Degenerative Diseases of the Nervous System

Information Leaflet

• alzheimer’s disease • parkinson’s disease • age related macular degeneration • multiple sclerosis

Yesterday, today and tomorrow

MEDICAL RESEARCH INTO DEGENERATIVE DISEASES OF THE NERVOUS SYSTEM

Blindness, loss of memory, tremor, paralysis, progressive debilitation - they were once considered just 'part of growing old'. Now, the inevitability of these disabilities is no longer just accepted.

 Palliative care - seeing aids for the blind, transport for the immobile and care for the demented - remains important, but it is not good enough. The community is demanding protection for future generations from these disabilities, and from the suffering they cause to the victims, and those who care for them.

It is also recognised that advances in treatment will not come without more understanding, for these diseases involve fundamental changes in body tissue, changes at the molecular level. They cannot be prevented or treated by good living, by diet or hygiene. To understand the cellular and molecular changes which underlie these destructive diseases requires research at the fundamental level.

The Sir Zelman Cowen Universities Fund is dedicated to making that research possible. We understand that fundamental research is uncertain and unprogrammable until some new discovery is uncovered, and enormously powerful when that new knowledge is developed. We understand also that without research, nothing will change.

This leaflet summarizes four of the most common degenerative diseases of the nervous system - Alzheimer's disease, Parkinson's disease, retinal degeneration, multiple sclerosis - the history, the present and the future of research and treatment.

There is hope for treatment and prevention of these diseases. That hope lies in increased knowledge, in research.

ALZHEIMER'S DISEASE - presenile dementia

This disease was recognised as a distinct condition just 90 years ago, by Alois Alzheimer, a German neurologist. The disease is a steady loss of brain function, the brain failing and degenerating in a healthy body. Its progress is relentless. After 5 to 10 years, death follows, usually from an 'opportunistic' infection like pneumonia, which takes advantage of the sufferer's immobility and failing general condition.

As the number of older citizens increases, the disease is becoming increasingly familiar - it affects 3 or 4 people in every 1,000 aged between 65 and 69, and 70-75 years in every 1,000 aged 85-89. Dementia can arise from many causes for some of which - like alcoholism and arteriosclerosis - the cause is clear. Alzheimer's disease is far and away the major cause of dementia and, with Australia's population aging, the suffering and cost caused by this disease are already a large part of the fabric of life - and death - of older people.

The cause of the disease is still not known despite intense investigation. There is some evidence of a familial factor related to a particular genetic form of fat metabolism. The correlation between this genetic form and AD is striking for the early onset of the disease, but not for later onset. Attempts to exploit this understanding to devise effective therapy have been intense but frustrating. Other studies have suggested a correlation with exposure to aluminium in drinking water; with occupational exposure to chemicals; with alcohol abuse; and with head trauma, hypothyroidism and depression. Conversely, smoking seems to offer some protection against developing Alzheimer's disease (provided you don't die from the diseases which smoking causes!). So many factors seem involved, but their common linkage to brain degeneration remains elusive.

Drugs have been tested which dilate the blood vessels of the brain, or increase its metabolism, without conclusive results. As knowledge has grown of the specific areas of the brain affected early in Alzheimer's a range of more targeted therapies has been devised. For example:

• Specific brain chemicals (neurotransmitters like acetylcholine, or their precursors) are offered.
• Attempts have been made to block the death of neurones, by interfering with the process of cell death, now known to involve the activity of several specific genes and the opening of specific ion channels in neuronal membranes.
• Attempts have been made to prevent the formation of 'free oxygen radicals' in brain tissue; such radicals are known to kill neurones.

And these approaches have been combined, in 'cocktails' of drugs. The results are disappointing. There are stories of improvement - and of deterioration - caused by such treatment. And no approach is available which will stop the relentless progress of the disease, even if symptoms are relieved for a time. Without more understanding, we remain helpless in the face of this disease.

