Chapter 1

The promise and the problems

1.1 Rare attempts have been made to transplant animal organs or tissue into human beings since the early years of this century. Interest in this procedure, known as xenotransplantation, has increased in the last few years because it is seen as one way of reducing the shortage of human organs for transplantation. Currently, this shortage severely limits the potential of transplantation for treating human disease.

1.2 The prospect of using animal organs and tissue for xenotransplantation raises important issues, both practical and ethical, which must be debated. Will xenotransplantation be scientifically feasible? If so, should it be permitted? Are there safety risks for recipients, or for the public at large? If so, how can patients and the wider population be protected? Should animals be used in this way? This chapter sets out the main issues raised by xenotransplantation to be discussed in the body of the report. First, however, it sets the scene by describing the increasing success of transplantation for treating organ failure and other conditions, and the increasingly acute shortage of human organs and tissue for transplantation.

Transplantation in medicine

1.3 For many conditions involving organ failure, transplantation has become routine, and is often the treatment of choice. In the early days, problems with organ rejection, and infections resulting from early immunosuppressive regimes, made transplantation a risky procedure. But a new generation of immunosuppressive drugs, and improved surgical techniques, now allow patients to receive transplants relatively safely and with considerable benefit. As Table 1.1 shows, more than four in five kidney transplant recipients live for at least a year, and over two-thirds live for at least five years. Other transplants are not as successful, but even in the least successful case of liver transplants, more than half the recipients live for longer than five years.
Organ transplantation offers several benefits. For some conditions, such as advanced heart failure, treatment with drugs or restorative surgery may not be possible and a transplant will provide the only way of replacing a failed vital organ. Heart or liver transplantation can offer many additional years of life for people who otherwise might not survive, as the one year and five year survival rates for liver and heart transplant recipients show (Table 1.1). Worldwide there are patients whose lives have been considerably extended following transplantation: by 23 years after liver transplants and 20 years after heart transplants.

Transplantation can not only increase the length of life, but also improve its quality. Even where there is an alternative form of treatment, such as dialysis for end-stage kidney failure, a transplant frequently offers a higher quality of life despite the drawbacks of the continuous immunosuppressive regime most transplant recipients require. Kidney transplant recipients are freed from the necessity of regular, uncomfortable and time-consuming treatment and are restored to a level of health not possible with dialysis. They are able to eat and drink freely, and to travel, in ways that people on long-term dialysis often cannot. Patient support groups describe heart transplant recipients who are able to climb hills, and undertake other activities, that they would not have been able to manage before the operation. Some transplant recipients participate in highly demanding sporting contests such as the Transplant Games.

It should be noted that, contrary to some misperception, transplantation is not particularly expensive. Estimates are very difficult to make, but it is possible to get a rough idea of the relative costs of different treatments. A kidney transplant operation costs in the region of £10,000. After that, the cost of immunosuppressive drugs and other follow-up treatment is about £3,000 a year. In contrast, dialysis costs about £18,000 a year if the patient is treated in hospital, and about £11,000 if the patient is treated at home. Thus, kidney transplantation is a more cost-effective

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treatment for patients with renal failure than long-term dialysis. The cost of other transplant operations varies according to how long the patient remains in hospital. Heart transplants cost about £10,000 - £18,000 and liver transplants about £15,000 - £18,000. Immunosuppressive drugs and other follow-up treatment after a liver transplant cost about £3,000 - £5,000 a year.2

The demand for organs

1.7 The success of transplantation, however, brings with it the problem of obtaining an adequate supply of human organs for such treatments. In the UK, the majority of human organs for transplantation come from donors who are brain stem dead but whose lungs are being artificially ventilated in an intensive care unit and whose hearts are still beating. Most of these people have suffered severe brain damage, mainly caused by brain haemorrhages or road accidents. Some organs, such as kidneys, can be removed from donors whose hearts are no longer beating. And kidneys, sections of the liver, and some tissues such as bone marrow, can be donated by living people. Live donation, however, is a major procedure and it is not possible for hearts. Thus, the supply of organs for transplantation is very restricted and falls far short of demand. Even if all human cadaveric organs were somehow made available for transplant, the supply would still not meet the potential demand.3 Meanwhile, as the benefits of transplantation have become more apparent, so the demand for this form of treatment has increased and the shortage of human organs has become more acute. This is illustrated by the figures for kidney transplantation, the most commonly performed transplant operation (Figure 1.1). In 1978, in the UK and the Republic of Ireland, 765 kidney transplant operations were performed, and 1,274 people remained on the waiting list. By 1994, the number of transplants performed that year had increased to 1,744, but the number of people remaining on the waiting list had increased to 4,970.4

