



IN THIS ISSUE FIND ABOUT

10TH ANNIVERSARY OF
THE TISSUE BANK AND
THE PROGRESS MADE

WHERE THE TISSUE BANK
HAS RELOCATED

CHANGES IN THE TISSUE
BANK'S ORGANISATION

NEW RESEARCH PROJECTS
SUPPORTED BY THE
TISSUE BANK

We have moved!

The Bank Statement

OF THE UK MULTIPLE SCLEROSIS TISSUE BANK

4

JANUARY 2009

Welcome to the fourth issue of our newsletter, designed to bring you up to date with what is happening at the Tissue Bank. Whether you are already a registered donor, still considering registering as one, or a relative or friend of someone who has donated tissue, we hope that The Bank Statement 4 makes for interesting reading.

On our 10th Anniversary in March this year the Tissue Bank was relocated. We moved into brand new, purpose built laboratories at the Hammersmith Hospital Campus of Imperial College, together with other neuroscience research groups previously based at Charing Cross Hospital.

The new address and telephone numbers for the Tissue Bank are >>>

**The UK Multiple Sclerosis Tissue Bank
Division of Neuroscience and Mental Health
Imperial College London
Hammersmith Hospital Campus
Burlington Danes Building
160 Du Cane Road
London W12 0NN
Tel. 020 7594 9734
Fax. 020 7594 9735**

Our e-mail and web page address stay the same –

ukmstissuebank@imperial.ac.uk
www.ukmstissuebank.imperial.ac.uk

The **emergency donor line number** stays the same

07 659 132 045

Please remember: only use this number to activate **an immediate 24h response** from the Tissue Bank.

10th Anniversary of the Tissue Bank

Anniversary

0th

Tissue Bank
 1 national tissue bank
 2 programme grants
 10 years in existence

In 1998 The MS Society established the Tissue Bank to operate as a facility for people living in Great Britain and Northern Ireland who want their tissue to be used in research into MS. By choosing to donate their tissue after death to research, people with MS and people without the

condition provide an invaluable resource for scientists whose meticulous research into what causes MS and how to treat it is totally dependent on human tissue. Over the past decade we have successfully grown into a truly national and international Tissue Bank. Our donor scheme covers all of the British Isles and tissue is supplied to research projects not only here but also across the world, from Japan to North America. Such success has only been possible because of the foresight and personal investment in MS research of all the individuals who chose to donate their tissue as well as their family members who assisted us in this process. It is also due to the enduring commitment of all the members of our team and generous funding from the Multiple Sclerosis Society of Great Britain and Northern Ireland. The funds were provided in five-year programme grants and so far the Tissue Bank has been successful in securing two of these. We are currently awaiting news about our application for the third five-year term.

We have promoted the Tissue Bank in different ways: notably by writing articles and giving talks about MS and research to groups and at conferences. The MS Tissue Bank

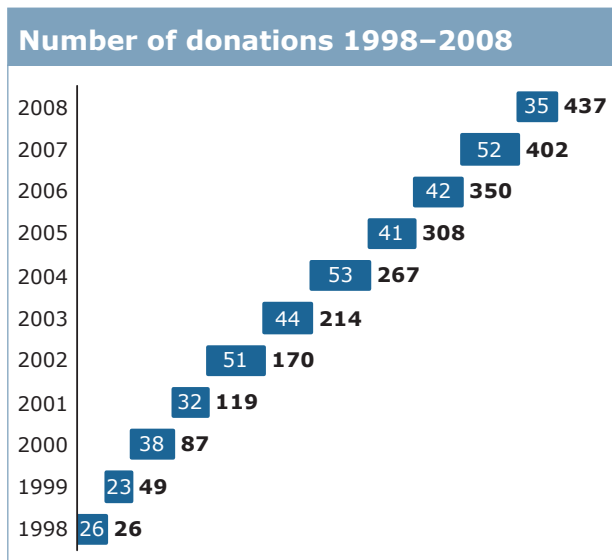
Anniversary

0th

Donor scheme
 5,342 registration packs
 3,678 registered donors
 437 tissue donations

has explored various ways of raising the awareness of multiple sclerosis and the importance of using human tissue for research. Most popular with groups and at conferences have been talks about multiple sclerosis and the very latest research, presented by key members of the

