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XENOTRANSPLANTATION, CONSENT AND INTERNATIONAL JUSTICE

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ABSTRACT
The risk posed to the community by possible xenozoonosis after xenotransplantation suggests that some form of 'community consent' is required before whole organ animal-to-human xenotransplantation should take place. I argue that this requirement places greater obstacles in the path of ethical xenotransplantation than has previously been recognised. The relevant community is global and there are no existing institutions with democratic credentials sufficient to establish this consent. The distribution of the risks and benefits from xenotransplantation also means that consent is unlikely to be forthcoming. Proceeding on the basis of hypothetical consent to a package of global health measures that includes xenotransplantation, as Rothblatt has recently advocated, is more problematic than she acknowledges. Given that it may place the lives of citizens of poor nations at risk to benefit the citizens of wealthy nations, xenotransplantation raises significant questions of international justice.

INTRODUCTION

Xenotransplantation is distinguished from other experimental surgical procedures by the fact that the risk inherent in the procedure concerns not merely the fate of the recipient, but also those surrounding him or her – indeed, arguably and ultimately, everyone in the world. Scientists involved in xenotransplantation research have themselves raised the theoretical possibility that the introduction of living non-human tissue into the human body may lead to the transmission or evolution of novel pathogens, which might then spread beyond the transplant recipient.[1] In the worst-case scenario, xenotransplantation could lead to the evolution of a new infectious virus capable of causing a pandemic of AIDS-like proportions.

A number of authors have noted that the risks to the community, involved in xenotransplantation, suggest that some form of 'community consent', as well as the consent of the recipient, is required for the procedure to

[1] G. Beauchamp. Ethics and Xenotransplantation. *Can J Surg* 1999; 42: 5–6: 5; P. Collignon & L. Purdy. Xenografts: Are the Risks So Great That We Should Not Proceed? *Microbes Infect* 2001; 3: 341–348; A.S. Daar & D. Phil. Ethics of Xenotransplantation: Animal Issues, Consent, and Likely Transformation of Transplant Ethics. *World J Surg* 1997; 21: 975–982: 977; J.Y. Deschamps et al. History of Xenotransplantation. *Xenotransplantation* 2005; 12: 91–109; J.A. Fishman & C. Patience. Xenotransplantation: Infectious Risk Revisited. *Am J Transplant* 2004; 4: 1383–1390; J. Greenstein & H.J. Schuuman. Solid Organ Xenotransplantation: Progress, Promise and Regulatory Issues. *J Commer Biotechnol* 2001; 8: 15–29: 23–25; P.D. Griffiths. Xenotransplantation: One Trotter Forward, One Claw Back. *Lancet* 2000; 356: 1049–1050; D. Louz et al. Reappraisal of Biosafety Risks Posed by PERVs in Xenotransplantion. *Rev Med Virol* 2008; 18: 53–65; Y. Moalic et al. Porcine Endogenous Retrovirus Integration Sites in the Human Genome: Features in Common with Those of Murine Leukemia Virus. *J Virol* 2006; 80: 10980–10988; Nuffield Council on Bioethics. 1996. *Animal to Human Transplants: The Ethics of Xenotransplanation.* London: Nuffield Council on Bioethics: 67–80; J. Stoye. No Clear Answers on Safety of Pigs as Tissue Donor Source. *Lancet* 1998; 352: 666–667; J. Stoye. Xenotransplantation and the Risk of Zoonoses. *Newsl Int Soc Chemo* 2000; 4(3): 5–6: 6.

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take place.[2] I would argue that these requirements place greater obstacles in the path of ethical xenotransplantation than has previously been recognised.[3] The relevant community is global and there are no existing institutions with democratic credentials adequate to establish this consent. The distribution of the risks and benefits from xenotransplantation also means that consent is unlikely to be forthcoming. Proceeding on the basis of hypothetical consent to a package of global health measures including xenotransplantation, as Rothblatt has recently advocated, is more problematic than she acknowledges. The circumstances in which Rothblatt imagines consent being provided are arguably ones in which the vulnerability of individuals in the Third World is exploited in order to secure their consent. This undercuts the moral weight of such consent. Thinking about the moral weight of democratic consent to xenotransplantation in various circumstances also draws our attention to the fact that, because xenotransplantation involves placing the lives of citizens of poor nations at risk to benefit the citizens of wealthy nations, it raises significant questions of international justice. The existence of deep inequalities in access to health care at a global level means that the distribution of the benefits of xenotransplantation and the risk of xenozoonosis is *prima facie* unjust. Taking concrete steps to address these inequalities will be a crucial stepping stone on the way to ethical xenotransplantation.

