Coping strategies for carers
Therapy programme reduces depression.

Alzheimer’s disease ‘in a dish’
Brain cells growing in gel recreate dementia.

‘I was driven by my patients’
How life has shaped one researcher’s work.

What does the future hold for dementia blood tests?

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Welcome to the first issue of the new research magazine from Alzheimer’s Society. ‘Care and cure’ is a fairly succinct way of describing our research programme, which funds research to improve quality of life for people with dementia and carers as well as into the condition’s biological causes.

This magazine was created in response to feedback from our Research Network, Friends of Research and staff. From all quarters, it was the same response: ‘We want to find out about the latest in dementia research and we want the right background information to understand it better.’

Care and cure magazine will have regular sections for news, features and insights into research.

This issue covers several exciting developments from the past few months, including the recreation of Alzheimer’s in a petri dish, the launch of Join Dementia Research to connect more research volunteers with studies looking for participants, and the announcement of a £30 million programme to kick-start pieces of research that have stalled.

In addition to these, we take an in-depth look at potential blood tests for Alzheimer’s disease and hear from Dr Elizabeta Mukaetova-Ladinska about how she became involved in dementia blood test research.

Ian Le Guillou
Editor
Care and cure
A new technique for growing brain cells has allowed researchers to see Alzheimer’s disease develop in a petri dish. The team, led by Rudolph Tanzi of Massachusetts General Hospital in Boston, found that growing the cells in a gel encouraged them to form connections and create a network just as they do in the brain.

The researchers mutated two genes in stem cells and allowed them to grow to become brain cells. These mutations are found in people with early-onset, inherited Alzheimer’s. As the brain cells grew in the gel, the researchers saw the clumps of proteins known as plaques and tangles that are the hallmarks of Alzheimer’s disease.

Previous attempts to recreate Alzheimer’s disease in the lab have struggled to produce both the plaques and tangles. Getting over this hurdle could mean that these cells are a more accurate representation of the disease in humans, though more research is needed to confirm this.

‘This new system – which can be adapted to other neurodegenerative disorders – should revolutionise drug discovery in terms of speed, costs and physiological relevance to disease,’ said Dr Tanzi.

The researchers started using this technique by trying to recreate the environment that the cells encounter in the brain. Rather than sitting on a dish or floating in a flask, the brain cells seemed to respond to being held in place in the gel structure, which contained many proteins that are found in the brain. This technique could have the potential to be used in research into other forms of dementia and neurodegenerative disease.
Coping strategies reduce depression in carers

Giving carers of people with dementia stress-coping strategies and emotional support can significantly reduce clinical depression and improve quality of life for the following two years, according to a study published in The Lancet Psychiatry.

The START (STrategies for RelaTives) trial, led by Professor Gill Livingston at University College London, randomly assigned 260 family carers of people with dementia who were free from depression to receive either the therapy programme (173 carers) or standard care (87 carers). People who took part in the therapy sessions were seven times less likely to develop clinical depression for up to two years afterwards.

Delivered by psychology graduates, the eight-week course included education about dementia, dealing with stress and where to get emotional support. It also looks at ways to respond if the behaviour of the person with dementia is challenging or difficult to deal with.

‘It is pleasing to see research that focuses on improving the wellbeing of carers while other researchers search for treatments and a cure,’ says Dr Doug Brown, Director of Research at Alzheimer’s Society.

For more information on this research visit www.bit.ly/1uqzIDV

‘Two-faced’ drugs can target the brain

Drugs to treat brain disease often literally come up against the same barrier. The blood-brain barrier is a layer of cells that protects the brain from potentially dangerous molecules or viruses, but it can also block out drugs designed to help.

Now tests in monkeys, recently published in the journal Science Translational Medicine, have demonstrated a way around this by using an antibody molecule that presents two ‘faces’.

One face targets an enzyme called BACE1, which is linked to Alzheimer’s disease as it produces the amyloid-beta that forms plaques in the brain. This is the part that could help to treat the disease, but on its own it could not reach the brain to do its job. The key is the second face, which attaches itself to a protein called transferrin that carries iron to the brain. By using the transferrin as a ‘guest pass’, the antibody can pass through the barrier and block the effects of BACE1.