Tissue Bank Team on a voluntary basis. Another effective way of raising the profile of the Tissue Bank and of recruiting individuals onto its prospective donor scheme has been through articles in MS Society publications such as *MS Matters*, *TeaMSpirit* and *Research Matters*. We continue to work closely with the MS Society so that its members can learn more about the work of the Tissue Bank and, should they wish, find out how to go about making their own significant contribution to research. This has resulted in people across the whole of the UK registering on our donor scheme. We are proud of the fact that, to our knowledge, ours is the **largest brain tissue donor scheme** in operation in the UK and Europe.



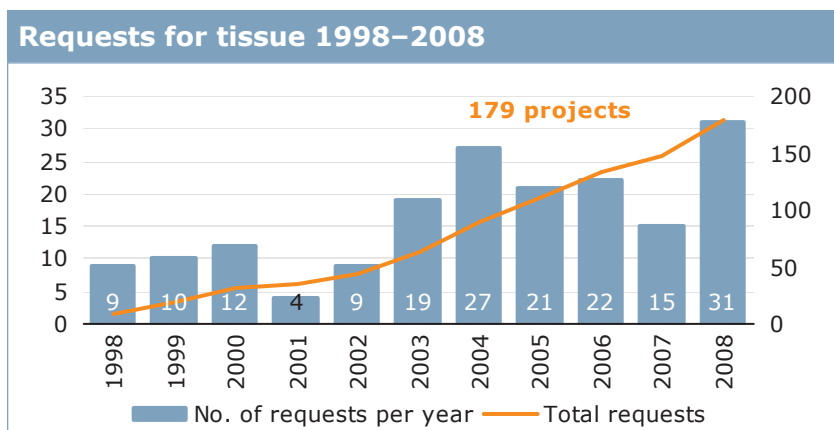
So far 5,342 individuals have been supplied with a Registration Pack and 3,678 people have registered as donors. The majority of individuals who wish to bequeath their brain and spinal cord to research are people living with MS (76%). However, it is also essential to receive control tissue from people who do not have MS. In an effort to recruit people without MS onto our donor scheme, we carried out a survey of the general public to find out what information the Tissue Bank could provide to make the process of tissue donation clearer.

We wrote about this in MS Matters and, as a result of this single article, 143 people registered as donors, one third of whom did not have MS. The graph on the left shows the rate at which we have accrued tissue over the last 10 years from 390 donors that had MS and 47 subjects without the condition. The specialised ways in which we process and preserve tissue ensure that the material will remain useable for many years to come and will be suitable for use in a wide range of research projects. Many of you have asked when we expect to have enough tissue and how much more tissue we need to collect. We do now have a considerable number of samples, which are continuously being requested worldwide. Demand for the high quality of tissue that we hold is increasing as researchers exploit the ever-changing clinical and pathological knowledge of multiple sclerosis in order to develop increasingly complex therapies.

0th Anniversary
Samples for research
 127 research groups
 179 research projects
 International resource

That is why **it is vitally important to keep collecting.** To date, the Tissue Bank has supplied a total of 6,442 individual tissue samples for use in research. These samples have been supplied to a total of 127 research groups working on 179 research projects. Of the 179 projects, about two thirds (69%) are being carried out within the UK, 22% in the European Community and the remainder (9%) in the rest of the world. We have become the major supplier of MS tissue in Australia and have now assisted in the setting up of an MS tissue bank in Sydney.

The rate at which these requests for tissue were received by the Tissue Bank is shown in the graph on the right; the line shows the progressive rise in the number of requests for tissue and the bars indicate the number of requests received each year.



