

Rivers of Fire - The untold story of neuropathic pain

27 August 2002, The Body Worlds Exhibition, London

Rivers of Fire was hosted by the Neuropathy Trust and held at the unusual but fascinating Body Worlds exhibition. Some of the country's leading diabetes, neurology and pain management specialists met with journalists at this important briefing to discuss the untold story of neuropathic pain.

The purpose of the meeting was to raise awareness of neuropathic pain amongst practitioners, via healthcare media, offering practitioners solutions for sharing both the management and the burden across both primary and secondary care.

A Growing Concern

Tony Dickenson, Professor of Neuropharmacology at University College, London clarified the size of the issue:

- There are 2 billion chronic pain days world wide
- Chronic pain affects two thirds of people over 65
- There are over half a million sufferers of neuropathic pain in the UK.

Dr Steve Allen, a Pain Consultant from the Royal Berkshire Hospital discussed the burden of mismanagement of neuropathic pain. As one example, he cited the fact that patients with chronic pain use health services 5 times more than the general population.

Dr Solomon Tesfaye highlighted poor glycaemic control as one of the most common causes of neuropathic pain, and that since the incidence of diabetes is set to rise dramatically over the next few years, the incidence of painful diabetic neuropathy is set to rise with it. Interestingly, Dr Tesfaye noted that the tightening of glycaemic control might not relieve the pain once established.

According to Dr Simon Ellis, Consultant Neurologist and visiting Professor in Neuroscience at Staffordshire University, the number of neuropathic pain sufferers is set to increase to one million by the year 2010.

The Patient Perspective

Neuropathic pain has a profound impact on quality of life; leading in some cases to a myriad of secondary conditions including depression, sleep disturbance and impaired physical and psychological functioning.

Andrew Keen from the Neuropathy Trust gave a powerful insight into the real impact this level of suffering has on patients' lives. A history of misdiagnosis and long waiting periods for referral to pain clinics leads to years of private, hidden suffering.

So profound was the sense of frustration and helplessness that Andrew was motivated to establish the Neuropathy Trust. Andrew firmly believes that even a modest increase in the awareness of neuropathic pain and peripheral neuropathy amongst healthcare professionals could go a long way to alleviating this suffering.

What Help is Available?

Dr Allen explained that the main goals of therapy are to reduce the pain as much as possible, to support the patient in coping with this pain during therapy and to improve their physical mobility and quality of life. To achieve this, a rational treatment approach must be developed. He highlighted that:

- In recent years a number of neuropathic pain treatments have



Dr Steve Allen at the Body Worlds Exhibition in London

been proven effective in large-scale clinical trials, and licensed therapies do now exist.

- The tricyclic antidepressants have historically been a first line although they are not specifically licensed for the condition
- Anticonvulsants have also been used
- Gabapentin is licensed for the treatment of all types of neuropathic pain
- More complex cases of neuropathic pain may require a multi-modal approach including adjunctive therapies such as transcutaneous electrical nerve stimulation (TENS), acupuncture, reflexology and in severe cases cognitive behavioural therapy

He concluded by stating that "Education of all those involved to understand the abnormal physiology and to use appropriate therapies will lead to significantly improved patient care."

A Role for Primary Care

As was the case with Andrew Keen, most patients visit their GP as the first point of call. Dr Nigel Higson, A GP from Hove and Chairman of the Primary Care Virology Group, explained the varying levels of understanding of the condition that exists in general practice. He agreed that whilst a tremendous effort would be required for

GPs to gain a deep understanding of neuropathic pain, they still have an extremely important role to play. In particular:

- Conditions such as trigeminal neuralgia, painful diabetic neuropathy and post herpetic neuralgia can and should be easily diagnosed in primary care
- These specific types of neuropathic pain can be treated with specifically targeted drugs
- Perseverance with traditional analgesics is rarely the answer
- Early referral to a pain specialist must also be considered when such treatment proves ineffective
- With increased awareness, and use of the appropriate course of treatment, GPs could achieve more for their patients, without necessarily increasing their workload
- When incorrectly managed the secondary symptoms such as sleep interference and depression are likely to increase a GP's workload

Dr Higson's final message to GPs was "If you can see it is neuropathic, treat it - if you can't treat it, see it as neuropathic."