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2 Another method of estimating treatment costs uses the QALY or Quality Adjusted Life Year, which tries to take account of the increase in life-expectancy and quality of life gained by treatment. This method has its difficulties, but it can give a rough idea of treatment costs. It indicates, for example, that a kidney transplant is about four times more expensive than a hip replacement, but confirms that it is a less expensive treatment for kidney failure than dialysis (Mason J et al. (1993) Some guidelines on the use of cost effectiveness league tables. British Medical Journal, 306:570-2).


Fewer heart transplants are performed, but the organ shortage is still acute: in 1994, 328 transplants were performed, but 320 patients remained on the waiting list. Unlike patients with kidney failure, who can receive dialysis, patients with end-stage heart failure often have no alternative form of effective treatment and many will die while waiting for a suitable donor organ. This means that the length of the waiting list underestimates the demand for heart transplants. In addition, the organ shortage means that the criteria for eligibility for transplantation are very strict: organs are transplanted into those for whom there is the most pressing need and the best chance that the operation will be successful. Many people who might benefit from a transplant if more organs were available never make it onto the waiting list for human organs. It is estimated that, if sufficient organs were available, the number of people in the UK who could benefit from heart transplantation would be five times the number that can currently hope to receive an organ. Since the incidence of heart failure increases with age, as the number of elderly people in the UK increases, the demand for heart transplants is likely to increase still further.

Figure 1.1  Number of kidney transplants and size of waiting list

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5 Figure reproduced with kind permission from UKTSSA information sheet (1995). Figures are for cadaveric kidney transplants.
1.9 It is not only organs, such as the kidneys, heart, liver and lung, which are transplanted, but also human tissue and cells. Hip replacements may involve transplants of bone and treatment of burns may require skin transplants. Less common is the transplantation of neural tissue for treating Parkinson’s disease and the transplantation of pancreatic islet cells for treating diabetes. The shortage of human organs is especially pressing, since they are usually required to treat otherwise terminal diseases that cannot be treated in any other way. In contrast, there may be alternatives to treating a condition if tissue is not available for transplantation, and the condition itself may not be so life-threatening. Moreover, much human tissue, like bone and skin, can regenerate and can, therefore, be obtained from living donors. Nevertheless, in addition to the difficulty of obtaining organs, there are also difficulties in obtaining supplies of human tissue and cells for transplantation. Further developments in transplantation are likely to lead to its use for treating a wider range of conditions and so to increased demand for human material for transplantation.

Reducing the shortage of human organs

1.10 How can the shortfall between the supply of, and the demand for, human organs and tissue be overcome? One approach is to try and reduce the demand through preventive measures to improve health: at present some transplants are required for conditions that should be avoidable. Another approach is to introduce measures to improve the supply of human organs and tissue. It is often suggested that, if the UK adopted measures similar to countries with a higher transplantation rate, it could increase its transplant activity. As discussed in Chapter 2, however, changing policy to improve human organ supply is a sensitive issue. In addition, certain factors affecting transplantation rates may be beyond the control of policy changes. In the UK, for example, the low number of organ donors is due in part to the wholly desirable decline in deaths due to road traffic accidents or brain haemorrhage.8, 9

1.11 Another possibility for reducing the human organ shortage is to develop artificial replacements for organs and tissue. These may be mechanical devices, like the battery-powered heart, or bioengineered structures incorporating human or animal material. Many of these developments hold promise for the future but, as discussed in Chapter 2, they remain problematic for the time being.

