

A PICTURE OF HEALTH 2009

A snapshot of HRB funded research



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Improving people's health through
research and information

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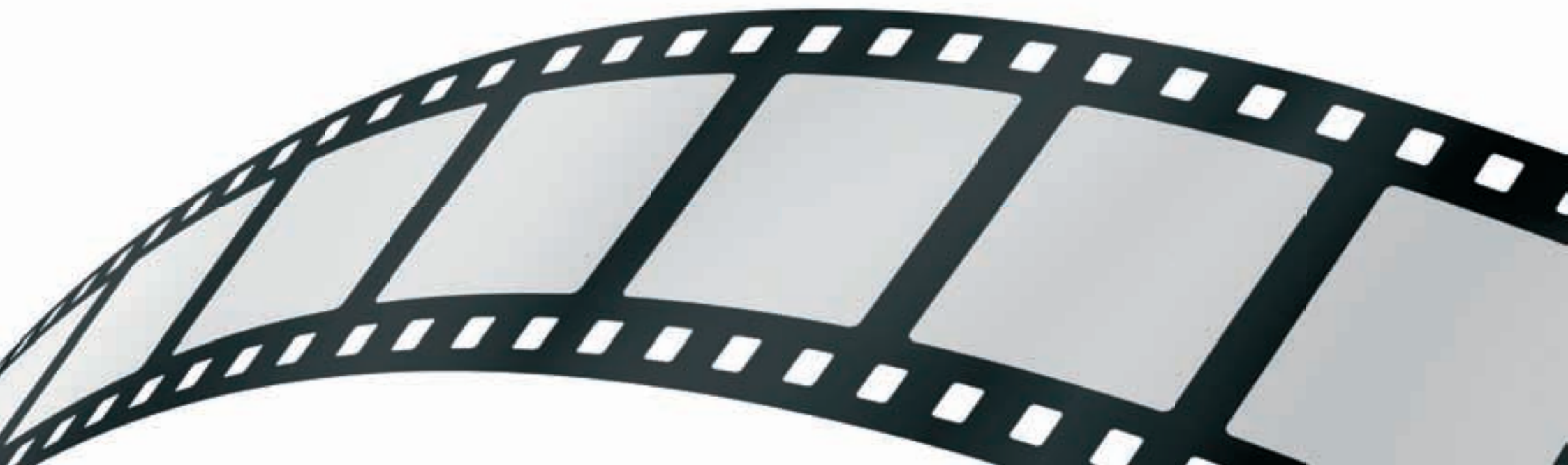
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FOREWORD



When we or our loved ones get sick, we want them to have the best treatment and care available. Health research is the driving force behind better treatments and new approaches to care. But health research also has a vital role to play in preventing illness. By providing the evidence for the best health policies and practices, you can also help prevent illness before you have to cure it. This improves people's lives as well as saving time and money.

The Health Research Board is the lead agency in Ireland that supports and funds health research. It currently has investments of €190 million throughout the hospital and third level system to support health research that improves people's health, enhances patient care and advances health service delivery. Our investments also create an environment to support the development and commercialisation of ideas and discoveries. These underpin a vibrant life sciences sector in Ireland which has a strong and positive impact on our economy.

In 2008, 107 different research projects were completed. The Picture of Health 2009 represents a snap shot of the outcomes from just some of those projects. The stories come from 55 researchers working in nine universities, eight hospitals and four research Institutes. The topics included range from babies health in the womb, to end-of-life care and span improving heart health, to medication safety. They highlight new discoveries and potential improvements to health service delivery, provide evidence to inform health policies and demonstrate the commercial benefits that can emerge as a result of health research.

We hope that the Picture of Health 2009 will give you a sense of both the scope and the impact of Irish health research.

A handwritten signature in black ink, appearing to read 'Enda Connolly'. The signature is fluid and cursive, with a long horizontal stroke at the end.

Enda Connolly
Chief Executive – Health Research Board

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STORIES FROM RESEARCH COMPLETED IN 2009


MEDICATION SAFETY



KEY RESULTS

- A new '*Let's Talk Medication Safety*' booklet is now available in all pharmacies in Ireland.
- Doctors can now target interventions more precisely to reflect the patient's behaviour.

Persistence (continuing to take medication) and adherence (taking medication correctly) are both necessary to extract the maximum benefit from a medicine.



Patients are often confused by the medication they have to take. Help is now at hand, thanks to the new, free, 30 page booklet *'Let's Talk Medication Safety'* which is now available at every pharmacy in Ireland (and is free to download at www.isqsh.ie). The booklet was put together by Hilary Dunne, CEO of the Irish Society for Quality and Safety in Healthcare (ISQSH) and colleague Maria Boyce with the aid of a HRB Strategic Research Partnership award. It explains all basic issues about medication and safety – for instance, differences between prescription and over-the-counter medicines, generic and branded drugs, how to read a label on a medicine, and storing medicines.

The booklet is based on patient perception surveys in which the researchers noted gaps where the safety of medication was concerned. For instance, patients reported they were often not told the reason for a new medication or about potential side effects. Patients and providers were both involved in compiling the booklet and,

Boyce says, ISQSH has received 'great feedback' on the project. Indeed *'Let's Talk Medication Safety'* won two awards (Finalist at the 2009 Crystal Clear MSD Health Literacy Awards and the ARAMARK Healthcare Innovation Awards).

Meanwhile, the HRB and the Irish Heart Foundation co-funded Dr Thomas Barron (TCD) in exploring two important aspects of patient medication-taking behaviour. Persistence (continuing to take medication) and adherence (taking medication correctly) are both necessary to extract the maximum benefit from a medicine. 'We believe there is a distinct difference between the patient who stops taking a drug altogether and the one who at least believes it is important but does not take it correctly,' explains Barron.

But conventional models of analysing prescription refill data do not capture the differences between persistence and adherence. Barron developed a new model that is able to separate out

these two elements and reveals the risk factors relating to each. He worked with prescription refill data from nearly 80,000 General Medical Services patients taking statins to lower their LDL-cholesterol.

The findings open up the possibility of targeting interventions more precisely to the patient's behaviour. For instance, the doctor might try persuasion of the benefits of the medication with the non-persistent patient. But help in organising a medication-taking routine – by special pill boxes, for instance – might be more appropriate for the non-adherent patient. 'Statins are a good example of medication where persistence and adherence may be poor, putting the patient at risk of heart disease, but this new model is applicable to other kinds of medication,' says Barron.



IMPROVING HEART HEALTH

KEY RESULTS

- A decrease in hospital admissions for those going through the prevention programme.
 - Mixed feelings of fatigue/sadness can help predict a recurrence of heart disease.
-

The aim of the SPHERE programme is to improve the aftercare patients get in general practice, thereby reducing the risk of relapse and premature death.

Heart disease is still a major public health problem in Ireland. That is why the HRB continues to fund studies that look at all aspects of the disease, ranging from prevention in the community and clinical work, through to fundamental work into molecular aspects of blood clotting.

Andrew Murphy, Professor of General Practice in the Clinical Sciences Institute, NUIG, used his HRB funding in the development of a major drive to help prevent recurrent heart attacks.

The aim of the SPHERE programme (Secondary Prevention of Heart Disease in General Practice, www.spherestudy.com) is to improve the aftercare patients get in general practice, thereby reducing the risk of relapse and premature death. The trial of SPHERE, co-funded by the Irish Heart Foundation, is a first for the Department of General Practice and also involved collaborators at TCD and QUB; it is the largest non-pharmaceutical clinical trial

ever undertaken on the island of Ireland. Over 900 patients in 48 different general practices took part in the study, with one group following the SPHERE programme and the other receiving usual care.

The involvement of two different healthcare systems – the Irish healthcare system and the National Health Service – makes this study of particular interest. SPHERE involves the design of tailored practice and care plans for the patient with heart disease, involving elements such as using medication for lowering cholesterol and blood pressure and encouraging the patient towards a healthier lifestyle.

Although much is known of these factors, which are so important in secondary prevention, the knowledge is not always applied consistently. ‘We found a decrease in hospital admissions for those going through the programme,’ said Murphy. ‘Current efforts should be maintained. There should also be a focus at a population level – everyone should, for example, try to keep

their blood pressure down.’ The findings of this study are to be published in the British Medical Journal.

Another HRB funded study indicates that care of the heart patient should also include attention to their mental health. Depression and heart disease are known to be linked. Some studies show that chronically depressed people are more likely to develop heart disease. Other research shows that depression after a heart attack makes recurrence more likely. In 2006 Dr Frank Doyle, RCSI, working with Principal-Investigator (PI) Dr Ronan Conroy, published research showing that depression made people with heart disease more likely to have further heart attacks and die.

But they were becoming aware that the tools used to screen for depression were rather ‘blunt instruments’ for this kind of work because depression is such a complex condition with many different symptoms relating to mood and cognition. ‘Depressed mood and the inability to feel pleasure are



Depression and heart disease are known to be linked. Care of the patient should include attention to their mental health.

agreed to be fundamental symptoms of depression,' Doyle explains. 'However, there is no agreement over whether fatigue is, or is not, a key symptom of depression.'

In the current study, Doyle applied three different screening tools for depression to a group of patients with acute coronary syndrome and monitored them for one year. Each measured depression in a different way, covering different symptoms. Only mixed symptoms of fatigue/sadness turned out to be predictive of a recurrence of heart disease. Anhedonia (inability to feel pleasure) and other typical symptoms had no influence

on the risk. The fatigue symptoms may arise from the heart disease itself, lack of sleep, or medication taken for the heart condition. One way of dealing with it may be to increase exercise levels, and there are some ongoing trials on this aspect.