The Neuropathy Trust is committed to a better future for all sufferers of peripheral neuropathy and neuropathic pain. Through education and communication to patients and healthcare professionals, the aim of the Trust is to raise awareness of these conditions and provide a lifeline to all sufferers.

For more information on the Neuropathy Trust please visit www.neurocentre.com, email rof@neurocentre.com or alternatively or send a medium sized SAE to The Neuropathy Trust, PO Box 26, Nantwich, Cheshire, United Kingdom, CW5 5FP.

Rivers of Fire was sponsored by an educational grant from Pfizer Ltd. With thanks to the Body Worlds Exhibition for our front cover picture

Stem Cells: Prospects for Research and Therapy

11 September 2002, London, UK

Key Points:

- ❑ Stem cells hold considerable therapeutic promise, but much more research is needed before they can be considered for clinical application
- ❑ The MRC is leading a co-ordinating national stem cell strategy that involves other relevant Research Councils and charities, regulatory agencies, the scientific and clinical community, patients, the public and industry
- ❑ The first national stem cell bank is to be established at the National Institute for Biological Standards and Control (NIBSC) in Hertfordshire in order to allow both academic and clinical access to ethically approved and quality controlled stem cell lines from a variety of sources
- ❑ This MRC initiative, along with the prioritisation of government funding for stem cell research and favourable legislation, should place the UK in a leading position in this exciting area of science

Stem Cells: Prospects for Research and Therapy was held at the Millenium Gloucester Hotel in London, a very comfortable venue for what turned out to be an exciting and positive discussion about the future of stem cell-based therapies. The event was led by the Medical Research Council (MRC), and co-sponsored by the Biotechnology and Biological Sciences Research Council (BBSRC) and the Economic and Social Research Council (ESRC). It aimed to showcase UK developments in this new field, including the newly announced MRC-funded stem cell bank in Hertfordshire, which will be co-sponsored by the BBSRC and has full backing of the UK government. This bank will enable academic, clinical and industrial access to ethically sourced, quality controlled, new and existing stem cell lines of all types; adult, fetal and embryonic. A panel of highly distinguished speakers was present giving a varied perspective on the wide range of issues (including politics, ethics, religion, regulation and fundamental and clinical research challenges) that must be considered in order to promote activity in stem cell work in the UK. Approximately 400 delegates attended this high profile event, including members of the research and clinical communities, research councils, charities, patient groups such as the Parkinson's Disease Society (PDS) and the Alzheimer's Society, consumers, representatives from pharmaceutical companies and from pro-life groups plus the media.

Lord Sainsbury, the Minister for Science and Innovation introduced the meeting and gave an account of the investment being made by the government into science and the government's interest in the potential of stem cell research; he announced the creation of 12 new career development fellowships dedicated to this field of interest, which will be jointly funded by the MRC, BBSRC, Alzheimer's Society, Parkinson's Disease Society, Diabetes UK, plus the Juvenile Diabetes Research Foundation of America. Professor Sir John Pattison from the Department of Health (DOH) then gave a brief history of the development of legislation for stem cell research and indicated how the DOH plans to work closely alongside the MRC in order to promote the success of the stem cell bank. He discussed how the UK was becoming the obvious home for stem cell research, due to its existing research infrastructure, its promotion of stem cell research as a priority for funding and its balance of regulatory impositions. An overview of the UK stem cell initiative was given by Professor Sir George Radda, the Chief Executive of the MRC, who stressed the importance of collaboration, partnerships, co-operation and communication with a range of stakeholders. He also outlined the planned operation of the UK stem cell bank, how it will be funded and governed, including the appointment of a high level steering committee to be chaired by Lord Patel, and in general terms spoke about the practicalities of the facility, such as the banking of samples, quality control and the accessibility of cell lines from the bank. In addition, Professor Dr Ron McKay from the National Institute of

Neurological Disorders and Stroke, Bethesda, USA, a international figure in the scientific stem cell arena, presented an elegant and considered overview of the potential of stem cells in research and therapy, and highlighted the scientific challenges facing the field.

