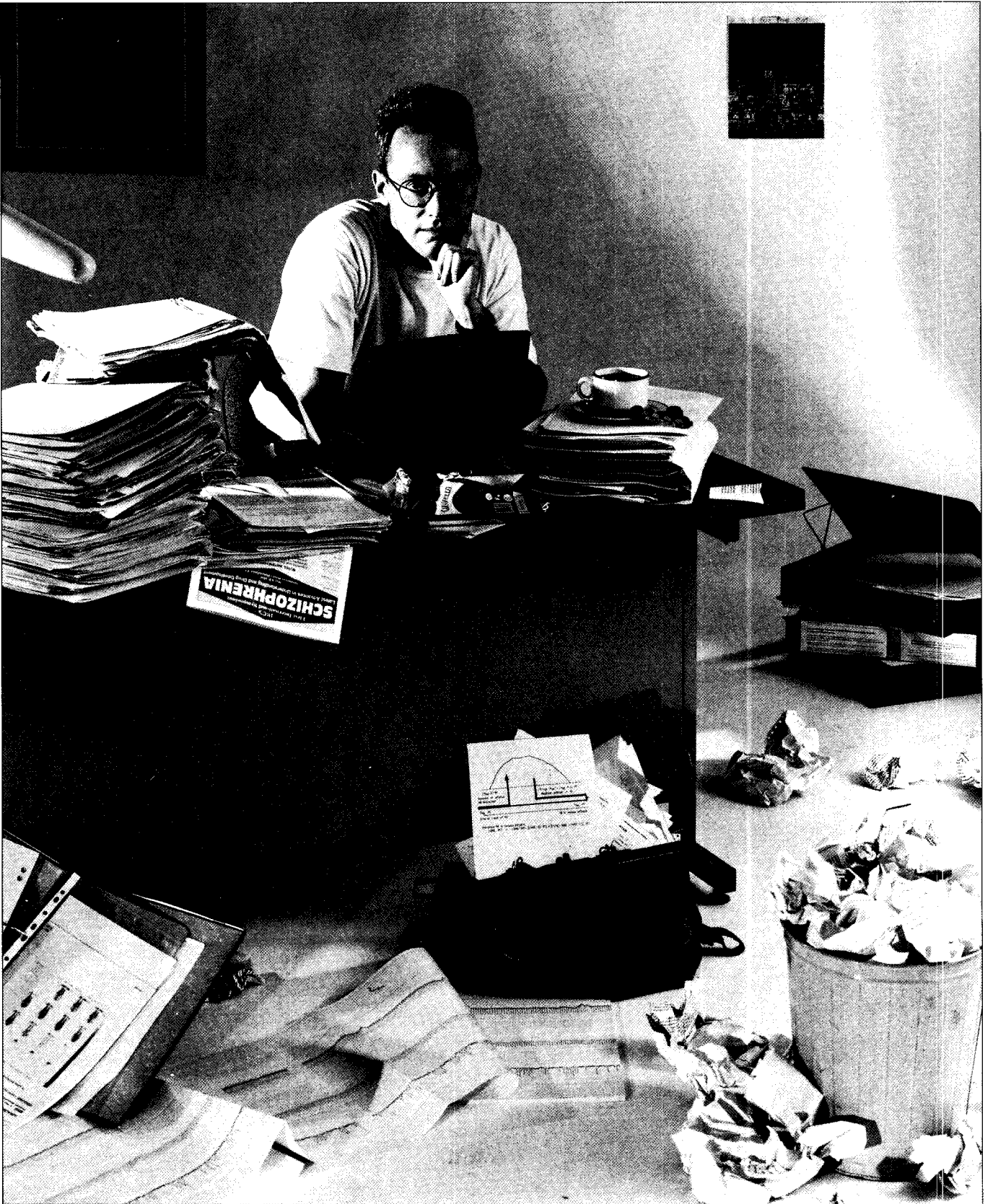
Back in 1989, another enzyme (11-HSD1, for obvious reasons) was cloned, but subsequently shown to work in the opposite direction (actually producing hydrocortisone) in tissues like liver and lung, and not in the kidney. By 1991 the race was on, with seven laboratories around the world (Dallas, Hanover (New Hampshire), New York, London (Ontario), Edinburgh, Lausanne and Melbourne) bending their backs. The result was a deadheat, and in a sense a counterintuitive one; in New York Perrin White cloned the enzyme from sheep kidney, and here we got the human enzyme. Aniko Naray-Fejes-Toth, who was born closer to Hanover in Germany than in America, has now got the rabbit enzyme, and we and the Canadians and the Scots the mouse.

Now it's obviously both comforting and immediately relevant to human high blood pressure to have the human gene and enzyme - but why all the other species, and particularly the mouse? There are two levels at which this question can be answered. First, there are occasional, but potentially very instructive, differences between species: for example, the human enzyme is not found in the adrenal gland, where hydrocortisone is made, but in the sheep levels in the adrenal are ten times higher than anywhere else: why?

Secondly, the mouse is the species very much most commonly used by the genetic engineers for so-called 'knock-out' experiments. In such experiments one copy of a particular gene is interfered with in a fertilized egg, and eventually mice are bred which are so-called heterozygotes - with one good gene and one which has been 'knocked-out'. When a male and female heterozygote are mated, one in four of the offspring (on average) will be normal, two will be heterozygotes like their parents, and one will be a so-called homozygote - i.e. will have both genes knocked out.

The prediction is very much that such homozygous knockouts will be the mouse-equivalents of Jamshid - that they will be extraordinarily sensitive to salt, and will have very high blood pressure from birth. The more interesting question, in a sense, is what will the heterozygotes be like - the mice with the capacity to make half as much 11-HSD2 as normal. Is this enough to cope - or are such animals predisposed to hypertension later in life (like human essential hypertensives), particularly in response to a combination of too much salt and too much stress (again, like human hypertensives)?

It's in fact highly unlikely that the bulk of human essential hypertensives are heterozygotes for 11-HSD2, and much more likely that a subpopulation of them have disordered enzyme activity in blood vessel walls rather than in the kidney. Now that we have the tools - the DNA code, the amino acid sequence of the enzyme - we can begin to ask these questions: in Dallas, and Lausanne, and wherever people are working on hypertension with all the collegiality, collaboration and competition that characterizes the best of medical research.



Gavin Lambert, not long before beginning to write his thesis. Note universal student requirements (black coffee, bulk chocolate) and touch of old Geelong (Gladstone bag).

Ten years ago Gavin Lambert successfully applied for a short-term position in Murray Esler's laboratory. He does not plan to leave until June 1995, when he will be taking up a Postdoctoral Fellowship in Neurosciences in Sweden. Gavin joined the Baker after an Honours degree from Deakin, and a couple of short stints as a laboratory assistant; now he is a coauthor on more than thirty scientific publications, and is off to conquer the world.

In barebones terms, Gavin worked as a Research Assistant for seven years, and then dropped his income to half for three years as a PhD student: from his bank manager's point of view, not necessarily a good thing. But for the future of the Baker, and for the sort of place we want Australia to become, Dr. Gavin Lambert will be a very important contributor. What he has done, under Murray Esler's guidance, is to take the techniques that Murray pioneered 15 years ago to measure neurotransmitter spillover from the heart and kidneys and other peripheral organs, and to apply these techniques to the brain.