THE PROMISE OF XENOTRANSPLANTATION

The development of powerful immunosuppressant drugs in the 1980s made possible the successful transplant of a range of vital organs between unrelated human beings. However, there currently exists a serious shortage of human donor organs available for transplantation, with the result that many people who are in need of a transplant die while waiting for a suitable donor organ to become available. This shortage seems likely only to worsen in the future. As improved nutrition and medical care lengthens the span of a human life and also increases the likelihood of sustaining those who suffer from what previously would have been fatal organ failures, the demand for compatible organs for transplant will continue to increase. Alternative social arrangements for the provision of donor organs seem unlikely to resolve this.[4]

As a consequence, attention has turned to whether it may be possible to use non-human animals as a source of organs for transplant.[5] The *Encyclopaedia of Bioethics* describes xenotransplantation as:

> any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (a) live cells, tissues, or organs from a non-human animal source; or (b) human body fluids, cells, tissues, or organs that have had ex vivo contact with live non-human animals cells, tissues, or organs.[6]

Recent research on xenotransplantation has concentrated on pigs and primates as possible sources of organs. However, a large set of pragmatic, conservation, ethical and scientific concerns have led most authors writing in the area to recommend against the use of primates.[7] Much current research is directed towards the development of genetically modified pigs, designed so that their organs are more compatible for transplant. This is done, for instance, by arranging for their cells to express surface proteins that fool the immune system into decreasing its

[2] A.S. Daar. Animal-to-Human Organ Transplants – a Solution or a New Problem. *Bull World Health Organ* 1999; 77: 54–61; M. Rothblatt. 2004. *Your Life or Mine: How Geoethics Can Resolve the Conflict Between Public and Private Interests in Xenotransplantation*. Aldershot, UK: Ashgate: 143.

[3] I should state at the outset that I will not be concerned with the ethical issues raised by xenotransplantation in relation to our treatment of animals in this paper. I do not think these issues are insignificant. However, I do not believe them to be distinct from questions about the treatment of animals in the course of other forms of medical research or, indeed, more generally. Moreover, the existing social consensus on the moral status of animals over-determines an answer to the question of the ethics of the use of animals as sources of organs for transplant; if we are prepared to breed and eat animals for pleasure, then we can hardly have any objection to breeding and killing them in order to save human lives.

[4] Xenotransplantation Working Party, National Health and Medical Research Council. 2003. *Animal-to-Human Transplantation Research: How Should Australia Proceed*? Canberra: Australian Government Publications: 15–19. Available at: http://www.nhmrc.gov.au/publications/synopses/_files/e55.pdf [Accessed 17 Oct 2008].

[5] There is, of course, the possibility that various stem cell therapies, therapeutic cloning, or the bioengineering of artificial organs, may at some stage in the future greatly reduce the demand for organs for transplant. However, at this stage it is not clear which, if any, of these technologies will come to fruition, or when, or what possibilities they will offer.

[6] A.S. Daar & L.E. Chapman. 2003. Xenotransplantation. In *Encyclopedia of Bioethics*. S.G. Post, ed. New York: Macmillan Reference: 2601–2612: 2602.

[7] M.A. Clark. This Little Piggy Went to Market: The Xenotransplantation and Xenozoonose Debate. *J Law Med Ethics* 1999; 27: 137–152: 141; Daar & Chapman, *op. cit.* note 6, p. 2604; Daar & Phil, *op. cit.* note 1, p. 976; M. Michaels. Infectious Concerns of Cross-Species Transplantation: Xenozoonosis. *World J Surg* 1997; 21: 968–974; Nuffield Council on Bioethics, *op. cit.* note 1, p. 72; H. Vanderpool. Commentary: A Critique of Clark's Frightening Xenotransplantation Scenario. *J Law Med Ethics* 1999; 27: 153–157: 154.

hostile response to the foreign tissue.[8] The hope is that it will eventually be possible to use this technique to overcome the currently insurmountable problems of tissue rejection following xenotransplantation. Indeed, researchers have already met with some success in this area – at least when it comes to pig to (non-human) primate transplantation.[9]

THE RISK OF XENOZOONOSIS

As both critics of xenotransplantation and xenotransplantation researchers themselves have noted, the transplant of whole animal organs into the human body raises the issue of how infectious agents that normally affect these organs will respond to the presence of the organ in its new environment.[10] Because their health depends on the health of animal tissue, xenotransplant recipients may suffer from a range of infections that would not normally affect human beings. Moreover, there is a danger that the presence of animal tissue which may harbour infection inside the human body will allow an infectious agent to adapt to its new environment and infect human tissue.[11] There is also the risk that any such infection may prove contagious and spread to affect other members of the community. Evidence is accumulating that a number of virulent pathogens, especially viruses, are the results of the agents moving between hosts of different species (zoonosis).[12] There is also some evidence that this change has been brought about by animals of different species being brought into regular, close proximity as a result of human agricultural practices.[13] The possible evolution of a new infectious agent as a result of cross-species organ transplantation has been termed xenozoonosis (or xenosis).[14] The risk of xenozoonosis subsequent to xenotransplantation is higher than it would otherwise be because persons who have received xenotransplants will be immunosuppressed.[15]