You can clearly trace a general rise in the number of requests received each year over the past 11 years. The distribution of this vast amount of material to a wide range and large number of studies demonstrates the effectiveness of the Tissue Bank in achieving its primary aim of supporting research into multiple sclerosis. In a recent survey our tissue users gave a high rating to their contact with the MS Tissue Bank and the quality of samples we supplied for their research projects. Without doubt the Tissue Bank is becoming an important European and International tissue resource for research into multiple sclerosis. What is more important is that this also translates into better research into the causes and treatment of MS. To date over 50 publications have resulted from this research, many of which have substantially changed the way we think about MS.

Changes in the Tissue Bank Team

0th Anniversary
Changes
 New team
 New strategies
 Joint tissue bank

In March 1998, Dr Abhi Vora was appointed to manage the new UK Multiple Sclerosis Tissue Bank. After nine years during which he shaped the successful operation, Abhi accepted a new challenge and moved to the Society for Endocrinology in Bristol. Abhi said how honoured he felt in having been able to help fulfil the wishes of all those who had bequeathed their tissues

to research. During time at the Bank, Abhi gave over 100 presentations at meetings of local branches of the MS Society. He said he had learnt so much about 'life' from meeting people living with MS and their families. We are very pleased that Dr George Gveric took over management of the Tissue Bank in January 2008. George has a long history of conducting research into MS using material donated by tissue donors. In fact George used to work at the previous MS tissue bank located at Queen Square in London.

Most recently our team has been strengthened by the arrival of Dr Bishan Radotra, who provides us with full-time neuropathology support and expertise. Research technicians, Ms Nirali Patel and Mr Iyob Ghebrenegus, also moved to new positions. They have been replaced by three new research technicians – Ms Natalie Woodman, Ms Claire MacDonald and Ms Julia Steele. They continue the excellent work that Nirali and Iyob carried out at the Tissue Bank by ensuring that tissue procurement and distribution to research groups are carried out in a timely and accurate manner.

Mrs Sue Fordham continues her sterling work as Administrator and Professor Richard Reynolds oversees the entire operation as the Scientific Director and Principal Grant Holder.

Tissue Bank Team •

Directors



Professor Richard Reynolds
Scientific Director



Dr Richard Nicholas
Clinical Director

Management



Dr George Gveric
Tissue Bank Manager



Mrs Sue Fordham
Administrator

Neuropathology Team



Dr Federico Roncaroli



Dr Stephen Gentleman



Dr Bishan Radotra

Technical support



Natalie Woodman



Claire MacDonald



Julia Steele

In the near future we will be joining forces with our colleagues from the Parkinson's Disease Tissue Bank. A panel of experts, including representatives of both the Multiple Sclerosis and Parkinson's Disease Societies, recommended this move on the basis of common working practices and research goals. The new joint tissue bank will be an important source of human samples for research into both inflammatory (Multiple Sclerosis) and neuro-degenerative (Parkinson's) diseases of the brain. By keeping the majority of the MS Tissue Bank team on board we made sure that our donors will receive the attention they deserve. We envisage that a number of projects will use this resource to study how inflammation and neurodegeneration influence each other in multiple sclerosis, thus contributing to better understanding of the disease process (see the research projects below).