TOWARDS A COMPREHENSIVE TOBACCO CONTROL POLICY IN IRELAND

KEY RESULTS AND FINDINGS

- A rapid and sustained improvement in respiratory symptoms amongst bar workers.
 - Two years on, a significant number of bar workers had quit smoking.
 - Many people are unaware of the link between second hand smoking and ear infections in children.
 - Combining the smoking ban with a comprehensive suite of tobacco control policies could save even more lives.
-

In Ireland, smoking and second-hand smoke exposure claim around 6,500 lives each year...

In Ireland, smoking and second-hand smoke exposure claim around 6,500 lives each year from lung cancer, heart disease and lung disease. In 2004, Ireland became the first country in the world to ban smoking in all workplaces (including bars and restaurants). The HRB has funded two studies that look at how policies aimed at reducing tobacco consumption are working in practice.

Dr Birgit Greiner (UCC) received HRB funding to look at how the ban has affected people's health, behaviour and awareness of the health impact of smoking. First, through the All-Ireland Bar Worker Study headed by Dr Shane Allwright, she discovered a rapid and sustained improvement in respiratory symptoms in a sample of bar workers following the ban. Second, she found that, two years on, a significant number of Cork bar workers had actually quit smoking. Those who continued to smoke did, initially, smoke less – an average of four cigarettes a day fewer one year on – although this went back up by three cigarettes a day at two years.

And, finally, Bernie Mulally worked with Greiner for her PhD on how people's awareness of the harm caused by second hand smoke (SHS) has changed between 1999 and 2006. There is a growing realisation that SHS is linked to heart disease, lung cancer and bronchitis although many still do not know of the link between SHS and ear infections in children. 'Smokers are now more aware that passive smoking is inflicting a risk,' Greiner says. However, smoking is still underestimated as a cause of death. Indeed, people believe that road traffic accidents are the leading cause of death in Ireland when, in fact, smoking causes 6,500 deaths a year – ten times as many as car crashes.

In another HRB study, Dr Zubair Kabir, Research Fellow at the Institute for a Tobacco Free Society, Dublin, examined the health outcomes of the Massachusetts Tobacco Control Program (MTCP) which was set up in 1993 (with state-wide smoke-free policies in 2004). His team looked at lung cancer deaths in the state and estimates there were about 23,500 fewer deaths than

expected (between 1977 and 2003), which can be attributed to anti-smoking policies. A decline in adult smoking in Massachusetts also helped prevent 425 deaths from heart disease between 1993 and 2003.

Kabir's team used computer modelling to look at how tobacco control measures such as increased taxation, indoor smoking bans, reducing young people's access to tobacco and anti-smoking ads can contribute to health outcomes. Such studies could be applied to Ireland to help achieve a truly evidence-based comprehensive tobacco control programme. Massachusetts is a good place to do this work – for 25% of its population have Irish heritage, their tobacco control measures predate the Irish ones by a decade, and Ireland's smoking rates are now falling as they did in Massachusetts. 'Although Ireland has a tobacco control policy, it is not yet comprehensive,' says Kabir. 'If such policies can work in Massachusetts, then they should work here as well.'

IMPROVING DENTAL HEALTH



KEY RESULTS

- Significantly lower levels of decayed, missing and filled teeth among Republic of Ireland children and adults compared to Northern Ireland.
 - Fluoridation is warranted as a public health measure to protect against tooth decay.
 - Research has important implications for water fluoridation programmes in other countries.
 - A strong evidence base for fissure sealant programme to guide future policy.
-



Good dental care can never start too early, which is why the HRB is supporting research that safeguards children's dental health. Under a HRB Research Project grant, Professor Martin Kinirons and Edel Flannery, UCC, have been creating a firm scientific foundation for the Health Service Executive (HSE) fissure sealant programme.

HSE dentists apply a plastic resin to the back teeth which seals the pit and fissure surfaces which may, otherwise, be a site for tooth decay. The process is carried out between the eruption of the molars and the onset of decay. However, there is variation in the timing of eruption of the molars between children and it is not known what impact this has on the optimal timing of fissure sealing. Flannery, who has a background in statistics, created a statistical model for the eruption of permanent molars using the mean eruption times and their variabilities from an all-Ireland database of children's dental health information. 'We identified the optimal timeframe to seal the

teeth, and looked at the impact of various risk factors for tooth decay,' she says.

Fluoridation of the water supply is another proven approach to improving dental health. It has the advantage of being freely available to all sectors of society, unlike fluoride toothpaste which depends on the individual to purchase fluoridated toothpaste and brush their teeth regularly with it. Although the effects of fluoridated water and toothpaste are additive, the question is whether water fluoridation is still warranted given the dramatic reduction in dental decay that has taken place over the last 30 years.

'It is important to keep looking at the impact of fluoridation', according to Helen Whelton, Associate Professor of Dental Public Health and Director of the Oral Health Services Research Centre, UCC.

With a HRB Research Programme grant, she and her team compared the dental health of children and adults in the Republic of

Ireland (ROI) and Northern Ireland (NI), looking at levels of tooth decay, (decayed, missing and filled teeth). In the Republic, 70% of the population live in areas where water has been fluoridated since the 1960s, whereas in NI, water is not fluoridated. The study found that although decay levels are lower than previously, it is still a widespread disease affecting both children and adults. The vast majority of adults examined had experienced decay in their teeth. However, there were significantly lower levels of decayed, missing and filled teeth among ROI children and adults compared to their counterparts in NI. Participants in ROI also had more teeth that did not require any treatment. The study concluded that fluoridation provides lasting protection from dental decay for both children and adults in Ireland and that its use as a public health measure is still warranted. 'These findings have important implications in relation to water fluoridation in other countries,' Whelton says.

Levels of tooth decay are significantly lower in the Republic of Ireland, where water is fluoridated compared to Northern Ireland.

As part of the evaluation of water fluoridation Tara Beecher, an applied psychology graduate, has studied the benefit of the reduction in decay in adults' teeth on their quality of life. Beecher reported that though general life quality is similar in both jurisdictions, Oral health-related quality of life was better in ROI than in NI.

But that is not the whole story, because fluoride has a downside. It can cause changes in the tooth enamel known as enamel fluorosis – ranging from barely noticeable white spots to stains and pitting. There is evidence that the prevalence of fluorosis is on the increase both in Ireland and internationally. With a HRB Fellowship, Dr Deirdre Browne of

Cork University Hospital has been working with researchers at the University of Manchester to develop an objective method of measuring enamel fluorosis.

This compares well with more traditional methods, which are very dependent on the nature of light conditions used to view the teeth and other factors. 'This is very important if you want to measure and monitor fluorosis over time,' she says. For instance, the amount of fluoride in the Irish water supply decreased in 2007 and Browne and colleagues want to know if this change will actually lead to a decrease in the rate of fluorosis.

She has also been looking at the aesthetic impact of fluorosis. A group of adolescents

were shown pictures of cosmetically whitened teeth, teeth affected by low level fluorosis and teeth affected by decay, and then questioned about their reactions. While decayed teeth were voted unappealing, there was no difference in participants' response to teeth with or without fluorosis – suggesting that fluorosis (which also has no known clinical consequences) is not really an aesthetic problem. Another part of Browne's study showed that fluorosis does not have a significant impact on quality of life – while the presence of tooth decay lowers it.




ADVANCING PALLIATIVE CARE

KEY RESULTS

- Most patients opted to be cared for at home, but only a third wanted to die there.
 - Very few patients wish to die in hospital, yet a significant number do.
 - Findings that will underpin palliative care services.
-

There was a strong demarcation line between the place the patient would like to be cared for while they are still in reasonable health, and the place where they wish to spend their final days.



It is often assumed - and other research has suggested this - that terminally ill patients would prefer to be cared for and to die in their own home. New HRB research challenges this assumption.

Dr Sinead Kelly, a palliative care specialist in cancer at St Luke's Hospital carried out the first study that asked patients themselves about these preferences. She worked with the home care team at Blackrock Hospice and carried out 58 interviews with patients and their carers.

She learned that there was a strong demarcation line between the place the patient would like to be cared for while they are still in reasonable health, and the place where they wish to spend their final days.

Most patients (91%) opted to be cared for at home but only a third wanted to die there. Another third said they would prefer to die in a hospice inpatient unit. A further 12.5% were undecided while 4.5% chose a nursing

home, 4.5% a private hospital, 8.5% home or hospice and 4% hospital or hospice.

'It may be that patients want to protect their families at the end of their lives and don't wish to be a burden on them or leave sad memories in the home,' comments Kelly.

'They may also have a positive view of hospice care through their own experience or the experiences of others.'

Patients are not asked directly about these matters - maybe because the subject is thought to be too sensitive and ethically challenging. Kelly believes this ought to change. 'I found patients were more than happy to speak openly about this - they wanted to help others have a choice and they wanted to be included. We shouldn't be acting as the gatekeepers in this matter.'

In Ireland, there are a number of policy documents focusing upon cancer and palliative care services which advocate a patient-centred approach. In particular, the *National Cancer Strategy* (DoHC 1996) and the Report of the National Advisory

Committee on Palliative Care (DoHC 2001) place a strong emphasis on patient preferences about where they would like to be cared for and where they would like to die.

At present, only 64% of patients succeed in dying in their place of choice. This research shows that very few wish to die in hospital, yet a significant number do. Patient preferences on place of care and place of death now need to be translated into genuine choices.

Most patients (91%) opted to be cared for at home but only a third wanted to die there. Another third said they would prefer to die in a hospice inpatient unit.

A photograph of a woman with long brown hair, wearing a light-colored top, sitting at the side of a bed. She is holding the hand of a man who is lying in bed, looking up at her. The man has a grey beard and is wearing a light-colored shirt. The bed has white pillows and a light-colored blanket. The background is a plain, light-colored wall.

SUPPORT FOR THE CARER

KEY RESULTS

- Caring itself has a positive effect on people's health.
- Carer educational programmes help people to cope more effectively with the experience of caring for someone with bipolar affective disorder.

‘Caring itself has a positive effect on people's health, it gives people a sense of importance – they are grounded in the world through a sense of responsibility.’