Now whereas the transmission of a signal down a nerve is an electrical phenomenon (which is also measured in the laboratory, by the technique of microneurography), at the waystations (in technical terms, synapses) nerves talk to one another by releasing little packets of chemicals, called neurotransmitters, which then fit in receptors (keyholes) on the downstream nerve. It's a bit like a mini-endocrine system, except where hormones go all over the body, neurotransmitters are confined to the very tiny cleft between two nerves - or a nerve ending and a muscle fibre, for example.

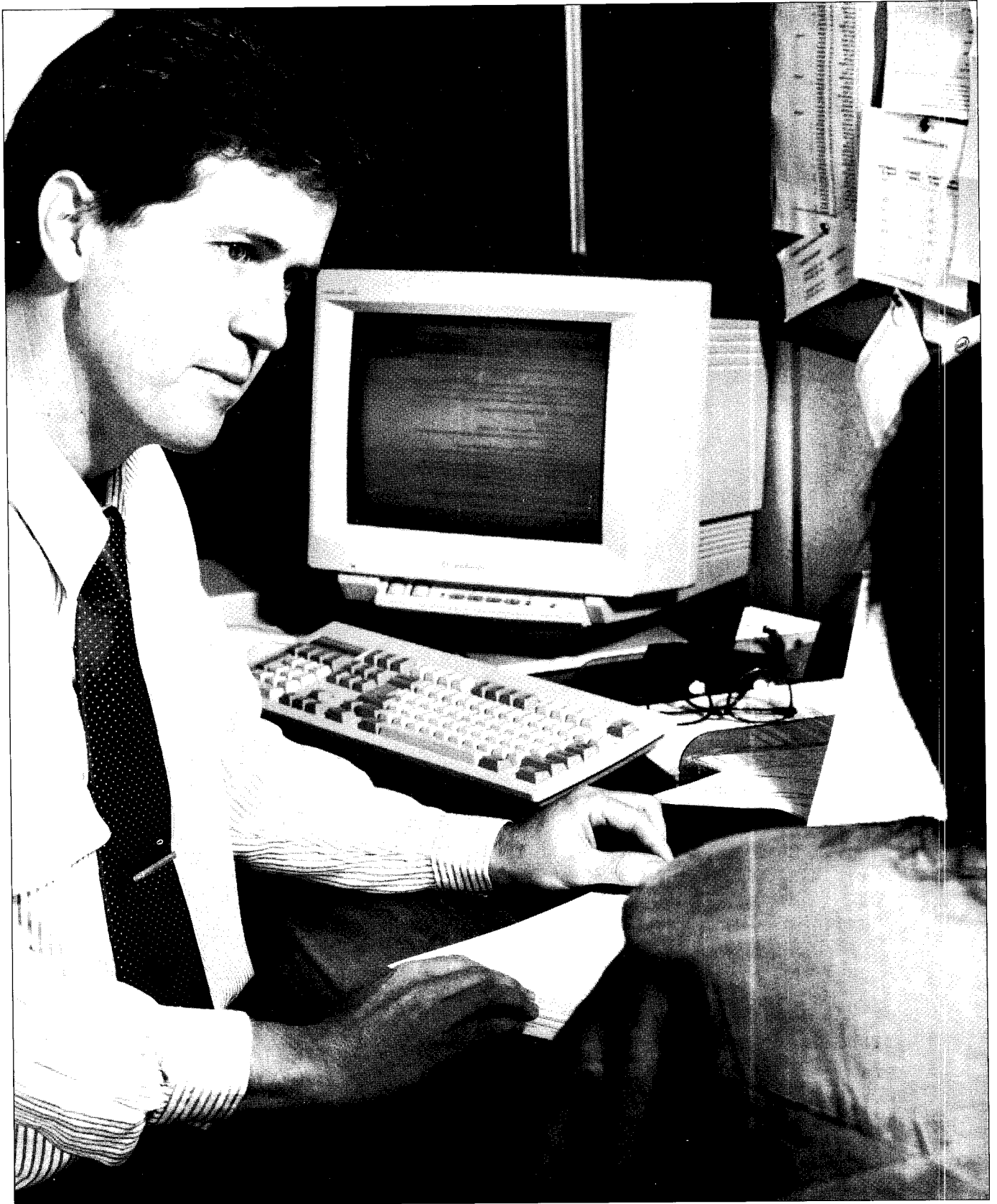
On the international scene, Murray is 'Mr. Spillover', having devised and refined a technique, involving the infusion of (gently) radioactive neurotransmitter molecules, to measure the amount of traffic down the nerves supplying a particular organ. In a whole variety of ongoing studies Murray - and Gavin, measuring plasma neurotransmitter levels as a Research Assistant - have shown the importance of increased nerve traffic (sympathetic activity, as it is often called) in the way the heart accommodates to heart failure, or from the kidney in hypertension.

For his PhD thesis, Gavin has measured neurotransmitter spillover from the brain, by sampling blood from the right and left jugular veins simultaneously. Put like that, it may sound relatively easy; in fact, there's a lot of things to make it rather complicated. First, the neurotransmitters, both natural and radioactive, are inactivated by enzymes lurking in the cleft between two nerves to various products, so that you have to measure four or six substances in plasma rather than one. Secondly, and importantly, in most people one jugular vein mainly drains the cerebral cortex - the outside, 'thinking' bit of the brain - while the other drains the subcortical, subconscious, more 'autonomic' structures.

What this means is that you may see different patterns in one jugular vein from the other, which at first sight may seem a problem, but in many senses is a real window of opportunity. The first studies Gavin did were to compare control and hypertensive subjects, and to compare release of neurotransmitters from the brain with sympathetic nerve traffic intensity measured by microneurography. What he showed was that hypertensive patients not only had increased activity in the sympathetic nerves - which Murray had already established - but also that they had higher levels of neurotransmitter release from the brain. Not all the brain - only the subcortical areas, draining down one jugular vein, including those parts of the brain known to be involved in blood pressure control.

Now in a cardiovascular research institute like the Baker you might sometimes gain the impression that control of blood pressure is the most important thing the brain does; a moment's reflection, even for the most single-minded of us, is proof that this is not the case. In addition to its range of subconscious activities, like control of blood pressure, the cortex is involved in a whole range of conscious activities. In disorders like depression and schizophrenia, it has long been suspected that there are abnormal patterns of neural activity and neurotransmitter release. Now, for the first time, Gavin and Murray are able to study such patients, focussing on the 'other' jugular vein, the one which happens to drain the outer, cortical 'thinking' part of the brain in most people.

In Sweden, Gavin will continue this line of investigation, now clearly in the province of cutting edge psychiatric research rather than in the cardiovascular area. It goes to show two things - that in 1994 the lines of demarcation between 'areas' of medical research are becoming increasingly blurred, and that 'the boys from Geelong' - as Murray refers to himself and Gavin - are poised to open a new field of enquiry for the Baker, that of the neurochemistry of psychiatric disease.



Public Health research means asking questions, listening to the responses and then analyzing the data. Here Chris Reid is doing it in microcosm, trialing a questionnaire.

The Baker does a lot of benchtop research - test tubes and centrifuges, rabbits and rats, cells and cell extracts. The Baker does a lot of clinical research, where people rather than laboratory animals are investigated in various ways, both normal 'controls' and patients with various cardiovascular disorders. What we do least of - which is in many ways a pity - is public health research, looking at people in society rather than patients in a laboratory. We may not do enough, but what we do is well done, thanks largely to Chris Reid.

