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EQUIPOISE

The Blood
Issue



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EQUIPOISE

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EDITORIAL

Welcome to the second edition of Equipoise. Our aim is to bring you interesting and challenging reports from the frontiers of our health and health services research; articles that will make you question and ponder but which are a pleasure to read.

We had great feedback on our first edition, so we know that many of you enjoyed reading about the human face of health sciences. If you have ideas for future themes for the journal or articles you'd like to see then please contact us. All our news and opportunities for research, education and training are available on our website (www.york.ac.uk/healthsciences) and you can follow us on Twitter: @HealthSciYork.

Here at York our Spring Term is upon us and the cold and dark of winter will soon give way to the energising light and air of the spring. In this issue, our theme is 'blood', which, for the ancient Greeks, was associated with both air and the spring. Blood, as one of the four humours (the other three being phlegm, black bile and yellow bile), was responsible for producing a 'sanguine' temperament in people. This was characterised by a joyful mood, sociable personality and pleasure-seeking behaviour. The Greeks recognised that you can have too much of a good thing though and too much blood meant uncontrolled energy and the need for bloodletting. Blood has an important symbolic meaning; so words such as bloodthirst, bloodbath, and blood money connect with us on an almost visceral level. Its colour represents life, fire, danger, violence, energy, speed, and passion – the stuff of strong emotion.

In this issue we hope to get your 'blood up' and get you thinking. Topics such as blood phobia; the (often unintended) societal impacts of blood tests for genetic disease; cancers of the blood; and the politics of the wound care industry all illustrate the many and varied ways in which this most precious of fluids affects our lives.

If your New Year's resolution includes a desire to learn, commission or undertake research, or develop yourself professionally, then we hope you'll get in touch to see if we can help.

Kate Pickett & Carl Thompson

“IT’S A BIT MORE THAN JUST BLOOD RESULTS”

ANTE-NATAL SCREENING AND THOSE AT RISK OF SICKLE CELL AND THALASSAEMIA

Identifying the genetic basis of disease, even in recessive disorders, is not straightforward and brings with it a host of practical and ethical issues. Downplaying these issues not only threatens families’ ability to make informed reproductive choices but also raises broader questions about the social consequences of genetic screening. Since 2001 antenatal (before birth) and neonatal (at birth) screening for sickle cell and thalassaemia has been a coordinated health service response. The programs are identifying more “carriers” than ever before and many examples of good practice exist. However, inadequate, ill-coordinated and poorly resourced services remain. The persistence of suboptimal elements of screening reflects a broader philosophical concern regarding the purpose of genetic screening and what it means to all those involved.

Sickle cell and thalassaemia are the most common, single-gene disorders in the UK. They directly affect at least 16,000 people with a further 240,000 people carrying the sickle cell trait and 214,000 people carrying the thalassaemia trait. If two trait carriers have a child, there is one in four chance that their child will be born with the disorder. Ante-natal screening enables parents to choose whether to continue with the pregnancy if a child is found to be affected. Traditionally, sickle cell and thalassaemia are thought of as diseases of particular ethnic groupings; sickle cell disorders (SCD) affect people of African-Caribbean or African origin, whilst thalassaemia more commonly occurs in Cypriot, South Asian and Chinese populations (and to a smaller extent, those of African-Caribbean descent). To some extent, this association still holds. Increasingly, however, ethnicity is becoming a far less reliable predictor of who carries a trait. National screening programmes have identified far more ‘white’ carriers than expected and the

increasing proportion of people identifying as ‘mixed heritage’ makes assuming the need for screening solely on the basis of ethnic origin an inadequate strategy.