Dr Michael Rosato

A decorative graphic of a film strip, consisting of a series of rectangular frames connected by a dark line, curving upwards from the bottom left towards the right.

The patient is often the main focus in medical and health research – however we should not forget the needs of the carer, whose role is vital as health and social care move, increasingly, into the community setting. There are two studies highlighted here, one looks at the impact on carers generally and the other at people caring for a specific illness.

Michael Rosato and his colleagues at the Centre for Public Health, Queen's University Belfast, carried out an investigation into the health of carers. While one might think that caring imposes a burden that might be detrimental to health, the study found that people providing informal care recorded lower mortality levels than those not providing care – and this was true for both males and females, of whatever age and even if they had reported an illness themselves.

'Caring itself has a positive effect on people's health,' says Rosato. 'It gives people a sense of importance – they are

grounded in the world through a sense of responsibility.' These findings contribute to the general debate on growing old in today's society. There are limits to what State health services can provide and informal care is going to become increasingly important. 'Caring has typically been characterised as negative – but these findings show it can also have positive aspects,' Rosato concludes.

The study reported here analysed the recently established Northern Ireland Longitudinal Study (NILS) and is a good example of what can be achieved using population databases - linking data routinely collected for administrative purposes. Similarly designed Longitudinal Studies cover the whole United Kingdom (UK) and the Queen's team use them routinely in various projects. These databases are becoming increasingly important as an information source for prospective studies on people's health.

Bipolar affective disorder (BPAD) is a serious mental health problem that affects around 0.5% of the population. Despite improvements in treatment, the condition is still lifelong and relapses are common. 'Bipolar disorder has a major impact upon families, who play an increasing role in the care of the patient,' explains Eadbhard O'Callaghan, Professor of Mental Health Research at UCD and St John of God Hospitaller Services. 'Despite this, there are very little research on how the burden on families might be decreased.' His research, funded by a HRB Project Grant, looked at whether a carer education programme might help both the carer and the patient.

A group of 47 carers of 33 patients was assigned to either carer education (40%), solution focused group therapy (40%) or usual care (20%). Education, led by psychiatric nurse Shane Hill and social worker Patrick Egan focused on issues such as medication, rehabilitation, coping with BPAD, and how to access services.

‘Bipolar disorder has a major impact upon families, who play an increasing role in the care of the patient’ Professor Eadbhard O’Callaghan.

Similar programmes have been used, with some success, in families caring for a person with schizophrenia.

Solution focused group therapy, which was led by two nurses, is a kind of talking therapy that concentrates on what participants want to achieve, but does not offer specific advice. Both interventions were delivered in five weekly two-hour sessions. The participants were followed up one and two years later to find out whether the burden on the carer had lessened. O’Callaghan’s colleagues also looked at psychological distress for carer and patient, and at the level of knowledge the carer had about BPAD. Knowledge did increase for

those in the education group whilst global burden decreased, but there was no change in the other two groups. The patient group did not benefit in terms of reduced relapse.

Many carers posed the question: ‘Why didn’t we have the chance of doing something like this years ago?’ It may be in the early stage of treatment that psychoeducational interventions have the most power to help the carer cope effectively with the experience of caring for someone with BPAD by equipping them with both the knowledge and skill to help their relative whilst maintaining their own wellbeing.

Of particular interest was the difficulty of recruiting people to the study – of 182 referrals, only 47 carers actually took part. O’Callaghan thinks that trials and interventions should start earlier in the course of a patient’s illness – maybe just after the BPAD diagnosis is made. Had the study been larger, there could have been more significant findings that would have helped these families.



A BETTER UNDERSTANDING OF BLINDNESS

KEY RESULTS

- Potential to start clinical trials of a new gene therapy treatment for retinal eye disease.
 - New understanding of retinal cell death opens up the possibility of new drug treatments for eye disease.
-

‘We may now have the beginnings of a rational drug development programme that could help those with retinal eye disease.’

Professor Tom Cotter



According to the World Health Organisation, 161 million people have a visual problem, with about 40 million of these having the clinical status of legal blindness. The most common causes of registered blindness in the developed world, including Ireland, are due to degeneration of the retina (called retinopathies). They include age-related macular dystrophy (AMD) and retinitis pigmentosa (RP).

While limited progress is being made in applying therapies for AMD, the loss of central vision, which is the hallmark of that disease, cannot be prevented. And there is no treatment, as yet, for those with RP. In both of these conditions, cone photoreceptors, the light-sensitive retinal cells responsible for daytime vision, degenerate and die. The HRB has supported two closely-related projects that create a new understanding of what happens to these retinal cells.

Professor Tom Cotter, UCC, has a long-standing interest in cell death in cancer, where damaged cells do not die when they should. 'I became interested in the other side of the coin – why cells die in degenerative diseases,' he says. In his experimental research, supported by a HRB research project grant, he investigated the molecular signals that trigger death in retinal cells.

The work involved using very fine layers of cells taken from retinal samples. 'The cells become stressed on exposure to a variety of genetic and environmental factors. They do try to survive but, if they cannot, a death pathway is triggered,' he explains.

This new understanding of retinal cell death could help us to understand the pathology of diseases like RP, which affects one in 3,000 people. 'We have now learned a lot about how cells die in the eye,' Cotter says. 'We also found that certain compounds can

modulate the stress that otherwise triggers cell death. Therefore, we may now have the beginnings of a rational drug development programme that could help those with retinal eye disease,' he concluded.

Meanwhile, Professor Peter Humphries, TCD, has been supported with a five-year Programme Grant for work investigating the genetics of RP and other retinal disease. His work has greatly advanced the understanding of the role of genes in photoreceptor cell death. Humphries has also carried out proof of principle studies of a gene therapy approach to retinal eye disease that could soon be taken into clinical trials.



FINDING OUT ABOUT RARE DISORDERS

KEY RESULTS

- A detailed three phase plan for rare disorders for the island of Ireland is now being put into effect, including:
 - Dedicated information website.
 - Family support service.
 - A National Centre for Rare Disorders.
 - A new treatment for nephropathic cystinosis.
-

A rare disorder is defined as affecting five or fewer people per 10,000 of the population. There are between 5,000 and 7,000 rare disorders, 80% of which are genetic in origin.

The HRB, and the Medical Research Charities Group, have supported a wide range of fundamental research into rare disorders and in finding ways to support those affected. A rare disorder is defined as affecting five or fewer people per 10,000 of the population. There are between 5,000 and 7,000 rare disorders, 80% of which are genetic in origin. Three quarters of those affected are children.

RehabCare, part of Rehab Group has been looking at the informational and support needs of individuals with rare disorders and their families, in a project funded by a HRB Strategic Partnership Grant. According to Sarah Jane Dillon (Rehab) RehabCare's interest began when the *Report of the commission on the status of people with disabilities-a strategy for equality* specified a need for a National Centre in Ireland to support those with rare disorders. They have looked for examples of best practice elsewhere – including work at the Norwegian Centre for Rare Disorders,

Frambu – and, in 2002, carried out the first survey on paediatricians' experience of rare disorders on the island of Ireland. RehabCare then went on to set up a rare disorder service for people with Prader Willi Syndrome and their families.

In the HRB study, RehabCare consulted with 23 families affected by 10 different rare disorders and both specialist health professionals and GPs on information, current social support and future support needs in this area.

- **Information.** Three quarters of GPs said they had difficulty providing families with their information needs on rare disorders. Families reported negative experiences such as receiving inaccurate or 'worst case scenario' information, particularly from unregulated sites on the Internet. There is also a need to set up a database of the exact number of people who have a rare disorder on the island of Ireland.

- **Support.** Lack of understanding about rare disorders was a considerable source of frustration for individuals and families affected. For this reason, peer support was rated as extremely important. Guilt – because of the genetic nature of many rare disorders – added to the stress felt by families.

'There is a need for Europe-wide support networks to be established for rare disorders,' Dillon says. 'The traditional support group model adopted for more common diseases isn't possible when so few families are affected'. Three quarters of GPs said that they had difficulty providing families with their information needs on rare disorders.

This project has highlighted many areas where changes are needed and RehabCare has set up a specialised project group which will put every effort into making sure these become a reality. Subject to funding they plan to set up:-

Lack of understanding about rare disorders was a considerable source of frustration for individuals and families affected. For this reason, peer support was rated as extremely important.

- A specialised website for rare disorders
- A family support service
- A National Centre for Rare Disorders

There is a European dimension to this work with the publication in June 2009 of the *European Council Recommendations on an action in the field of rare diseases*, which is a political commitment requiring Member States to establish and implement plans for rare disorders by the end of 2013.

Individuals with rare disorders also need new and better treatments. With funding from the Medical Research Charities Group (co-funder Cystinosis Foundation of Ireland) Professor Donald Cairns of the Robert Gordon University, UK has been working towards an improved drug for nephropathic cystinosis. An inherited inability to handle the amino acid cystine means that toxic levels build up and damage the kidneys in this rare disorder. There is an existing drug, Cystagone, but it smells and tastes so bad that many of the young people affected by the disorder don't want to take it, Cairns explains. 'We have now made a number of pro-drugs, that is (drugs which are not

active in their ingested form), which will turn into an active drug in the body,' he says. 'We are also working on a number of non-oral formulations that may be easier to take.'

'Within the next year, we should have enough data to take the drug into clinical development so that it can actually benefit patients with nephropathic cystinosis.'
Professor Donald Cairns

A close-up, high-magnification image of several rod-shaped bacteria, likely MRSA, in shades of pink and purple. The bacteria are elongated and have a textured surface.

FIGHTING INFECTION

KEY RESULTS

- **Potential for commercial development of MRSA vaccine.**
 - **The combined use of anti-inflammatory drugs and antibiotics could be more effective in treating infection.**
 - **Rapid molecular methods are available for early detection of MRSA.**
-

‘We aim to identify the most efficient and cost effective methods possible to address the very serious problem in Ireland caused by hospital acquired infections.’

