Bio Factsheet

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Tissue and Organ Transplants

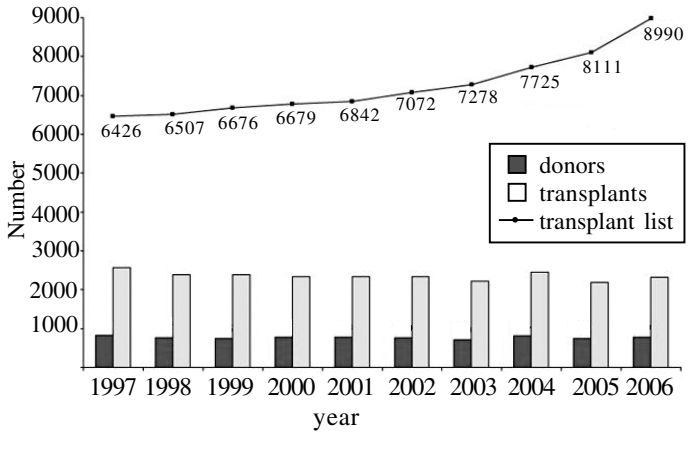
Transplants are a favourite synoptic topic; and ethical issues are becoming more common on all of the A level specifications.

This Factsheet summarises:
- The main types of transplant
- The difficulties that have to be overcome to stop rejection
- Ethical issues surrounding transplants
- Typical exam questions you are likely to face

An organ transplant is the moving of a whole (or part of) an organ from one person's body to another. It is always done to help patients whose organ has failed in some way or is diseased.

Over 2,300 transplant operations are performed annually in the UK (Fig1), but there are over 7,000 people on the waiting list to receive a new organ – this reflects a shortage of supply. This gives rise to a number of **ethical considerations** surrounding the circumstances under which someone should donate an organ for transplant.

Fig 1. Transplants UK



Types of organ transplantation

Kidney and heart are the most commonly performed transplant operations. However, a whole host of other organs and tissues from the body can be transplanted nowadays from the liver, pancreas and intestines to heart valves and bone marrow.

Most transplant operations involve transplantation from one human to another with similar immune systems so that the tissues **'match'**. However, it is possible to **transplant across different species (xenotranplantation)**. Some doctors believe this could be a means of solving the **supply problems** we are currently facing. However, it raises a number of ethical, religious and safety issues which will have to be resolved.

Table 1 Key terms

Term used	Description
Allograft	Transplant between genetically different members of the same species
Isograft	Transplant between genetically identical members of the same species (e.g. identical twins or even a clone)
Xenograft (xenotransplantation)	Transplantation from one species to another (e.g. a pig to a human)
Domino transplant	Transplanting 2 organs at a time. For example, if a patient needs new lungs it is easier to transplant the lungs and heart together. The recipients heart can then be used for another patient.

A brief history of transplant technology

Although there are some accounts of experimental transplants taking place as early as second century BC, the time-line below gives details of the first successful documented examples.