The researchers at biotechnology company Genentech previously described this antibody in 2011 after tests in mice showed that it could halve the concentration of amyloid in the brain. They have since re-engineered the molecule to reduce side effects and have now shown that it can also halve amyloid levels in monkeys, an important step before human trials.
Researchers who discovered cells in the brain that work like a GPS system have been awarded the 2014 Nobel Prize in Physiology or Medicine. The prize was split between John O’Keefe and married couple May-Britt and Edvard Moser, who studied the brain’s ability to recognise where we are and where we are going.

John O’Keefe was honoured for his discovery of ‘place’ cells – brain cells that activate when we are in a specific place. This discovery was made in 1971 by studying rats and recording the signals from individual cells as the rats moved around a room. The combination of many place cells allows the brain to build a map of the environment and determine where we are.

The Mosers worked in Professor O’Keefe’s lab at University College London before returning to their native Norway to build their own research group. It was there in 2005 that they first discovered ‘grid’ cells by also studying the movement of rats. These cells activated as the rats moved around, essentially charting their navigation. The combination of these with the place cells form an ‘inner GPS’, as the Nobel committee described it.

These cells are found in the hippocampus and entorhinal cortex, regions of the brain that are both often affected by Alzheimer’s disease. The discoveries of these cells have helped scientists to better understand why people with dementia can become lost easily.

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Antioxidants found in cocoa known as flavanols can improve brain function by increasing blood flow to an area of the brain affected by ageing. Although the amount of flavanols actually found in chocolate would be too small to have an effect, this could prompt further research into their effects on dementia.

A new technique to detect inflammation in the brain was presented at the Society for Neuroscience conference in Washington DC. A tracer molecule has been developed that highlights areas of inflammation in PET brain scans in mice. Inflammation appears to be a significant part of Alzheimer’s disease and this development could help to monitor the effects of potential drugs.

Thinning of the retinas could be a predictor for frontotemporal dementia, according to researchers at University of California, San Francisco. They found that people with genetic mutations that cause frontotemporal dementia tended to have thinner retinas. This deterioration appeared before the participants developed symptoms and could be one of the earliest observable signs.
Developing a blood test for Alzheimer’s disease is a hot topic in dementia research and hardly a month goes by without another story appearing in the news. These tests are getting more and more accurate, but what are they and what can they be used for?

Why blood?
Currently, the only way to fully understand the biochemical changes in someone with dementia is to take brain samples after death. It is not feasible or desirable to carry out surgery to get brain samples in order to get a diagnosis and predict the progression of the disease. All that doctors can do now is to use imaging technology, such as PET scans, that allow them to see the build-up of proteins in the brain.

‘The primary reason for focusing on blood is that, compared to other tissues, it’s quite easy to access,’ says Dr Richard Dobson, a researcher at King’s College London. ‘And it can be lower cost, relatively, to screen for signatures in the blood than through a PET imaging scan.’

As the blood circulates it picks up proteins and other chemicals from different parts of the body. This means that blood samples can say a lot about what’s happening inside us – that is, if we know what to look for.

Lots of choice
There is a lot of research currently trying to find markers of dementia in blood. Several new blood tests have received a lot of publicity in the past year. They are all looking for subtle changes to chemicals in the blood that are linked to Alzheimer’s disease, but come in several different varieties (see Tests in the media, right).

These results sound promising but they might still be some way from being reliable enough to be used more widely. ‘Most of these markers are at the validation and replication stage,’ says Dobson.

Potential blood tests for Alzheimer’s disease get a lot of attention from people with dementia, families, researchers and the media. We take a closer look at why blood tests are so popular and where they could start to make a difference.
‘We have to think about them in the context of normal ageing changes and other disease changes. We have to be careful about how specific these signals that we’re identifying are for Alzheimer’s and dementia.’