Chris' official title is "Manager of Clinical Trials and Services". This he does, as the major domo of the Alfred and Baker Medical Unit, but he also has another life, that of a long-term, part-time PhD student. In 1994 Mr. Chris Reid became Dr. Chris Reid - and in 1995 he will remain at the Baker, but have responsibility for the second Australian National Blood Pressure Trial, a \$15 million multicentre Australian and New Zealand trial of angiotensin converting enzyme inhibition in the prevention of cardiovascular mortality.

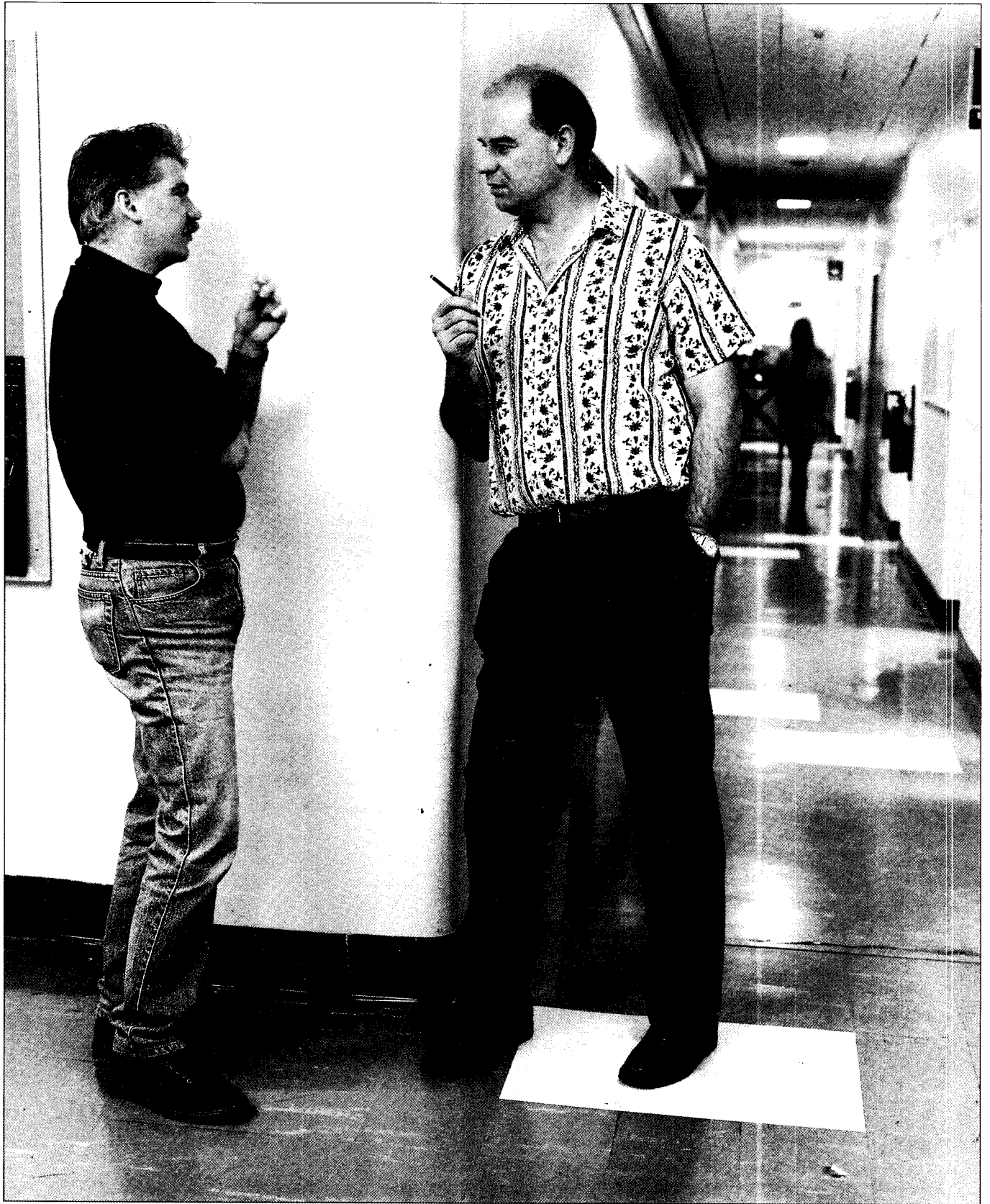
What public health is properly focussed on is health maintenance and disease prevention, rather than how best to close the stable doors on the remaining horses. Early in his time at the Baker Chris was responsible for the development of Heart Track, a program of investigation and evaluation of cardiovascular fitness and relative cardiovascular risk. This program, which involves a history, physical examination and blood analysis, then computes a risk figures; the person so assessed can then try and improve his or her relative risk, for example by exercise or diet, and the group of which he or she is a member can be assessed as a whole, and conclusions drawn. The program was used extensively by the Victorian Police, by BP (Australia), Glaxo, Woodside and other companies to empower their staff, and to give the company insight into their staff health profile as a whole.

A more recent study has involved the use of a questionnaire, administered to a very large group of men and women primarily recruited by the Anti Cancer Council of Victoria, designed to try and pinpoint those at serious but hitherto unsuspected risk of coronary artery disease. Of those identified as in a relatively high risk category, 14% were shown to be suffering from unrecognized coronary artery disease; for such people in particular the appropriate measures (both life style and pharmaceutical) can be expected to very much lower the incidence of morbidity and premature mortality. Cardiovascular disease is not like arthritis, where age and wear and tear gradually cause a build-up in severity of symptoms; a heart attack or stroke often comes 'out of the blue', so that any warning signs are worth heeding.

Some of Chris' studies are 'intramural', involving him plus Baker/ABMU colleagues; others are much broader based. One of the latter sort is the HEART project, an acronym for the Hypertension Evaluation Action Research Trial. This is a study done in collaboration with the National Heart Foundation and the Royal Australasian College of General Practice, and is taking place in the industrial western suburbs of Melbourne. It's been known for some time that high blood pressure is unevenly distributed across the socioeconomic scale; the higher you are, in socioeconomic terms, the less likely you are to have high blood pressure. In Footscray, the current best estimates are that between 35 and 40% of people over 40 have hypertension, around 2.5 times the national average.

With the advent of effective antihypertensive drugs, it's become relatively easy to control high blood pressure, without too much in the way of side effects. It's also expensive - and the drugs are often battling uphill against the sorts of lifestyle factors that influence blood pressure. Some of these are within the hands of the individual patient, more or less - for example, exercise and salt intake; others are in a much harder basket, for example weight loss and quitting cigarettes. Some of the lifestyle factors - for example, the stress not of a challenge successfully met but of a seemingly inescapable social situation - are the province of society as a whole, however much they impact on the individual.

What Chris and his colleagues are doing in Footscray is to see whether attempts to modify lifestyles can be successful, and if so the extent to which they can add to or even replace drug therapy. The betting is on the former rather than the latter; after a day at the meatworks mung beans and meditation are a difficult bill of goods to sell. But we need to know, to use resources optimally and to extend the cover of care to all those who need it; and it is Chris, and his trials (and sometimes tribulations) that are going to give us answers, however much the rest of us may do at the benchtop.



At the Baker, where the laboratory design of yesteryear favours privacy over interaction, corridor conversations are doubly invaluable. Fortunately, the corridors of yesteryear are wide enough to accommodate both Roger Evans (left), and Ian Smith.