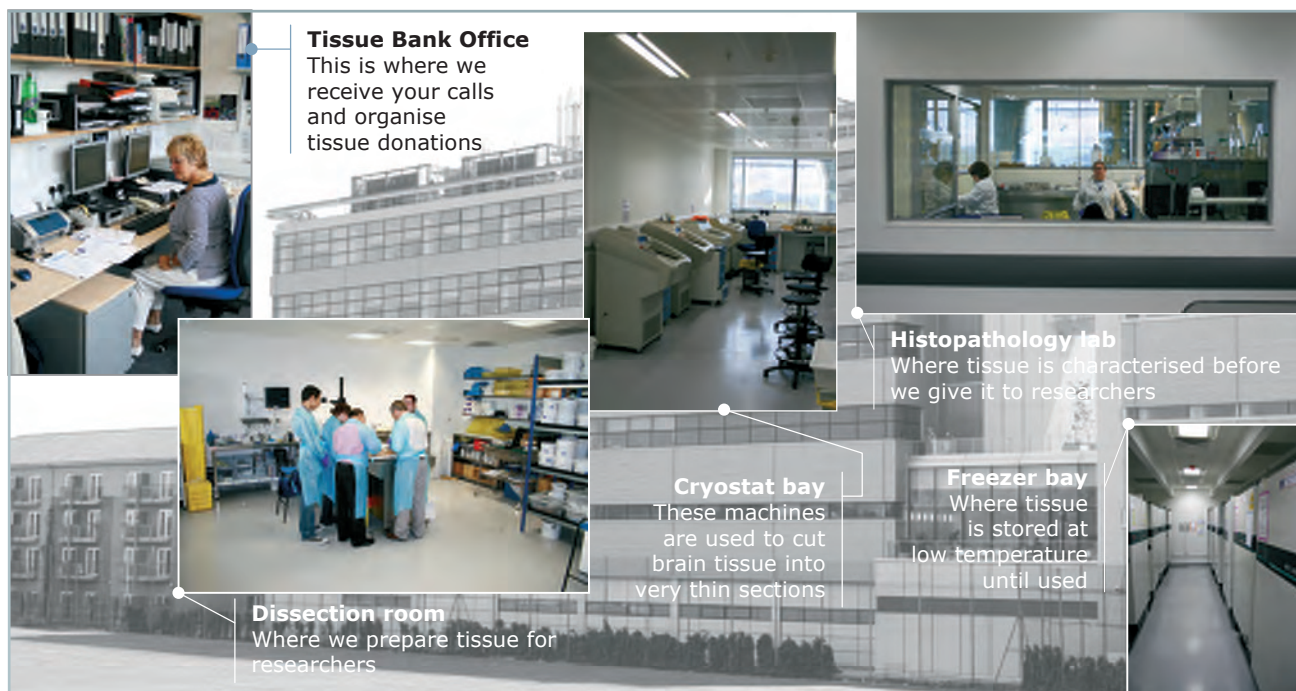
Where the Tissue Bank has relocated

In 2006, the Rector of Imperial College decided that the Tissue Bank together with other Neuroscience research groups based in Charing Cross Hospital should move to the Hammersmith Hospital Campus in White City. It took two years to implement this

decision and finally on 13 March 2008 the Tissue Bank moved into its new, purpose-built laboratories, funded by Imperial College and the Wolfson Foundation.

The new premises are shared with the Parkinson's Disease Tissue Bank and provide us with opportunities to better interact with other research groups working on the brain, which is crucial to finding technical solutions to many of our tissue banking problems.

It is often said that a picture is worth a thousand words so here is a collage of the layout, new laboratories and offices.



Tissue Bank Office

This is where we receive your calls and organise tissue donations

Histopathology lab

Where tissue is characterised before we give it to researchers

Cryostat bay

These machines are used to cut brain tissue into very thin sections

Freezer bay

Where tissue is stored at low temperature until used

Dissection room

Where we prepare tissue for researchers

New science projects supported by the Tissue Bank

The main role of the tissue bank is to support MS research that will lead to the prevention of MS and development of new drugs. The three latest research projects of the 179 projects that the Tissue Bank has supplied with tissue are interesting examples of how research is currently progressing. Each of these particular projects is being carried out in the UK and illustrates how research using human tissue is uncovering and piecing together new information. It has long been known that in MS there is evidence of damage to myelin, often referred to as white matter. Evidence is now emerging that nerve cells in the grey matter are also damaged. Moreover, the slow progression in disability experienced by many people living with MS may actually be due to the destruction of these nerve cells. The first project provides some evidence of how nerve cells may be damaged while the second project demonstrates nerve cell loss in an area of the brain concerned with memory. Normally the sensitive cells of the brain are protected from potentially harmful substances present in the circulation of the blood by the so-called blood-brain barrier. The third project actually shows the breakdown of this barrier within the MS brain.