Ante-natal screening presents parents with difficult and complex choices. Despite the challenges involved, parents are generally positive about being offered screening when pregnant. People generally favour the provision of information and discussions about the implications of testing. Two significant dimensions of the “decision challenge” faced include the lack of knowledge about the condition and the confusing array of tests offered during pregnancy. Couples say this can make it difficult for them to understand the consequences of what they are agreeing to. Mothers, for example, often accept screening (and the possibility of termination) because they do not wish to be judged as ‘bad mothers’. Rejecting screening, when they are considered at risk, leaves them open to accusations of irresponsibility. Furthermore, mothers tend to agree to testing on the assumption it will show their unborn child is healthy and do not expect to have to make a decision on whether to continue the pregnancy or not.

It may not just be professional competence that leads to mothers expressing a high degree of trust in healthcare professionals. Mothers accept doctors and nurses as a source of ‘authoritative knowledge’, especially as they struggle to make sense of the multiple risks associated with pregnancy. They are, therefore, happy – at least initially – to be directed by practitioners as long as it provides news of a healthy baby. Professionals for their part admit they have often received little training in this kind of difficult decision making involving parents. Advice to parents often reflects a complex interplay of professional and personal beliefs – which are themselves

Traditionally, sickle cell and thalassaemia are thought of as diseases of particular ethnic groupings; sickle cell disorders (SCD) affect people of African-Caribbean or African origin, whilst thalassaemia more commonly occurs in Cypriot, South Asian and Chinese populations

not divorced from broader social assumptions about disability.

It is an awkward and uncomfortable prospect, but it is impossible to escape the implicit eugenic implications of screening. Mothers are well aware of this, as they point out how the offer of a test, already presupposes that sickle cell and thalassaemia are undesirable. Prospective parents say that decisions about termination are informed by the perceived severity of the condition, along with negative perceptions of society's treatment and support (or lack of it) for people with disabilities and long-standing conditions.

Despite advocating informed choice, genetic screening programmes, by their very nature, cannot help but reduce the incidence of the condition. To add to the confusion, underlying economic models in their attempt to inform, suggest reducing the numbers of people with the condition makes screening cost-effective. The numbers of terminations for sickle cell and thalassaemia, for example, have increased since the introduction of coordinated screening programmes. This raises the question of who really benefits from offering screening: the individual, or society?

Aside from a somewhat bounded view of individual choice-making, organisational constraints also act to restrict couples' options. Timely screening is particularly important for informed choice, since most women

are reluctant to consider termination beyond three months into their pregnancy. Policy aims to offer screening to 90% of mothers by ten weeks gestation. It fails. At most, 45% of mothers are offered screening, but in some areas of the UK it's less than 12%. The problem cannot be explained by mothers who report the pregnancy later than others: 74% of women – irrespective of ethnic origin – consult for pregnancy before ten weeks' gestation. Organisations simply lack the capacity to deliver. The problem of timely screening is further compounded by a failure to engage with fathers, something that is essential when screening for recessive disorders. Studies show that fathers would like more involvement in their partners' pregnancy, frequently describing themselves as 'bystanders', 'outsiders' and 'disengaged' from ante-natal care. Black fathers also have to counter the institutional assumption

that they prefer not to be involved – something for which there is no evidence. Sickle cell and thalassaemia has long held a leading role in (institutional) racism.

Little more than twenty years ago, most doctors and nurses had little understanding of sickle cell and thalassaemia. Much has been achieved since then. Whilst services have evolved and developed, the dissemination of good practice remains a struggle. Service coordination, evidence-based practice, inter-agency collaboration and strategic leadership represent key challenges, as does the need to provide equitable care, wherever a person might live. A particular problem associated with antenatal testing is the failure to ground choices in parents' perceptions and experiences (rather than professional assumptions), while acknowledging fundamental tensions between choice and prevention – tensions which lie at the heart of genetic screening.

Professor Karl Atkin is currently leading two projects exploring the social consequences of screening. One funded by (NIHR) Research for Patient Benefit, explores how best to involve fathers in the ante-natal screening process (PB-PG-0610-22196). The other funded by the ESRC examines the impact of being identified a carrier of sickle cell or thalassaemia, across the life course (www.esrc.ac.uk/my-esrc/grants/RES-062-23-3225/read).