Twenty years ago, the treatment of hypertension was reasonably effective if - and it was a big if - the patients could be convinced to keep taking their medication. People with mild or moderate hypertension usually felt fine until they started taking their tablets. The side effects - ranging from itchiness to impotence - meant that some patients stopped taking their medication, and worried about their blood pressure, and others persisted and worried about the side effects. In both instances the resultant stress was hardly calculated to help in terms of blood pressure control.

Over a decade ago we saw the introduction of angiotensin converting enzyme (ACE) inhibitors, which ushered in a new era of antihypertensive therapy. Angiotensin is a very powerful vasoconstrictor, an agent which causes blood vessels to narrow and thus raise blood pressure; in addition, it stimulates the adrenal gland to produce the salt-retaining hormone aldosterone. Blood loss, for example, is a powerful stimulus to angiotensin formation; the resultant vasoconstriction keeps the blood pressure near normal levels, despite the smaller blood volume, and the salt (and with it water) retention helps replenish circulating volume.

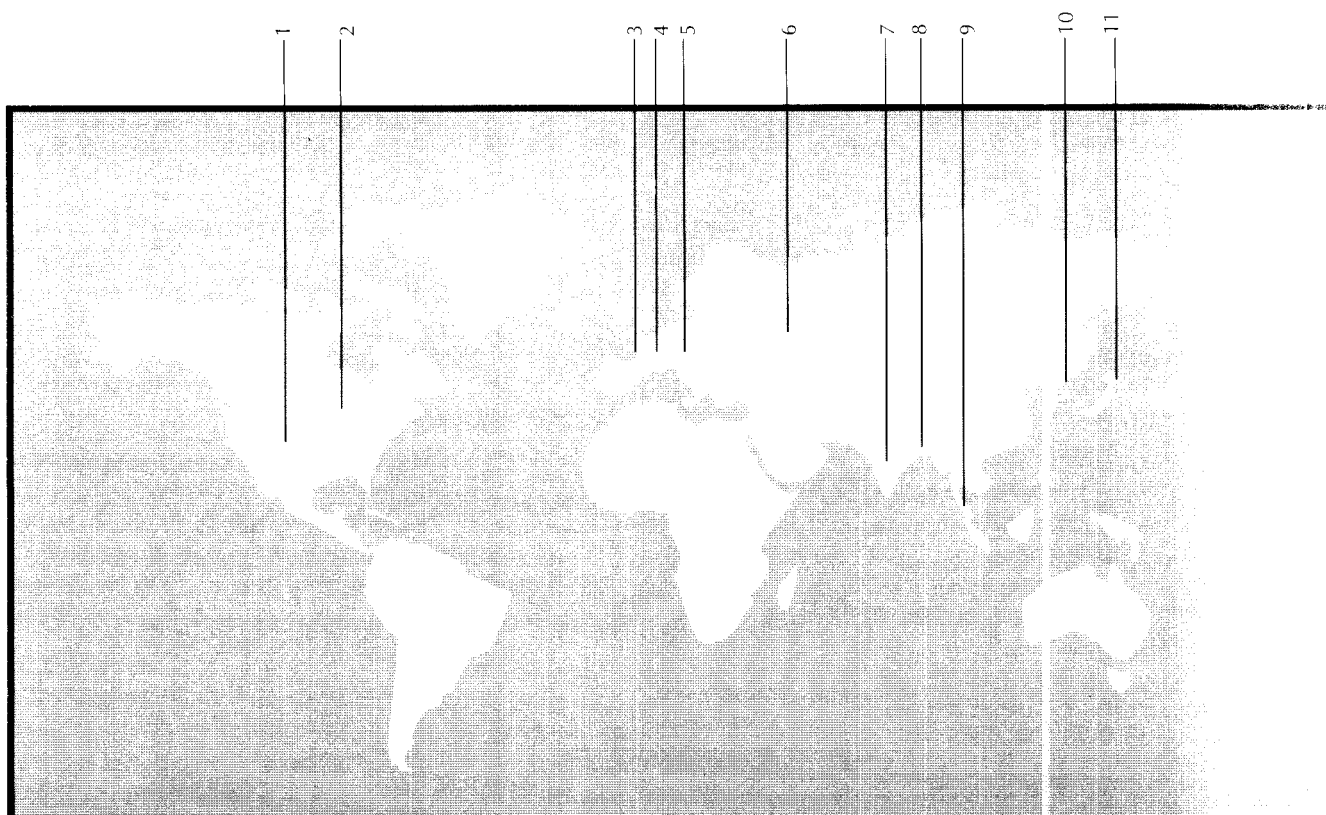
Like many active agents in the body, the peptide angiotensin is formed by being clipped off a much longer precursor protein (called angiotensinogen) by an enzyme (called renin). Again, like many other active agents, the initial enzyme product is itself inactive, and needs to be converted to the active agent by a second enzyme - in this case, for obvious reasons, called angiotensin converting enzyme. This series of steps may seem complicated, but it's the way we've evolved so that some measure of control can be built into the system, so that it doesn't just happen all the time - which would be disastrous.

Now the fascinating thing about ACE inhibitors is that not only are they much better tolerated by patients but that they seem to be effective in lowering blood pressure in patients whose angiotensin is not elevated. This unexpected bonus reflects the fact that the enzyme which we blithely call angiotensin converting enzyme is actually rather more a jack of all trades; like many such enzymes, it cleaves proteins between particular amino acid building blocks, and thus has a number of possible objects of its affections.

Among this number is bradykinin, which ACE cleaves and inactivates. Bradykinin is ying to angiotensin's yang: bradykinin relaxes blood vessel walls, and thus lowers blood pressure. ACE inhibition thus reduces the cleavage and inactivation of bradykinin - so that it lasts longer in the circulation, and is thus better able to lower blood pressure. If all this sounds increasingly complicated, there's nothing wrong with your hearing. To unravel just what is happening requires a blend of background and expertise, which is where Ian Smith and Roger Evans make an excellent team. Ian is an internationally acknowledged expert on the enzymes that cleave proteins; Roger is a superbly trained cardiovascular physiologist, with years of experience in measuring the effects of various treatments on blood pressure in the rabbit, and more importantly thinking about them. Together they make a very powerful team, and together they have found that a second enzyme, more soberly called endopeptidase 24.15, is probably more important than ACE in cleaving bradykinin. They have also established that in all the studies published to date the effects of 24.15 and ACE have been thoroughly confused, which probably is a major factor in why it has to date been overlooked.

There are at least two reasons why Roger and Ian's studies are potentially very important. First, they should help chart the details of how blood pressure is controlled at the level of vasoactive (constrictor or dilator) peptides; without such baseline data we will continue to be using drugs on a trial and error basis. Secondly, though ACE inhibitors are much better than antihypertensives of two decades ago, they are not the final answer. If both raising bradykinin and lowering angiotensin is useful in lower blood pressure, then a combination of an ACE inhibitor and a 24.15 inhibitor would be the logical way to go. Ian and Roger are currently trying very hard to answer the above question. In a decade from now, as well as the 22 operationally identical ACE inhibitors on the Australian market, we may have a combination or broad spectrum enzyme inhibitor - for even more effective blood pressure control.

Our World Health role...

