The Thomas Willis Oxford Brain Collection

The Thomas Willis Brain Collection is an initiative by the Clinical Neurosciences Departments of Oxford University and the John Radcliffe Hospital in Oxford.

The prospective collection of brain tissue for teaching and research has a long history in Oxford, and the Thomas Willis Brain Collection has evolved from the internationally renowned OPTIMA project (Oxford Project To Investigate Memory and Aging) that has been studying the clinical and pathological correlates of aging and dementia for almost 20 years.

Other areas of interest and close collaboration with clinicians within Oxford and the Thames Valley are the study of movement disorders such as Parkinson's disease and motor neuron disease. Brains from patients with demyelinating diseases such as multiple sclerosis are also part of the Collection. More recently, an appeal has been launched to raise awareness of the importance of brain tissue donation to help research into autism spectrum disorders, together with Professor Anthony Bailey from the Department of Psychiatry.

The aim of the Thomas Willis Oxford Brain Collection is to facilitate and encourage modern scientific research into the pathological and molecular basis of neuropsychiatric diseases by offering clinically and pathologically well-characterised brain tissue to local as well as national researchers who work with us on a collaborative basis.

The Collection is embedded within the Department of Neuropathology in the new West Wing of the John Radcliffe Hospital which opened in 2007 (left).

The Collection is partly funded by the NHS, the University and a grant from GlaxoSmithKline.

All tissue is held according to the standards set out by the Human Tissue Authority. The management board of the Collection comprises neuroscience consultants, scientists, members of the Oxford Hospitals bereavement team and a lay representative. Proposals for research on tissue held within the Collection are reviewed by the board and require approval by a local research ethics committee. (Olaf Ansorge).

Who was Thomas Willis ?

The Oxford Brain Collection is named after Thomas Willis, an enlightened Oxford Physician of the Seventeenth century who greatly advanced our understanding of the structure and function of the human brain. He and his colleagues at Oxford were amongst the first doctors to critically apply scientific methods to the study of brain diseases. He worked together with Christopher Wren who prepared beautifully detailed engravings of the anatomy of the brain. Wren later became London's most famous architect, designing St Paul's cathedral and many other landmarks.

Thomas Willis is most famous for the discovery of the ring of blood vessels at the base of the brain, known to this day as 'The Circle of Willis'. You can read more about Thomas Willis' life and times in the book 'Soul made Flesh' by Carl Zimmer, Heine-mann, London, 2004. (Olaf Ansorge).
Why do research on human brains?

Before recent advances in computer-aided imaging of the living brain the only opportunity available to us to examine a brain thoroughly was when it could be biopsied or removed after someone’s death and studied in such a way as to reveal any pathology that might have affected it such as a stroke, a tumour or a more subtle disease such as Alzheimer’s disease. This approach has led to major discoveries that benefit living patients to this day. Examples include the realisation that Parkinson’s disease is due to death of nerve cells that produce dopamine, a chemical that can be substituted for with an oral medicine; and that strokes are often the result of partial blockage of blood vessels in the neck that can be successfully operated upon.

What is the value of this approach to examining and investigating human brains after death in the light of rapid progress of non-invasive techniques and the decoding of the human genome?

While modern imaging techniques undoubtedly have revolutionised the diagnosis of many neurological diseases, their impact on the understanding of the cellular and molecular basis of underlying disease processes remains currently limited. Although there is great hope to be able to use specific molecules as imaging tracers, the identification and characterisation of suitable molecules largely depends on the direct study of brain tissue with modern biological techniques.

Similarly, while advances in genetics have helped to identify many mutations or genetic variations that cause, or contribute to the risk of developing, specific neurological diseases, the cascade of pathological changes in the human brain triggered by these genetic changes remains largely unknown.

Identification of a disease gene is nowadays generally followed by an attempt to model the disease process in laboratory animals. This has been very successful in identifying early pathological events in disease progression and possible targets for therapy. However, many models incompletely recapitulate human disease, and some treatments that have been successful in animal models are not effective, or may even be harmful, in humans. As a result it is increasingly being realised that data derived from such experiments should be critically examined for congruence with the human disease whenever possible.

These examples make it clear that direct scientific investigation of human brain tissue remains essential if we want to advance our understanding of neurological disease. Similarly, while advances in genetics have helped to identify many mutations or genetic variations that cause, or contribute to the risk of developing, specific neurological diseases, the cascade of pathological changes in the human brain triggered by these genetic changes remains largely unknown.

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Oxford Bereavement Services

In the aftermath of the Kennedy and Isaacs reports on post mortem and retention of tissue, many people involved in pathology and care of the bereaved thought that no-one would ever again give consent for a medical interest post mortem examination. No-one who had any contact with families making retained organs enquiries can doubt the depth and extent of their distress. Many families were reassured while others remain angry with a deep sense of betrayal. For a few the process of enquiring had a positive outcome because, for example, it was possible to answer

(continued overleaf)
examination, location of suture lines and how to access findings. When necessary we can discuss the case with a pathologist and arrange a letter or meeting with a clinician.

Requesting consent works best when one starts with a conversation with the family. Eye contact and non-verbal communication are vital in establishing whether a family is giving consent reluctantly, which is a concern for us in case of later regrets and feelings of guilt. Other families are keen to consent either because of the information that will be obtained or an altruistic desire to help others. This informal discussion helps the Coordinator establish whether it is appropriate to offer the opportunity to donate tissue including whole organs for research. Families are often surprised at our interest in normal brains but when their use as control tissue is explained they respond very positively. For most of these families disposal seems a non-issue and most give consent for later incineration at an unspecified date in the future (we explain that this may be many years hence). Completing the form can be done easily after this conversation and without it dominating the communication.