BLOOD, WOUNDS AND INTERCESSIONS

“The last thing the surgeon said to me, on the afternoon of the procedure: ‘For you, this is a big thing, but remember, to us it is routine’ ...When I sit up and see the wound in my abdomen, I am pleased to see that it has a spiral binding, like a manuscript...Within a few days, the staff are tampering with my spiral binding when the whole wound splits open. Blood clots bubble up from inside me... We see things that never should be seen; our inside is outside, the body’s sewer pipes and vaults exposed to view, as if in a woodcut of our own martyrdom.”¹

SS. Cosmas and Damian
dressing a chest wound.
Oil painting by Antoine de Favray.
Credit: Wellcome Library, London



This is part of author Hilary Mantel's description of life as a patient going to hospital for a 'routine' operation which resulted in months of recovery: "After that initial cut, nothing went on time or to plan, and it was no one's fault." The edges of Mantel's surgical incision were held together by stitches, "spiral binding", but sometimes surgically closed wounds split open due to infection, tissue loss or other factors and cannot be stitched or stapled closed again and sometimes surgical wounds just have to be left open in order to heal. This can be distressing for patients, their carers and indeed clinicians who are left feeling that they are, "seeing things that never should be seen".

The Wounds Group at the University of York focuses on how to deliver the best healthcare for people with chronic wounds such as leg ulcers, pressure ulcers, diabetic foot ulcers and open surgical wounds (also known as surgical wounds healing by secondary intention). Often these wounds are caused by a complex mix of factors. Our aim is to improve wound care and patient outcomes by identifying effective treatments and promoting their use. There is currently very little good quality information about these complex and chronic wounds. For example, we do not know how many people have open surgical wounds, the full impact of wounds on patients and the NHS, how best to treat them and how long they take to heal.

What we do know is that chronic, complex wounds are common, distressing and costly. The total financial cost of wound management to the NHS was estimated at £2.3–£3.1 billion per year in 2005/6.² With an ageing population and more chronic disease, this has risen since and is set to keep on rising. Wound care management is one of the largest segments of the UK medical technology sector with a turnover exceeding £1bn in 2009.³ However, wound care remains something of an evidence wilderness with systematic reviews of evidence revealing a predominance of small, underpowered, and methodologically flawed trials.^{4,5,6} It is a sector in which practice becomes reliant on custom, opinion and marketing and where systematic reviews are being portrayed as a means of rationing access and reducing patient and professional choice.⁷

Products used to prevent and treat wounds, for example wound dressings, pressure relieving surfaces and Negative Pressure Wound Therapy (the "small, heavy black box" used on Hilary Mantel's open wound to, "vacuum out the cavity and gradually close its walls") are classified as devices rather than medicinal products. The focus of the European regulatory process (the CE marking often seen on products) is on safety assessment, viability, and competitiveness of such devices, not clinical effectiveness. This leaves

uncertainty about outcomes in clinical practice.⁸ Clinicians using 'quick to market' innovations are in effect using unproven technology in uncontrolled experiments. While devices that have not been tested for efficacy may not be actively dangerous, neither might they produce the effects promised to clinicians by their marketing. In short, patients may not be receiving effective treatment.

Rather than filling the evidence gap with good quality evidence, it is more profitable under the current system of regulation for medical device companies to market the promise of solutions through boundless wound management 'innovation'. Once a device is launched onto the market, the incentives to conduct quality research on clinical use are reduced because good quality research is expensive and can reveal that lucrative products/solutions with strong market positions are not nearly as efficacious as their marketing implies.