Professor Hilary Humphreys

A stylized graphic of a film strip, showing several frames, curving upwards from the bottom right corner of the page.

The emergence of antibiotic resistant bacteria has become a serious worldwide public health problem.

The most well-known being *Methicillin-Resistant Staphylococcus Aureus* (MRSA). Professor Tim Foster, TCD, and his group have been working on the mechanisms of *S. Aureus* infection since the early 1990s, with funding from both the HRB and the Wellcome Trust. One possible outcome of this research would be an effective vaccine against MRSA. In 1994, they isolated a surface protein from the bacterium, called clumping factor A (ClfA). ClfA binds to a blood protein called fibrinogen in a key step of the infection process. ClfA has the potential to form the basis of a vaccine.

In the current project, PhD student Joan Geoghegan has made an important discovery that has led to a fundamental rethink of how ClfA binds to fibrinogen. Geoghegan successfully mapped the surfaces of these two proteins and pinpointed where they lock into one another. This revealed that there are two

binding sites for fibrinogen on ClfA. The team have also been working with a monoclonal antibody that binds to ClfA. 'This antibody has potential as a treatment for MRSA infection,' says Foster. 'It blocks fibrinogen binding which, essentially, doesn't allow the bacteria entry into the body. It could also be used as a preventative measure - during emergency surgery for instance, when the patient is particularly vulnerable to infection.'

Foster and his team have also been looking at how the immune system responds to ClfA, with a view to developing a vaccine. Some variants of ClfA have been identified that appear to provoke a stronger immune response; these could be potential candidates for an MRSA vaccine, and Foster's group is in talks with companies who may wish to take this to commercial development. They have just received a new HRB grant for vaccine development and are also supported by Science Foundation Ireland for MRSA research.

Until recently, much research on meningitis has focused upon community-acquired infection caused by *Neisseria meningitidis*. However, meningitis is also a complication of neurosurgery involving medical devices, with the common skin bacterium *Staphylococcus epidermidis* being largely responsible. In a separate HRB Research Project, Professor Hilary Humphreys, RCSI and Beaumont Hospital, has been investigating the tendency of these bacteria to evade the immune response by forming a biofilm (or 'slime') on the surface of the medical device. These bacteria are also relatively antibiotic resistant as antibiotics cannot effectively penetrate into such biofilms.

The researchers concluded that the relationship between the bacteria, medical device and host (patient) is a complex one. PhD student Niall Stevens found that besides forming a biofilm, it appears that *S. epidermidis* also induces an immune response, opening up the possibility that combined use of an anti-inflammatory drug



with an antibiotic may help the patient overcome such infections. There are also drugs in development that can attack or prevent biofilm formation, which may prove to be useful additional therapies.

The HRB also awarded Humphreys an MRSA translational research grant for work being carried out with the Dublin Dental School and Hospital, the Health Protection Surveillance Centre and the National MRSA Reference Laboratory at St James's Hospital, Dublin. They learned that one predominant strain accounts for one out of 20 isolates at Beaumont Hospital and have also identified six different strains of community MRSA in Ireland.

Rapid molecular methods are being used for early detection of MRSA and the researchers are looking at how Beaumont Hospital can better control MRSA through patient isolation and rapid decontamination. Humphreys explains that, ideally, existing Irish hospitals would be replaced by larger, newer ones with single rooms and a full

complement of infection control staff – with everyone being scrupulous about hand hygiene. 'Currently this is not the reality in Ireland. Part of the solution, therefore, must be to undertake research here to identify the most effective and cost efficient methods possible to address the very serious problems in Ireland caused by hospital acquired infections, and that is what we aim to do.'

Rapid molecular methods are being used for early detection of MRSA and the researchers are looking at how Beaumont Hospital can better control MRSA through patient isolation and rapid decontamination.



HELPING CHILDREN OVERCOME CHALLENGES

KEY RESULTS

- New website (www.helpfriendstell.com) developed to help young people deal with revelations of sexual abuse.
- Validation of the updated DEAP tool means better diagnosis of speech disorders for Irish children.

‘Young people have a strong need for containment – they must be sure it is safe to tell and their revelation will be kept confidential.’

Ms Rosaleen McElvaney

All children face challenges, but some are more serious than others. It is well known that children will often keep sexual abuse secret for many years and, indeed, some never tell. Therefore, abuse may continue and opportunities for intervention are missed. Observing this in her own practice, Ms Rosaleen McElvaney, TCD, sought to dig deeper into the process leading up to a revelation of sexual abuse with a study coming, for the first time, from the child's perspective. Supported by a HRB Fellowship, she carried out 22 interviews with young people who had experienced abuse, using a grounded theory methodology that encourages free narrative.

She identified the main issues around the 'tell/don't tell' dilemma. 'Young people have a strong need for containment – they must be sure it is safe to tell and their revelation will be kept confidential,' she says. She also noted a 'cyclical adaptive' process, whereby the young person goes through the same conflict – which she likens to a 'pressure cooker' effect – each time the revelation is

made over the years that follow. 'There is often a kind of active withholding going on, which is very dynamic and quite deliberate and part of the process leading up to telling,' she explains.

During the study, McElvaney was struck by how few people some of her participants had told of their experiences of sexual abuse. Often the school or immediate family were completely unaware of what had happened.

Young people will often turn to their peers with this kind of confidence and it is important that these friends know how to handle the information sensibly. She has been impressed how astute some of these young confidants are – but all children need to know how to deal with information of this kind. Therefore, she wants policy

change with initiatives, rather like anti-bullying schemes, established in schools so that pupils who have experienced sexual abuse can get the help they need as soon as possible.

A speech disorder represents another challenge for a child, especially if it is not recognised and dealt with early. Another study showed that children with speech disorders need early diagnosis and intervention to help their development. With HRB funding Margaret Leahy (TCD) has adapted and validated the Diagnostic Evaluation of Articulation and Phonology (DEAP) tool, which has been developed by world speech development expert Barbara Dodd of the University of Queensland to meet the specific needs of children speaking what is known as Hiberno-English (that is, native Irish children).

In DEAP's original format, Irish and English children are likely to get different scores because of the different ways the English language is used in the two locations.

The tool developed is valid, reliable and ready to use. It allows for accurate and timely diagnosis and more appropriate intervention. With its use, Irish children can expect better diagnosis of any speech disorders.

Therefore, an Irish child could be diagnosed with a speech problem when none exists – or the converse could be true - because the original DEAP is not specific to the way the Irish child uses the language.

Leahy's study has involved around 300 children from Dublin city, Dublin county and the west of Ireland. They are now extending this study to get a more representative sample. The research takes account of the way Irish people use 'r' and 't' and 'ing' for instance, and how and at what rate these differences develop in children.

'Speech is a complex area, even though it is taken so much for granted,' Leahy explains.

The DEAP looks at the various aspects of speech, and is thereby able to distinguish accurately between normal and delayed development, and actual speech disorders.

There are differences in how Irish and UK-based children develop various sounds.

The tool developed is valid, reliable and ready to use. 'It allows for accurate and timely diagnosis and more appropriate intervention,' says Leahy. With its use, Irish children can expect better diagnosis of any speech disorders.

There are differences in how Irish and UK-based children develop various sounds. Therefore an Irish child could be diagnosed with a speech problem when none exists - or the converse could be true. This adapted tool overcomes the issue.



BETTER MANAGEMENT OF BLOOD SUPPLIES

KEY RESULTS

- The use of formal blood stock management processes has greatly reduced wastage and blood going 'out of date'.
 - Detailed analysis and understanding of why people do and do not donate blood in the North and South.
-

A study sought to support Irish hospitals in maintaining a high level of blood availability at reasonable cost.

Blood saves lives, and is a vital resource both for emergency and elective treatments. Professor Anthony Staines, DCU, and colleagues across the island of Ireland have completed a programme of work – the Transfusion Research Network, Ireland – examining some of the many sides of the blood supply. This was co-funded by the HRB and the Health and Social Care Trust Research and Development Office, NI. The first part was a study of blood stock management in Irish hospitals. Using the same ideas used by supermarkets to control stocks and avoid wastage, the study sought to support Irish hospitals in maintaining a high level of blood availability at reasonable cost.

If blood runs out in an emergency it will be found, but this can be very costly. The biggest impact of poor stock management is either excessive outdating of blood, or having to cancel elective surgery, as the blood required is not available. Previous studies found a very high wastage of blood in Irish hospitals, due to blood not being

used before it's 'use-by date'. We worked with transfusion staff to develop, implement and deploy a statistical model to support more efficient ordering of blood. As a result of this work, the use of formal stock management had greatly increased and the level of wastage has fallen.

The second part of the work was a study of attitudes to and knowledge of donation. A large telephone survey was conducted in the North and the South, which asked people what they thought of donation, and for non-donors, why they did not donate. The team found great goodwill towards the transfusion services, North and South, and a good level of general knowledge about transfusion. People didn't donate, at least partly, for logistical reasons, and the research team have had very constructive discussions about their findings with the two transfusion services. In a related study they looked at the flow of patients through a donor clinic, using operations research methods similar to those used by transport planners, to identify some of the logistical problems.

The third part was a very detailed qualitative study to see how people understand the risk of receiving blood. The researchers worked with adults and with the parents of babies who needed transfusion to understand how they saw the risks and benefits of transfusion for themselves and their children. This study identified the key factors that lead to heightened risk perceptions of blood transfusions for patients and parents. Risk perceptions were not found to be based solely on statistical information about blood transfusion, but could also be strongly influenced by patients interpersonal relationships with medical staff and their overall confidence in the medical system.