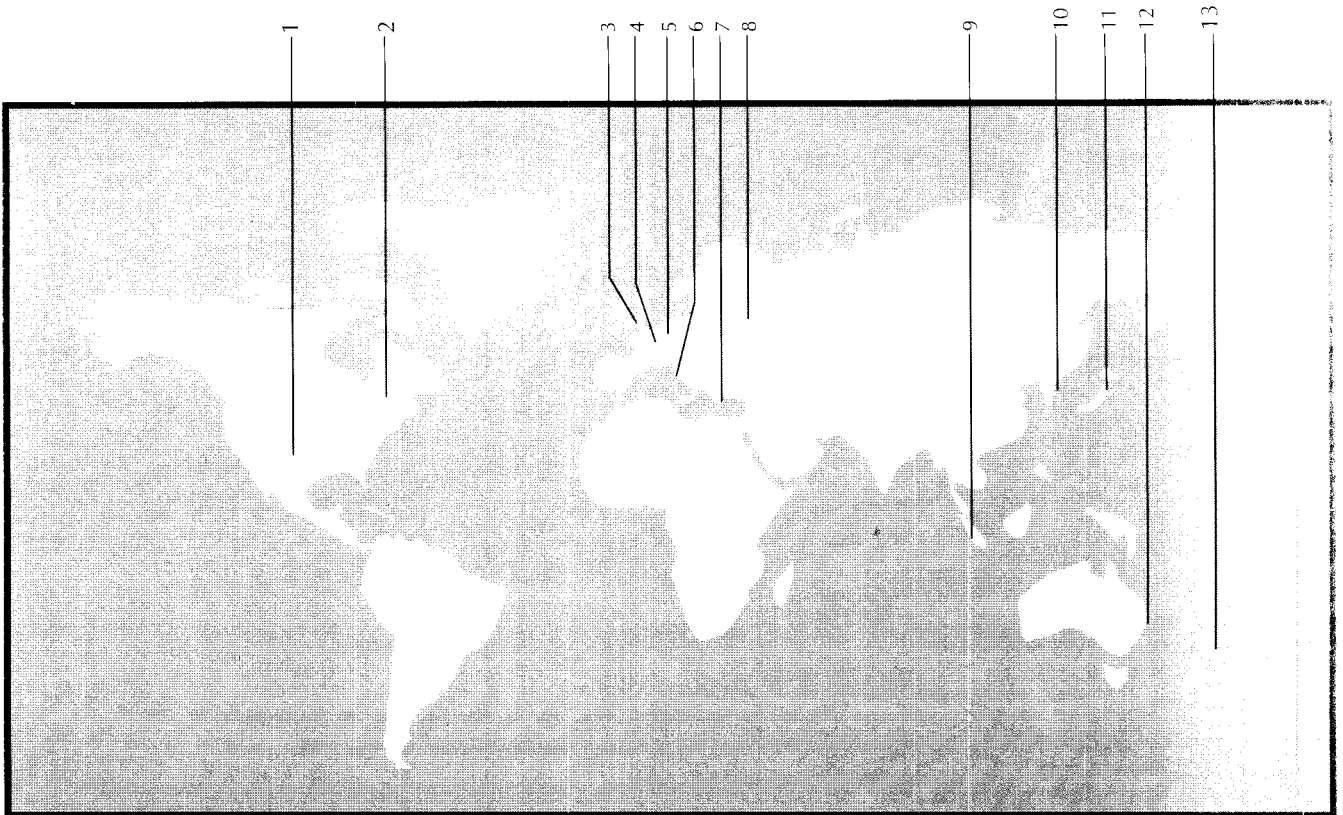


1994 - Visiting Scientists at the Baker Institute

- | | | |
|----|--|--|
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Ms Jeanne Howard
Assoc. Professor John Pintar
Dr. Barbara Roland
Assoc. Professor Bob Mazzeo | New York , USA
Wisconsin , USA
New Jersey, USA
California , USA
Colorado, USA |
| 2 | Dr. Patricia Provencher | Quebec, Canada |
| 3 | Ms. Trine Fischer Hansen | Copenhagen, Denmark |
| 4 | Dr. Martin Wehling | Munich, Germany |
| 5 | Dr. Paolo Ferrari | Berne, Switzerland |
| 6 | Dr. Alexy Nickashin
Dr. Nikolai Routkevitch
Dr. Byzova Tatiana Vladimizovna
Dr. Dimitri Sviridov
Dr. Elena Lukochkova
Dr. Valdimir Nikolsky | Moscow, Russia
Moscow, Russia
Moscow, Russia
Moscow, Russia
Moscow, Russia
Moscow, Russia |
| 7 | Dr. Mario Vaz | Bangalore, India |
| 8 | Dr. Zaw Lin | Yangon, Myanmar |
| 9 | Dr. Ruszymah Idrus | Kuala Lumpur, Malaysia |
| 10 | Dr. Xiao-Jun Du
Dr. Lu Y Liang | Beijing, China
Guilin, China |

OUR PLACE IN THE WORLD

and where we went to tell the news



1994 - Seminars, meetings and lab visits by Baker staff

1. Atlanta, Boulder, Boston, Charleston, Columbia, Cleveland, Chicago, Dallas, Houston, Hawaii, Iowa City, Indianapolis, Los Angeles, Las Vegas, Milwaukee, New York, Nashville, Portland, Seattle, San Diego, San Francisco, Squaw Valley, Santa Barbara
2. Calgary, Edmonton, Halifax, Kingston, Ottawa, Quebec, Toronto
3. Cambridge, London, Gleneagles, Newcastle, Oxford, Glasgow, Bristol, Manchester
4. Courbevoie, Nice, Les Adrets, Paris, Lyon, Nijmegen, Stasbourg
5. Frankfurt, Heidelberg, Berlin, Hanndorf, Regensburg, Cologne, Munich, Vienna, Berne, Goteborg, Stockholm
6. Budapest, Rome, Milan
7. Jerusalem, Tel Aviv
8. Moscow
9. Singapore
10. Hong Kong
11. Osaka, Tokyo
12. Adelaide, Ayers Rock, Canberra, Coolum, Coolangatta, Day Dream Is, Gold Coast, Hobart, Lorne, Marocohydore, Melbourne, Philip Is, Perth
13. Auckland, Christchurch, Queenstown

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BOARD MEMBERS REPORT

BOARD MEMBERS REPORT FOR THE YEAR ENDED 31 DECEMBER 1994

The Board of Management present their report together with the financial statements of the Institute for the year ended 31 December, 1994 and the auditors' report thereon.

Board Members

The Board Members in office at the date of this report are:

Mr. N. O'Bryan, President
Professor J.W. Funder, Director
Mr. R. E. Barker
Mr. W.P. Gurry
Dr. P.G. Habersberger
Professor S. Holdsworth
Ms. F. Howarth
Dr. G.P. Johnston
Mr. W.A. Krickler, AM
Mr. W.G. Philip, AM
Professor R. Porter
Mrs. M.S. Ross

Principal Activities

The principal activities of the Institute are medical research into the basic causes of cardiovascular disease, to use this knowledge to help prevent heart and vascular disease in the community, and to improve medical and surgical treatment. No significant change in the nature of these activities occurred during the year.

Operating Result

The consolidated deficit of the Institute for the year amounted to \$432,462 (1993: deficit \$546,147). Income tax is not applicable.

Review of Operations

A review of the operations of the Institute during the year has been included in the President's and Director's report. The Institute's activities continued to be dedicated to medical research into the basic causes of cardiovascular disease. The Institute is a body corporate under an Act of Parliament and has no share capital.