We are working to fill the evidence gap with quality, reliable, independent evidence, develop innovative ways of reliably evaluating technologies and – crucially – to increase public engagement and involvement in our work. As part of our portfolio we have successfully undertaken five large Randomised Controlled Trials in the past ten years and are currently investigating whether a wounds register can be developed to provide much needed information about wounds and wound care. We are also working with the James Lind Alliance, clinicians, patients and Third Sector organisations in a partnership to identify priorities for future pressure ulcer research (JLAPUP).⁹

Hilary Mantel wonders if "there is a little saint you can apply to, if you're a person with holes in them?" She has trouble identifying an appropriate one because the saints she can think of have been, "...pierced suddenly by the fiery lance of God's love, whereas I was pierced by prearrangement, in a hospital just off the M25." Suitable saints to intercede on behalf of patients with chronic wounds are hard to find in an increasingly secular society. However, the odd clinician scientist has risen to become part of the 'cult of celebrity'. So, instead of saints, those of us seeking to publicise concerns about this seldom heard sector try to attract the attention of celebrity "nerd cheerleaders" and spread the word that by taking a long hard look at market relationships in healthcare and by making the most of the possibilities of rigorous evaluation we begin to see parts of the industry that "never should be seen".¹⁰

What we do know is that chronic, complex wounds are common, distressing and costly. The total financial cost of wound management to the NHS was estimated at £2.3–£3.1 billion per year in 2005/6. With an ageing population and more chronic disease, this has risen since and is set to keep on rising.

Dr. Mary Madden is a research fellow in the Wounds Group which is part of the Health Services and Policy team. She is currently investigating the treatment outcomes that matter most to patients and other stakeholders; working with patients, carers and clinicians to identify and prioritise shared healthcare uncertainties; exploring the extent of industry influence in knowledge production and the positioning of evidence based medicine in opposition to clinical knowledge and as an obstacle to innovation.



CLOSER TO DEFEATING CHILDHOOD CANCERS?

Hematological malignancies – cancers of the blood and bone marrow – account for around 10% of all cancer diagnoses and represent the fourth most frequently diagnosed cancer in both males and females in economically developed regions of the world. Whilst there are over 60 recognised disease subtypes, which differ widely in clinical presentation, treatment requirements and prognosis, these cancers have traditionally been grouped as leukaemia, lymphoma or myeloma. Haematological malignancies are, however, relative

newcomers to the cancer world, as it wasn't until the 19th century that the first cases of leukaemia were described, thousands of years after Hippocrates first described tumours of the skin and breast. Nowadays haematopathology – the study of the pathology of these malignancies – currently represents one of the most rapidly advancing and changing areas of clinical research.

It was Anton van Leeuwenhoek's development of the primitive compound microscope in the 17th century that sparked activity in this area. In the late 18th century, this led to the description of the different

components of blood (red cells, white cells etc.). However, almost 100 years passed between the discovery of white blood cells and the reporting of "leukaemia" in 1845 by Virchow, who introduced the term "leukemia" simultaneously with Bennett who referred to the disease as "leucocythaemia".

Virchow pioneered the way with the identification of different types of leukaemia which were described as splenic and lymphatic, the former associated with splenomegaly and the latter with large lymph nodes and cells in the blood that resembled those in the lymph nodes.

Today, the developments in aligning genetic and chromosomal abnormalities with different subtypes have resulted in treatment protocols that are now defined according to the underlying disease characteristics with both “good” and “poor” biological indicators identified. And, as a result, well over 90% of children in the “good” risk group are now cured in the developed world.

splenic and lymphatic types already described. Again it was improvements in microscopy and the development of methods to differentiate cell types that allowed leukaemia to be classified as myeloid (arising from granulocytes in the bone marrow) and lymphoid (arising from lymphocytes, nongranular cells). By 1913 it became possible to classify leukaemia as chronic lymphocytic, chronic myelogenous, acute lymphocytic, myeloblastic, monocytic, or as erythroleukemia.