Xenotransplantation researchers are aware of these risks and studies have been carried out (and are ongoing) to try to quantify them.[16] Researchers are also developing techniques to try to eliminate or at least reduce them.[17] It has been suggested that the source animals for transplants could be bred and raised in isolation from other animals so as to be disease-free.[18] Unfortunately, this technique will not protect recipients from infection by agents they come into contact with after the operation, nor will it eliminate the risk posed by the existence of porcine endogenous retroviruses (PERVs), which are present in the genetic code of the cells of all pigs.[19] Consequently, much recent work on xenotranplantation consists of research dedicated to evaluating and reducing the risk of xenozoonosis due to PERVs.[20]

[8] P. Bucher, P. Morel & L.H. Buhler. Xenotransplantation: An Update on Recent Progress and Future Perspectives. *Transpl Int* 2005; 18: 894–901; D.C. Cooper. Clinical Xenotransplantation – How Close Are We? *Lancet* 2003; 362: 557–559; Deschamps et al. *op. cit*. note 1, p. 103; OECD. 1999. *Xenotransplantation: International Policy Issues.* Paris: OECD Publications: 9; 31.

[9] L. Buhler et al. Pig Kidney Transplantation in Baboons. *Transplantation* 2001; 72: 1743–1752; E. Cozzi et al. Maintenance Triple Immunosuppression with Cyclosporin A, Mycophenolate Sodium and Steroids Allows Prolonged Survival of Primate Recipients of hDAF Porcine Renal Xenografts. *Xenotransplantation* 2003; 10: 300–310; Greenstein & Schumman, *op. cit.* note 1, p. 18; D. Lambrigts, D.H. Sachs & D.K.C. Cooper. Discordant Organ Xenotransplantation in Primates: World Experience and Current Status. *Transplantation* 1998; 66: 547–561; *Lancet*. Xenotransplantation: Time to Leave the Laboratory. *Lancet* 1999; 354: 1657.

[10] Fishman & Patience, *op. cit.* note 1, p. 1384; OECD, *op. cit.* note 8, p. 34.

[11] Any transplant of living animal tissue into the human body involves some risk of cross species infection. However, it is whole organ transplants, which seem to involve a much larger risk of xenozoonosis, that will be the focus of my argument in this paper. While my arguments may apply to cell therapies, the extent to which they do will be a matter of scientific dispute in which I am not especially qualified to participate.

[12] F.H. Bach, A.J. Ivinson, & C.H. Weeramantry. Ethical and Legal Issues in Technology: Xenotransplantation. *Am J Law Med* 2001; 27: 283–300: 285; J.H. Barker & L. Polcrack. Respect for Persons, Informed Consent and the Assessment of Infectious Disease Risks in Xenotransplantation. *Med Health Care Philos* 2001; 4: 53–70: 55; Collignon & Purdy, *op. cit.* note 1; Daar, *op. cit.* note 1, p. 56; Griffiths, *op. cit.* note 1, p. 1050.

[13] Clark, *op. cit.* note 7, p. 139.

[14] Fishman & Patience, *op. cit.* note 1, p. 1384.

[15] Daar, *op. cit.* note 2, p. 77; Michaels, *op. cit.* note 7, p. 969; Nuffield Council on Bioethics, *op. cit.* note 1, p. 69; OECD, *op. cit.* note 8, p. 35.

[16] Collignon & Purdy, *op. cit.* note 1. See also the sources cited in Bucher et al. *op. cit.* note 8, p. 897.

[17] A. Ravelingien et al. Proceeding with Clinical Trials of Animal to Human Organ Transplantation: A Way Out of the Dilemma. *J Med Ethics* 2004; 30: 92–98; Fishman & Patience, *op. cit.* note 1.

[18] Barker & Polcrack, *op. cit.* note 12, p. 61; Michaels, *op. cit.* note 7, p. 971; OECD, *op. cit.* note 8, pp. 68–69.

[19] B. Bartosch et al. Evidence and Consequence of Porcine Endogenous Retrovirus Recombination. *J Virol* 2004; 78: 13880–13890; Griffiths, *op. cit.* note 1, p. 1049; OECD, *op. cit.* note 8, p. 36; Stoye, 1998, *op. cit.* note 1, p. 666.

[20] See, for instance, Louz et al. *op. cit.* note 1; S. Magre, Y. Takeuchi & B. Bartosch. Xenotransplantation and Pig Endogenous Retroviruses. *Rev Med Virol* 2003; 13: 311–329; U. Martin et al. Absence of PERV Specific Humoral Immune Response in Baboons After Transplantation of Porcine Cells or Organs. *Transpl Int* 2002; 15: 361–368; Y. Martina et al. Mice Transgenic for a Human Porcine Endogenous Retrovirus Receptor Are Susceptible to Productive Viral Infection. *J Virol* 2006; 80: 3135–3146; S. Miyagawa et al. A Novel Strategy for Preventing PERV Transmission to Human Cells by Remodeling the Viral Envelope Glycoprotein. *Xenotransplantation* 2007; 13: 258–263; Moalic et al. *op. cit.* note 1.