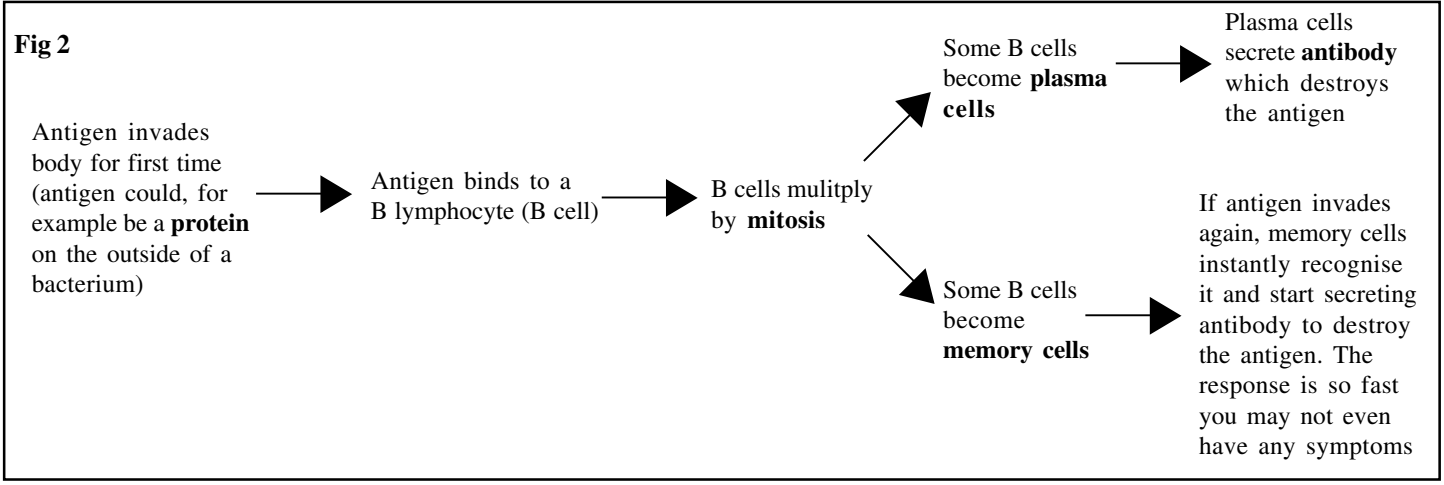
1905	First successful cornea transplant performed by Eduard Zirm (In China the main source of organs for transplant is from executed prisoners)
1954	First kidney transplant by Joseph Murray, USA
1966	First pancreatic transplant by Lillehei and Kelly, USA
1967	First successful heart transplant by Christiaan Barnard, South Africa
1981	First heart-lung transplant by Bruce Reitz, USA
1986	First successful double-lung transplant by Joel Cooper, Canada
1998	First live-donor partial pancreatic transplant by David Sutherland, USA
2005	First successful partial face transplant, Devauchelle and Dubernard, France
2006	First successful penis transplant by Hu Weilie, China

Transplant biology

The main difficulty relates to the patient's immune system. Because the donor organ doesn't belong to the patient, **the immune system** sees it as **foreign/antigenic** and launches an attack on the newly transplanted tissue. L**ymphocytes** release **antibodies** which attack the organ and this leads to **rejection**.

The flow chart shows what happens when an antigen enters our body (Fig 2)

Fig 2



If this is not controlled, the patient often dies. Drugs which **suppress** or slow down the patient's immune system were first discovered in the late 1950's. These so-called **immunosuppressants** (the most famous of which is called **cyclosporine**) revolutionised transplantation surgery because they stopped the organ being rejected.

However, suppressing the patient's immune system makes them more likely to get other infections. The challenge is to develop a drug which stops rejection but doesn't suppress the immune system to the extent that the patient becomes vulnerable to infections.

Typical Exam Question

Gene therapy is used to treat the genetic disorder, ADA deficiency. Affected individuals are unable to produce the enzyme adenosine deaminase (ADA). Without this enzyme, T lymphocytes, a type of white blood cell, cannot provide immunity to infection.

T lymphocytes are produced in bone marrow. A bone marrow transplant from a genetically matched donor can provide a permanent cure for ADA deficiency.

(a) Suggest why bone marrow for a transplant is obtained from a genetically matched donor. (1 mark)

(b) Explain why treatment of ADA deficiency by gene therapy must be repeated at regular intervals, whereas a single bone marrow transplant can provide a permanent cure. (2 marks)

Markscheme

(a) to .prevent. rejection / immune response; 1

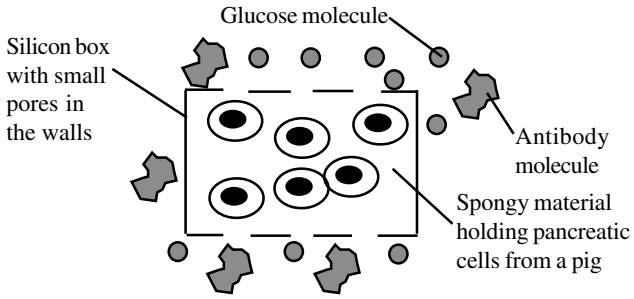
(b) T lymphocytes have a limited life span / do not reproduce;
bone marrow provides continual supply of T lymphocytes; 2

Often in synoptic topics like this, you will be asked to apply basic principles to unfamiliar topics or to combine bits of knowledge of different areas of the specification– the secret is not to panic! The following question combines transplants with glucose regulation.

Typical Exam Question

Many diabetics inject insulin because their pancreas has stopped producing it. Attempts have been made to transplant pancreatic cells from human embryos into diabetics but these foreign cells are often destroyed by the diabetic's immune system.

The diagram shows a new type of transplant which has been tested in rats.