Significant advances in laboratory techniques have continued over the last 100 years. This has not only underpinned progress in disease classification, but has also enabled the development of improved treatment regimens resulting in improved survival. But it is with respect to childhood leukaemia, first described as the acute form in 1857 that we have seen the most dramatic changes in survival. Acute leukaemia is the most common type of cancer seen in children, but is nevertheless rare, accounting for approximately 600 cases each year in the UK. Acute lymphoblastic leukaemia represents 80% of these cases and has a striking and unique age distribution with incidence increasing rapidly after birth, peaking between 2–5 years of age, before declining and rising again after the age of 45 (www.hmrn.org). In the early part of the 20th century, survival from this disease was extremely poor, but headway was made in 1948 with the observation that temporary remission could be obtained through the use of folate antagonists, and in 1962 it was the first systemic malignancy to be cured by chemotherapy. However, despite the many advances in classifying leukaemia subtypes, until the late 1960s all acute leukaemias in children were grouped and treated together. It was only the observation that acute myeloid and acute lymphoid leukaemias responded differently to treatment that enforced and established the use of new technologies to

distinguish between them, coupled with the identification of biological features associated with the different types.

Today, the developments in aligning genetic and chromosomal abnormalities with different subtypes have resulted in treatment protocols that are now defined according to the underlying disease characteristics with both “good” and “poor” biological indicators identified. And, as a result, well over 90% of children in the “good” risk group are now cured in the developed world. However, treatment is very expensive and very lengthy, and in less advantaged economies many children still die, assuming they even survive to be diagnosed. Even in the UK where all children have access to the same treatments, inequalities in survival have been documented according to socio-economic status.

Childhood leukaemia is undoubtedly one of the success stories in terms of advances in the development of strategies to combat haematological malignancies. As technologies such as gene sequencing and gene expression profiling become routine diagnostic tools that are no longer confined to research laboratories, it seems inevitable that we will witness dramatic prognostic advances for other “blood and bone marrow” malignancies as well. Indeed, stratified or personalised medicine, following the in-depth genetic profiling of malignancies and the development of targeted therapies, is becoming a realistic option for the near future.

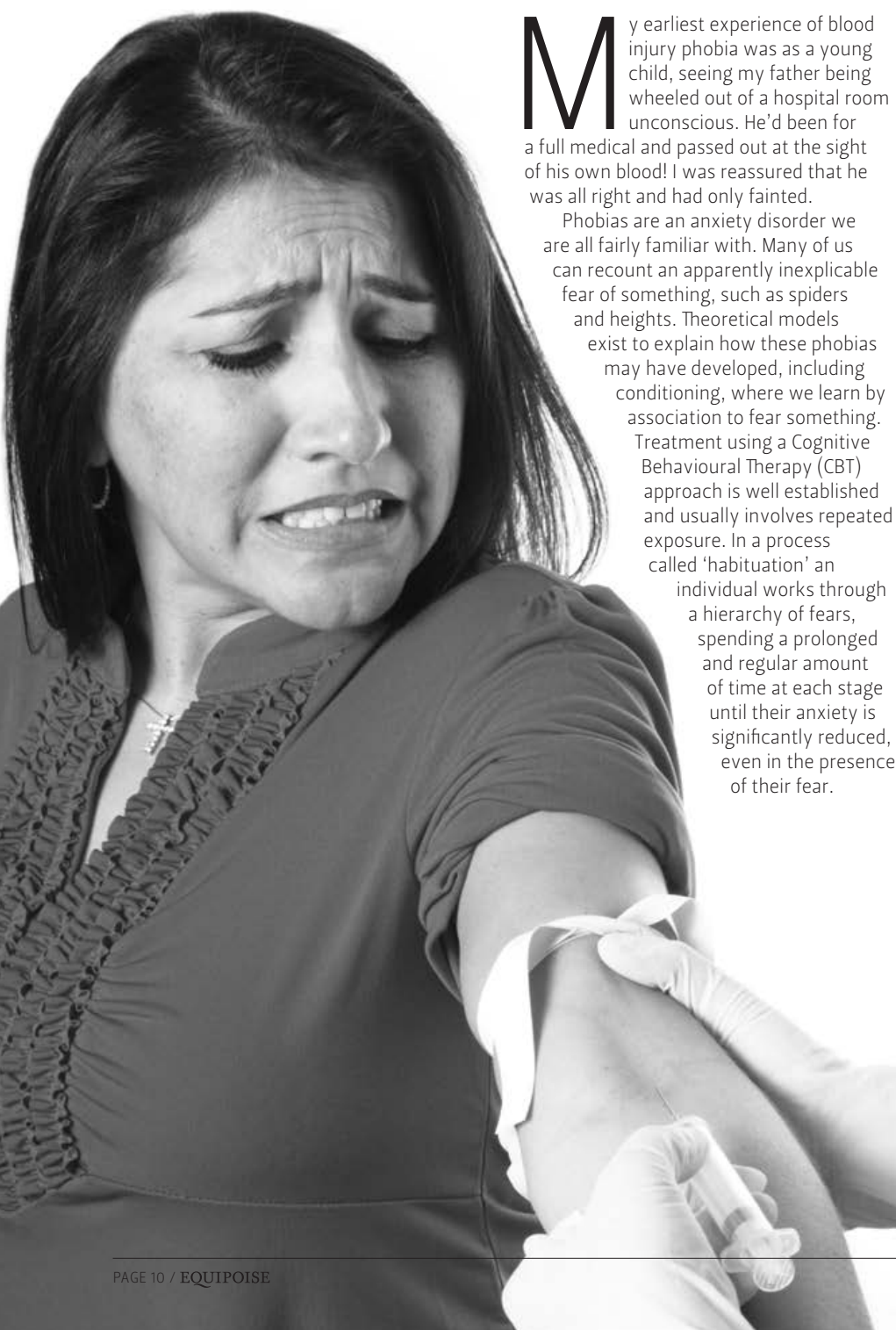
Dr. Tracy Lightfoot's research interests are in cancer epidemiology, particularly haematological malignancy and childhood cancer. She is programme leader for the Department of Health Sciences innovative distance-learning MSc course in Haematopathology: www.york.ac.uk/healthsciences/gradschool/masters/msc-haema/