10th

HOW ARE NERVE CELLS DAMAGED IN MS?

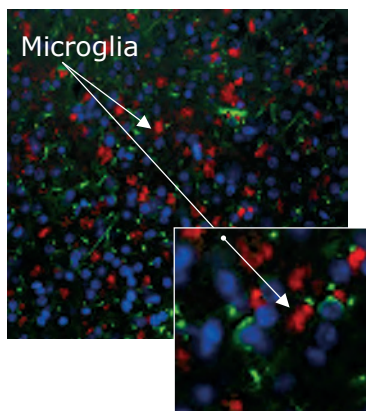
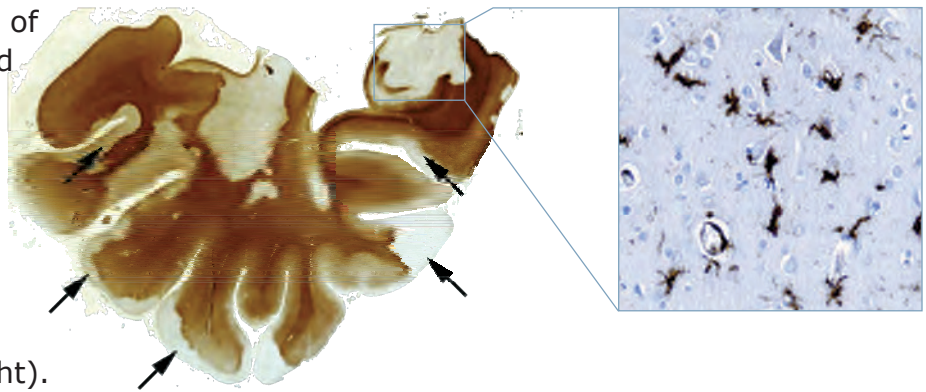
PROFESSOR SETH LOVE

INSTITUTE OF CLINICAL NEUROSCIENCES
UNIVERSITY OF BRISTOL

Although MS was long regarded as a disease that mainly affects white matter, recent studies have demonstrated **extensive loss of myelin in the outer layers of cerebral cortex** in most patients. The image of a section of brain from a MS patient has been

labelled with an antibody to a myelin protein (brown colour). The cerebral cortex (grey matter) runs along the surface of the brain, and this region is extensively demyelinated, as shown by the patchy loss of brown staining (arrows)

(the arrows indicate some of the demyelinated regions of cortex). The demyelinated cortex contains large numbers of activated microglia, the resident inflammatory cells of the brain which when labelled with a specific antibody appear dark brown (picture on the right).



Professor Love and his colleagues have been interested in finding out how the nerve cells are damaged by the microglia. In particular, they have been investigating whether some of the damage results from **destruction of the perineuronal net** (a delicate layer of tissue that surrounds and protects nerve cells) by microglia and whether the damage also involves the generation of highly toxic reactive oxygen species, through the activity of an enzyme called myeloperoxidase. They have found that there is indeed loss of the perineuronal net, although some of this may be secondary to the death of nerve cells that the net surrounds; further work is in progress to clarify this.

In addition, Professor Love's team has demonstrated that the cortical plaques contain elevated levels of myeloperoxidase. When the team then labelled sections of cortical plaques with an antibody to myeloperoxidase, the myeloperoxidase was present in a subset of microglia. In the picture above, the microglia that contain myeloperoxidase are stained red, the astrocytes (scar cells) within the cortical plaque are stained green and the cell nuclei blue (Figure 3). The findings indicate that **reactive oxygen species** derived from activated microglia may be involved in cortical demyelination and damage to nerve cells in MS. It may be possible to prevent this damage using drugs that "dampen down" microglia.

