

## Could a pig's heart save your life?

In 2016 it was announced that researchers in the US had kept a genetically engineered pig's heart beating in a baboon for three years. This wasn't just idle research. Every year, several million people die world-wide because of transplant shortages. There simply aren't enough human organs from tragedies like road accidents to go around. For years, scientists have been working on a radical solution – to use organs from animals. This is known as xenotransplantation.

Xenotransplantation may sound like science fiction but doctors and scientists have been trying to develop it for decades. Back in 1984, Stephanie Fae Beauclair, generally known as 'Baby Fae' was born with a heart defect that would have killed her within a week or so. At that time transplants using infant human hearts were almost always unsuccessful. The surgeon, Leonard Lee Bailey, was a pioneer in animal-animal transplants so decided to try using a baboon heart. The hope was that this would allow Fae to live long enough for a second operation to replace the baboon heart.

In many respects the surgery was a success. However, Fae died 21 days later as the heart was rejected by her body. Nevertheless, her sad story marks the beginnings of serious attempts at xenotransplantation. There are two big questions about xenotransplantation: Is it feasible? and Is it ethical?

### **The biology of xenotransplantation**

Our immune system is a wonderfully complicated collection of cells and organs that helps to protect us against foreign bodies that can cause disease. Our immune system contains highly specialised cells that attack these foreign bodies, such as invading viruses and harmful bacteria. The long and short of how this works is that each of us has the physiological ability to recognise that our body and its organs are 'ours' and that invading objects are not. The net result is that while the white blood cells and other components of our immune system attacks foreign biological objects inside us, they do not attack us. The advantage of this is obvious. Disease-causing organisms can be attacked and destroyed without the body turning against itself.

However, the immune system can go wrong in various ways. For example, it may over-react to foreign bodies. This is what happens with allergies such as hay fever. In the worst case, such over-reaction can cause death (e.g. the fatal shock experienced by some people on eating nut products or being stung by a bee/wasp). The other main way the immune system can malfunction is by starting to attack parts of its own body. This is what happens in a number of chronic diseases including rheumatoid arthritis.

It is because the immune system normally works so effectively that people receiving human-to-human transplants generally have to be given large doses of immunosuppressive drugs. As their name implies, these drugs damp down the immune system and so prevent it from rejecting the transplanted organ. Unfortunately, patients with suppressed immune systems

are less able to fight off germs so they are more likely to catch infections – and with a weakened immune system even common diseases can prove very serious. With the latest immunosuppressive drugs, though, this is now less of a problem.

When it comes to transplanting non-human organs, such as a pig's hearts, into humans, an extra difficulty arises. Within hours of the transplant, even if immunosuppressive drugs are used, so called hyperacute rejection typically sets in and the transplant fails. It is to try and overcome this problem that pigs are being genetically engineered to carry a single human gene. This gene results in the pigs producing a human protein on the surface of their internal organs. As a result, it is hoped that when these organs are used in transplants, hyperacute rejection will be avoided.

Rejection isn't the only problem that we face if we receive a transplant from another species. Pigs are the species of choice for human xenotransplantation, partly because they are about the same size as we are, partly because they are easy to keep in captivity and partly because their physiology is surprisingly similar to us, despite them being less closely related to us than apes and monkeys. However, pigs carry what are called porcine endogenous retroviruses, endearingly abbreviated to 'PERVs'. This is a problem because a lot of nasty human diseases result from viruses that come from other species. For example, swine flu comes from pigs and the 2009 flu pandemic was caused by swine flu and led to about 250,000 human deaths.

### **Is there a need for xenotransplantation?**

Each year tens of thousands of people have their lives saved as a result of human-to-human transplants. However, each year far more people die who would have lived had they received a transplant. Indeed, the large majority of people waiting for a transplant never receive one. So what can we do about this?

The purchase of human organs – a market-led 'solution' to the shortage – is, by-and-large, illegal, though a number of countries permit the sale of human eggs, sperm and blood. In addition, Iran is one of the very few countries that permits the sale and purchase of kidneys. If you are interested, the going rate is only about US\$4,000 – and waiting times for kidney transplants in Iran have come down as a result.

The reason why most people waiting for an organ transplant never receive one is simply that there aren't enough human organs to go around. There are several reasons for this. For one thing, the number of people who would benefit from a transplant continues to rise. This is partly because of advances in transplant surgery which mean that more organs (e.g. lungs) can now be transplanted than used to be the case. In part, too, this is because a greater range of medical conditions can now be treated by transplantation than used to be the case.

Another reason is that only a very small proportion of deaths result in organs that are suitable for transplants. Deaths from motor vehicle accidents provide a high proportion of suitable organs, yet, thanks to improvements in road safety (seat belts, improved car design,

better road layouts, more speed limits, tougher driving tests, greater use of motor cycle helmets), the number of people killed in such accidents is reducing in those countries where transplant surgery is fairly common.

A final reason for the shortage of human organs is that many countries have some sort of 'opt in' rather than 'opt out' system for organ donation. This can mean that for a transplant organ to become available: (a) the dead person needs previously to have expressed a wish for their organs to be used for transplantation (e.g. by carrying a donor card); (b) a doctor must ask relatives to consent to this; (c) no close relative must object to the transplant.