State of Affairs

- (a) During the year an amount of \$600,277 being the total amount held for Ethel Mary Baillieu, Bertalli Family, William Buckland, Lang, Laura Nyulasy, Edgar Rouse and Ruby Wallace research funds was transferred to the Capital Fund. These were previously reported within the accumulated surplus of the Specific Purpose Fund. The transfer of these funds has no impact on the result for the operating year.
- (b) The Institute is intending to finance the redevelopment of the Institute. Although at the date of this report no formal contracts have been entered into with a construction company, it is expected costs of approximately \$14.0 million will be incurred in respect of this project. Federal and State Government grants totalling \$8.0 million are due to be received towards the cost of this project. Additional funds of \$6.0 million are being sought from the Institute's private sector supporters of which \$2.4 million has been raised to date.

Events Subsequent to Balance Date

There has not arisen in the interval between the end of the financial year and the date of this report any item, transaction or event of a material and unusual nature likely, in the opinion of the Board of Management of the Institute, to affect significantly the operations of the Institute, the results of those operations or the state of affairs of the Institute in subsequent financial years.

BOARD MEMBERS REPORT

Board Members Benefits

Since the end of the previous financial year, other than one Board Member who is a Director of a firm of Stockbrokers which has received, or become entitled to receive, fees for services rendered to the Institute on normal commercial terms, no Board member has received or has become entitled to receive any benefit, by reason of a contract made by the Institute or a related corporation with any Board Member or with a firm of which a Board Member is a member or with an entity in which any Board Member has a substantial financial interest other than the Director of the Institute, Professor J. W. Funder, who receives a salary.

Dated at Melbourne this 3rd day of April 1995

Signed in accordance with a resolution of the Board of Management



Board Member
Norman O'Bryan
President



Board Member
John W. Funder
Director

FINANCIAL REPORT

BAKER MEDICAL RESEARCH INSTITUTE CONSOLIDATED INCOME AND EXPENDITURE STATEMENT YEAR ENDED 31 DECEMBER 1994

INCOME	Note	1994 \$	1993 \$
Government and Statutory Bodies	3	4,923,539	4,835,109
Baker Benefaction		901,266	843,399
Alfred Hospital		185,000	169,750
Fundraising, Corporate & Private Support		1,853,360	1,164,793
Investment Income		272,182	291,630
Clinical Services		243,263	258,122
General Income		543,823	345,763
Total Income		8,922,433	7,908,566
EXPENDITURE			
Salaries and Wages		5,798,948	5,280,864
Consumable Supplies		1,002,853	1,112,718
Scientific Equipment		64,286	12,926
Depreciation		515,209	522,386
Laboratory Support Costs		716,723	610,748
General Overheads		757,419	623,855
Administration		438,540	243,317
Public Relations/Fundraising		60,917	47,899
Total Expenditure		9,354,895	8,454,713
CONSOLIDATED DEFICIT FOR YEAR	7	(432,462)	(546,147)
Represented by:			
Deficit from Operations		(739,552)	(31,062)
Surplus from Capital Fund		184,840	40,204
Surplus / (Deficit) from Specific Purpose Fund		122,250	(555,289)
Consolidated Deficit for Year		(432,462)	(546,147)

The accompanying notes form an integral part of these financial statements

FINANCIAL REPORT

BAKER MEDICAL RESEARCH INSTITUTE CONSOLIDATED BALANCE SHEET AS AT 31 DECEMBER 1994

	Note	1994 \$	1993 \$
ASSETS			
Current Assets			
Cash at bank and in hand		665,696	111,685
Debtors		267,614	346,603
Stock on hand	2(9)	137,508	0
Prepayments		98,196	134,303
Investments (at cost)	8(a)	1,905,819	1,295,634
Total Current Assets		3,074,833	1,888,225
Non - Current Assets			
Plant & Equipment	9	1,764,873	2,006,572
Investments (at cost)	8(b)	3,784,218	3,157,066
Total Non - Current Assets		5,549,091	5,163,638
TOTAL ASSETS		8,623,924	7 051 863
LIABILITIES			
Current Liabilities			
Creditors		392,274	123,335
Prepaid Grant	10	1,600,000	0
Total Current Liabilities		1,992,274	123,335
Non - Current Liabilities			
Provisions	11	901,888	766,304
Total Non - Current Liabilities		901,888	766,304
TOTAL LIABILITIES		2,894,162	889,639
NET ASSETS		5,729,762	6,162,224
FUNDS			
Accumulated Funds			
Operating Fund	4	(1,956,505)	(1,216,953)
Capital Fund	5	4,942,863	4,157,746
Specific Purpose Fund	6	741,916	1,219,943
Asset Revaluation Reserve - 1/1/93		2,001,488	2,001,488
TOTAL FUNDS	7	5,729,762	6,162,224

The accompanying notes form an integral part of these financial statements

FINANCIAL REPORT

BAKER MEDICAL RESEARCH INSTITUTE STATEMENT OF CASH FLOWS FOR YEAR ENDED 31 DECEMBER 1994

	Note	1994 \$	1993 \$
Cash Flows from Operating Activities			
Receipts from Granting Bodies		6,881,450	4,857,434
Donations and Bequests		2,766,194	1,987,865
Payments to Suppliers & Employees		(8,536,564)	(8,349,804)
Dividends Received		167,538	134,987
Interest Received		94,617	173,681
General Income		614,360	628,920
Net Cash from / (used in) Operating Activities	14(b)	1,987,595	(566,917)
Cash Flows from Investing Activities			
Payment for Investment Securities		(822,868)	(67,123)
Proceeds from sale of Investment Securities		280,426	20,328
Payment for Plant & Equipment		(273,511)	(527,470)
Net Cash used in Investing Activities		(815,953)	(574,265)
Net Cash Increase /(Decrease) in cash held		1,171,642	(1,141,182)
Cash at beginning of the financial year		1,407,319	2,545,884
Effects of Exchange rate changes on cash held in foreign currencies		(7,446)	2,617
Cash at the end of the financial year	14(a)	2,571,515	1,407,319

The accompanying notes form an integral part of these financial statements

BAKER MEDICAL RESEARCH INSTITUTE NOTES TO AND FORMING PART OF THE ACCOUNTS

1. Incorporation

The Thomas Baker, Alice Baker and Eleanor Shaw Medical Research Institute was incorporated as the 'Baker Medical Research Institute' ("the Institute") under the Baker Medical Research Act 1980.

2. Summary of Significant Accounting Policies

Set out hereunder are the significant accounting policies adopted by the Institute in the preparation of its accounts for the year ended 31 December 1994. These policies have been consistently applied unless otherwise indicated.

(a) Accrual basis

The accrual basis of accounting has been used with revenues and expenses being recognised as they are incurred, and brought to account in the period to which they relate.

(b) Historical cost

The financial statements have been prepared on a historical cost basis and except where stated do not take into account current valuations of non-current assets.

(c) Fund accounting

The Institute operates on a fund accounting basis and maintains three funds; Operating, Specific Purpose and Capital Funds. The work of the Institute is financed from grants, investment income and donations of both general and specific natures. Income of a specific nature is used in accordance with the terms of any relevant convenants. The amount of grants received for specific purposes during the year but unspent at year end, will be expended in the next financial year. The Institute's capital fund comprises the unspent capital donations, bequests and receipts from fundraising activities.

