# Obtaining and using human tissues for research: ethical and practical dilemmas

The wide publicity given to the inappropriate retention of organs at post-mortem has resulted in new regulations governing the use of all human samples. Ethical review and explicit consent are required, even for research using urine samples. This editorial argues that the result, far from protecting patients, is now damaging patients' interests.

## THE VALUE OF HUMAN TISSUE IN RESEARCH

Human tissue can be of value in medical research. Wherever it can be used instead of animal tissue, this is preferable on scientific as well as humanitarian grounds. However, there are many types and sources of human tissue, from whole hearts or brains of babies, through excised haemorrhoids, to faeces or sputum, which contain human cells.

The potential research uses of tissue vary enormously; from merely reviewing microscope slides in the histopathology archive, through genetic testing for an inherited predisposition to incurable disease, through the growth and commercial exploitation of living human cells, to the production of biological weapons. Consequently the ethics of using human tissues in research are complex, and guidance intended to cover all eventualities rarely does so in a logical fashion.

## AUTOPSY SAMPLES

Before the year 2000 the best guidance on using human tissue in research in the UK was provided by the Nuffield Council on Bioethics (1995). This report concluded that patients should be empowered to control the uses to which their tissues are put. Patients should be informed that surplus tissue may be used in research. Consent for a surgical resection or biopsy could then be regarded as consent for any ethically acceptable use of the tissue removed, unless the patient lodges a specific objection. The report included a detailed discussion of what constitutes ethically acceptable use.

Before 2000, most pathologists assumed that their post-mortem practice complied with this guidance, because the consent forms in use at that time mentioned that 'tissue samples' might be removed. The investigations into paediatric autopsies in Bristol and Alder Hey showed this assumption to be wrong. It is a basic principle of consent that the patient must be adequately informed. Patients and relatives did not realize that 'tissue' might include whole organs, and so the post-mortem organ retention scandal began. The Retained Organs Commission was established and efforts continue to put matters right.

At present, autopsies conducted with the consent of relatives are rare (mainly because of reduced rates of requesting rather than more refusals), but those which do take place are accompanied by detailed information on what may be removed and how samples may be used. The circumstances under which archive samples may be used for research is still under consultation by the Retained Organs Commission (Department of Health, 2002a); most archives are currently 'frozen'. The Body Worlds exhibition of plastinated human specimens was very popular, but fear of controversy means that most pathology museums are unavailable even for teaching.

## SURGICAL SPECIMENS AND BIOPSIES

Post-mortem tissues are often perceived as being all that remains of a loved relative, whereas when diseased tissue is removed from living patients, most are glad to be rid of it and are happy for it to be used for the benefit of others (Start et al, 1996; Medical Research Council (MRC), 2001a). Nevertheless a series of changes have been made which fail to recognize this distinction.

The MRC rejected 'abandonment' of surplus surgical tissue in favour of 'gifting' and indicated that consent is necessary for research use (MRC, 2001b). The Department of Health (2002b) has followed a broadly similar line. This poses practical problems even when research use is contemplated before the operation, but there are far larger problems with the use of archival samples. 'Consent' has widely been interpreted as meaning explicit consent, needing a signature on a consent form. The new guidance recognized that in some circumstances it may be unethical to pester patients for consent to study samples taken long ago, and that sometimes it may be 'impractical' to obtain consent. But what is impractical? Demands by research ethics committees (RECs) for explicit consent to tissue use have since proved their impracticality too late, when the project is cancelled.

The UK limb of at least two multinational trials has been abandoned because of REC insistence on explicit consent, while identical research proceeded in other developed countries without consent (I Ellis, personal communication, 2001; author's personal experience, 2002). Harder to quantify is the research which is now not even attempted and the impact on the research element of training. One problem is regarding research as a single entity. Merely reviewing histopathology slides may now require REC approval, and the REC may feel it is 'playing safe' to demand explicit consent even for such an innocuous activity. But is it?

## ONE RIGHT, TWO CONSEQUENCES

It is now accepted that patients should be empowered to control how their tis-

sues are used. The consequence of this right is that it is immoral to use tissue samples in research against the patient's wishes. However, the second logical consequence is that it is surely also immoral to prohibit the use of tissue samples if the patient wants to contribute to research, or even if the patient is merely content for such use to proceed. This second consequence has been widely ignored, perhaps because RECs assume that consent is easy to obtain. The larger number of abandoned research projects indicates that, in the case of archival tissue samples, it is not.

## THE 'HELICOBACTER TEST'

It is instructive to recall the circumstances of the discovery of *Helicobacter pylori*, the main cause of gastritis and peptic ulceration. A histopathologist examining inflamed gastric biopsies noticed structures resembling bacteria. He then reviewed 100 biopsies to test for a correlation between active gastritis and the presence of such structures (Marshall and Warren, 1984).