There are several features of the risk of xenozoonosis that will be important for the argument that follows. First, it is important to recognise just what is being risked. In the worst-case scenario, xenotransplantation might lead to the creation of a new viral pandemic of similar (or even worse) lethality to the AIDS pandemic or the influenza pandemics that occurred early last century.[21] Xenotransplantation therefore risks the deaths of millions of people.[22] Second, this risk is (probably) very small.[23] Researchers are unlikely to proceed with xenotransplantation if they thought there was any significant likelihood that this would occur. However, third, the precise magnitude of this risk is currently unknown and may well remain unknown despite the best efforts of research scientists to quantify (and reduce) the risk before proceeding.[24] A 2003 commentary on the state of xenotransplantation research concluded:

> . . . there is now less concern about transfer of porcine endogenous retroviruses than previously. Nevertheless, there is still much to clarify about the potential hazards of exogenous viral infection because, with the exception of cytomegalovirus, few studies have been done.[25]

It is worth noting in this context that 'less concern' does not equate to 'no concern'. It is exceedingly difficult to find an authority on xenotransplantation who is prepared to go on record as saying that there is *no* risk of xenozoonosis involved. The dilemmas that concern me here will occur as long as there is *any* risk of xenozoonosis involved in xenotransplantation at all. Finally, it is likely that the only way to resolve the question of the magnitude of the risk involves taking it.[26] Until human trials of whole organ transplants are carried out we can achieve at best a theoretical understanding of the risks involved.[27] Even then, as I will argue further below, we may not know the real level of risk for a period of decades.[28]

Epidemiologists and xenotransplantation researchers have suggested that a number of steps could be taken to minimise and manage these risks when xenotransplants first begin to be performed.[29] Ideally, transplant recipients will need to be monitored by medical and health authorities and to provide tissue and body fluids specimens to them until the risk of xenozoonosis is judged to have been eliminated.[30] Given the nature of the risks involved and the lack of data available about them, this is likely to mean for the rest of their lives. Moreover, for this monitoring to achieve its purpose, it must be possible to reliably track all xenotransplant recipients for the same period. This will require xenotransplant recipients to give up their right to privacy and confidentiality, as medical authorities must be able to pass relevant information on to other parties and organisations involved in monitoring.[31] It arguably might also involve restrictions on their freedom of movement to travel to regions where such monitoring would not be possible.[32] Furthermore, xenotransplant recipients will also have to agree to restrictions on their ability to serve as blood or tissue donors.[33] They may also have to consent to an obligation to inform their sexual partners, and other persons with whom they are in regular intimate contact, of their status as xenotransplant recipients.[34] Given that it is foreseeable that compliance with these requirements may be onerous and that recipients may not wish to participate in monitoring after their operation, even where they have consented to do so, penalties for non-compliance may need to be established and imposed. These penalties might range from administrative and financial penalties, in the form of fines or denial of access to social services, to the

[21] L.P. Knowles. Xenotransplantation: Full Speed Ahead, Slow Down. *Hastings Cent Rep* 1999; 29(4): 47.

[22] F.H. Bach et al. Uncertainty in Xenotransplantation: Individual Benefit Versus Collective Risk. *Nat Med* 1998; 4: 141–144: 142; Rothblatt, *op. cit.* note 2; Xenotransplantation Working Party, National Health and Medical Research Council, *op. cit.* note 4, p. 102.

[23] Fishman & Patience, *op. cit.* note 1; Louz et al. *op. cit.* note 1; Nuffield Council on Bioethics, *op. cit.* note 1, p. 73.

[24] Bach et al. *op. cit.* note 22, p. 142; Nuffield Council on Bioethics, *op. cit.* note 1, pp. 73, 76; OECD, *op. cit.* note 8, p. 35; Rothblatt, *op. cit.* note 2, p. 67.

[25] Cooper, *op. cit.* note 8, p. 559.

[26] R.E. Gold & W.A. Adams. Reconciling Private Benefit and Public Risk in Biotechnology: Xenotransplantation as a Case Study in Consent. *Health Law J* 2002; 10: 31–75: 40; Nuffield Council on Bioethics, *op. cit.* note 1, p. 72.

[27] Louz et al. *op. cit.* note 1.

[28] In discussing the ethics of a surgical procedure, it is normally possible to consider it in a research setting and in a clinical setting. In the case of whole organ transplants from animal sources, however, this distinction is not so clear. The risk of xenozoonosis may remain even in circumstances in which xenotransplantation has become a routine surgical procedure. As this is the risk that generates the ethical dilemmas that interest me here, my argument will apply to xenotransplantation in both clinical and research settings.

[29] Fishman & Patience, *op. cit.* note 1.

[30] Michaels, *op. cit.* note 7, p. 972; H. Vanderpool. Critical Ethical Issues in Clinical Trials with Xenotransplantation. *Lancet* 1998; 351: 1347–1350: 1348; Xenotransplantation Working Party, National Health and Medical Research Council, *op. cit.* note 4, p. 110.