(d) Principles of consolidation

The Institute's accounts have been prepared on a consolidated basis. All inter-fund transactions have been eliminated on consolidation.

(e) Plant and equipment

Items of plant and equipment are recorded at cost and Board's valuation and are depreciated over their useful lives using the straight line method.

(f) Land and building

The land and building occupied by the Institute is not included as an asset as the Institute does not have title to the property. The estimated replacement cost of this building is \$11 m.

(g) Change in accounting method

In previous years it was Institute policy that items of stocks of consumable scientific and administrative items purchased in the course of normal operations out of grant income were not taken into account at balance date as assets but written off at the time of purchase.

Commencing this year, the Institute has adopted the policy of capitalising stock on hand at year end in order to comply with accounting standards. As a result of this change in accounting policy, stock of \$137,508 has been brought to account in the Balance Sheet. Expenditure within the Income and Expenditure Statement has been reduced by the same amount.

(h) Stocks

Stocks of consumable scientific and administrative items are stated in the Balance Sheet at the lower of cost and net realisable value. Cost is determined by the average cost method from computerised stock records.

(i) Tax status

The income of the Institute is exempt from income tax pursuant to the provisions of section 23(e) of the Income Tax Assessment Act. The Institute is also exempt from other government levies such as payroll tax and sales tax but not fringe benefits tax. Donations of \$2 or more made to the Institute are income tax deductible to the donor.

(j) Employee entitlements

The Institute has fully provided for accrued leave for all staff as at 31 December 1994. Long service leave entitlements are provided for staff with ten or more years of service.

(k) Foreign exchange transactions

The Institute maintains bank accounts in the USA and UK for the purpose of receiving donations and for the purchase of equipment and supplies. Foreign currency at balance date is translated at exchange rates at balance date. Exchange gains and losses are brought to account in determining the surplus or deficit for the year.

(l) Comparative figures

Where necessary comparative figures have been adjusted to conform with changes in presentation in the current year.

3. Government and Statutory Bodies	1994	1993
	\$	\$
National Health & Medical Research Council	3,835,563	3,840,852
Victorian State Government	652,490	672,735
National Heart Foundation	435,486	221,522
Victorian Health Promotion Foundation	0	100,000

	4,923,539	4,835,109
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4. Operating Fund

Balance at beginning of year	(1,216,953)	(1,185,891)
Deficit for year	(739,552)	(31,062)

Balance at end of year	(1,956,505)	(1,216,953)
------------------------	--------------------	--------------------

5. Capital Fund

The Institute's capital fund comprises the unspent capital donations, bequests, receipts from fundraising activities and capital grants from government. Each year the Board allocates a proportion of this income to supplement the research operations of the Institute. From time to time the Institute is the beneficiary under various wills and trust agreements. Such bequests and legacies are an unpredictable source of income each year. The amounts shown as income in the Income and Expenditure Statement represents the net result applicable for the operating year. The current fund balance is:

Balance at beginning of year	4,157,746	4,117,542
Surplus for year	184,840	40,204
Transfer from Specific Purpose Fund - refer note 6	600,277	0

Balance at end of year	4,942,863	4,157,746
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6. Specific Purpose Fund

Specific purpose funds comprise funds provided to the Institute for special purposes other than through normal fund raising activities. Institute accounting records are kept as to identify expenditure charged against income from these funds. All such income and expenditure is incorporated in the consolidated Income and Expenditure Statement.

During the year an amount of \$600,277 being the total amount held for Ethel Mary Baillieu, Bertalli Family, William Buckland, Lang, Laura Nyulasy, Edgar Rouse and Ruby Wallace research funds was transferred to the Capital Fund. The transfer of these funds has no impact on the consolidated result for the year. The current fund balance is:

Balance at beginning of year	1,219,943	1,775,232
Surplus / (Deficit) for year	122,250	(555,289)
Transfer to Capital Fund	(600,277)	0

Balance at end of year	741,916	1,219,943
------------------------	----------------	------------------

7. Fund Balances

Balance at 1 January 1994	6,162,224	4,706,883
Asset Revaluation Reserve at 1.1.93		2,001,488
Surplus / (Deficit) for year		
operating fund	(739,552)	(31,062)
capital fund	184,840	40,204
specific purpose fund	122,250	(555,289)

	(432,462)	(546,147)
--	------------------	------------------

Balance at 31 December 1994	5,729,762	6,162,224
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FINANCIAL REPORT

8. Investments (at cost)	1994	1993
	\$	\$
(a) Current		
Short term deposits	1,905,819	1,295,634
Total Current Investments	1,905,819	1,295,634
(b) Non - Current Investments		
Shares and Debentures	3,719,186	3,089,434
Trust Units	65,032	65,032
Government and Semi - Government Stock	0	2,600
Total Non - Current Investments	3,784,218	3,157,066
Total Investments	5,690,037	4,452,700

The Institute's investments are shown at cost. As at the 31 December 1994 the market value of the Institute's non-current investments was \$4,798,116 (1993: \$4,855,242)

9. Plant and Equipment

Plant and Equipment (at cost and Board's valuation)	2,802,468	2,528,958
Less: Accumulated Depreciation	1,037,595	522,386
Total Plant & Equipment - net book value	1,764,873	2,006,572

10. Prepaid Grant

This amount represents the first capital works grant from the Federal Government for the redevelopment of the Institute. In accordance with our accounting practices, income and expenditure associated with the redevelopment project will be brought to account in the period to which they relate.

Prepaid Grant	1,600,000	0
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11. Provisions

Employee Entitlements		
Annual Leave	349,588	261,873
Long Service Leave	285,841	237,972
Deferred Maintenance	266,459	266,459
Total Provisions	901,888	766,304

12. Remuneration of Board Members

(a) The names of each person who held office as a Board Member of the Baker Medical Research Institute during the financial year ended 31 December 1994 are:

D.F.Hogarth (until Dec'94)	W.A. Kricker
N. O'Bryan	J.Loy (until June '94)
J. W. Funder	W.G.Philip
R. E. Barker	R.Porter
P. G. Habersberger	M.S. Ross
S. Holdsworth (from June '94)	G. Ryan (until June '94)
F. Howarth (from Dec '94)	R. Wells (from June - Dec '94)
G. P.Johnston	

(b) Other than one Board Member who is a Director of a firm of Stockbrokers which has received, or become entitled to receive, fees for services rendered to the Institute on normal commercial terms, no Board Member has received or has become entitled to receive any benefit, by reason of a contract made by the Institute or a related corporation with any Board Member or with a firm of which a Board Member is a member or with an entity in which any Board Member has a substantial financial interest other than the Director of the Institute, Professor J.W. Funder, who receives a salary.

13. Superannuation

The Institute operates a cumulative type superannuation plan under which all employees are entitled to benefits on retirement, disability or death. Employees contribute to the plan at various percentages of their salaries. The Institute also contributes to the plan at rates related to employer contributions and pursuant to an award set down under a national wage case. Funds are available to satisfy all benefits that have been vested under the plan in the event of termination of the plan or voluntary or compulsory termination of employment of each employee .

14. Notes to the Statement of Cash Flows

(a) Reconciliation of Cash

For the purpose of the statement of cash flows, cash includes cash on hand and in the bank and investments in the money market instruments, net of outstanding bank overdrafts.

