

Bristol and the Brain

Alzheimer's disease and other dementias affect one in fifty people over 65 and one in five people over 80 – approximately 650,000 in total in the UK.

The Bristol Dementia Research Group is a joint venture between the NHS and the University of Bristol. It is led by Professor **Gordon Wilcock** who has good news about the future.

TREATING ALZHEIMER'S

There are many causes of dementia, but three occur more frequently than the others. Alzheimer's disease is the most common cause, irrespective of age, although most of those afflicted are older than 70 years. It usually starts with memory problems and sufferers will then go on to develop more problematic

researchers in Europe and the United States, including some of us who work in Bristol. These showed that a chemical messenger called acetylcholine, important to memory cells, was particularly reduced in people with Alzheimer's disease. Once this was established, medical researchers and the pharmaceutical industry joined

prescribed. It works on a different chemical messenger system from the others and may help protect brain cells from some of the potentially harmful changes that occur in the brain in Alzheimer's disease. It is still waiting to be assessed by the National Institute for Clinical Excellence and should be freely available from, and paid for by the

Our understanding of what causes dementia and our ability to treat it have been transformed

symptoms, eventually becoming increasingly dependent on other people for their daily needs. The two other main causes of dementia are known as Lewy body dementia, which is associated with abnormal structures (Lewy bodies) found in certain areas of the brain, and vascular dementia. The latter was previously thought to be caused by a number of small strokes but we now know that it is more frequently the result of damage to very small blood vessels within the brain substance. Some people have more than one cause for their dementia and it is not unusual to find, for example, that a person suffering with Alzheimer's disease also has vascular damage to the brain.

The first drugs for Alzheimer's

The existing treatments for Alzheimer's are based upon our knowledge of the biochemical changes in the brain and were first described in the 1970s by groups of

together to try to find ways of combating the reduction in acetylcholine.

The first treatment that showed promise, Tacrine, was evaluated in centres in the United States and Europe, Bristol being one of the first two European centres to undertake a trial. Although it had unpleasant side-effects in some people, it did help a significant number of patients with Alzheimer's disease. This drug worked by conserving the decreasing amounts of acetylcholine present in the brain in this condition.

Three newer drugs, including one that we in Bristol had a large part in identifying and evaluating, are now available on prescription to people with mild to moderate Alzheimer's disease, and help perhaps 50-60 per cent of those to whom they are given. These are Aricept (also known as Donepezil), Reminyl (Galantamine) and Exelon (Rivastigmine). They all work in a similar way but have subtle differences in their pharmacological properties.

More recently a new drug, Ebixa (Memantine), has been licensed for people with moderate to severe dementia caused by Alzheimer's, extending the spectrum of severity for which medicines can be

National Health Service. Again, Bristol has played an important part in the early evaluation of this drug, and also its potential use in conditions other than Alzheimer's disease.

Other treatment approaches

Recently in the newspapers and other media there has been information about the apparent benefits of:

- hormone replacement therapy
- various pain killers given to people with arthritis
- substances such as antioxidants
- some medicines used to lower cholesterol levels in the blood

There is indeed evidence that some people destined to develop Alzheimer's disease and who take these compounds for other conditions, may develop their Alzheimer's disease later in life than they otherwise would have. If this is true it probably represents a general protective effect on brain cells rather than being a specific treatment for Alzheimer's disease.

Most doctors are wary of prescribing some of these medicines to people who already have Alzheimer's disease as some of them can cause significant problems. The →

→ mechanism for delaying the onset of the disorder may well be different from that required to treat that disorder once it has become established.

Treatment to stop brain cells dying

The current medicines are designed to help the brain cope with reduced production of some chemical messengers and thus delay the onset of the symptoms of Alzheimer's. They probably have little, if any, effect upon the process of brain cell death itself. We therefore need treatments that will prevent the cells from dying and a number of these are under development. One widely explored approach has involved developing strategies to stop an apparently harmful protein called amyloid, from damaging cells. Potential medicines to achieve this are just beginning to be evaluated in early clinical trials, and if successful may be available in five years or so.

Another approach is based on our knowledge that brain cells need special proteins to keep them alive and help them fulfil their normal function. In Alzheimer's disease it seems that some of these proteins do not manage to travel from the site where they are made to their site of action. We are exploring ways of making one of these substances and delivering it to the cells that are known to be important for memory processes, in the hope that this will enable them to survive the damage that the Alzheimer's disease process can cause. This is very experimental and we do not know yet whether it will be possible to try it out in people with the disease.

Now that we have treatments that are beginning to make an impact on Alzheimer's disease, many research centres, including Bristol where we have nearly 30 people working in our research programme, are looking to develop ways of making the diagnosis even earlier so we can offer these drugs at the earliest opportunity. We are also developing tests that will help us to determine how effective these treatments are, in ways that really matter – e.g., in improving a person's ability to regain control over their day-to-day life and have a more meaningful relationship

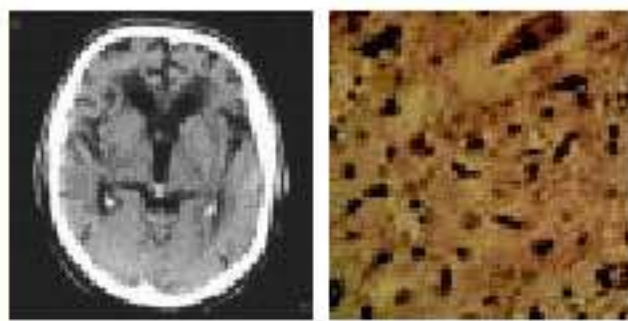
with their families. Additionally, we are looking at the genetic make-up of people who have Alzheimer's disease, not just to discover genes that increase the risk of developing this condition, but also to see if we can use this knowledge to better target the treatments that are currently available and which we are developing for the future.

The Future

There have been major advances in the past ten years in the development of treatments for people with Alzheimer's disease that really do help with the symptoms in many sufferers. In the longer term, it is probable that we shall have a number of different medicines that will work on different stages of the Alzheimer's disease process. Even more exciting are the medicines on the horizon that show promise in terms of preventing brain cells from dying, rather than just treating the symptoms. If, as seems likely, some of these medicines will also benefit people with other conditions that cause dementia, we shall be well on the way to helping millions of people. ■

BRACE is a registered charity established to support the work of Professor Gordon Wilcock and his research team. If you would like to donate something towards this front-line research, please contact the Appeals Office:

The BRACE Appeals Office, Blackberry Hill Hospital, Manor Road, Fishponds Bristol BS16 2EW. Tel: 0117 975 4831 www.alzheimers-brace.org



CT scan of the brain Alzheimer's plaques.