[31] Bach et al. *op. cit.* note 12, p. 291; Clark, *op. cit.* note 7, p. 145.

[32] Bach et al. *op. cit.* note 12, p. 292.

[33] Vanderpool, *op. cit.* note 33, p. 1348.

[34] Clark, *op. cit.* note 7, p. 141; Daar & Phil, *op. cit.* note 1, p. 977; P.S. Florencio & E.D. Ramanathan. Legal Enforcement of Xenotransplantation Public Health Safeguards. *J Law Med Ethics* 2004; 32: 117–123: 118.

detention of recipients who are uncooperative.[35] Finally, recipients may have to be – if necessary, forcibly – isolated and quarantined in the event that they are shown to be harbouring a xenozoonotic infection.[36]

Note that the need for long-term medical monitoring of transplant recipients is unlikely to lapse even if xenotransplantation generates no evidence of xenozoonotic infection in the first recipients. The mere fact that a large number of xenotransplantations have been performed successfully over a period of years without any sign of xenozoonosis occurring will *not* serve to establish that the risk of such an event can be ignored. The pathogens that are of most concern as possible agents of xenozoonotic infection are retroviruses, which may have very long latency periods.[37] Thus even if xenozoonosis occurred shortly after an operation, without specific monitoring directed to this purpose, such an infection may not be detected for many years. It is also possible that xenozoonosis would only occur in very particular (and exceedingly rare) circumstances and it may therefore be many years before we can be confident that all possible circumstances that may prove favourable to xenozoonosis have been exhausted without any such event occurring.

The nature and extent of these mechanisms to minimise the risk of xenozoonosis render the extent to which informed consent to such restrictions is possible and the moral weight of such consent when it is secured extremely problematic. However, these issues have been extensively discussed elsewhere and are not my concern here.[38] Instead, I want to focus on the difficult questions about how we should respond to poorly defined – indeed unknown – risks and, in particular, by whom the decision to proceed in the face of such risks should be made.

JUSTICE AND THE DISTRIBUTION OF RISK

As Bach et al. have argued, of the risk of xenozoonosis arising from xenotransplantation:

> Because the risk is societal and not merely individual, the decision whether to undertake the procedure involves more than ensuring the ability of the surgeon and the transplant team, the capacity of the institution, and the willingness of the patient. Where the risks are collective, the public must not only be educated about the risk but must also be involved in decision-making.[39]

All of those whose interests are at stake – indeed, whose lives are at risk – have the right to participate in any decision about proceeding with xenotransplantation. As Daar observes, this is a right to participate in decision-making and not just in consultative processes aimed at gauging public attitudes as part of the process of drafting the regulations that will govern decisions made by surgical teams or ethics committees.[40] Otherwise, regardless of how much consultation has taken place, those people who are making the decisions about whether (or when) to proceed with xenotransplantation will be deciding whether to risk the lives of others. This expresses a profound disrespect for the autonomy of the persons whose lives are risked without their consent.

This conclusion raises two immediate difficulties. The first is that the relevant community is clearly global.[41] The second is that the vast majority of this community have nothing to gain from xenotransplantation and everything to lose.

Most discussions of xenotransplantation describe the relevant body which must provide consent as 'the public' and then treat this as a *national* constituency.[42] However, the set of persons who must be included in decision-making about xenotransplantation is the *global* population, because the risk posed by xenozoonosis is not restricted to the citizens of the nation in which experiments are taking place.[43] In a world in which tens of thousands of people travel internationally each day, infectious agents pay little attention to borders. There is a real possibility (indeed, some would say, likelihood) that any infectious agent created in the process of xenotransplantation would spread to become a global health problem.[44] Moreover, even if it were possible to be confident in our ability to confine any emergent epidemic to national

[35] Florencio & Ramanathan, *op. cit.* note 34, p. 120.
[36] Barker & Polcrack, *op. cit.* note 12, p. 66; Rothblatt, *op. cit.* note 2, pp. 58–64.
[37] Fishman & Patience, *op. cit.* note 1, p. 1385; Florencio & Ramanathan, *op. cit.* note 34, p. 117.
[38] Bach et al. *op. cit.* note 12; Barker & Polcrack, *op. cit.* note 12; Beauchamp, *op. cit.* note 1; D.M. Bowman. Bioethical and Legal Perspectives on Xenotransplantation. *Monash Bioeth Rev* 2004; 23(3): 16–29; Clark, *op. cit.* note 7; Daar & Phil, *op. cit.* note 1; Florencio & Ramanathan, *op. cit.* note 34; R.E. Gold & W.A. Adams. Reconciling Private Benefit and Public Risk in Biotechnology: Xenotransplantation as a Case Study in Consent. *Health Law J* 2002; 10: 31–75; Nuffield Council on Bioethics, *op. cit.* note 1.
[39] Bach et al. *op. cit.* note 22, p. 142.
[40] Daar, *op. cit.* note 2, p. 57.
[41] Rothblatt, *op. cit.* note 2, p. 140.
[42] Bach et al. *op. cit.* note 12, p. 300; Bach et al. *op. cit.* note 22, pp. 141–143; Barker & Polcrack, *op. cit.* note 12, p. 65; Clark, *op. cit.* note 7, p. 139; Florencio & Ramanathan, *op. cit.* note 34, p. 121. A notable exception here is Rothblatt, *op. cit.* note 2.
[43] Rothblatt, *op. cit.* note 2, pp. 141–144.
[44] S. Herz. Before Pigs' Germs Fly: Xenotransplantation and a Call for Federal Action. *Camb Q Healthc Ethics* 2001; 10: 441–444: 441; OECD, *op. cit.* note 8, p. 43.