‘At the moment we’re just looking at one aspect: we’re looking at the RNA or at proteins or at metabolites. One great thing to do will be to combine these different modalities. The technology is there now to generate this data.’

**Power of screening**

An accuracy of 90 per cent might sound good enough for a test to diagnose people, but in reality it is still far too low. Most people do not develop dementia and this means there would be far too many people given false diagnoses, with damaging consequences.

Although these tests have a long way to go before they could be used for diagnosis, they could be useful in recruiting people for clinical trials to test new drugs. Scientists suspect that to find new drugs for Alzheimer’s disease they will have to try them in people at a very early stage in the disease — potentially even before symptoms appear.

‘Drug trials have more chance of succeeding if you can identify people in this preclinical stage. That’s why we’re interested in finding blood markers of these brain changes,’ explains Dobson.

‘That’s where you’ve got real potential to slow down disease progression before too much damage is done.’

We already know that there are changes in the body’s chemistry long before the signs of dementia appear. The key is spotting these changes in a way that is reliable. With current technologies, this requires PET imaging scans of healthy people and looking for signs that Alzheimer’s disease will develop. However these signs might only exist for one in 10 of study participants, meaning that perhaps 1,000 volunteers would need to be screened in order to recruit 100 suitable people for a trial.

Dobson says this just isn’t sustainable. ‘You have a really high failure rate in identifying people suitable for the clinical trial and it’s very expensive.’

This is where even an imperfect blood test could be useful. ‘Even if the blood marker isn’t that amazing, say 80 or 90 per cent, it doesn’t have to be. Even if it was just like a coin toss, that greatly reduces the number of people you have to scan.’

This is why the focus for a lot of blood test research is to help clinical trials. If trial recruitment can be improved, then it might help to stop the trend of large clinical trials failing when the drugs do not have an effect on the participants. Focusing on recruiting people earlier in the disease could be crucial in delaying the development of dementia or preventing it completely.

**Looking ahead**

Improving clinical trial recruitment might not sound ambitious, but it could have a big impact within just a few years. And that’s not all that blood tests can do. There is research into providing a definitive diagnosis of dementia, predicting the progression of the disease and telling the difference between forms of dementia.

These tests might not be ready just yet, but in the meantime blood tests are likely to keep appearing in the media and getting public attention.

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**Tests in the media**

- In March, a team from Georgetown University published the results of a blood test that predicted Alzheimer’s disease three years in advance with 90 per cent accuracy. They identified 10 different fat molecules that were linked with the disease by studying healthy people and noting who developed Alzheimer’s disease. However few people in the group developed the disease, so the 90 per cent claim may not be reliable.

- Then in May, researchers announced another blood test that worked by searching for proteins. This study involved many more participants and had an accuracy of 87 per cent, but only for the progression from mild cognitive impairment to Alzheimer’s disease.

- A couple of months ago, researchers in Australia developed a test that looked for small molecules known as micro RNA. These molecules help to control the activities of cells and certain ones allowed the researchers to predict dementia years in advance with 91 per cent accuracy.
For decades my research focused on measuring proteins extracted from the brain tissue of deceased people with dementia and understanding their clinical meaning so that I could use that knowledge in the care of my patients. However more recently my research moved on to developing a blood test for dementia. This change was driven by my patients who I saw in the clinic.

‘Isn’t there a quicker way to diagnose my father?’ relatives would ask me, as I was explaining the need for brain scans. ‘Could a blood test help you know whether she has dementia or is just confused?’ they would ask when discussing their mother’s diagnosis.

Why do we not have a blood test for dementia? Or any simple test that could provide us with a diagnosis and help us begin treatment as soon as possible? Those were the questions I also started asking myself, both as a neuroscientist and a clinician, while the first reports on blood proteins for dementia started emerging.

Platelet cells found in the blood have certain similarities to the brain’s nerve cells. Platelets contain many of the different proteins found in the nerve cells, and in similar amounts. Our research has identified similar protein changes in platelets as those found in the brain tissue of people with dementia. We were also able to design novel methods to measure them, and confirm that these proteins found within the platelets also changed in people with dementia. These findings confirm further the complexity of the dementia process that can now also be detected in the blood.