'Blood saves lives, and is a vital resource both for emergency and elective treatments.'
Dr Anthony Staines



HEALTH SERVICES RESEARCH – A LIFELONG PROJECT

KEY RESULTS AND FINDINGS

- Health services research provides evidence for policy and planning decisions.
- Children with medical cards attend the doctor and hospital more often.
- There is a need to ensure that children without medical cards are not missing out on care because of cost.
- Asthma in young children is linked to maternal eating habits during pregnancy.
- 90% of older people are living well and independently in the community and feel valued in society.
- Research findings will inform Cardiovascular Health Strategy and help plan services for older people.

Health services research is increasingly important, because it provides a vital body of knowledge that can inform future health policy developments. The HRB has funded a number of important projects on issues such as, how children's health is affected by parental and grandparental factors, health service utilisation by different population groups, and the challenges faced by our ageing population.

Dr Una Fallon, UCD and HSE, who held a HRB Primary Care Fellowship, used the Lifeways Cross Generational Study to investigate patterns in health service utilisation in a cohort group of 1,000 families across three generations. 'The ability to look across the generations for risk factors is unique, internationally,' she says. Lifeways, set up in 2000, has already produced several significant findings, including:

- Children with medical cards attend the doctor more often, have more hospital admissions, and are more likely to have

asthma. The policy implication is that children without medical cards may be missing out on care because of cost barriers.

- Asthma in young children is linked to mothers eating fewer fruits and vegetables during pregnancy. This finding highlights the new area of 'nutrigenomics' – the way genetic and environmental factors interact during the antenatal period.
- Grandparents can affect a child's health. A child's birth weight – which can affect his or her health throughout life – depends upon the mother and the grandmother's own weight and their level of education. Both genetic and environmental factors are likely to play a role.
- Nearly 40% of women who have planned their pregnancies do not take folic acid (recommended to prevent spina bifida). We need to consider whether the health message on folic acid could be better conveyed.

'The value of the Lifeways study is based on it being continued and maintained, and to date the HRB has been our main source of support,' Fallon says. She adds that there is an urgent need to support development of electronic surveillance systems to capture primary care use and chronic disease prevalence. This would help not only future research but also in planning services and policy. She would also like to see new ways of publishing and discussing findings in this area. 'We need to prioritise good health services research. Our service is unique and complex and it is difficult to publish Irish health services research in international journals. But we need our own evidence to make planning decisions.'

Professor Hannah McGee (RCSI) used her five-year HRB Programme Grant to carry out a number of studies within the Healthy Ageing Research Programme (HARP). As the Irish population ages, it is important to develop a scientific understanding of what we mean by successful ageing and what role health and social services can play.

‘We found that over 90% of older people are living well in the community, and feel valued in society.’

Professor Hannah McGee

HARP aimed to:-

- Evaluate how health/social services enable or impede successful ageing.
- Compare health and social service experience in the Republic of Ireland and Northern Ireland (two neighbouring, but different, health systems).

General community samples of older people (1,000 each in the Republic and Northern Ireland) and similar samples of stroke and heart failure patients were assessed. These conditions provide examples of chronic and acute/life-threatening conditions affecting older people.

The stroke study showed how patients in Northern Ireland, in a system with GP

incentives for chronic care and audits of acute services, had a better quality of care profile than those in the Republic. The study on heart failure showed higher than anticipated mortality and many deficits in self-care that should be addressed by more thorough chronic disease education. For instance, clear explanations about the reasons for daily weighing in heart failure are needed to encourage patient alertness to changes in fluid retention.

The HARP community study had encouraging results. ‘We found that over 90% of older people are living well and independently in the community, and feel valued in society. This gives us a positive message on ageing in today’s Ireland.’ McGee comments. But she warns that the

study found that about 10% were in poor health and experienced social isolation. Services need to be appropriately targeted, therefore, to this vulnerable group.

Another good feature of HARP is building research and policy-informing capacity to support successful ageing – they have already produced four PhDs in gerontology, for example. Lessons learned are already contributing to the upcoming national longitudinal study on ageing (TILDA) – a project that will follow over 8,000 Irish people age 50+ years over the coming decade.

‘This study aims to understand ageing, inform policy and improve life for older people in Ireland.’

Professor Hannah McGee



SPOTLIGHT ON LOW BACK PAIN

KEY RESULTS AND FINDINGS

- Waiting times for physiotherapy in the public health system are not found to be detrimental to low back pain.
 - Clinical psychologists could have an important role to play in back pain management.
 - A more evidence-based approach to the treatment of low back pain is needed among both physiotherapists and doctors.
-

‘It is the type of treatment patients receive for back pain, rather than how long they wait for it that is important.’

Dr Deirdre Hurley



Low back pain is a common and disabling problem, often associated with high costs in terms of work absence and disability payments. Doctors, physiotherapists and patients need new and more effective ways of approaching the condition, and two HRB-funded researchers have been very active in this area.

There are evidence-based guidelines recommending referral for physiotherapy if low back pain persists beyond six weeks, to prevent the condition becoming chronic. However, in Ireland, the two-tier health system means that those receiving physiotherapy in a public setting may have to wait for treatment, compared to those who are treated in a private clinic who do not have to wait. We do not know what impact the waiting time has on the outcome in low back pain.

Dr Deirdre Hurley, Senior Lecturer in the UCD School of Physiotherapy and Performance Science, has carried out a

randomised clinical trial of the public versus the private setting of physiotherapy for low back pain with Dr Sarah Casserley-Feeney, Lecturer, Institute of Technology, Sligo. One hundred and sixty patients were recruited into the trial, some of whom also took part in focus group discussions about their experiences. Participants, aged 18-65, came from either two areas of Dublin or from Sligo. They were followed up at three, six and 12 months for functional disability, pain and psychosocial measures such as anxiety, depression and beliefs about their back pain. No difference in outcomes was found between the public and private groups, showing that the waiting times for physiotherapy involved in the public health system are not detrimental to low back pain. Functional disability and pain improved in both groups but there was no improvement in psychosocial measures – in other words, although the patients' condition improved, they did not feel any better about it.

'It is the type of treatment patients receive for back pain, rather than how long they wait for it, that is important,' Hurley says. A cognitive element, where the patient works on their beliefs about back pain and other psychological aspects of the problem, could be important, according to recent international research. Unfortunately, there are few clinical psychologists available in Ireland's health system to either deliver the therapy or train physiotherapists to include it in their practice.

Exercise is widely accepted to be important in the management of low back pain and, in this trial, the participants did receive advice on exercise.

Exercise is the key and there is evidence to support this. Therefore, the introduction of the Back to Fitness classes is welcome; they also help with the psychosocial aspect and are currently being trialed by Hurley and others compared to usual physiotherapy and a walking programme.

‘Low back pain is one of the most common conditions presenting in primary care and, unfortunately, treatment outcomes are all too often unsatisfactory.’

Dr Padraig MacNeela

In general, however, a more evidence-based approach to the treatment and management of low back pain is needed among both physiotherapists and doctors, Hurley believes. She would like to see the new multidisciplinary European guidelines on this topic adopted more widely in Ireland (www.backpaineurope.org).

Meanwhile, Dr Padraig MacNeela, NUIG, and his team have been investigating how GPs make their treatment decisions on low back pain. He comments that low back pain is one of the most common conditions presenting in primary care and, unfortunately, treatment outcomes are all too often unsatisfactory. There is a

huge element of uncertainty - both as to the cause of the pain and its prognosis.

In this study, 28 GPs judged the case studies of 40 patients. The research was carried out using judgement analysis – an approach based upon weighting given to different information cues which, in this study, were mobility, self-esteem, sleep, treatment motivation and self-reported pain. The researchers analysis found that the doctors relied upon information cues about mobility and self-reported pain to make their judgement on the patients’ current pain severity. To judge the likelihood of future disability, the doctors looked at all information cues, save the patients’ reports

on sleep. When the patient asked for increased pain medication, doctors tended to rely mainly on the self-reported pain cue.

Overall, the latter was the most important cue – that is, the doctors paid the most attention to what the patient told them about their pain, relative to other issues related to low back pain. There was much variability on how much attention doctors paid to psychosocial aspects of low back pain, like self-esteem. The doctor’s key task is to avoid future disability relating to low back pain and this study revealed that there was great variation in how they assess this risk. The research has already been disseminated to doctors in the HSE west region.



PROTECTING BABIES' HEALTH

KEY RESULTS AND FINDINGS

- **Babies of diabetic mothers show different heart formation as early as 14 weeks.**
- **Changes are more marked in women with poorer diabetic control.**
- **Pregnant women who smoke are more likely to have babies with restricted growth.**

‘Conceiving while diabetic control is good will minimise any possible effect diabetes will have on the developing baby.’
Professor Fionnuala McAuliffe

The HRB has funded two projects which examine how aspects of a mother's health can affect their babies. With a HRB Project grant, Professor Fionnuala McAuliffe, UCD, looked at the effect that pre-existing diabetes in the mother has upon the health of the unborn child. The hearts of these babies can sometimes have structural defects or may not pump well. They also seem to have a somewhat higher risk of dying in the womb than babies carried by non-diabetic mothers.

McAuliffe set out to investigate the possible link between heart dysfunction and risk of foetal death. She found that babies of diabetic mothers who died in utero had much thicker hearts than those of non-diabetic mothers. This led her on to a prospective study where the hearts of fetuses of a group of 30 type 1 diabetic mothers were monitored throughout pregnancy with echocardiography and compared with fetuses carried by a similar group of non-diabetic mothers. The former tended to have enlarged hearts and had an impaired 'squeeze' function. 'Even as early as

14 weeks, differences in foetal heart function between the two groups were found,' she says. 'Moreover, the changes were more marked among those women with poorer diabetic control.' Happily, there were no deaths in this group and, once out of the diabetic environment, the babies' heart function seemed to return to normal.

However, other studies have looked at the offspring of diabetic mothers at the age of 7-10 years and there are some subtle blood test differences compared to children of non-diabetic mums. And in adult life, the children of diabetics also seem to run an increased chance of cardiovascular disease, type 2 diabetes and obesity. 'Even when the foetus is out of the diabetic environment of the womb, the susceptibility to disease in later life may still persist,' McAuliffe comments.