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

	1994	1993
	\$	\$
Cash	665,696	111,685
Deposits at call	1,905,819	1,295,634
Total as above	2,571,515	1,407,319

(b) Reconciliation of Net Cash provided by Operating Activities to Deficit

Operating Deficit from Operating Activities	(432,462)	(546,147)
Effects of Exchange rate changes on cash held in foreign currencies	7,446	(2,617)
Depreciation	515,209	522,386
(Profit) / Loss on sale of investment	(84,710)	(20,328)
Changes in net assets and liabilities		
Decrease (Increase) in debtors	78,990	(102,734)
Increase in inventories	(137,508)	0
Decrease (Increase) in prepayments	36,107	(38,357)
Increase (Decrease) in creditors	268,939	(346,491)
Increase in prepaid income	1,600,000	0
Increase (Decrease) in provisions	135,584	(32,629)
Net cash from / (used in) operating activities	1,987,595	(566,917)

15. Redevelopment of the Institute

The Institute is intending to acquire, under Committee of Management, property from the Royal Victorian Institute for the Blind to redevelop the Institute. Federal and State Government grants totalling \$8.0 million are due to be received towards the cost of this project. Additional funds of \$6.0 million are being sought from the Institute's private sector supporters. As at the date of this report, a total of \$1.8 million had been received of which minimal costs associated with the project have been paid.

Although at the date of this report no formal contracts have been entered into with a construction company, it is expected costs of approximately \$14 million will be incurred in respect of this project.

INDEPENDENT AUDIT REPORT

TO THE BOARD OF MANAGEMENT BAKER MEDICAL RESEARCH INSTITUTE

Scope

We have audited the financial statements of the Institute for the year ended 31 December 1994 as set out on pages 36 to 42. The Directors are responsible for the preparation and presentation of the financial statements and the information contained therein. We have conducted an independent audit of the financial statements in order to express an opinion on them to the Board of the Institute.

Our audit has been conducted in accordance with Australian Auditing Standards to provide reasonable assurance as to whether the financial statements are free of material misstatement. Our procedures included examination, on a test basis, of evidence supporting the amounts and other disclosures in the financial statements, and the evaluation of accounting policies and significant accounting estimates. These procedures have been undertaken to form an opinion as to whether, in all material respects, the financial statements are presented fairly in accordance with Australian accounting standards so as to present a view which is consistent with our understanding of the Institute's state of affairs, the results of its operations and its cash flows.

The audit opinion expressed in this report has been formed on the above basis.

Audit Opinion

In our opinion, the financial statements of the Institute are properly drawn up:

- (a) so as to give a true and fair view of the state of affairs of the Institute as at 31 December 1994 and its results and cash flows for the financial year ended on that date; and
- (b) in accordance with Australia Accounting Standards.

Price Waterhouse
Chartered Accountants

Melbourne
3rd April, 1995

EA Alexander
Partner

BAKER MEDICAL RESEARCH INSTITUTE STATEMENT BY BOARD MEMBERS

In the opinion of the Board Members of the Baker Medical Research Institute:

- (a) The financial statements and notes to the accounts set out on pages 36 to 42 are drawn up so as to present a true and fair view of the state of the Institute's affairs as at 31st December, 1994 and of its results for the year ended on that date;
- (b) As at the date of this statement there are reasonable grounds to believe that the Institute will be able to pay its debts as and when they fall due; and
- (c) The consolidated financial statements have been made out in accordance with applicable Accounting Standards.

Signed at Melbourne this 3rd day of April 1995 in accordance with a resolution of the Board.

Norman O'Bryan
President

John W Funder
Director

Donors 1994

Major Donors 1994

The Institute is grateful for major contributions to its work from:

National Health & Medical
Research Council of Australia
Victorian Government
National Heart Foundation
National Institutes of Health (USA)
Australian Kidney Foundation

Merck Sharp & Dohme
IRI Servier & Compagnie -
Developpement
Takeda Chemical Company

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Westfold, Prof K C
Wicks, Dr W G
Williams, Mrs G E
Woolfe, Mr Kenneth W

Certificates of Appreciation

In addition to the various Charitable Trusts, Foundations and Estates listed in the 1993 Annual Report, a Certificate of Appreciation was also presented to the following at the 1994 Annual General Meeting:

Ashton Mining Limited
Baillieu, E L & C, Limited
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Buchanan, Mrs A M E
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Jeffrey, Miss D
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Kerr, Mrs Kathryn
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Myer AC, Mr S B
National Mutual Life Association
Roach, Mr I
Robertson, Mrs R
Robertson, Mr B
Rotary Club of Doncaster
Row, Mrs P S
Scott, Mr D W
Smith, Mrs M
Snowy Nominees
Tattersall Sweep Consultation
VEADA
Wade, Mr E A
Ward, Mrs Alston
Webster, Mrs Ruth

Donors 1994

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Alfis, Mrs Koula
Allan, Mrs Bonnie
Anderson, Thelma Ivy
Atkinson, Theo

Batty, Leonard
Benton, Mr Graeme

Bowden, Mr A
Brasher, Mark
Brooks, Mrs V
Bull, Mrs May

Burns, Mr J H
Butterss, Betty
Campbell, Bethol Rose
Capewell, Mrs Ivey
Capper, Bill

Carthew, Leila
Chambers, David
Chappell, Jane

Cutton, Amy
Davenport, Rita
Davies, Mr J
Davies, Reggie
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Eastwood, Olive Ruby
Ellis, Douglas Raymond
Evans, Alan Rae
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Greenaway, Mrs Eileen
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Hodge, Cecil
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Maguire, Agatha
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Tony Campbell
Dr D C Hodge
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Salter, Mr H K
Scovell, A. McKenzie

Senn, Don
Smith AM, Mr James R.
Smith AM, Mr James R.
Smith AM, Mr James R.
Smith AM, Mr James R.

Smith AM, James
Smith AM, James (Jim)
Smith AM, James Robert
Smith AM, James Robert
Smith AM, James Robert
Smith AM, James Robert
Smith AM, James Robert
Smith AM, James Robert
Smith AM, James Robert
Smith AM, James Robert
Smith AM, James R. (Jim)

Smith AM, Jim

Smith AM, Jim

Smith AM, Jim
Smith AM, Mr J R
Smith AM, Mr J R
Smith AM, Mr James R.
Smith AM, Mr Jim
Smith AM, Mr Jim
Smith AM, Mr Jim

Stahl, Lesley
Steen, Keith
Stott, Jack
Teasdale, Nelva Irene
Virgona, Clare
Wagstaff, Mr E
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Alcatel Australia Limited
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Family
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Mrs M White
Mrs D C Cresswell
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Marjorie Rose

We gratefully acknowledge the very considerable support of many donors who have made smaller but equally valuable contributions to our work, some over a period of many years.

DIRECTORY

AUDITOR

PRICE WATERHOUSE

215 SPRING STREET, MELBOURNE, VIC 3001

SOLICITORS

BLAKE DAWSON WALDRON

101 COLLINS STREET, MELBOURNE, VIC 3001

ANNUAL GENERAL MEETING

MONDAY 1st MAY

BAKER MEDICAL RESEARCH INSTITUTE

5.00 pm

BAKER MEDICAL RESEARCH INSTITUTE

COMMERCIAL ROAD, PRAHRAN

P.O. BOX 348, PRAHRAN, VICTORIA 3181 AUSTRALIA

TELEPHONE (03) 522 4333

FAX (03) 521 1362