Today, even this simple review would require submission of a 16-page application form to a REC, which would probably want patient consent before research could proceed. The chances of *H. pylori* being discovered under current guidelines seem remarkably slim, so one of the greatest recent advances in medical therapeutics would be blocked. Thus, guidance which was designed to protect patients' rights may actually damage them. The 'Helicobacter test' for new legislation asks: under the proposed system of regulation, could *H. pylori* still be discovered? The current system fails that test, and the Department of Health's (2002b) proposals are little better. We have not resolved the uncertainty about when it is better to use archives without consent than not to use them at all.

## THE WAY FORWARD?

The only way to satisfy the wishes of all patients in this context is to know the wishes of all patients. Otherwise, excised tissues will be used against the wishes of the patient, or use will be prohibited against the wishes of the patient.

Recording the patient's wishes in the notes is only part of the answer – information must remain available. Consent forms get lost, and researchers need consent to examine the case notes to find information about consent – catch 22 (MRC, 2000). Formal consent is not currently recorded for blood, sputum and urine samples. The Royal College of Pathologists (2001) argued that an ideal system would actively record the wishes of all NHS patients, but such an undertaking would be massive, and despite the benefits of enhanced patient autonomy there is no political will to pay for it.

When human tissues are needed in teaching and laboratory quality control, the Department of Health (2001) has indicated that implied consent is sufficient. Patients should be informed of how their tissues may be used and invited to register an objection. This is cheaper and easier than seeking explicit consent from each patient, but is implied consent adequate for research? Current guidance concludes that it is not, but this regards research as a single entity.

Implied consent is insufficient to authorize controversial research, but 98–99% of patients will give consent if asked explicitly for non-controversial research which carries no risk of producing anything which may harm the tissue donor (C Womack, personal communication, 2002). If patients are given adequate information about how surplus tissue may be used for the benefit of all, is it unreasonable to invite those who object to register their objections, to facilitate the wishes of the 98% who wish research to proceed?

## KEY POINTS

- 'Human tissue' encompasses material with a wide range of emotional importance, from urine samples to children's hearts.
- 'Research' similarly encompasses a broad range of activities not readily amenable to logical control by simple guidelines.
- The reaction to the organ retention scandal has resulted in new restrictions which are seriously inhibiting research. This is damaging patient care.
- The problem of tissue being used against the wishes of the patient has been largely replaced by the problem of prohibition of tissue use against the wishes of the patient.
- To resolve this we need a system which records the wishes of all patients. To do this using explicit consent would be laudable but expensive. Implied consent would be cheaper but is currently regarded as inadequate.

## CONCLUSION

It seems that measures designed to protect patients' rights are actually undermining the right of patients to contribute to medical research and to benefit from the results of that research. The pendulum has swung too far, and a sensible equilibrium has yet to be regained. HM

**Peter N Furness**
*Professor of Renal Pathology and Honorary Consultant Histopathologist*
*Department of Pathology*
*Leicester General Hospital*
*Leicester LE5 4PW*

Department of Health (2001) *Good practice in consent implementation guide: Consent to examination or treatment.* Department of Health, London: 23 (www.doh.gov.uk/ consent/implementationguide.pdf)
Department of Health (2002a) *Retained Organs Commission: A consultation document on unclaimed and unidentifiable organs and tissue.* Department of Health, London (www.nhs.uk/ retainedorgans/consultregframework.htm)
Department of Health (2002b) *Use of Human Organs and Tissue: A Draft Interim Statement for Consultation by the Department of Health.* Department of Health, London (www.doh.gov.uk/tissue/interimstatement.htm)
Marshall BJ, Warren JR (1984) Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* **i:** 1311–15
Medical Research Council (2000) *Personal Information in Medical Research.* MRC, London (www.mrc.ac.uk/PDFs/PIMR.pdf)
Medical Research Council (2001a) *Public Perceptions of the Collection of Human Biological Samples.* MRC, London (www.wellcome.ac.uk/en/images/biolcoll_3182.pdf)
Medical Research Council (2001b) *Human tissue and biological samples for use in research: Operational and ethical guidelines.* MRC, London (www.mrc.ac.uk/pdf-tissue_guide_fin.pdf)
Nuffield Council on Bioethics (1995) *Human tissue: Ethical and legal issues.* Nuffield Council on Bioethics, London (www.nuffieldfoundation.org/bioethics/)
Royal College of Pathologists (2001) *Transitional guidelines to facilitate changes in procedures for handling 'surplus' and archival material from human biological samples.* Royal College of Pathologists, London (www.rcpath.org/transition.html)
Start RD, Brown W, Bryant RJ et al (1996) Ownership and uses of human tissue: does the Nuffield bioethics report accord with opinion of surgical inpatients? *BMJ* **313:** 1366–8