THE FOUNDATION FOR SCIENCE AND TECHNOLOGY

LECTURE AND DINNER DISCUSSION SUMMARY SHEET

Science, society and xenotransplantation

Held in the rooms of the Royal Society on 22 February 2000
Sponsored by the Foundation's Shared Sponsorship Scheme:
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In the Chair:
The Rt Hon the Lord Jenkin of Roding

Speakers:
Dr David White, Director R & D, Imutran Ltd;
Professor John Harris, Institute of Medicine & Bioethics, University of Manchester;
The Rt Rev Lord Habgood PC, Chairman, UK Xenotransplantation Interim Regulatory Authority.

Many speakers justified the need for some alternative to allotransplantation by the mismatch world wide between the demand for human organs and their supply. Techniques for and the success rate of allotransplantation have been improving but it seems that the availability, especially in the UK, of suitable organs is reducing. One speaker suggested that there were not enough young dead because of the widespread use of seat belts and increasing safety of cars. Another commented that it was an illusion that a person's body remained intact after death; it was either consumed by fire or worms!

The UK system for 'opting in' by potential organ donors came in for much criticism especially as relatives frequently overrode the wishes of the deceased and refused permission for the removal of organs. Several suggestions were made for improving the UK supply including the possibility of presumed consent and 'opting out' rather than 'opting in'. Suggestion included payment for live organ donations under carefully controlled arrangements; someone reported that a Canadian company had bought a live kidney through an Internet auction for $63,000. One speaker commented that Empress Maria Theresa of Austria had enacted a law, still in force, that all dead bodies were the property of the state. However it was argued that there would have to be some 'opting out' procedure for those with religious or other scruples, to which another speaker responded that the result might well be the death of a potential recipient. It was pointed out that there were similar discussion at the turn of the last century about anti smallpox inoculation; as a result of severe conciencious objection laws smallpox had been eradicated. Speakers gave examples from several countries, notably Spain and Belgium, where regulatory arrangements

made organs more readily available, but in all cases a considerable gap remained between demand and supply and one kidney researcher felt that parliament would never enact mandatory donation legislation.

There was widespread agreement that allotransplantation alone was unlikely to provide a solution for many years and some alternative was necessary. No real alternative emerged during the discussion other than xenotransplantation.

Extensive research is underway both in academic research centres and by commercial organisations such as Imutran Limited. There are already limited examples of xenotransplantation, in particular the successful use pig's insulin with minimal side effects and pig's heart valves over the past 40 years, although it was pointed out that these were pickled before transplantation and were not live tissue. Activity in Russia and China was mentioned, including the use of live pig's skin for burns and the use of pig's spleens to treat patients with systemic infections. Patients have retained living pig's cells for up to 8 years with no apparent adverse effects. It was pointed out however that Aids took many years to emerge and there appeared to be no effective monitoring arrangements or regulatory authority. Imutran had to monitor the Russians themselves to obtain useful data, and they have found no adverse effects so far.

A speaker explained that pigs rather than primates are mostly used as potential 'donors' not only because the risk of cross infection is much greater from primates to humans than from pigs, but also because pig's organs provide a better size match and because there is likely to be greater public antagonism to the use of primate organs. The two main clinical issues are the problems of rejection and the dangers of cross infection.

Vigorous hyperacute rejection can occur within minutes of transplantation but research suggests that if the pig organ is given a donor DNA identifier by micro injection this might be overcome. A speaker reported that pig's kidneys have been successfully transplanted to monkeys which have survived for at least 78 days, and a baboon has survived for a month with a heart transplant. However there is frequently a rejection crisis after 60 days which is not yet well understood.

One speaker described a trial in which 200 patients with Parkinson's disease were successfully treated using implanted human cells and argued that the use of pig's foetal neural tissue might be equally successful as the risk of cross infection is minimised because brain infections do not travel to the rest of the body as would happen with the transplantation of whole organs such as the liver. Another speaker argued that this trial was flawed because Parkinson's patients were known to improve through the placebo effect and that judgment should be withheld until the completion of the more extensive phase 2 trials.

The possibility of cross or retro-viral infection was of concern to many speakers especially as the use of immuno-suppression drugs increased susceptibility to infection. The worry was whether PERV would affect humans, however one speaker claimed 217 primate xenotransplantation organ recipients had shown no sign of infection. The speaker also cited the successful use of pig's skin for burns, but another speaker questioned the validity of this as the skin was used more as a dressing than tissue replacement and was discarded once the burn had healed. Someone argued that no one knows what caused the cross species HIV infection, but this view was hotly contested.

A few speakers voiced ethical concerns but one commented that there was no great religious objection and the Nuffield Council on Bioethics had not raised serious ethical issues. Someone pointed out that we eat pork which provides a precedent for rearing pigs for human use and that an excellent living environment is provided for the pigs. Another speaker claimed that pigs can be reared with all human pathogens excluded to produce organs cleaner than human organs, but this conflicts with the provision of an excellent environment. There was a general concern that pioneering new medical techniques is very expensive, driven by the self interest of large corporations who monopolise the available expertise. It was emphasised that the major ethical concern was that people were dying every day for want of an organ transplant, someone quoting India where 3000 transplants are undertaken for every 100,000 needed.

Many speakers voiced the need for informed public opinion, and criticised the press for fermenting irrational, emotional and negative responses to complex issues. One speaker claimed the UK public is badly served by medical correspondents who are ignorant and do not understand the subject (with the honorable exception of The New Scientist), contrasting this with the USA where the press are much more informed and Germany where they are highly educated, knowledgeable and check back before publishing. There was much discussion on how to discourage the press from overdramatising risks and we were told that the House of Lords report on Science and Society, due out shortly, will address this.

There was considerable discussion about regulatory issues, and the role of UKXIRA. It was explained that there was not yet any comprehensive statutory regulation and the role of UKXIRA, as an interim body, was to provide a focal point, establish procedures for clinical trials and review all available evidence. They sought to strike a balance between setting impossible standards, which drove research to less demanding countries, and having laxer standards which opened the possibility of another HIV or BSE epidemic. No applications have yet been approved but a few have been submitted. One speaker claimed any use would need rigorous containment and life long surveillance, but another asked if it was realistic to require organ recipients to use barrier contraceptives for life, avoid pregnancy

or never father a child, notify all journeys abroad and avoid close contact with others.

Many speakers acknowledged that a great number of people die for lack of available organs and that zero risk in developing xenotransplantation was impossible. The challenge, as one speaker put it, was to move forward by small steps, reducing risk, building confidence and bringing about a long term informed debate.

David Firnberg

Some definitions:

Xenotransplantation: the transplantation of organs, tissues or viable cells from one species to another.

Allotransplantation: the transplantation of organs, tissues or viable cells from one human to another

UKXIRA: United Kingdom Xenotransplantation Interim Regulatory Authority.

PERV: porcine endogenous retrovirus

The discussions were held under the rule that nobody contributing to them may be quoted by name after the event. None of the opinions stated are those of the Foundation for Science and Technology, since, by its constitution, the Foundation is unable to have an opinion.

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