Animal-to-human transplants: the ethics of xenotransplantation

Preface

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Transplantation is a revolutionary form of treatment for organ failure. Its success has been due largely to the discovery of immunosuppressive drugs, which are constantly being improved and updated. The success of transplantation meant that many patients were able not only to live longer but also to have a drastically improved quality of life. This in turn meant different priorities for the health service and, even though transplantation is probably not more expensive than keeping patients with organ failure alive, such financial burdens cannot be disregarded. The success has been so outstanding that demand is clearly outstripping supply. The problem of insufficient donor organs has been compounded by the, fortunate, decrease in road accidents and, with experienced gained, greater selectivity of organs by surgeons. I am one of the fortunate beneficiaries of transplantation. Magdi Yacoub saved my life with a heart and lung transplant when it was found that I was suffering from a terminal form of pulmonary hypertension. It is six years on and I am enjoying life to the full.

The inadequate supply of suitable human donor organs for transplantation has led to a search for possible alternatives, namely xenotransplantation and, more recently, tissue engineering. Xenotransplantation, or animal-to-human transplantation, has been performed for quite some time (e.g. treated porcine valves into human hearts). However, transplantation of whole organs is still at a very early stage. The setting up of a Nuffield Council working party into xenotransplantation was a very welcome development because there were many important issues that needed to be dealt with. These included the shortfall of human donor organs, a problem that was exacerbated recently by the Alder Hey enquiry with nationwide repercussions; the growing uncertainty concerning the potential risk of disease transmission; and public concerns about the use of genetic modification of animals and wider aspects of animal welfare. The Working Party was engaged in a wide public consultation, involving people from all walks of life, as well as calling on the expertise of relevant groups. The report was made public and the Working Party concluded that research into xenotransplantation should continue subject to rigorous regulation to ensure protection for potential human recipients and care for animal welfare. In addition, it was stated that clinical trials are not to commence until such time as the Advisory Committee on xenotransplantation is in place and has given its approval. The Working Party concluded that the animal of choice should be the pig rather than any primate and that the use of transgenic pigs is ethically acceptable. All procedures should be carried out in accordance with the Home Office Animals (Scientific Procedures) Act 1986. If xenotransplantation becomes a treatment of choice, its introduction into the NHS should be overseen by the Super Regional Service Advisory Group. They must ensure that counselling of xenograft recipients is provided, including discussion of the possible psychological impact of xenotransplantation, and that the follow up of patients should include every step during post-transplant life.

The report deals with the problem of transplantation, the demand for organs and how the reduction in human organ availability can be combated. It explains how xenotransplantation raises ethical concerns and places importance on moral convictions. It considers alternatives to xenotransplantation and stresses that the supply of human organs should not be curtailed, with encouragement for organ donation given extra emphasis. The Report goes on to consider the practice of animal care, the transmission of infectious diseases and the problem of unknown infective agents that can be transmitted to humans, consent to participation in clinical trials, the implications for the NHS and the personal and social effects of xenotransplantation.
After the Report

The Report recommended that the Department of Health establish an Advisory Committee to monitor clinical trials in the field of xenotransplantation, assess potential risks, maintain a register of xenograft recipients and assess the impact of xenotransplantation on individual patients. As the Council’s Report was being prepared, the Government established an Advisory Group on the Ethics of Xenotransplantation, chaired by a member of the Nuffield Council, which reported in 1997 and endorsed this recommendation. The UK Xenotransplantation Interim Regulatory Authority (UKXIRA) was subsequently established to ‘provide a focal point for xenotransplantation activity in the UK, provide a means of regulating xenotransplantation and in particular, to provide a process through which applications to undertake xenotransplantation in humans can be considered, and to consider the underlying evidence about xenotransplantation developments and to consider whether clinical trials can be justified’.1

Despite cautious optimism about xenotransplantation around the time the Report was written, it remains the case today that no clinical trials involving whole organs have been conducted in the UK, and UKXIRA state in their most recent Annual Review that ‘the likelihood of whole organ xenotransplantation (particularly for heart transplantation) being available within a clinically worthwhile time frame may be starting to recede’. This hints at new developments in transplant research which may yet obviate the need to use animal organs. These include improvements in organ donor systems, the development of artificial organs like the Jarvik 2000 robotic heart, and advances in tissue engineering techniques. However, commercial bodies are continuing to research the possibilities of xenotransplantation in the UK and abroad. At the same time, debate about its ethical acceptability continues. In 1999, the Council of Europe called for a moratorium on clinical trials in the field. In September 2001 the Pontifical Academy for Life in the Vatican announced that it had considered the ethical issues surrounding xenotransplantation and concluded that the use of animals to save human lives was justified.

Future developments

Tissue engineering is a relatively new, multidisciplinary science that aims to develop methods of growing tissues outside the body which can be subsequently implanted back into the body to help restore or replace the function of damaged or diseased tissues. The general principle involves combining living cells with a natural or synthetic support or scaffold to produce a three-dimensional living tissue construct that mimics the tissue it has been designed to replace (Fig 1).

1 UKXIRA Annual Review 2000
A major advantage of this approach is that tissues can be designed to grow in such a way that they match more precisely the requirements of the individual in terms of size, shape, mechanical strength and immunological compatibility, minimizing the need for further treatment. Key to the success of tissue engineering is a supply of cells that can grow to form the desired tissue. Whilst cells isolated from tissue biopsies are useful, they are usually not the best source as they tend to grow rather slowly. However, stem cells can overcome such problems. A stem cell can be described as an “immature” cell that is able to divide rapidly for many generations giving rise to large numbers of stem cells (i.e. self-renewal). These cells also contain all the information required to form a variety of different tissues. Providing the cells are maintained under the appropriate conditions, it is possible to grow specific types of tissue. There are number of different types of stem cell, including stem cells isolated from the bone marrow, brain stem cells, fetal cord blood stem cells and embryonic stem cells. This has been the subject of another Nuffield Council on Bioethics report. The full potential, as well as the limitations, of these various stem cell sources to supply cells and tissues for regenerative transplants remain to be determined and requires both in vitro experiments and in vivo animal models.

What the future holds

(a) More basic research is needed into xenotransplantation i.e. the problems that might occur before clinical trials begin.

(b) Increased public awareness is needed to improve the current rate of donor organ donation, particularly in view of the temporary set back due to the Alder Hey report and consequent public sensitivity.

(c) Further developments in the fields of cell therapy and tissue engineering.
The Nuffield Council’s Report was the first to tackle the ethical and regulatory issues raised by xenotransplantation, and did so comprehensively, recommending clear guidelines and cautious approaches to future work in this area which have been broadly followed by the UK government.