10th

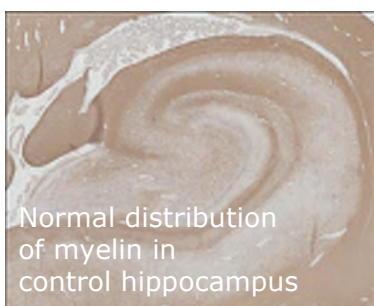
WHY IS MEMORY AFFECTED IN MS?

DR DIMITRI PAPADOPOULOS

DEPARTMENT OF CELLULAR AND
MOLECULAR NEUROSCIENCE
IMPERIAL COLLEGE LONDON

It has recently been recognised that cognitive deficits such as impairment of memory, verbal fluency and planning skills are common in multiple sclerosis. Approximately **40–60% of MS patients have some form of cognitive deficit**. It occurs in all disease types, and is often present from the early stages of

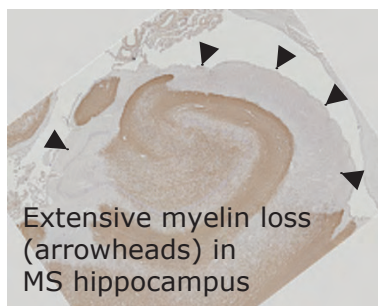
MS, sometimes despite minimal physical disability. Although physical problems are a fundamental aspect of living with MS, cognitive deficits can have a profound impact on the quality of life and patients own perception of the disability in both workplace and private life. The **most frequent cognitive deficit is memory impairment**. In MS it



Normal distribution
of myelin in
control hippocampus

is the memory of events, time and places and acquisition and storing of new memories that is most affected. This pattern of memory loss points to an area of the brain called the **hippocampus** (from Greek word for seahorse) which contains neuronal cells known to play a critical role in recording memories.

The studies of the MS hippocampus by Dr Papadopoulos show that this area is commonly



Extensive myelin loss (arrowheads) in MS hippocampus

affected by demyelinated plaques of varying sizes. In a group of 50 MS brains with disease durations ranging from 11 to 56 years, plaques were detected in 52% of samples and covered on average one third of the surface area suggesting that demyelination in the hippocampus is very extensive. Apart from myelin loss there was also a **significant loss of neuronal cells** in the hippocampus (50% of cells in plaques and 25% of cells in surrounding white matter) frequently coupled with **shrinking of the brain tissue**. The extent of neuronal loss was similar to that seen in dementias such as Alzheimer's, which strongly suggests that tissue shrinkage and neuronal loss in the hippocampus could be at least partly responsible for the memory problems seen in MS. These studies are aimed at better understanding the disease processes in the hippocampus and are vital for designing better drugs to prevent or treat cognitive deficits associated with MS.

10th

HOW CAN THE BRAIN BECOME SUSCEPTIBLE TO DAMAGE?

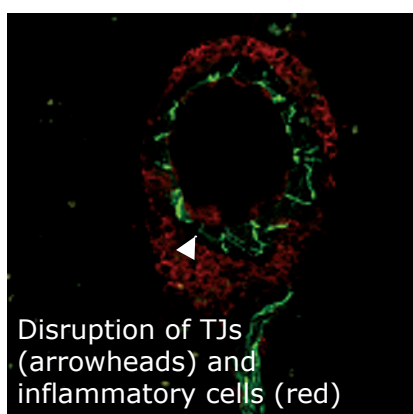
DR STEPHEN MCQUAID

TISSUE PATHOLOGY LABORATORY
ROYAL GROUP OF HOSPITALS, BELFAST

• In multiple sclerosis **leakage of blood vessels**

in the brain has consistently been demonstrated in both lesions and normal-appearing brain matter. In early MS, where this is most prominent, it is associated with and probably caused by inflammation. The protective 'barrier' role of the blood-brain barrier