Of course, a need for transplants doesn't automatically translate into a need for xenotransplants. Better health education might lead to less of a demand for hearts and other organs if we exercised more and weren't so overweight. If only more of us carried donor cards and gave permission for our dead relatives' organs to be used in transplants the need for xenotransplants would be reduced. In addition, though it is still too early to be sure that they will ever work, significant advances are being made in artificial organs, made from metal and plastic. Finally, advances in tissue culture, cloning and stem cell research hold out the hope that more and more human organs may be grown from a patient's own tissues. One advantage of this approach is that there should be few or no rejection problems.

### **Welfare considerations of the animals involved**

The extent to which animals can suffer is still argued but there is increasing acceptance that certain of our closest evolutionary relatives have the brain power that suffering requires. A growing number of biologists and philosophers agree that, at the very least, most mammals can suffer.

So would xenotransplantation lead to significant amounts of animal suffering? Consider, first of all, the pigs that are likely to be used. Companies involved in research on xenotransplantation maintain that their pigs are extremely well looked after. Indeed, in my experience, the animals used in the research are looked after better than are pigs on most pig farms in terms of the conditions in which they live.

However, there is more to the welfare of the pigs than their housing. For a start, the pigs are subjected to a number of surgical procedures. A general anaesthetic is needed to flush out the eggs from sows. In addition, if and when clinical trials begin in earnest, it seems likely that so-called 'gnotobiotic' (germ-free) animals will be needed. Such animals would probably be obtained by what is sometimes euphemistically called 'surgical derivation'. This means that shortly before birth, the entire uterus with the piglets would be removed (surgical hysterectomy) from the mother. The piglets would then be raised in isolation and in sterile conditions. From the pigs' point of view, this doesn't sound like much of a life (pigs are social creatures).

Furthermore, it is not only pig welfare that needs to be considered. Current research aimed at improving the success of xenotransplantation has meant that thousands of primates (captive-bred macaques and wild-caught baboons) have already been used in surgical

operations as recipients of the transplants. While many of these operations are deemed a research 'success', this, of course, is to view the procedure from the perspective of the surgeons and scientists involved (and perhaps, ultimately, the patients and shareholders who may benefit). From the point of view of the non-human primates, every such operation leads to considerable pain and a dramatic shortening of lifespan.

### **Changing the nature of animals**

Let us assume that xenotransplantation will require genetically engineering pigs through the insertion of one or more human genes into pig DNA. This involves changing the 'nature' of the pigs in at least some sense. Is this morally acceptable?

A frequent cry against genetic engineering of any sort is that 'It's unnatural'. However, this objection is difficult to defend. After all, what is 'natural'? In everyday language smallpox, tidal waves and death are natural whereas vaccines, mobile phones and foreign holidays aren't. In other words, there doesn't seem to be much of a relationship between what is 'natural' and what is good.

Nevertheless, the 'It's unnatural' argument can be defended in a number of ways. For a start, a number of religions argue that, at least to some extent and in some sense, nature is good. In the Jewish and Christian traditions, the understanding is that on the sixth day 'God saw everything that he had made, and behold, it was very good'. Death and decay entered the world through sin, but even after the Fall sufficient of God's goodness is present in the creation for much that is natural to be good. Around this notion there has built up an entire theology of natural law.

Nor is it only within religions that nature has been seen as an indicator of goodness. To this day there is a considerable body of opinion holding that 'natural' practices are desirable in such separate activities as child nutrition (e.g. 'breast is best') and agriculture (organic farming) and food (fresh rather than processed).

Aside from psychological reasons for the success of appeals to nature, one great advantage of nature is that it has been around for quite a while. Consciously or otherwise the thought may be 'Our ancestors successfully brought up their children, farmed and prepared their food in these ways so traditional approaches must be OK'. After all, and quite logically, one cannot be sure about the long-term consequences of any new technology (including genetic engineering), only of practices that have been around for a considerable time and so are now considered 'natural'.

However, to what extent does the genetic engineering in question in this particular technology really change the nature of pigs? From the pigs' point of view, it can be argued hardly at all'. The practicalities of genetic engineering have significant welfare implications but it seems difficult to argue from a pig's perspective that the genetic engineering itself has changed its nature. The pig's behaviour is no different; its mental capacities and experiences are unchanged. The only difference is that it produces an extra internal protein. Traditional breeding, on the other hand, has resulted in very significant changes to the natures of farm

animals (increased tolerance of high stocking densities, increased domesticity, massive changes in milk, wool and meat production, etc.).

### **How would you feel?**

How would you feel about the thought of a pig's heart inside of you? It is difficult to predict. Some people might not like the idea – but then the alternative may be death, which most of us don't like much either. When human-to-human heart transplants first started, some commentators said that they were deeply immoral yet we seem to have got used to them very rapidly and most people with a heart transplant are deeply grateful to have had it. If pig-to-human transplants really do take off, it will be very interesting to see how people feel about them.

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