The promise of xenotransplantation

1.12 The demand for human organs and tissue for transplantation exceeds their availability and the gap between supply and demand is likely to increase (Chapter 2). In these circumstances one possibility is that the imbalance could be redressed by using other animals as sources of material for transplantation into human beings. Pig heart valves have been used in human heart surgery for 30 years. Attempts to transplant animal organs into human beings are far more ambitious. To date this has not been successful. The best result was recorded in the case of one patient who lived for nine months in the 1960s having received a transplanted chimpanzee’s kidney.

1.13 The major hurdle in the way of successful xenotransplantation is preventing the rejection of transplanted animal organs. This is a problem even with human organ transplantation: the recipient’s immune system mounts an attack on the transplanted organ, which it sees as foreign. The immune response to organs or tissue from a different species is much stronger. Two main approaches are being used to overcome this problem. First, in the United States, the use of baboons is being investigated, on the basis that baboons are closely related to human beings and so the immune response to baboon organs or tissue will not be too strong. The second approach is to use pigs that have been modified genetically so that their organs do not cause such a strong immune response when transplanted into human beings. These two approaches are described in more detail in Chapter 3.

1.14 Xenotransplantation offers promise, not only for organ transplantation, but also for the transplantation of tissue and cells. Xenotransplantation of animal bone, skin, bone marrow, pancreatic islet cells, and fetal neural tissue have all been suggested. Xenotransplantation of tissue is a less drastic procedure than organ xenotransplantation. The immune response is less vigorous for small pieces of tissue which do not have a major blood supply running through them and the surgical procedure is likely to be less risky. The impact on the recipient may also be less severe since it seems that people attach more significance to organ transplantation than to the transplantation of tissue or cells. Moreover, as mentioned above, it is the shortage of human organs that is particularly acute. For this reason, the discussion in this report will largely concern the xenotransplantation of organs. Much of what is said about organs, however, will also apply to xenotransplantation of tissue and cells. Where xenotransplantation of tissue or cells raises particular issues, these have been discussed. The transfer of molecules between species lies outside the scope of the report (paragraph 3.8).

1.15 Recent developments suggest that xenotransplantation teams are making progress in controlling the immune response to animal transplants in order to prevent rejection. Even if this becomes possible, there is also the question of whether animal organs and tissue will be able to perform all the necessary functions in a human body.
Nevertheless, it is looking increasingly probable that many of the biological obstacles to xenotransplantation will eventually be overcome.

1.16 Proponents of xenotransplantation argue that there would be significant benefits if it were to become a successful and widely available treatment. Most importantly, enough animals could be reared to provide sufficient organs and tissue to overcome the present shortage of human organs and tissue for transplantation. This would eliminate the decline in health, the considerable anxieties, and the loss of life associated with the current long waits for human organs and tissue. Instead, xenografts could be offered as and when they were needed. Xenografts could also be offered to a wider group of patients who might benefit from transplantation but who are currently not eligible for a human organ or tissue transplant. Successful xenotransplantation of genetically modified organs and tissue would also eliminate the need for the careful matching of the organ or tissue with the recipient, required in transplants between human beings in order to reduce rejection by the immune system. This would be of particular benefit to people for whom it is currently more difficult to find compatible organs and tissue: for example, people from ethnic minorities for whom there is a shortage of donors with the same or similar tissue type.

1.17 Xenotransplantation would also avoid the need to consult the relatives of dead people about organ donation at times of great stress and emotional turmoil. If there are alternative sources of organs, it will not be necessary for relatives to make such difficult decisions. The need to perform transplant operations at very short notice, as occurs when human organs become available, would also be avoided: patients and health care workers could prepare themselves for the operation in advance. Transplantation would become an easier service to coordinate and administer, and this might bring savings in cost.