boundaries, the risks of such epidemics may still be difficult to contain. Once xenotransplants become available anywhere in the world, individuals from jurisdictions where they are not available are likely to travel across borders to secure them. When they return home, they will bring the risk of xenozoonosis with them.[45]

Thus, if the consent of the public whose lives are being risked is required for xenotransplantation to be ethical, then this means a process of global consent is required. Just as a small group of potential xenotransplant recipients has no right to risk the lives of their fellow citizens without their consent, citizens of any one nation have no right to risk the lives of citizens of other nations without their consent.[46]

Yet it is exceedingly difficult to imagine how such consent might be granted or secured. It would require the existence of a global political forum in which all persons could vote or – more realistically – in which the interests of all living persons were represented. It would also require an informed debate on the costs, benefits, and ethics of xenotransplantation to take place amongst all nations, peoples, and constituencies. There is no body in the world today with the democratic credentials to make any of this plausible.

In the face of these practical difficulties, it might be argued that the requirement of *actual* consent from the global population should be waived in favour of some form of *hypothetical* consent.[47] Perhaps it will be ethical to proceed with xenotransplantation when it is reasonable to believe that the procedure *would* receive majority support from a fully informed global community, if such a debate and vote were possible.

However, on first analysis at least, given the nature of the distribution of the costs and benefits of xenotransplantation, it seems extremely unlikely that xenotransplantation would gain consent from a genuinely democratic global political forum.

The vast majority of humanity, namely the poor in the Third World, stands to gain nothing from the development of xenotransplantation. It may be true, as the OECD's *Xenotransplantation: International Policy Issues* suggests, that, to a certain degree, *some* citizens of Third World nations stand to benefit from xenotransplantation, if it should turn out to be a cheaper and more accessible procedure than existing remedies for organ failure.[48] However, any such benefit will be confined to those wealthy enough to afford it. Given the expense of the surgical facilities and expertise that are required to successfully transplant organs, regardless of the source of the organ, xenotransplantation will never be available to any but a small minority of citizens in the Third World. The vast majority of people would clearly stand to benefit more if the funding and research effort dedicated to developing xenotransplantation in the First World were invested in basic health infrastructure in the Third World.

The risks involved in xenotransplantation are also distributed in such a way as to discourage majority support for the procedure. They are borne most by the very group that is least likely to benefit. If a new infectious agent *did* emerge as a consequence of xenotransplantation, it is likely to impact most heavily on the poor in the Third World because of the lack of health-care infrastructure. A disease that can be contained and treated in a prosperous industrial society, with a democratic government and a modern health care system, may cause tens of thousands of deaths in another part of the world where poverty, oppression, war or civil disorder prevent the relevant epidemic control procedures or treatments being instituted – as has been illustrated dramatically in the past three decades by the spread and impact of the HIV virus.

Note that both of these observations apply, though perhaps not to the same degree, to the distribution of the costs and benefits *within* nations as well as between them. There exists a large class of people within most nations (the possible exceptions being the European social democracies) who are effectively excluded from the enjoyment of the benefits of advanced surgical techniques because of their socio-economic status. These people – the poor – also bear the brunt of the costs associated with disease and other health problems. They have little to gain and much to lose from xenotransplantation.

Thus if a genuinely democratic decision were possible about whether or not to proceed with xenotransplantation research it seems highly unlikely that global consent would be forthcoming. Xenotransplantation will therefore also fail to meet the requirement of hypothetical consent.

ROTHBLATT'S PROPOSED SOLUTION

Rothblatt has argued that a way through this impasse can be found by taking measures to ensure that people in the

[45] Bucher et al. *op. cit.* note 8, p. 898.

[46] Rothblatt, *op. cit.* note 2, p. 141.

[47] In her discussion of the possibility of global consent to xenotransplantation, Rothblatt moves quickly from a discussion of the democratic credentials that would be required of any organisation that tried to claim a global mandate for xenotransplantation research to a 'role-play' wherein she imagines how discussions conducted within such an organisation might proceed.

[48] OECD, *op. cit.* note 8, pp. 71, 80.

Third World will in fact benefit from the availability of xenotransplantation.[49] There are in fact two mechanisms whereby they might benefit.