So far we have used DoH consent forms and hand written in the additional consent to retention of the brain for generic research purposes including as normal control tissue. Whilst ensuring our new forms are fully compliant with the Human Tissue Act and Codes of Practice, we will include a specific section for this purpose. This will add to our portfolio of forms that includes one specifically for removal of central nervous system tissue only and another under development that allows someone to consent in life to post mortem removal of tissue with space for relatives to confirm their agreement after death. Relatives are also given the choice of whether they receive follow up communication including a letter of thanks from a consultant pathologist and information about research.

Our links with the Neurosciences clinicians including the Neuropathologists allows families to derive some comfort from the fact that their bereavement will be of assistance in disease prevention and treatment in the future. (Anne Wadey, on behalf of the Oxford Bereavement Team)

100 years of Alzheimer’s Disease

2006 was an important year for Alzheimer’s disease (AD) research as it marked 100 years since Alzheimer’s description of a clinical case of this disease with its characteristic pathology (see images).

This centenary celebration has spawned many reviews of 100 years of research and assessments of where our understanding of the disease has reached.

As two of many, Steven Chance and I, from this department, contributed an article to a special centenary issue of the Journal of Alzheimer’s Disease. This issue was launched at an international meeting of the US Alzheimer’s Association, held in Madrid in July 2006. The tone of the meeting was optimistic that the future will bring improved treatment and management of AD.

Much research work now takes place in animal models of the disease but there is still an important need for studies of humans with the condition (and hence for our brain collection). Particularly urgent is a reliable test (biomarker) that will enable AD to be diagnosed at an early stage when treatment has the best chance of being effective. Such a test would assist in trials of the effectiveness of new interventions if it could reliably detect those at high risk of developing full-blown disease.

Local research by the Oxford Project to Investigate Memory and ageing (OPTIMA) has made samples available to assist in finding such a biomarker. OPTIMA is also directing a trial of the use of vitamins to prevent the development of AD. Our brain bank has this year provided samples to several studies here and abroad that aim to promote understanding of AD. More information on these studies will be provided in forthcoming Newsletters.

[Images show characteristic pathology of Alzheimer’s disease: an ‘amyloid plaque’ stained for the molecule betaA4 (left) and neurofibrillary tangles stained for the protein tau (AT8). (Margaret Esiri; images Olaf Ansorge)]
Profile: Brian Adams — Lay Member of the Board

As the representative member of the Oxford Radcliffe Hospital Trust (ORH) Patient and Public Panel on the Management Committee of The Thomas Willis Oxford Brain Collection (TWOBC) I feel that I should give a short explanation of how and why I - a lay person - comes to be in the privileged position of meeting at regular intervals with the distinguished and very interesting fellow members of the Management Committee.

The panel

The ORH NHS Trust Patient and Public Panel has evolved from a consensus within the NHS that public involvement is important in promoting innovation and change. During 2000 and 2001 several government documents promoted such involvement in NHS services. The Kennedy Report on the Royal Bristol Infirmary in July 2001 recommended that perspectives of patients and the public be taken into account. In the early part of 2003 David Lammy, Parliamentary Under-Secretary of State for Health in his ‘Involving Patients and the Public: Policy Guidance’, stated that “Patient and public involvement is not an end in itself but a way of achieving three fundamental objectives:

- strengthened accountability to local communities
- a health service that genuinely responds to patients and carers
- a sense of ownership and trust.”

The ORH Trust has established many innovative and easily accessible ways of involving patients, carers and the public and to listen and respond to those people's views. This strengthens accountability to organisations and communities in the ORH Trust's area, promotes a perception that we have a health service that genuinely responds to patients and carers, and builds up mutual trust between the ORH and the public that it serves.

My panel membership

Following a career that spanned printing technology at production managerial level, scientific and technical academic publishing production management, and lecturing and teaching, I retired to pursue other interests. I became involved in a variety of organisations and committees as diverse as The National Printing Heritage Trust, The George Eliot Fellowship, running weekly painting workshops for a local art society, and serve as a Parish Councillor.

Seeing a ‘call’ for interested persons to come forward for consideration as serving members of the ORH Trust's planned Patient and Public Panel I submitted my name and was appointed a Panel Member. I was present at the inaugural meeting of the Panel held on 15th September 2003 and since then have enjoyed serving in a variety of capacities.

In addition to the ongoing work of the Panel I spent one year on a Research Ethics Committee, was a member of Discharge Planning Focus Group and the Infection Control Focus Group, and am regularly a member of the ORH Environmental Quality Audit teams. Currently, I am also a lay member of Dr. Tutton's group that contributes to her ongoing ethnographic study of patient care on a trauma unit, and this my lay membership of the TWOBC Management Committee.

My role

I hope that the foregoing puts the work of the Patient and Public Panel into focus. Whilst I am very conscious that I do not have any medical training or expertise, I do have interests, experience and enthusiasms that I feel I may usefully draw upon to add to a debate. Thus, as a lay member of the TWOBC Management Committee I hope to express the view of an independent lay member of the public and try to contribute in some minor way to the work of the committee, and at the same time discharge the role given to me by the Patient and Public Panel.

(Brian Adams)