In a paper just published in *Diabetes Care*, McAuliffe has shown that the cord blood of newborn babies of diabetic mothers has enhanced levels of two known biomarkers of cardiac disease – troponin and brain

natriuretic peptide (BNP). Babies born to mothers with higher sugar levels during pregnancy showed further elevated troponin levels. 'These findings add significantly to our understanding of foetal programming,' she says.

She adds that she would not want diabetic would-be mothers to be overly worried that they will harm their babies because of their medical condition. What this research shows is that diabetic mothers should not become pregnant until their diabetic control is good (which can take up to a year, as getting sugars down does not happen overnight). Conceiving whilst the diabetic control is good will minimise any possible effect diabetes will have on the developing baby. Many pregnancies, including those of diabetic mothers, are unplanned, therefore effective contraception is essential in this group of women.

Notably, 23% of the babies of smoking mothers fell into the bottom 5% of the birth weight range, compared to only 6% of those born to non-smokers.

Another study showed that babies of women who smoke while pregnant are also at risk – through restricted growth in the womb. One theory is that smoking increases levels of thromboxane, a molecule involved in activation of blood platelets, and this, in turn, somehow restricts growth of the foetus. Therefore, current clinical practice is to give low dose aspirin, which inhibits thromboxane production, during pregnancy.

Dr Carmen Regan (Coombe Hospital) used a Research Project grant to investigate whether there is, in fact, any real link between smoking, thromboxane and growth restriction. With Dr Caoimhe Lynch, she measured thromboxane levels and foetal growth rates in a group of 60 pregnant smokers at 28, 32, 36 weeks and at birth,

and compared them with 60 pregnant non-smokers.

‘Our results showed an increase in thromboxane with smoking and confirmed that smoking leads to growth restriction. But we were puzzled to find that there is no direct association between thromboxane and growth rate. Thromboxane is not the player, so there is no role for aspirin.’

‘Notably, 23% of the babies of smoking mothers fell into the bottom 5% of the birth weight range, compared to only 6% of those born to non-smokers.’ Regan commented. Smoking could cause growth restriction either because the smoking mother tends to have a poorer nutritional status as well, or because some component

in cigarettes is directly toxic to the foetus. Regan comments that nicotine, for instance, constricts blood vessels and is also a cellular toxin. The evidence tends to argue against the nutritional status theory, because the measurements show a global growth restriction.

When the foetus is malnourished, the head tends to be spared and is of normal size, so growth restriction is not uniform. Regan now wants to look at some of the basic physiology of pregnancy and what role thromboxane and platelet activation might play in the implantation of the foetus in the womb lining.



NEW DIRECTIONS IN CANCER RESEARCH

KEY RESULTS

- Pre-clinical experiments show 60% cure rate for new combined immunotherapy and gene therapy treatment. Clinical trials are imminent.
 - Potential to be effective against gastrointestinal cancers which are currently hard to treat.
 - Possible new biomarker for bladder cancer.
 - Identification of gene defects open up possibilities of new cures for bone marrow cancer.
-

The aim of immunotherapy is to restore the immune response to a tumour.

The HRB supports a wide range of cancer research with €35 million invested in clinical trials, molecular studies and research into the causes and prevention of cancer. For instance, Professor Gerald O'Sullivan, UCC, used a Research Project grant to start developing a new cancer treatment known as immunotherapy. Cancer cells often have the ability to evade the immune system and therefore grow unchecked. 'Those patients who do have an immune response to their cancer do better than those who do not,' comments O'Sullivan. The aim of immunotherapy is to restore the immune response to a tumour. O'Sullivan's team has been developing an immunotherapy that is also a gene therapy (gene therapy is the insertion of genes into an individual's cells to treat a disease). Therapies with a dual action like this are more likely to be effective.

So far, this particular research looks very promising, with as many as 60% of treated animals being cured in pre-clinical experiments. 'We showed that when the

gene therapy made the tumour immune reactive, its growth rate then slowed down. More importantly, secondary growths were also inhibited.' This means that this treatment could be given either as a cure for the cancer, as well as prior to surgery. O'Sullivan has permission to proceed to clinical trials with his gene delivery system. He envisages it being given as an injection into the tumour on an out-patient basis. Where internal cancers, such as gastrointestinal cancers, are concerned, the gene therapy could be delivered by endoscope. He sees the treatment being particularly applicable to this group of cancers, which are often resistant to standard chemotherapy.

In another study, Professor Anthony Staines, DCU, has been involved in several international collaborations in work on multiple myeloma, a bone marrow cancer, which is more common in Ireland than elsewhere and for which long term survival rates are poor. One project funded by the HRB is the European Union's EPILYMPH

project, led by the International Association for Research into Cancer, which is looking into the epidemiology of the disease.

'We are also working with Dr Mark Lawler at St James's Hospital, on the genetic risk of multiple myeloma and a genetic defect in DNA repair has been identified. This is a very significant finding,' says Staines.

Staines is also the founder of the Multiple Myeloma International Consortium which is involved in various projects. Their research has found that there is an occupational element in the risk, with cleaners and farmers having a higher risk possibly because of exposure to environmental chemicals.

Meanwhile, the discovery of biomarkers – molecules that act as a 'signature' for cancer – is probably the newest area of cancer research. With the support of a HRB North-South grant, Dr Amanda McCann, UCD Conway Institute of Biomolecular and Biomedical Research, worked with Professor Elaine Kay, Beaumont

These findings are particularly important for a group of bladder cancer patients, where the cancer has not yet invaded the bladder muscle.

Hospital, and Professor John Fitzpatrick, Mater Hospital, on identifying new biomarkers in bladder cancer. Examination of bladder tumour samples showed that a protein called E-cadherin tends to move from the cell membrane to the cytoplasm of the cell in bladder cancer. E-cadherin's normal role is to help cells to adhere to one another and this shifting might imply that cells in the tumour are becoming more mobile, allowing them to spread more easily throughout the body.

These findings are particularly important for a group of bladder cancer patients (classified as pT1G3), where the cancer has not yet invaded the bladder muscle. There's some debate over whether the whole bladder should be removed in such patients. The presence of E-cadherin in the cytoplasm might have

some predictive significance as a biomarker – indicating those patients whose cancer will spread and who need more aggressive intervention. McCann and her collaborators have also been looking at a biomarker called IGF-2 in urine. A patient presenting with blood in their urine will usually need cystoscopy – an invasive examination of the bladder – to see if they have cancer. Patients with bladder cancer turn out to have a higher level of IGF-2 in their urine, opening up the possibility of using a biomarker-based urine test in addition to – or even in place of – cystoscopy to diagnose bladder cancer.

McCann has also been looking at changes in cancer-related genes known as epigenetic changes – which, put simply, are a significant change in the gene's 'signature'.

In a paper just published online in the Human Molecular Genetics the Conway team and colleagues at St Vincent's University Hospital, the National Centre for Medical Genetics, Crumlin, and Cancer Research UK, Cambridge, found epigenetic changes in prostate cells under low oxygen conditions (hypoxia). The cells began to show some of the characteristics of cancer cells – becoming resistant to cell death, more able to migrate and to produce chemical messengers that can enhance survival of prostate cancer cells. Hypoxia is a feature of many tumours – and of the ageing prostate. These new findings increase our understanding of the mechanism of hypoxia-induced changes through epigenetics.



MINING AND MANAGING HEALTH INFORMATION

KEY RESULTS

- **The combined patient database and patient clinical records brings researchers and clinicians closer together.**
 - **A practical model now exists to inform how other such systems should operate.**
 - **New Biobank Information Management System increases the pace of knowledge discovery.**
-

‘It will speed up the knowledge discovery process enormously if we can share information.’

Professor Jane Grimson



Research and clinical practice often occur in two separate worlds. Research findings are not always readily accessible to clinicians whose patients have participated in a study. And there is a wealth of information in the clinical setting that could be put to good use by the research scientists – if only they could get hold of it. Getting research into practice is a worldwide difficulty. HRB Health Information Systems infrastructure awards are just one means by which this difficulty can be overcome.

Dr Ronan Hearne, Cluain Mhuire Service, in Dublin, and colleagues, are building an information bridge between the research lab and the clinic. The St John of God/ Cluain Mhuire Hospital Adult Mental Health service is already known internationally for research into adult psychosis. They have now developed a research database system which interfaces directly with clinical records. The database supports the service's Delta and Detect first psychotic episode research projects in the east coast area. Around 1,500

different items are uploaded per year for each participant and then a clinically relevant subset is transferred to the fully integrated electronic patient record. Also, demographic, service use and treatment information is transferred from the patient record onto the research database.

A major challenge of setting up this system was keeping patient data anonymous for research purposes while also interfacing it with an electronic patient record, where the patient's identity is required. This required the creation of two, interlinked databases.

One has patient identifiers and is used to input research data. This one transfers and receives information from the patient clinical electronic records. The other is an anonymised replica of the first and is used to provide data for research purposes. The stage is set now for mutual enhancement of psychiatric research and clinical practice at Cluain Mhuire/St John of God.

'Clinicians would not usually have such high quality information about their patients,' says Hearne. Put simply, the project brings clinicians and researchers much closer together. What is more, the interfaces and connectivities involved in setting up this two-way interaction are applicable to other research systems; the proof of concept that has been shown in this project acts as a model for building interfaces between other research databases and clinical record systems.

The Irish Prostate Cancer Research Consortium (PCRC) brings together four universities and six hospitals to accelerate discoveries that will improve the treatment and prognosis for Irish men with the disease. Since 2003, PCRC has been collecting clinical specimens and data from patients. However, all this information needs organising into a high quality biobank system so that its value and potential can be extracted.

Clinicians would not usually have such high quality information about their patients.