PARKINSON'S DISEASE - paralysis agitans

Parkinson's Disease was first described by the English neurologist James Parkinson in 1817, but for a long time it was viewed by many as 'early ageing'. It is not; it is a specific disease, with a specific lesion, recognised in 1919 by the Russian neurologist Tretiakoff. It is almost as common as Alzheimer's disease, affecting 1 person per 2,000 in their late 60's, rising to 6% among those in their late 80's. It too is a cruel thread in the fabric of life and death of older Australians.

The disease has some features in common with Alzheimer's disease. It is degenerative; again the brain fails in a healthy body. And it is also relentless, slowly progressing until an opportunistic infection ends the suffering of the victim, and relieves the burdens of the victim's carers. However, the site of the degeneration is very specific; neuroanatomists call the site the substantia nigra ('black stuff'), a small but critical group of neurones in the stem of the brain. We know also the special chemical used by these neurones (it is called dopamine), and we have learnt that giving the patient dopamine (actually a precursor molecule called DOPA) will...
dramatically relieve the symptoms of the disease. The tremor and immobility dissolve away; the patient is 'released', as though a chain had dropped away.

The use of DOPA, developed over 30 years ago, gave great relief to patients and its success gave great hope of other therapies, of which many have been tried. The use of DOPA and related drugs remains, however, the mainstay of treatment. That is because later years of research have been disappointing, and even DOPA does not stop the relentless progress of the disease. The levels required to help the patient steadily increase, until side effects become difficult to manage.

So the search for new approaches continues intensively. Research and clinical teams around the world are testing:

- protection of the brain from oxygen radical accumulation (as in Alzheimer's disease)
- the transplantation of healthy 'black stuff' neurones from foetal human brains
- treatment from outside the head with low-level magnetic fields.

Each of these new approaches is based on a line of research, usually incomplete, and tested sooner rather than later because of the suffering of victims. None has provided the dramatic breakthrough which came with the use of DOPA; and without more knowledge - more research - no more breakthroughs will be made.

### AGE RELATED MACULAR DEGENERATION (AMD)

This disease is the major cause of blindness in older people. It rarely causes complete blindness and does not threaten life, but it robs the sufferer of 'central' vision, the part of the visual field we use to read, to recognise people, to watch things around us. It cuts the sufferer off from the written word, from the faces of grandchildren and friends, and causes great loss of quality of life to hundreds of thousands of older Australians, affecting 35-40% of those over 80 years.

As with Alzheimer's and Parkinson's disease, this blindness was once considered just part of aging. For many years now, that acceptance has been put aside and ophthalmologists and scientists have sought the cause, and a treatment. The disease strikes the retina, the thin sensitive membrane which lines the back of the eye and detects light. The detector cells - called photoreceptors - die, particularly over the central part of the retina. In many cases their death is precipitated by an abnormal growth of blood vessels. In many other cases the photoreceptors die without clear cause leaving this critical area of retina functionless and the sufferer unable to read or see faces.

What causes it? As with the other degenerative diseases, the cause is elusive. 'Age' is a risk factor, but that is not really an explanation. Some studies have shown raised blood levels of antibodies to retinal tissue, but it is not clear if this is the cause of the disease or the result. Some studies have described, and others have questioned, a link with diabetes. Some have suggested a weak familial tendency, others a link to exposure to sunlight. Studies of ethnic groups, pigmentation levels and environmental factors have revealed only weak correlations.

With so little known of the cause, effective treatment remains elusive.

- Early attempts tried vasodilators, dietary and lifestyle changes, and vitamin supplements.
- Some cases - 'disciform, macular lesions' - are treated with laser therapy, which cannot restore the retina but hopefully will stop the spread of the lesion. However, laser treatment risks damaging vessel growth.
- The hypothesis has been tested that in AMD, the damage is caused by free oxygen radicals, and there are some reports that vitamin E therapy limits the damage. The success, here too, is limited and partial.

- One European study has tried X-ray therapy, with limited success.
- Recent trials of eye injections of anti-inflammatory agents have yielded encouraging results, limiting the loss of vision for some patients.

