

The xenotransplantation research debate: time to involve the community

Medical practitioners need to be involved in the community debate

ON 8 JULY 2002, the National Health and Medical Research Council released a discussion paper¹ and draft guidelines for xenotransplantation research, with the aim of promoting widespread community debate of the issues involved. In the discussion paper, xenotransplantation is defined as the placement of animal cells, tissues or organs into humans, and includes the exposure of human tissue or cells to animal cells. Examples include the external perfusion of blood through a "bioartificial liver" (ie, an external apparatus containing pig liver cells which are separated from the perfused human blood by a semipermeable membrane), or culture of human skin cells on mouse fibroblasts for later use in treating burns. This definition excludes implantation of inert, sterilised animal tissues, as currently used to create artificial heart valves.

The concept of xenotransplantation has arisen because of an ongoing shortage of human donor organs. The discussion paper provides information on this shortfall, and measures pursued in Australia and overseas to try to improve organ donation rates. As there is general acceptance that the demand for donor organs is such that even increased human donation will not overcome the problem, the complex issues attending the shortage of human donors are not pursued further in the discussion paper.

So, what are some of the matters requiring community consideration and debate? A key issue is the risk that an infectious agent could cross from an animal to humans, and produce unknown infectious risks for the general community. Cross-species transmission of most known viral and bacterial pathogens is preventable by appropriate breeding, housing and testing of source animals. However, there is serious concern that a virus, such as the endogenous retrovirus present in the pig genome (the pig is currently the preferred source of organs), could "reactivate" in human recipients and, theoretically, later infect close contacts, healthcare workers or the wider community. Although experimental work has demonstrated that isolated human cell lines can be infected with porcine endogenous retrovirus (PERV), retrospective testing of 160 patients exposed to date to pig xenotransplants, such as islet cells or neural cells, or to external perfusion using pig liver cells, has not revealed evidence of PERV infection.²

This risk of infection brings a new ethical dimension to how consent for xenotransplantation research might be given. The discussion paper emphasises that not only will any potential recipient need to be fully informed of any risks, but so too will close contacts of the recipient and members of the healthcare team. An additional ethical issue relates to how a prospective recipient might reasonably choose between risking an experimental therapy or waiting for a human organ transplant.

Another issue which requires community debate is the potential use of genetically modified pigs to overcome the intense rejection reaction which, so far, has made xenotransplantation unfeasible. While experimental work to date has involved minimal genetic manipulation, more extensive modification (which could be seen to significantly alter the essential nature of the animal) may not be acceptable ethically or to our community.

In all human research, a key ethical principle is that the putative benefits must outweigh the known and theoretical risks. Weighing this balance for any human xenotransplantation research proposal will not be an easy task. The draft guidelines outline multiple conditions which must be met before research can be approved. One such requirement is obtaining convincing data of the efficacy of animal-to-animal experiments (eg, pig-to-baboon xenotransplantation) before pig-to-human trials can be contemplated.

A further issue relates to which group of individuals should be empowered to weigh up these benefits and risks and give approval for such human research on the community's behalf. The discussion paper recommends that this should be a task for a national committee, whose membership would include people with relevant scientific, ethical and regulatory expertise, as well as community members. Local human research ethics committees would play a role in monitoring the research, and could reject a proposal, but could not approve a proposal unless it had also received approval from the national committee.

The full text of the document, entitled *Draft guidelines and discussion paper on xenotransplantation*, is available on the National Health and Medical Research Council (NHMRC) website,¹ or can be obtained from the NHMRC at PO Box 9848, Canberra, ACT 2601. The document contains advice on how to make a submission by the closing date of 6 September 2002. Submissions will be carefully considered by the working party in making its final recommendations to the Council. The NHMRC regards xenotransplantation research as one of the more important issues for community consideration, and wishes to actively involve medical practitioners in the debate. Medical practitioners are invited to either develop and communicate their own views, or to assist in stimulating debate in the wider community.

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1. National Health and Medical Research Council. Draft guidelines and discussion paper on xenotransplantation. Canberra: NHMRC, 2002. Available at: <http://www.nhmrc.gov.au/issues/xeno.htm> (accessed July 2002).

2. Paradis K, Langford G, Long Z, et al. Search for cross-species transmission of porcine endogenous retrovirus in patients treated with living pig tissue. *Science* 1999; 285: 1236-1241. □