1.18 For some, xenotransplantation would be preferable to some of the current or proposed methods of obtaining human organs and tissue. Despite legislation in many countries prohibiting this, the buying and selling of human organs, especially kidneys, continues.10 If xenotransplantation were successful in reducing the shortage of organs and tissue, such ethically unacceptable commercial dealings might stop. Proponents of xenotransplantation have pointed out that, in addition, it might provide an alternative to the use of human tissue from aborted fetuses, and to methods for obtaining human organs such as elective ventilation or live donation, all of which have their difficulties (Chapter 2). However, xenotransplantation itself raises important and wide-ranging ethical concerns which need to be addressed before a judgement can be made about its acceptability. The range of these concerns is set out below.

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10 Arguments against commercial dealings in human tissue were set out in a previous report of the Nuffield Council on Bioethics (1995) *Human Tissue : Ethical and Legal Issues.*
Ethical concerns

1.19 Xenotransplantation raises the question of how far, if at all, and in what ways it is acceptable for human beings to use other animals as a source of organs and tissue for transplantation. Even if one accepts in principle the use of animals in medicine and in medical research, their use in xenotransplantation may raise particular difficulties. The use of primates such as baboons would concern many. The use of genetically modified animals, which is likely to be necessary if pigs are to be used for xenotransplantation, also merits special consideration. And if the use of animals to supply organs for xenotransplantation is considered ethically acceptable in principle, can the welfare of the animals be adequately taken into account? These and other issues are discussed in Chapters 4 and 5.

1.20 Public health issues arise from the prospect of xenotransplantation. The transplantation of animal organs or tissue raises the possibility that infectious organisms of animals may be transferred into the human population. Xenotransplantation, like any major innovation, may have wide-ranging and unpredictable effects. It is necessary, therefore, to identify principles which would provide a basis for dealing with the remote, and unquantifiable, hazards that xenotransplantation could bring. This is discussed in Chapter 6.

1.21 The treatment of early recipients of xenografts may raise serious ethical issues. So far the survival times for recipients of xenografts have been poor and, in effect, early recipients are being used as experimental subjects for the development of the technology (Table 3.1). The principles that should govern early clinical trials for xenotransplantation are discussed in Chapter 7.

1.22 Widespread introduction of xenotransplantation could have implications for the health care system. There will be cost implications, particularly in a cash limited health care system like that of the UK. It is possible that xenotransplantation would displace other, perhaps more worthwhile, activities. The cost implications of xenotransplantation, and how the health service might control the introduction of xenotransplantation, is considered in Chapter 8.

1.23 Xenotransplantation may also have social implications. It needs to be assessed in the context of the wider debate about modern medicine and attempts to prolong life. Possible personal effects of xenotransplantation on those who are recipients need to be considered. It is impossible to say in advance what form and intensity these will take. Finally, it is important to consider how the use of animals as sources of organs might affect people's willingness to donate organs. These issues are discussed in Chapter 9.
1.24 The extent and importance of these ethical issues raises the question whether existing regulatory structures are adequate for managing the development of xenotransplantation. In Chapter 10 the different strands of the discussion are drawn together and suggestions are made for the appropriate regulation of xenotransplantation. The Working Party considers that the range of issues raised by xenotransplantation and the potential consequences of its practice are so great that there is a need for a national body to keep developments constantly under review.

The importance of moral convictions

1.25 In considering the ethical issues raised by xenotransplantation, great emphasis was placed by the Working Party on the importance of the moral convictions that people hold. It is sometimes argued that ethics and morality can be distinguished. According to this argument, codes of ethics are seen as derived by a process of abstract reasoning from first principles that are timeless and universal. Morality, by contrast, is seen as a set of rules, norms and expectations, specific to a particular culture and a particular time, which rests on tradition, sentiment and sympathy. Even where ethical systems prescribe respect for the beliefs of ordinary people, the rationality of those beliefs is often questioned.

1.26 Ethical deliberation does not take place in a vacuum, however, but in a social and historical context that is continually changing. There are no timeless solutions, and ethical debate cannot be separated from the domain of social life. Equally, people’s moral convictions are not just rooted in the force of tradition but are the results of sincere and mature reflection. This was reflected in the submissions received by the Working Party on the subject of xenotransplantation.