What do these findings mean for people with dementia, their families and medical professionals?

‘It is too early to claim that we have a blood test we can use in our clinics to diagnose dementia. However the identified proteins in blood cells bring us closer to developing not only a diagnostic test for dementia, but also to be able to differentiate distinct forms of dementia and monitor the progression of memory and behavioural changes, as well as monitor the response to treatment using the currently available drugs. With our engineering colleagues we are now developing a technique to provide a quick and reliable measure of blood proteins. Our aim is to have a hand-held tool that we can use routinely in dementia screening.

Over the last three decades, my professional work has been a marvellous and rewarding U-shaped journey from bedside to laboratory research and neuroscience, and back to the bedside. It was inspired by, in the words of the late psychiatrist Elisabeth Kübler-Ross, the ‘most beautiful people we have known… those who have known defeat, known suffering, known struggle, known loss’—my patients, their families, carers and my own family. Without them, their natural curiosity and life stories, this research would have not happened.

For more information visit alzheimers.org.uk/careandcure
Michael Head, a researcher at University College London, approached Alzheimer’s Society when his study into scabies in nursing homes was stalled. Scabies are contagious parasitic mites that can spread easily in residential care but are difficult to diagnose and manage in older people. As over 60 per cent of care home residents have dementia, the researchers were having trouble getting the study approved by their research ethics committee. ‘We had an ethical conundrum on getting consent from people without capacity,’ explains Head.

The Society put forward two of our Research Network volunteers, Sylvia Wallach and Tricia Best, both with experience of dementia in care homes, to work with the research team and improve their study design. ‘Being involved in the study was helpful for me to see what was happening in research,’ says Wallach.

‘In my parents’ care home there had been a suspected case of scabies and they were subjected to being covered in cream to treat it. The outbreak was never confirmed, but all staff and residents had to go through the treatment. So I had a personal interest in the study because of my parents, but I was also able to help on another level.’

The problem for the study was getting consent on behalf of residents quickly enough to study an outbreak of scabies as soon as it started. Informed consent might not be possible from a person with dementia and getting written consent from all the families involved would take too long. ‘I had been involved in another study looking at pain issues and put Michael in contact with the principal investigator. That study got verbal assent over the phone and then got written consent afterward,’ Wallach recalls.

Head applied this process to his study design and this time received ethical approval. Having spent the initial pilot grant to look into this project, the team led by Professor Jackie Cassell at Brighton and Sussex Medical School was able to get another £170,000 to expand the study. ‘We wouldn’t have got that if we didn’t have ethical approval in place,’ says Head.

‘We have covered six outbreaks so far. The study is still ongoing but we’re getting really good data. We’re looking to see if people with dementia have a higher risk of getting scabies, but we can’t say that for sure right now.’

‘We’re now also looking at influenza cases in care homes, so this has a snowball effect, leading to further studies on infectious controls in care homes and people with dementia.’

How public involvement saved my study

The involvement of people affected by dementia is a central part of the Alzheimer’s Society research programme. One example of this is how our Research Network volunteers saved a project by helping the researcher to get ethical approval.

‘Being involved in the study was helpful for me to see what was happening in research.’

Sylvia Wallach

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Neuro-MAP will ask pharmaceutical companies for drug projects that have stalled and need help to progress. There are many potential drugs that are patented, but that stop being investigated when research priorities move to fields that are viewed as being more commercially rewarding.

A total of £30 million is expected to be made available through Neuro-MAP, with each charity selecting projects that have promise for the people they represent. They will only invest money until the drug has been developed enough to encourage further commercial investment for large-scale trials.

Dr Doug Brown, Director of Research and Development at Alzheimer’s Society said, ‘Too many potential drugs are languishing in laboratories because the companies that own them have moved in other directions. Innovative projects like this will help demolish the barriers to dementia research and that’s why we’re delighted to be working as part of it.’