He also proposed the cellular theory of the origin of leukaemia, which has been fundamental to present-day understanding of the condition. At the time, controversy surrounded the claim that leukaemia was a separate disease, but as the number of case reports increased along with pathological and clinical details, it gradually became accepted in its own right.

A further breakthrough came at the end of the 18th century with the discovery that bone marrow was the source of blood formation, and leukaemia was recognised as a disease of the bone marrow, with the myelogenous subtype added to the

BLOOD INJURY PHOBIA

A UNIQUE AFFLICTION



My earliest experience of blood injury phobia was as a young child, seeing my father being wheeled out of a hospital room unconscious. He'd been for a full medical and passed out at the sight of his own blood! I was reassured that he was all right and had only fainted.

Phobias are an anxiety disorder we are all fairly familiar with. Many of us can recount an apparently inexplicable fear of something, such as spiders and heights. Theoretical models exist to explain how these phobias may have developed, including conditioning, where we learn by association to fear something. Treatment using a Cognitive Behavioural Therapy (CBT) approach is well established and usually involves repeated exposure. In a process called 'habituation' an individual works through a hierarchy of fears, spending a prolonged and regular amount of time at each stage until their anxiety is significantly reduced, even in the presence of their fear.

Blood injury phobia (sometimes called needle phobia), is one of the most common phobias (Ost & Sterner, 1987). An initial surge of anxiety raises the heart rate and blood pressure, but unlike all other phobias, a rapid drop then occurs (vasovagal syncope) and this does actually lead to fainting. It is thought that this is an evolutionary response developed to reduce the risk of injury (Antony & Watling, 2006). This clearly has significant implications for treatment.