First, Rothblatt argues that an adequate regime of international surveillance for outbreaks of xenozoonotic disease requires the extension of basic health care to the one billion persons who are currently denied it.[50] In order to have the capacity to detect a xenozoonotic infection in time to have any chance of containing it, it would be necessary to establish institutions to make possible the detection and identification of outbreaks of infectious diseases as they occur. This would require establishing a network of basic health centres capable of collecting the required tissues samples and of noting and reporting any symptoms that might reflect xenozoonosis, and also the education and training of sufficient health-care workers to staff them. In order to encourage people to attend them, these centres would have to offer basic health care at prices low enough to make it available to everyone. Finally, reducing the risk of the emergence of a destructive xenozoonotic pandemic will require improving the living conditions and basic health of the poor, who may otherwise function as a reservoir for infectious agents. Thus, securing *public* health at a global level, in the face of possible xenozoonoses, will require extending basic health care to include the millions of poor around the world who are currently denied it. Rothblatt suggests that the cost of such a health system could be funded via the imposition of a US$13,000 tax on the cost of each xenotransplant.[51]

Second, in order to ensure that citizens in developing nations would benefit from the development of xenotransplantation, a certain number of xenotransplants could be set aside for those who would otherwise be excluded from benefit.[52] That is, an international organisation established for this purpose could work to ensure that for every X number of xenotransplants taking place in the First World a (smaller) number, Y, would be made available to individuals randomly selected from among those who have appropriate medical need in the Third World. By ensuring that some of the benefits of xenotransplantation would flow to the Third World, this 'xenotransplant tithe' would shift the risk/benefit calculation for people in the Third World towards a clear net benefit. It would also go some way towards addressing the otherwise problematic *distribution* of risks and benefits so that it was no longer the case that the lives of some were being risked for benefits that would flow solely to others.

It would clearly be in the interests of people in the Third World to consent to these arrangements. Thus, according to Rothblatt, as long as we are willing to 'bundle' xenotransplantation with the extension of basic health care to the Third World and also ensure that some xenotransplants are made available to poor citizens in Third World nations, we can assume consent would be forthcoming and continue with xenotransplantation research trials and eventual therapy.[53]

EXPLOITATION AND HYPOTHETICAL CONSENT

However, considering the justice of proceeding with xenotransplantation as a question of hypothetical consent elides the question of the justice of the choice being presented to the Third World in the first place. Hypothetical consent – like actual consent – is only morally weighty if the conditions under which we imagine it being granted are themselves appropriate. There is an ethical impasse here that Rothblatt neglects; we need to consider the ethics of the process whereby consent might be secured. The existence of this impasse is obscured by failure to distinguish between two different circumstances in which communities in the Third World might be asked to consent to xenotransplantation research taking place in the First World.

One possibility is that First World nations choose not to proceed with trials of xenotransplantation until a more equitable distribution of health-care resources at a global level is achieved and all human beings have access to basic medical care. At this point the First World might offer residents in the Third World a share in the benefits of xenotransplantation through a 'xenotransplant tithe' of the sort Rothblatt advocates. As it would clearly be in the interests of citizens in Third World nations to have access to this technology, we can safely presume that they would consent to xenotransplantation trials (and, eventually, therapies) taking place in these circumstances. Note, however, that even in this scenario the question of just how many xenotransplants would be offered to the Third World, and at what cost, is likely to be controversial. While citizens in Third World nations would benefit as long as some minimum threshold number of xenotransplants were made available, the overall distribution of benefits would still be skewed heavily towards the First World.

[49] Rothblatt, *op. cit.* note 2, pp. 142–156.
[50] Ibid: 141–150.
[51] Ibid: 153–155.
[52] Ibid: 145.
[53] Ibid: 144.

A second, more likely, but also much more problematic, possibility is that the Third World might be offered a choice between the status quo wherein a billion people are denied access to basic health care and a scenario in which resources are redistributed to the Third World to make basic health care possible as part of a package of measures associated with facilitating xenotransplantation research in the First World. In this case, the Third World's access to basic health care is tied to the question of their willingness to consent to xenotransplantations being carried out in the First World. Rothblatt's treatment makes it clear that she imagines access to basic health care being granted *in exchange for* consent to the risks concomitant with xenotransplantation taking place in the First World.[54]

It is probably true that, if this was the choice they were offered, citizens of Third World nations might well choose to endorse xenotransplantation. However, the moral weight of this (hypothetical) consent is now surely called into question. What we have now appears to be a case of *exploitation* wherein the vulnerability of a third-party is used to secure their consent. The First World would be using the vulnerability of the Third World to secure benefits that are clearly unevenly distributed between them.