The project will be managed by MRC Technology, an independent UK organisation that helps bridge the gap between basic research and commercial application. A portion of any revenue generated from drug sales will be shared with the charities to be reinvested into further research.

Charities unite to bring new life to stalled research

Alzheimer’s Society has come together with other charities to form the Neurodegeneration Medicines Acceleration Programme (Neuro-MAP), which aims to develop new drugs to treat brain diseases.

An online service to help match research volunteers with studies and trials is being rolled out throughout England. Join Dementia Research has been trialled in some regions and the register of studies is now being expanded.

The service has been developed by the National Institute for Health Research in partnership with Alzheimer’s Society and Alzheimer’s Research UK. It will make it easier for people to take part in research by having studies listed in one place and screening based on eligibility criteria. Join Dementia Research is open to people with and without dementia, as healthy volunteers are often needed in studies for comparison. Each study will have its own criteria for recruiting volunteers, so it is important to have a large pool of potential people to select from. People signing up to the service are not obliged to take part in any study, even if they find a match.

To find out more, please see www.joindementiaresearch.nihr.ac.uk or call our National Dementia Helpline on 0300 222 1122.
The knowledge generated by dementia researchers is impressive, but for that knowledge to make a difference it must be used in practice. We need to mobilise research knowledge, move it out of the realms of academia and into the hands of people with dementia, carers, commissioners, doctors, nurses, care workers and Alzheimer’s Society staff and volunteers.

Much is already being done to enable the discovery and creation of new knowledge about dementia, as well as the development of new or improved medicines and diagnostic tools. But the Society recognises the gap between research knowledge and practice, something that our evolving Research and Development team is working hard to remedy.

One example of successful research development is the FITS (Focused Intervention Training and Support) project. FITS is an evidence-based training programme for care home staff that aims to reduce the inappropriate use of antipsychotic drugs in people with dementia. FITS was funded by the Society from its ‘proof of concept’ stage, where training was carried out across 12 care homes to test whether the idea would work. Impressively, the programme was shown to reduce the use of antipsychotics by 40 per cent in comparison to usual care, without worsening behavioural symptoms.

Once the project came to an end, the baton was taken up by another group of leading researchers. To test its effectiveness, FITS was scaled up and delivered to 67 care homes across the UK. The result was a dramatic 30 per cent reduction in inappropriate antipsychotic drug prescription in people with dementia.

There are many components to putting research into practice, one being effective dissemination. This is getting the right messages to the right people at the right time, increasing the chances of new knowledge being used. The researchers and Research Network members involved in FITS have been hard at work sharing the findings to help improve care. Most recently FITS featured at the annual Alzheimer’s Europe conference, this year’s UK Dementia Congress and the G7 meeting in Osaka, Japan.

Now we’re also taking an active role in exploring how to make FITS available to care homes across the UK. There are lots of strategies that are needed to enable uptake of knowledge including ways to change personal, professional and organisational behaviour. A great deal of work is also needed to understand how to do this effectively.

We all play important roles in making the best use of research knowledge, whether it’s spreading the word or campaigning. Together, we can further enable research to make a positive impact on the lives of people affected by dementia.
About us

Alzheimer's Society is the leading support and research charity for people with dementia, their families and carers.

Since 1990, Alzheimer's Society has funded £30 million of cutting-edge dementia research. We aim to increase our investment in our research programme to around £10 million a year by 2017. This money funds important research that will help us to improve the quality of life of people with dementia, by tackling questions related to the causes of dementia, investigating good practice in care and treatment, and pursuing a cure.

Research Network

One distinctive feature of our ground-breaking research programme is the integral involvement of people with dementia and carers.

As part of our Research Network, volunteers with direct experience of living with dementia inform our research priorities.

If you have been a carer for someone with dementia or you have dementia and are interested in joining the Research Network, please contact Anna Grinbergs-Saul, Research Engagement Officer, for an application form or apply online at alzheimers.org.uk/researchnetwork

Alzheimer's Society maintains editorial independence over the content of this magazine.

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