The second session focused on governance of discovery and development and started with Mrs Suzi Leather from the Human Fertilisation and Embryology Authority (HFEA), who talked about how embryo donation for research will be controlled and the importance of informed donor consent.

The National Institute for Biological Standards and Control (NIBSC) in Hertfordshire, an agency that assures the quality of biological medicines, has been chosen as the home of the UK Stem Cell Bank. Dr Stephen Inglis and Dr Glyn Stacey from this facility described how they intend to manage the bank given their unique expertise in safety monitoring of human therapeutics, prior experience of cell-banking and experience in standardisation. Mrs Elizabeth Allanson from the Medicines Control Agency, the regulatory body that evaluates and accredits standards of Good Manufacturing Practice (GMP) in the UK, discussed a system of accreditation that should come into force in April 2003, that will provide the general public with the assurance that tissues and stem cells are handled in accordance with an appropriate quality control system. A clear message from these presentations was the high degree to which the success of the bank will depend on a two-way dialogue between the staff at NIBSC and the researchers and clinicians working with stem cells. The UK bank intends to store and make available non-GMP lines for basic research purposes and standardised GMP lines for use in clinical applications. Good practise controls will need to be implemented during the selection and retrieval of tissue, during testing and processing and finally during storage and delivery of the GMP lines to ensure consistency and quality; a monumental task given the inherent variabilities that exist! The morning session was concluded by some valuable and thought provoking discussions on the ethics and morals of stem cell research by Professors Ruth Chadwick from Lancaster University and Robin Gill from the University of Kent at Canterbury (both of whom were members of the MCR Stem Cell Bank Advisory Committee).

In the afternoon, the talks moved on to the importance of stem cells in basic research. Professor Nadia Rosenthal from the European Molecular Biology Laboratory in Monterotondo, discussed how the expression of insulin growth factor1 (*IGF1*) via a muscle specific transgene is able to mobilise stem cells in the bone marrow following injury to muscle, and how these stem cells can migrate specifically to the site of damage in order to induce some repair. Professor Cheryl Tickle (University of Dundee) highlighted the importance of basic developmental biology for enhancing our understanding of stem cells and their differentiation, since embryos are the natural environment of

stem cells and the construction of tissue and organs occurs here. Professor Roger Pederson, who moved from the USA to the University of Cambridge on an MRC International Appointment in order to continue to study embryonic stem (ES) cells, described his work with human ES cells, and in particular the definition of conditions that encourage them to differentiate into clinically useful cell types, for example, pancreatic b cells for the treatment of diabetes and cardiomyocytes for heart disease. The Director of Research and Development of the company Stem Cell Sciences UK, Dr Tim Allsopp, discussed the potential of human ES cells in high throughput screening for the purpose of drug discovery; in particular, the generation of healthy cells for research, healthy patient-specific cells for the treatment of disease and disease-specific cells for drug discovery.

The clinical session commenced with a presentation on haematopoietic stem cells, one of the most well characterised stem cell systems, by Professor Tony Green (Department of Haematology, Cambridge). In a series of very elegant studies he described how the position of the regulatory element (the +19 enhanceosome) for the stem cell leukaemia (SCL) gene (known to have an important role in the specification of haematopoietic stem cells, which give rise to all the cell types of the blood), was elucidated and the discovery that a complex of 3 proteins was required to bind to this key enhancer in order to activate it. This was followed by another presentation on the haematopoietic system from Dr Adrian Thrasher from Great Ormond Street Hospital, who went on to discuss how patients with severe combined immunodeficiency syndrome (SCID), have been treated with stem cells derived from the bone marrow that have been genetically modified to express the cytokine receptor gamma (gc) chain, a mutation in the gene of which causes X-linked SCID.