1.27 Wherever people are involved in making judgements about questions of life and death - whether as scientists, doctors, patients, relatives or loved ones - these judgements are made against the background of their relationships with human beings and with other animals. These relationships are already in place as the ground from which any moral or ethical system grows. Just as a craftsman’s ability to make fine judgements depends on long experience of working with the materials, so the sensitivity of individuals to the needs of others and their capacity to respond to them depends on the historical unfolding of their social relationships, both with human beings and with other animals. Thus, a sense of what may reasonably be done to human beings and to other animals necessarily depends on the sensitivity developed through these relationships.

1.28 In considering the ethical issues raised by xenotransplantation, the Working Party recognised that the capacity to make ethical or moral judgements depends on this sensitivity and that any judgements which had no basis in such experience would carry little practical or motivational force. An attempt has been made to identify
principles that will have such a basis but which, at the same time, reflect a critical appraisal of present practice and possible innovation.

**Basic assumptions**

1.29 This report is based on two assumptions of pluralism. The first is a recognition that it is unrealistic to expect complete consensus across society on the issues addressed in the report. The aim of the report is to seek as much common ethical ground as possible. But it is important to recognise and acknowledge differences of opinion. This will help to inform future debate, to try and ensure that, whichever direction society chooses to take, its decision will be based on principles that can be justified as reasonable to most of its members, and to take account of the views of those who dissent from the majority decision.

1.30 The second assumption is that no single ethical framework can capture all the reasonable perspectives that may be taken on the issues raised by xenotransplantation. The report does not, then, present a particular ethical theory and its application to all the various questions that arise. This would be bound to leave out reasons and values which would not be captured by the theory. Instead, the Working Party attempted to take into account all the salient considerations, to give them whatever weight seemed reasonable, and then to make judgements where appropriate.

**Method of working**

1.31 The Working Party met 11 times between February 1995 and January 1996. The inquiry was announced in the press in April 1995 and submissions were invited from interested parties. Annex A describes the consultation process in more detail. Written submissions were invited from a wide range of groups and individuals thought to have a possible interest in the issues raised by xenotransplantation. Copies of the consultation letters and information pack are presented in Annex B and those contacted are listed in Annex C. Annex D lists those from whom submissions were received. The Working Party members are grateful to all those who responded.

1.32 The Working Party recognises that the submissions received could not be taken as representative of public opinion as a whole. Their value lay in indicating the range of views on xenotransplantation. Almost all the issues discussed in the report were raised in some form in the submissions and the Working Party has drawn considerably on the thinking set out in them. From the submissions, three main points emerged:
where responses indicated an overall stance, many were in favour of the further development of xenografts. Most were cautious in this, weighing perceived advantages and disadvantages and specifying the need for a number of safeguards. Views here ranged from those who felt that the present legislation, guidance and codes of practice adequately accommodated developments in this area, to those who wished to see a broadened and continuing development of new regulatory mechanisms;

- a number of respondents expressed the firm view that in no case should xenotransplantation proceed because of their principled objections to the use of animals. In some cases they derived from particular religious convictions. On the whole, the case against xenografts was argued in carefully documented detail: critics were aware of and cited the latest research, and their arguments touched on most or all of the areas of concern that are discussed in the report;

- the weight of comment, regardless of the views expressed, centred on the use of animals.

Use has been made of quotations, selected from the submissions received, throughout the report.

The language used in the report

1.33 The terms xenotransplantation and xenografting are used interchangeably. The term organs and tissue has been used when referring to the xenotransplantation of animal organs, tissue and cells. Where appropriate, organs, tissue and cells are referred to specifically. The term animals should be taken to mean non-human animals. The Working Party accepts that a limitation of this convention is its suggestion that human beings are separate from other animals, but felt that it could be justified in terms of brevity and clarity. Similarly, the term primates should be taken to mean non-human primates. The term source animal, rather than donor animal, has been used in recognition of the fact that an animal has no choice in whether its organs or tissue are removed for human use. To avoid confusion, the term cost has been reserved for discussion about the financial implications of xenotransplantation. The term harm refers to possible disadvantages either for human beings or for other animals. There is a glossary, defining technical terms, in Annex E.