Professor Jane Grimson, an electronic medical records expert, and Dr Geoff Bradley's High Performance Computing team at TCD have developed a Biobank Information Management System (BIMS) that allows researchers to track samples and share data.

There are two types of BIMS user. A research nurse acts as 'gatekeeper' to the system, inputting data at their site only. The data is anonymised but has a study identifier that can link it back to the patients' clinical records. Meanwhile, researchers can see all the information they need to, but are not able to identify a patient. BIMS has been set up in two stages.

First, standard operating procedures were set up at all PCRC sites to make sure all

the data was collected in the same way, leading to an infrastructure that has now been in use since late 2007. Now they are developing a system with more functionality, where researchers will be able to add in research findings and share more data as it is collected. Spin-offs include the funding of two PhDs in biobanking. 'Developing BIMS, the first system of its type in Ireland, has involved extensive discussion with the Data Protection Commissioner to ensure patient confidentiality is protected', says Bradley.

BIMS is being developed along the lines of biobanks elsewhere and in other therapeutic areas – allowing researchers access to larger population samples. 'It will speed up the knowledge discovery process enormously if we can share information,'

says Prof Grimson. The main hope for this project is that biomarkers will be discovered that will help doctors to better predict prognosis in prostate cancer and so tailor treatment more precisely to the patient.

A Biobank Information Management System (BIMS) allows researchers to track samples and share data.



WHAT'S UP DOC?

UPDATES ON PREVIOUS
YEAR'S RESEARCH



AUTOMATED COLON SCREENING

COMMERCIAL DEVELOPMENT OF DIAGNOSTIC TOOL FOR AUTOMATED COLON CANCER SCREENING FROM HRB SEED FUNDING.

In 2004, HRB funded research led by Professor Paul Whelan (DCU) and his team described promising results when their virtual colonoscopy (VC) system was tested against conventional colonoscopy at the Mater Hospital. In VC, X-ray scans are taken and used to build a 'virtual model' of the colon through the generation of 2-D and 3-D images. Their system used computer vision software that allowed computer-aided diagnosis (CAD) for automated reading of the images of the patient's colon created by VC.

In conventional colonoscopy, scans are normally read by two radiologists. However, CAD has the potential to act as the second reader, combining the skills of both the human expert and the computer.

The DCU team has since received funding from Science Foundation Ireland to develop a prototype of their VC-CAD system. More recently, Enterprise Ireland helped them to commercialise it and they are now in the process of licensing it to a UK company, where it will soon be included in their suite of medical imaging products. The system differs from some other VC products in using low dose X rays – so more scans can safely be carried out. It is also especially good at imaging and interpreting the flat polyps that may be more indicative of cancer than stalked polyps.

VC combined with CAD will offer an alternative to those who have a familial risk of cancer – who may realise they need regular screening but do not wish to have repeated colonoscopy. The DCU system has already been tested on hundreds of patient datasets from key hospitals in the United States and Europe, with good feedback from gastroenterologists and radiologists.

HRB FUNDED RESEARCH IS THE FIRST IN EUROPE TO GATHER DATA ON THE SERVICE REQUIREMENTS FOR AGEING SPECIAL NEEDS PATIENTS

In 2003 a HRB study led by Professor Mary McCarron, Head of the School of Nursing at TCD, highlighted that people with Down's syndrome live longer than they used to, thanks to improved delivery of health care. However, adults with Down's syndrome are far more susceptible to dementia than the general population, with up to 40% showing signs of dementia beginning from age 35 years.

Her findings are helping to redesign services for this group. The findings include that quality of life is better in community-based homes and specialist dementia units, and that specialist dementia units are preferable to institutions, where patient needs and associated costs increase.

In light of her research, the School of Nursing and Midwifery at Trinity College has developed a Post Graduate Diploma in Specialist Nursing: Intellectual Disability and Dementia to provide urgently needed specialist nurses, and will soon launch an Interdisciplinary Masters in Dementia.

She has recently been granted funding to include a supplement on intellectual disability in the Irish Longitudinal Study on Ageing. The data she is gathering, using a sample drawn from the National Intellectual Disability Database, offers the first opportunity in Europe to ensure that the same level of data guiding policy and service provision in ageing will be available for special needs patients as well as the general population.



**RESEARCH
REDESIGNS END
OF LIFE CARE
FOR SPECIAL
NEEDS PATIENTS**



**RESEARCH LEADS TO
COMMERCIAL SPIN OFFS.**

**BYE-BYE BACTERIA
DENTIST CLEANS UP**

Professor David Coleman, Dublin Dental School & Hospital, TCD, was originally featured in Picture of Health in 2004. He was then looking at ways of reducing bacterial counts in the water cooling and suction systems that are part of dental chair units (DCU). These waterlines are easily contaminated with biofilms (an aggregate of micro-organisms in which cells are stuck to each other and/ or to a surface). 'The risk of infection for the patient and dental staff has been known about for 40 years, but there were very few effective practical solutions,' Coleman says.

But now a practical solution has been developed by Coleman through scientific collaboration with Planmeca, a major medical device manufacturer based in Helsinki, Finland. Dental School researchers worked with the company's engineers to develop the automated Planmeca Water Management System (WMS™). DCUs fitted with the WMS™ system can now be found in hundreds of single dental surgeries around the world as well as in large dental hospitals in North America and Canada and throughout Europe.

During the last three years Coleman has worked with the Irish water technology company Trustwater (Clonmel) and Enterprise Ireland and together they have developed fully automated, self-cleaning, biofilm control systems for Dental Hospitals. These simultaneously control the quality of water in hundreds of dental chairs and their associated water distribution system. The system guarantees water whose purity is ten times better than that of drinking water. Additionally, the new system also saves money as there are no chemicals and consumables are recyclable. Its installation at the Dublin Dental Hospital paid for itself within a year. Whatever worries the dental patient may have, the level of purity of the water used in treatment need not be one of them! The Copenhagen Dental School is now also equipped with the system and installations at several other large Dental Schools in Europe are currently in progress. Coleman says the system is also being applied to reduce the infection risk from other medical devices. 'All of this has come from an initial, small, project grant from the HRB,' he says.

STROKE PATIENTS BENEFIT FROM IRISH INNOVATION

In 2004, we wrote about research that the HRB had funded on the Stroke Activity Scale (SAS), a simple, but effective tool that physiotherapists can use to measure a patient's progress during post-stroke rehabilitation. The SAS takes only a few minutes and needs no special equipment or training. These assessment scales are important for showing both therapist and patient what progress is being made and making the best use of rehabilitation resources.

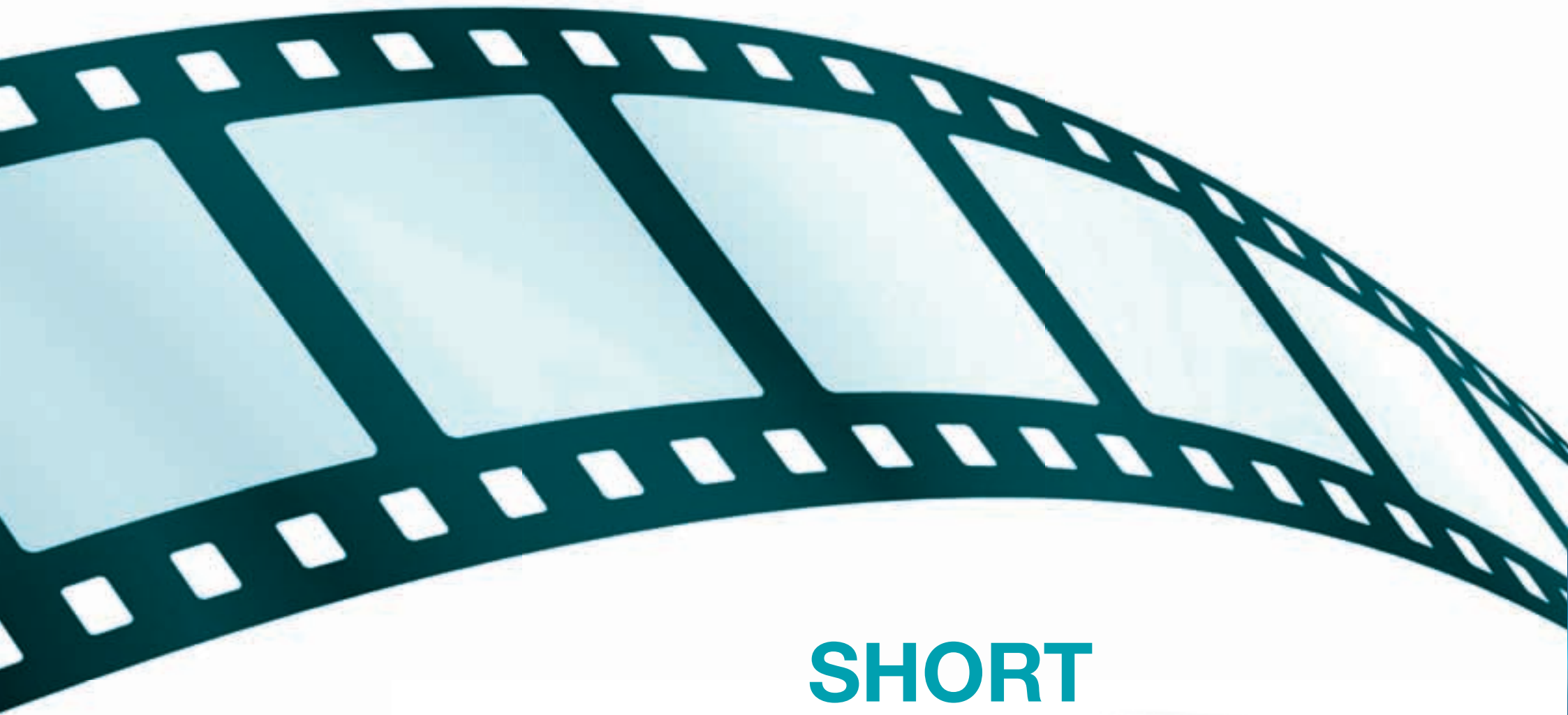
Dr Frances Horgan, Senior Lecturer in Physiotherapy, RSCI, has continued to develop the SAS. Her research findings contradict previous findings by others that suggested patients reach a 'plateau' of recovery a few months after the stroke. Contrary to this belief, Horgan has found that modest improvement in movement skills may continue beyond this point. Therefore, physiotherapy services ought

not to be discontinued if the patient can continue to benefit from them.