For AMD, as for the other diseases, each attempt at a treatment follows a line of argument, an idea, data. And again, because of the urgency of suffering, the therapy is attempted before we fully understand the disease. After many years of research and trials, it is clear that effective treatment will not come without greater understanding. We must either put up with this suffering in those we care for, and eventually in ourselves, or make the research possible which alone can provide a basis for effective treatment.

### MULTIPLE SCLEROSIS (MS)

This devastating disease results not from the death of nerve cells but of the cells which insulate them. These cells (oligodendrocytes) form the fatty myelin sheath which wraps nerve fibres. They die in a range of conditions collectively called 'demyelinating' diseases of the nervous system. The most important of these diseases is called multiple sclerosis.

The disease occurs worldwide, though its frequency varies from as low as 5 people per 100,000 in low risk areas to 30-80 people per 100,000 in higher-risk areas (Europe, Canada, the US, southern Australia, New Zealand). Most sufferers are between 20 and 40 years of age when diagnosed. With modern treatment most will live for decades (the mean survival time after diagnosis is 30 years). During this time they will suffer repeated attacks characterised by weakness or paralysis, blindness, loss of sensation. Any part of the nervous system can be a focus for the attack. Recovery is common, but successive attacks are typically more severe, and the recovery poorer.

The cause is not known. The mainstay of treatment is suppression of the immune system, because the myelinating cells are destroyed by the patient's immune response. It is still not understood, however, why this autoimmune activity occurs and immune suppression, though it will relieve an attack, does not halt the overall progress of the disease. Epidemiological studies suggest that sufferers are infected by the time they are 14 by an agent - perhaps a virus - whose devastating effects become apparent only 10 or 20 years later. However, a viral agent has not been identified in the cause of MS and studies of the relation between MS and other viral diseases which affect the nervous system (measles, rubella, herpes zoster) have not shown a clear relation. Studies of the occurrence of MS in twins suggest a genetic component to an individual's susceptibility.

MS shares with the other diseases discussed here a long, relentless progression, with years of suffering and struggle for the patient and his or her carers. The patient can be brought through the crises, but the underlying disease process cannot be stopped, because it is not understood. The only hope for effective treatment is understanding, the understanding which comes from research.

### About our Fund ……..

Since 1978 the Sir Zelman Cowen Universities Fund has provided millions of dollars for the support of medical research in a wide range of disciplines - the development of cultured skin for the treatment of burns and infection, the management of maturity onset diabetes, the control of pulmonary blood flow, fundamental research into the function of the heart and central nervous system, the molecular biology of AIDS and of other infectious diseases, and the study and early diagnosis of Alzheimer's disease.

This work, done at the University of Sydney and the Hebrew
University of Jerusalem, has contributed to the increasing power of medical science to deal with human disease in all its forms - to diagnose, to cure and, where no cure is available, to treat.

All grants made by the Fund are disbursed to the University of Sydney for projects nominated by the Fund’s Trustees at both Universities

We understand that the power of modern medicine comes from its ability to combine knowledge with care, and that its impotence in the face of some diseases comes from ignorance, from what we do not know.

With this understanding the Trustees affirm the Fund’s long-term goal, to aid the gaining of knowledge which will relieve human suffering, through basic medical research.

To give this commitment concrete form at the University of Sydney, a grants program has been established in the Fund’s name, to distribute funds on the most rigorous basis, that of competitive, peer-review.

The program is administered by a Scientific Advisory Committee comprised of the following neuroscientists chosen for their distinction and breadth of expertise:

• Professor Max Bennett B Eng, DSc, FAA  
  Professor of Physiology, University of Sydney

• Professor Liam Burke BSc PhD  
  Emeritus Professor of Physiology, University of Sydney

• Professor Bogdan Dreher MS PhD DSc  
  Professor, Department of Anatomy & Histology, University of Sydney

• Dr John McAvoy BSc Phd  
  Professor of Experimental Ophthalmology, Save Sight Institute

• Professor Ian Mc Closkey FAA, FTS FRACP  
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The job of the Committee is to distribute funds to the right group, with the right project, at the right time.

To make a tax-deductible donation to the Fund, complete the slip opposite and mail to the Fund.

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