Triggers to this response are many and varied. An example I recall vividly was when I was teaching a fairly new group of students approaches for working with phobias. After setting them all going to develop their ideas, I noticed one of them was looking rather pale. He had been keen to look at treatment for blood injury phobia because he himself was a sufferer, but the mere mention of the word 'blood' had activated a reaction in him. We rapidly left the classroom, sat down together and he was given a very practical demonstration, which he immediately put into action, of a key element of treatment for this phobia: applied tension (Ost et al, 1989). In applied tension, the individual learns to tense the muscles in their body, arms and legs. The process is not unlike applied relaxation but in reverse. His colour rapidly improved, and he was left highly convinced of the effectiveness of this approach and of his need to address his phobia!

Blood injury phobia can be very serious and even life threatening, as the fear of blood, and associated cues (including needles), can mean vital treatment is avoided. In my clinical practice I have worked with people with diabetes, and other chronic conditions, who would rather neglect their health than have to put themselves through the trauma of a medical procedure. Exposure, used in conjunction with teaching people to use applied tension to raise their blood pressure is an effective treatment to help people overcome this phobia. The challenge is to raise awareness, so that people seek treatment and do not damage their health through fear and lack of understanding.

Megan Edwards delivers CBT courses at the University of York, she has a special interest in CBT for physical health problems, Body Dysmorphic Disorder and the role of shame on the development and maintenance of psychological health problems. She is in practice in Liaison Psychiatry one session per week and is developing a new programme for CBT in long-term conditions.



ATTENTION HEALTH SCIENCES ALUMNI

The Department of Health Sciences is very pleased to be able to announce the launch of its new Alumni Engagement Strategy to complement the University's newly launched service for alumni, YorkSpace (www.yorkspace.net). This includes a new website dedicated to Health Science alumni and mailouts to those alumni for whom we do not have an email address.

We are very keen to link up with former students and staff, to hear success stories and interesting career routes, and those unexpected twists and turns which happened post education. Have you achieved a long-held ambition in the field of Health Sciences? Have you changed direction completely? Are you thinking of returning to study? Have you worked in an exotic or far-flung destination? Do you have any advice to offer our current

students? We want to hear from everyone with a story to tell us about what happens to our students once they leave York.

If you are interested in reconnecting with the department, there are a variety of ways you can do so, through the website (www.york.ac.uk/healthsciences/alumni), via the Facebook page (www.facebook.com/YorkHealthSciencesAlumni), through YorkSpace (www.yorkspace.net) or via email (dohs-enquiries@york.ac.uk).

If you do decide to reconnect with us we will endeavour to keep you updated with exciting developments in the department, key new areas of teaching and research and changes which we think will be of interest. At the same time we hope that you may find some old friends and familiar faces as well as broadening your network of contacts in the future.

If you have any suggestions for topics that interest you as an alumnus, or anything you would like featured in future articles, please contact us at dohs-enquiries@york.ac.uk.

NOTES, REFERENCES AND FURTHER READING

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Funded postgraduate study opportunities

The Department of Health Sciences at the University of York has a number of **PhD study opportunities** available to begin **October 2013** for talented students.

Reducing Tobacco Use in South Asians (ref: PHD2013SID)

Applications are invited for a full-time 3-year PhD studentship in tobacco control research in south Asians, funded by NHS Leeds and hosted within the Department of Health Sciences at the University of York, commencing October 2013. This PhD will be supervised by Dr Kamran Siddiqi.

Healthcare Inequalities Research (ref: PHD2013DOR)

Applications are invited for a full-time 3-year PhD studentship in health care inequalities research, funded by the University of York and hosted within the Department of Health Sciences, commencing October 2013. This PhD will be supervised by Professor Tim Doran.

Medical and Nursing Student Socialisation and Identity Formation (ref: PHD2013ALL)

Applications are invited for a full-time 3-year PhD studentship in Health Sciences/Health Services Research funded by the University of York and hosted within the Department of Health Sciences, commencing October 2013. This PhD will be supervised by Professor Helen Allan.

Visit the Department of Health Sciences website:

www.york.ac.uk/healthsciences/gsp



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