Following on from their testing and validation work, the SAS has been requested both nationally and internationally by therapists working with stroke patients. It is hoped to be included in a new cardiovascular health policy from the Department of Health and Children entitled *"Changing Cardiovascular Health": Overview of recommendations of the Cardiovascular Health Policy*.



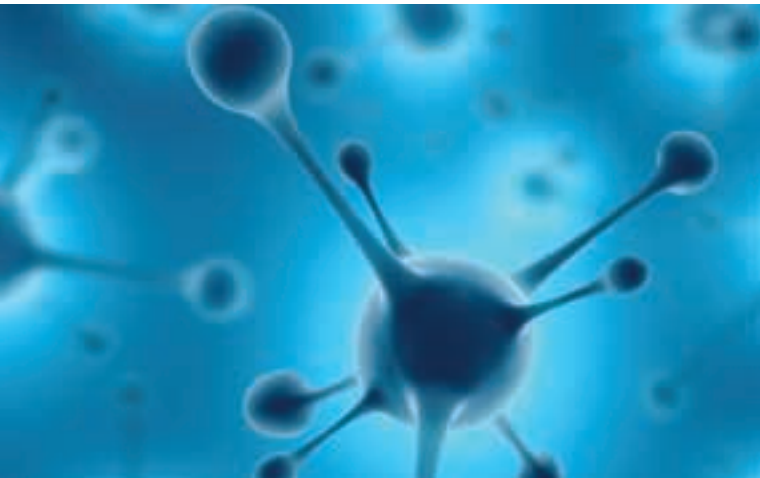
**MEASURING
MOBILITY AFTER
A STROKE**



SHORT **STORIES**

GENE THERAPY FOR BRITTLE BONE DISEASE

Aided by a HRB North-South grant, Professor Jane Farrar, TCD, laid the foundations for a gene therapy approach to brittle bone disease. A defect in the collagen gene is responsible for brittle bone disease. In this project, she explored the possibility of delivering a normal collagen gene via bone marrow stem cells (BMSCs).



Experiments showed that bone marrow stem cells can be delivered either intravenously or directly into the bone marrow. It is also possible to 'silence' the defective collagen gene prior to delivering the normal one. Now the cells have been implanted into a mouse model of brittle bone disease and the impact of delivery of a normal collagen gene on bone health is being investigated.

TASTING SHAPES AND HEARING COLOURS SYNAESTHESIA

Synaesthesia is a heritable condition that arises from 'cross talk' between perceptual systems – a stimulus to one sense sets off an experience in another one. Those affected can 'taste' shapes and 'hear' colours. The condition is surprisingly common - the incidence is estimated at one in 2,000 in the UK population and one in 2,500 in an Australian study - and



it has much to tell us about how areas of the brain's cerebral cortex are connected. Dr Kevin Mitchell (TCD) has studied synaesthesia in a number of Irish families, using brain imaging.

One key discovery is that synaesthetes process visual stimuli differently – even when these do not lead to synaesthesia – suggesting that the cerebral cortex is wired somewhat differently. Mitchell and his team are building a new theory of synaesthesia and will analyse DNA samples from the families to see which genes may be involved.

SPOTLIGHT ON BRAIN CHEMICALS

Glutamate is a neurotransmitter (a chemical that transmits information from one nerve cell to another) that plays an important role in brain activity. Abnormalities of glutamate have been implicated in a number of brain disorders, including schizophrenia, Alzheimer's disease and Parkinson's disease. Until now, glutamate has mainly been studied in cells. However, it would be more useful to study its activity in the living brain and the ability to do this is a long sought after goal of neuroscientists.



Professor John Lowry (NUIM) has now developed a special electrical biosensor for glutamate that can track its activity within the living brain.

The project has been extended to develop a dual sensor that also detects levels of hydrogen peroxide produced by glutamate – a lucky side effect given that recent research has shown that hydrogen peroxide also plays an important role in brain function. As a result of this research Lowry successfully filed a patent application and has signed licence agreements with a Dutch company (Solvay Pharmaceuticals). The group have also secured funding from Enterprise Ireland to commercialise related aspects of this research and are establishing a campus company to drive this work.



As a result of this research there is a patent pending, a licensing agreement in place and a campus company established.

PREVENTION OF LIVER DISEASE COMPLICATIONS

End stage liver disease can cause the 'replumbing' of the blood supply between the liver and the rest of the body. Abnormal vessels called portal shunt vessels divert blood past the liver, thereby reducing its detoxification and metabolism functions. They also cause increased blood pressure (portal hypertension) around the liver. Professor James Docherty, RCSI, has investigated the involvement of certain



biochemical messengers in the formation of these portal shunt vessels and how various small molecules might block their action. The drug thalidomide is showing potential as one such blocking agent, and its use opens up the possibility of new treatment for end stage liver disease.

LIVING WITH KIDNEY DISEASE

Patients with end stage renal disease (ESRD) must usually have either haemodialysis therapy or, if one is available, a kidney transplant. Aoife Moran, DCU, explored the patient experience of ESRD through 16 in-depth interviews with individuals in Ireland undergoing haemodialysis. She learned that 'time' is an important preoccupation for these patients. Waiting around for, and during, haemodialysis was referred to as 'killing time' or 'wasting time'. Participants looked forward to the opportunity for a kidney transplant but, here too, waiting was an issue with three major



elements – 'hope', 'uncertainty' and 'being on hold'.

In general, they said, nurses were unaware of these emotional issues, being more focused on the physical and technical aspects of treatment. Clearly, there are lessons to be learned that could enhance the wellbeing of the patient with ESRD. By offering recommendations for nurses and other health professionals Moran is hopeful that her research will contribute to more effective, patient-centred care for those patients undergoing haemodialysis therapy for ESRD.

NEW WAYS OF MANAGING PAIN

Patients with multiple sclerosis sometimes resort to cannabis (even though it is illegal to do so) for relief of pain. Why is cannabis so effective? Dr David Finn, NUIG, has shown that cannabis-related compounds – endocannabinoids – are among the body's natural painkillers. They play a role in regulating both pain itself and the memory of it. Endocannabinoids work by regulating production of pain producing proteins called cytokines.



These findings open up the possibility of finding new approaches to managing pain based upon the actions of naturally occurring cannabis-related substances within our bodies.

UNDERSTANDING ACUTE LUNG INJURY

Acute injury to the lung is common in pneumonia and septic shock patients and appears to be linked to the ventilation procedures that are so common in intensive care situations. Professor John Laffey, NUIG, has looked at the role of carbon dioxide, a waste product of respiration, in reducing the risk of lung injury. If ventilation rates are slowed, carbon dioxide levels rise and the blood becomes more acidic.

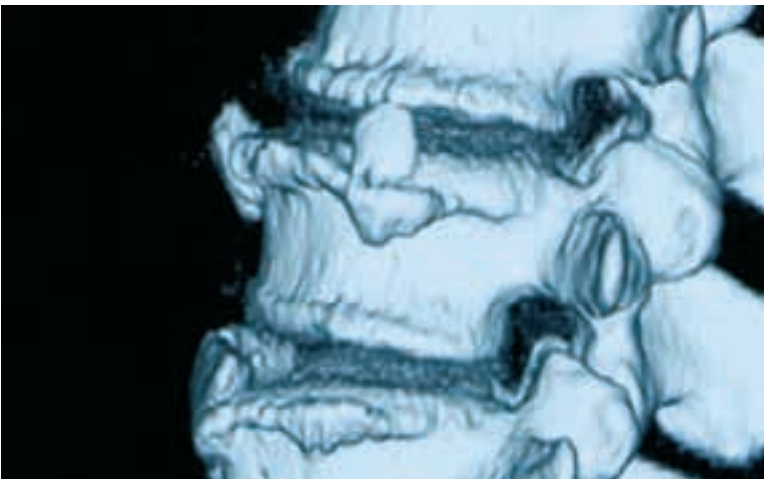
Laffey's experiments have shown that this subsequent blood "acidosis" protects the lungs in the earlier stages of pneumonia and septic shock. His results suggest that



allowing carbon dioxide levels in the blood to rise may protect against lung injury. As a result of his HRB funding Laffey has secured a major piece of EU funding from the European Research Council of over €1 million to further his research.

STEM CELLS FOR SPINAL CORDS

The great hope is that stem cells might be used, one day, to restore mobility through spinal cord repair. Dr Kieran McDermott, UCC, has been looking at the stem cells from which all of the different cells in the spine originate. He found that three specific genes, Pax 6, notch and Hes, hold the key to cell differentiation.



Their spatial and temporal distribution guide the stem cells down the right path. Interaction between these three molecules, and others yet to be discovered, is crucial to understanding how a stem cell can become a specific type of spinal cord cell. These new findings bring the possibility of spinal cord repair a step closer.

RHEUMATOID ARTHRITIS DISCOVERY

Rheumatoid arthritis is characterised by progressive joint damage and disability arising from an inflammatory process in the joints. Immune cells enter the synovial fluid in the joint and start to attack cartilage and then bone. Dr Ursula Fearon, UCD, investigated the role of two particular proteins in this destructive process.



She used a new synovial explant system (a technique to isolate and replicate cells and tissues) that better mimics the real joint than animal models or experiments with cartilage cells alone could do. Both proteins cause cells to invade the joint and lead to cartilage breakdown. The findings may lead to new RA therapies based on blocking the action of these particular proteins.



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