Of course, arguments about exploitation in the context of relations between the First World and Third World are often controversial. Certainly, it is implausible to hold that all agreements made in conditions of inequality are exploitative. However, two features of agreements are widely believed to make it more likely that they are exploitative. First, where the inequality that facilitates the agreement is one that the powerful party has deliberately engineered – or at least one that they have the power to alter and are morally culpable if they fail to do so – we are more likely to judge the situation exploitative.[55] Second, if what is agreed to is something that is *prima facie* unjust, or that we have independent grounds to criticise, this may also indicate the presence of exploitation.[56]

Arguably, both of these features are present in the (imaginary) scenario in which the Third World agrees to xenotransplantation trials in exchange for access to basic health care. The global inequality in wealth and living conditions that is reflected in the different standards of health care available in different nations is the result of a history – and, indeed, an existing set of global institutions – wherein First World nations have promoted their interests at the expense of the interests of Third World nations. That is to say, First World nations, to some extent at least, are responsible for the plight of the poor in the Third World.[57] Moreover, the nature and extent of this inequality are such that they establish a clear obligation on wealthy nations to address them as a matter of moral urgency.[58] Providing the poor in the Third World with basic health care would, in fact, only be to grant them what they are already owed. As I observed above, there is also a real question about the justice of what the Third World is agreeing to in this scenario. Even if some xenotransplants were made available to citizens of the Third World, populations in the Third World would still be agreeing to bear a disproportionate amount of the risks in order to gain few of the benefits of xenotransplantation.

Thus the second, more plausible, interpretation of Rothblatt's suggestion arguably does involve exploitation. Note that I have not denied that it would be in the *interests* of the Third World to see xenotransplantation research proceed. What I *have* denied is that we can proceed on this basis to presume the type of consent necessary to placate concerns about the distribution of the risks and benefits of xenotransplantation. If the scenario in which we imagine consent being granted is one in which those providing the consent are being exploited, such hypothetical consent tells us little about the ethics of the policy or procedure.

The implications of Rothblatt's discussion are therefore more subtle and complex than they first appear. She is right to note that it will be unethical to proceed with xenotransplantation until citizens in Third World nations have access to basic health care. However, any suggestion that this should be provided in exchange for consent to xenotransplantation vitiates the moral weight of that consent by endorsing exploitation. Instead, access to health care should be provided as a matter of justice before the question of consent to xenotransplantation is raised. Even then, the question of the justice of the distribution of risks and benefits of xenotransplantation will need to be addressed.

[54] Ibid: 146.

[55] J. Reiman. Exploitation, Force, and the Moral Assessment of Capitalism: Thoughts on Roemer and Cohen. *Philos Public Aff* 1987; 16: 3–41.

[56] A. Wertheimer. 1996. *Exploitation*. Princeton, NJ: Princeton University Press: 207–246.

[57] M. Chossudovsky. 2003. *The Globalization Of Poverty And The New World Order*. 2nd ed. Ontario, Canada: Global Outlook; T.W. Pogge. 2002. *World Poverty and Human Rights: Cosmopolitan Responsibilities and Reforms*. Cambridge: Polity Press: 1–26.

[58] Pogge, *op. cit.* note 57, pp. 1–26; P. Singer. 2002. *One World: The Ethics of Globalisation*. Melbourne: Text Publishing.

CONCLUSION: XENOTRANSPLATATION AND INTERNATIONAL JUSTICE

Despite the very real benefits it would offer, if it were to become a safe and effective procedure, there seem to be profound ethical difficulties standing in the way of xenotransplantation at this point. Given the profound global inequalities in access to health care that exist today, the risk of xenozoonosis involved in xenotransplantation means that the community which can reasonably expect to receive the benefits of xenotransplantation – the wealthy in the First World – is substantially distinct from that which is subject to most of the risks from xenozoonosis – the poor in the Third World. This means that proceeding with xenotransplantation involves risking the lives of others without their consent and with little prospect – and in some cases, none – of their benefiting. This sacrifice of the interests of some in order to secure benefits for others will be unethical according to Kantian ethics or, indeed, any ethics that is sensitive to features of the distribution of risks and benefits across persons. While the risk of xenozoonosis cannot be eliminated, the only way to negotiate the difficult question of the justice of the distribution of the risk of xenozoonotic infection is to eliminate the grotesque inequality in access to health care that produces this distribution.

Requiring that global access to basic health care be available before xenotransplantation trials or therapy proceed might appear to constitute an insurmountable ethical barrier to xenotransplantation. It is difficult to discern the political will to dedicate the funds required to achieve this in any First World nation today. However, as Rothblatt and others have observed, it is well within the power of First World nations to ensure that citizens in Third World countries have access to basic health care.[59] It would require the redistribution of wealth, but not the elimination of inequality nor a politically prohibitive drop in living standards in the First World. It is only the lack of political will that stands in the way of achieving this.[60] It would reflect poorly on the xenotransplantation research community indeed, if medical researchers and policymakers were more willing to risk the lives of people in the Third World than to confront the political task of putting forth this basic demand for justice, in the First World.

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[59] Pogge, *op. cit.* note 57, pp. 1–26; Singer, *op. cit.* note 58.

[60] Moreover, as Rothblatt notes, the prospect of xenozoonosis subsequent to xenotransplantation may even offer a way to mobilise the necessary political will. It is in the interest of citizens in First World nations to ensure that citizens in Third World nations have access to basic health care in order to minimise the risks of xenozoonosis should xenotransplantation become available.