

Globe and Mail

Health Warning: that pig cell may be a Trojan horse

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Xenotransplantation and *xenozoonosis*. Fancy words. But words whose meaning we can't afford to ignore. The transplantation of animal tissues and organs into humans (xenotransplantation) holds out promise of tremendous benefits to humankind. There is, however, a risk posed by this new medical technology: namely, that animal diseases may be enabled to cross the species barrier (xenozoonosis), thereby threatening public health.

This risk is difficult to quantify, but the worst-case scenario - a major new epidemic - is extremely serious. Thus, the ethics of xenotransplantation goes beyond the issue of individual consent and enters the region of justice. When is it morally justifiable for individuals, in pursuing their own benefit, to impose risks on society?

Early in September of this year, Maribeth Cook became the world's first stroke patient to receive a transplant of cells taken from a litter of 12 pig foetuses. Approximately 30 million of these pig brain cells were injected into the stroke-damaged part of Ms. Cook's brain. When she showed signs of early improvement, some newspaper headline writers were quick to proclaim: "Transplanted brain cells from pig foetuses give stroke victim new lease on life". The truth, sadly, is more complex.

Doctors will not know for some considerable time whether the implantation of brain cells from pig foetuses will confer genuine lasting benefit on stroke patients such as Maribeth Cook. Moreover, it will take an even longer period of time before scientists can be confident that she didn't also receive a disease-causing pig virus. One wonders whether, when her doctors informed Ms. Cook of her individual risk from this highly experimental procedure, they also informed her of the potential risk she could pose to her family, her friends, her colleagues, and to society at large.

Nevertheless, despite these fears and uncertainties, powerful corporations have invested powerful amounts of money in this new technology - US \$1 billion, in the case of pharmaceutical giant Novartis. Designer pigs, genetically engineered for medical purposes, could be worth a fortune. If serious problem of cross-species

rejection can be solved, then the implantation of animal organs could potentially deliver effective treatment for patients suffering from diabetes, Parkinson's disease, liver failure, multiple sclerosis, and stroke. Equally important, the technology could also eliminate long waiting lists for donor lungs, kidneys, and hearts. The supply of organs would become unlimited.

In the United States, the Food and Drug Administration has already tentatively approved a procedure which uses pig livers, functioning outside the human body, while they wait for a human organ donor. The British bio-tech company, Imutran, is genetically modifying pigs so that their livers will not be rejected by the human immune system during this "bridging" transplant.

Why pigs, you ask? Well, humans have lived in close association with pigs for a very long time. We breed, herd, handle, cook, eat them, and tan their skins, mostly without noticeable ill effects. Moreover, their organs are a convenient size for transplanting to humans, which makes them a favourite donor animal.

Unfortunately, scientists have discovered that there are at least two variants of the porcine endogenous retrovirus (PERV) that cannot be eliminated, both of which are capable of infecting humans. The danger is that these viruses, or others not yet discovered, could behave like HIV, which causes AIDS. That is, after transplantation they could lie dormant for years, spread through pathways such as blood donation or sexual activity, until they finally and fatally reveal themselves.

The spectre of zoonosis may sound as if it's an import from some science-fiction scenario, but the evidence is strong that viruses can cross species: examples include Ebola, the Hong Kong flu virus (H5N1), and HIV itself. When they do, their nature sometimes changes dramatically, in ways which are difficult to predict. A virus which produces no symptoms in pigs has the potential to cause serious disease if transmitted to humans through xenografting.

Consider. Virologists have only just discovered, by examining archived blood and tissue, that a man who received a baboon liver transplant in 1992 was, apparently, infected by a baboon virus. Had he survived the transplant by more than a few months, would he have become sick as a result of this simian virus? Could he have transmitted the virus to others? Because no one, at present, can answer such questions, there is great uncertainty about the risks attaching to clinical xenotransplantation. The species barrier between humans and other animals has evolved over millions of years. The available data simply do not permit any reasonable assessment of the magnitude of the risk posed by crossing this barrier.

Thus, society is confronted with a genuine ethical dilemma. If we proceed rapidly with xenotransplantation, many lives might be saved, and many more individuals who would otherwise be condemned to illness and disability might have the quality of their lives transformed. But, if we permit this technology to become widespread, we run a small but real risk of seriously endangering public health. Moreover, some of the steps we might take to reduce this risk seem impractical and oppressive: for example, a lifetime of monitoring every xenotransplantation patient to ensure that such patients never donate blood or engage in unprotected sex. Even then, a pandemic cannot be ruled out.

We cannot, then, avoid the basic ethical question: Which risks are worth taking for which benefits? Xenotransplantation is a technology with enormous life-saving potential. But no one can say with confidence how great or small is the risk associated with transferring body parts and tissues from animals to humans. Since the risks are unknown, a high degree of controversy is unavoidable. This leads us, inevitably, to the next question: when there is no consensus, who should decide?

Usually, individual patients decide for themselves whether the benefits of a medical procedure outweigh the risks. In this case, however, society has a lot at stake. Tragically, the value of protecting public health may sometimes have to outweigh benefit to individual patients. The precautionary principle requires that when a new technology is being introduced, the burden of proof should rest with those developing the technology, to prove its safety *in advance*, rather than on critics to prove harm.

A group of eminent scientists, led by two Harvard professors, has used the journal **Nature Medicine** [22nd January] to call for a moratorium on all clinical xenotransplant trials. The proposed moratorium would give experts time to discover potential harms and benefits and, equally important, it would allow time for informed public debate. Alas, this sensible proposal conflicts with the prevailing gung-ho attitude of many scientists and their corporate sponsors. It seems to be the case that unless governments are ready to impose strict regulations, the decision will be to proceed full-steam ahead. Canadians might look for regulatory leadership to the Health Protection Branch of the Federal Government, but critics have documented the Branch's worrying track-record, and there are serious doubts about its independence and integrity.

In a democratic society, when serious issues of public health and welfare are

at stake, the ultimate decision should be a political one. Citizens are entitled to shape policy through informed public debate. Especially when the range of scientific uncertainty is wide, society cannot simply put its faith in “the experts”. Science policy is much too important to be left to the pharmaceutical industry, or to the scientists.

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