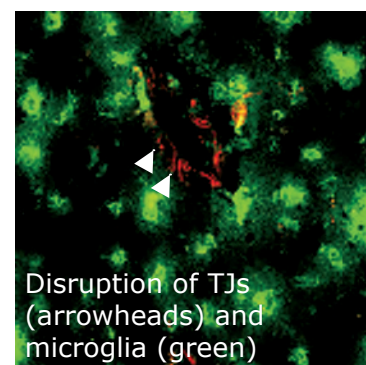
requires the presence of **tightly sealed joints (TJs)** between the cells that line the interior of blood vessels in a 'tile-like' formation. The accumulation of white blood cells and their migration through the walls of blood vessels, damage these crucial TJs. Vessels with imperfect joints are leaky to blood proteins and this is bad news for the nerve cells, the myelin sheaths and other cells of the brain, which require a tightly regulated environment in order to work properly. The importance of this process in MS is underlined by the fact that some **new therapeutic drugs** have been specifically designed **to prevent inflammatory cells sticking to blood vessel** walls and thus starting the inflammatory process.



Disruption of TJs (arrowheads) and inflammatory cells (red)

The McQuaid team has undertaken a series of microscopic studies on the two main clinical types of MS, primary and secondary progressive. As a result of this work we have identified **significant levels of abnormality in presence of TJs** at the blood-brain barrier in both actively demyelinating and chronic lesions and also in the normal appearing white matter that surrounds these lesions. In the two pictures below, very thin slices of MS tissues from lesions were stained with green or red dyes to detect the TJ proteins ZO-1 (left) or occludin (right) and with dyes that detect inflammatory cells.

In both examples disruption of the TJs (arrowheads) is associated with the presence of inflammatory cells (left) or with activation of microglial cells (right) in the brain. The presence of such **disrupted 'grouting'** at the blood-brain barrier in MS may play a role in continuing development of new lesions or in older lesions may contribute to the relative inefficiency of repair mechanisms. Future therapies that potentially would restore the damaged blood-brain barrier in



Disruption of TJs (arrowheads) and microglia (green)

MS may help to facilitate nerve cell protection (neuroprotection), remyelination and reduce that immune pathology that is considered to be so destructive in MS.

Enquires and contact numbers

General information: If you would like to find out more about the Tissue Bank or talk about donating tissue to research please ring our office number and speak to Sue or George. You can also call the MS Society helpline on 0808 800 8000. Alternatively send us an e-mail with your questions using the following address - ukmstissuebank@imperial.ac.uk or check our website.

Donor registration: If you are interested in registering on our donor scheme please request the Registration Pack. The Pack contains all the information you will need to decide whether registering is right for you, and all the forms that will allow you to register once you have made the decision. We even include a free-post envelope to return your signed forms.

Branch talk availability: Why not invite us to one of your branch meetings? We can explain what tissue banking is all about and talk about the latest MS research. We will also be glad to contribute an article to your branch newsletter.

Visits to the tissue bank: The tissue bank has an Open Day in in March, May, September and November (dates are flexible). The spaces are limited to a maximum of 15 persons and the visit has to be arranged through your local MS branch manager. Please note that disabled parking spaces are limited. For further details please ring us on 020 7594 7204.

What to do when your details change: If any details, such as your name, address, telephone number or your GP change please ring our office number 020 7594 9734 and inform us. Also please remember to update any change of details for your next-of-kin.

Emergencies: If you need an immediate response from the Tissue Bank or want to report the death of a donor please ring our 24-hour emergency number **07659 132 045**.

This *Bank Statement* was written by Abhi Vora and George Gveric. We thank Professor Seth Love, Dr. Dimitri Papadopoulos and Dr. Stephen McQuaid for presenting their research studies.



The Tissue Bank is most grateful to Merck Serono for generously meeting the cost of printing and posting *The Bank Statement*.