The potential for treatment of neurological diseases has been an area of intense interest and Professor Anne Rosser (University of Wales College of Medicine), described results of the ongoing MRC-funded trial of neural transplantation in Huntington's disease in the UK, and how the numbers of patients treated with this devastating inherited disorder could be vastly increased by the application of stem cells. Finally, Dr John Sinden, the Chief Scientific Officer at the company ReNeuron, discussed the development of stem cells lines from fetal and adult sources which he believes represent the the closest route to clinical application; he also announced that his company was keen to deposit such lines in the UK stem cell bank.

An anticipated highlight of the conference was a talk by the actor Christopher Reeve, to give the patient's perspective on stem cell research and treatment. This had been pre-recorded,

but unfortunately on the day of the conference, the video failed to arrive, so a disappointed audience was treated to a few selected quotes from the transcript. Mr Reeve, having suffered a riding accident 7 years ago leaving him with severe spinal cord injury and quadriplegia, was quoted as saying "some people are able to accept living with disability, I am not one of them". "We should push politics and economics aside and let science proceed", he went on, demonstrating the devastation caused to the lives of patients suffering with such disabilities and the huge support for research to continue. Mrs Linda Kelly, the chief executive of the Parkinson's Disease Society, stepped in at short notice to speak eloquently about the work of the society and the importance of stem cells research to patients suffering with Parkinson's disease.

The meeting was concluded with an interactive question and answer session between the audience and the speakers in which a number of issues were raised; for example, about both the ethics and practicalities of embryo donation, about the merits of adult versus embryonic stem cells and about raising the expectations of the public too soon regarding the therapeutic outcomes of the research. Not often does a topic of scientific research lead to such prolific social, political and media interest, but overall one came away from this meeting with the feeling that, although there are still fundamental scientific questions to be addressed, and despite the considerable ethical concerns about some of the stem cell sources, there exists the political, social and scientific will to allow the potential of stem cells for the treatment of disease to be fully developed in years to come.

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Further reading on stem cells:

- Weissman IL *et al.* (2002). *Stem cells-scientific, medical, and political issues.* N.Engl.J.Med.346:1576-79
 Prockop DJ (2002). *Adult stem cells gradually come of age.* Nature News and Views 20:791-2
 Anderson DJ (2001). *Stem cells and pattern formation in the nervous system. The possible versus the actual.* Neuron 30:19-35
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 Weissman IL (2000). *Translating stem and progenitor cell biology to the clinic: barriers and opportunities.* Science 287:1442-46
 Pedersen RA (1999). *Embryonic stem cells for medicine.* Sci Am. 280:68-73

The Christmas Symposium 2002 The Human Genome Project: what can it do for neuroscience?



An afternoon and evening of talks and discussions exploring this exciting topic and its potential impact on neuroscience

Wednesday, 11th December, 2002

2.00pm to 6.00pm

At the Sir Alexander Fleming Lecture Theatre, Imperial College, Exhibition Road, London, SW7

Chaired by **Nancy Rothwell** (Manchester) and **Ruth McKernan** (Merck)

Steve Brown (MRC Genetics Unit, Harwell) Mutagenesis in the mouse: towards new models of neurological disease

Tony Bailey (Institute of Psychiatry, London) 'Deep amidst the genome: identifying autism susceptibility loci'

David Porteous (Edinburgh) Cracking the nut of psychiatric genetics

Sabine Bahn (Babraham) Gene expression in complex neuropsychiatric disorders: new approaches to old problems

Jonathan Flint (Oxford) Anxious genes

During the afternoon, Nancy Rothwell, President of the BNA, will present the BNA Awards for 'Public Service' to Majorie Wallace (SANE) and for 'Contribution to British Neuroscience' to Richard Morris (Edinburgh).

A 'seasonal' reception follows for all our delegates to attend.

Admission will be FREE for BNA members and BNA student members (non-members £30) but tickets MUST be obtained in advance.

Email: events@bna.org.uk to reserve your ticket. These will be distributed with the final programme, venue map and travel details in November.

Members will be allowed to bring ONE additional person each as a guest.

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