(a) (i) Explain why this transplant is not destroyed by the rat but can respond to changes in the rat's blood glucose concentration. (2 marks)

(ii) Suggest why there might be controversy if this transplant was used in humans. (1 mark)

(b) Explain how the cells in the transplant control the blood glucose concentration of the rat. (3 marks)

Markscheme

(a) (i) antibody too big to get through pores (and attack cells);
glucose small enough to (diffuse) enter / hormones can leave;
protects from lymphocytes / no antigen on silicon box; 2 max

(ii) killing animals to use for human (transplant);
religious objections;1 max

(b) rise/fall in rat blood sugar means more/less glucose enters (diffuses) into box;
detected by animal pancreas cells that release insulin/ glucagon;
insulin (diffuses) into rat's blood;
insulin/glucagon makes rat's cells take up/release more glucose; 3 max

Safety

Another major problem with transplantation surgery is the risk of transmitting a blood-borne disease. If the donor is **HIV+** (the virus that leads to **AIDS**) or carries **hepatitis** (a liver disease), then it is likely that this will be transmitted to, (or caught by), the patient receiving the organ. All donors are screened in developed countries like the UK, but in the developing world efficient screening cannot be guaranteed.

The supply of donor organs

The largest supply of donor organs comes from people who have died but whose organs are still functioning and healthy (for example following a car accident). Currently in the UK a donor must give consent for organs or tissues to be used in this way by carrying a Donor Card (see www.uktransplant.org.uk for further information). If a recently deceased person is suitable as a donor, but hasn't consented by the donor card scheme, their close family (or next of kin) can give permission on their behalf for donation to occur.

The situation in the UK is an example of an **'opt-in' system**. That is to say doctors cannot use tissues unless they have permission. However, some countries (e.g. Spain, Poland and Brazil) operate an '**opt-out' system'** . This means that it is assumed that everyone gives consent or permission for organ donation on death, unless they have specifically said no or 'opted-out'. Such countries have a much greater supply of organs.

Some groups in the UK are currently campaigning for the system to be changed from an opt-in to an opt-out approach to increase the supply. Critics argue that this is a very personal decision which shouldn't be interfered with by the State.

It should be noted that you don't have to be dead to be an organ donor. It is possible to donate a kidney or part of your liver (a **lobe**) and still live healthily. These are so called **"Good Samaritan" donors** who usually (although not exclusively) donate to members of their family.

The ease of organ transplantation has been improved in recent years by big leaps in the technology used to preserve the organ for transplant outside the body. A very recent development has come about as a result of the work by Professor Ian Megson and his team at the University of Edinburgh. They invented a preserving fluid, containing nitric oxide, which helps to prevent blood from clotting inside the organ. This means it can spend longer outside the body without being too badly damaged before being transplanted into its new owner. This could facilitate transporting organs internationally for specific donors, improving the chances of a tissue match".

Ethical issues

Saviour siblings are children whose tissues can be used to treat a brother or sisters with a diseased organ or tissues. Pre-implantation embryo selection is used to ensure a tissue match. This practice is allowed, but very controversial

Ethics is the study of moral principles and how they relate to human behaviour.

Just because scientists and doctors *can* do something, doesn't mean to say that they *should.* It is up to citizens, elected politicians and ethics committees within hospitals and universities to decide on ethical questions and debates within Biology and Medicine. *The Human Tissue Act 2004* in the United Kingdom and *Human Tissue (Scotland) Act 2006*, is the current law which regulates what can be done in this area. One recent change to the law is the fact that if a person has consented to donate their organs after death (for example through the donor card scheme), their relatives cannot override this decision after they die.

Some of the ethical debates and questions surrounding organ donation include:

- Ensuring the supply of organs for donation. The relative merits of 'opt-in' and 'opt-out' systems. Should organs for donations be brought and sold? If governments won't regulate their supply, then a black market tends to arise, especially from developing countries to the west.
- **Genetically engineering** pigs to be used for organ donation so that they **match** and are not rejected by humans' immune systems. There is also a risk of an infection jumping from one species to another.
- Some religious groups object to the use of animals in this way or to the transplant of tissues from one individual to another.

Practice Questions

1. (a) Why is it necessary to suppress a patient's immune system following a transplant? (3)
   (b) Explain the term xenotransplant (2)

2. Mice have been bred so that they lack light sensitive cells in the retina of their eyes. Scientists have then attempted to cure their blindness by transplanting cells into the defective eyes. They have used both stem cells and cells from the retina of adult mice. Neither approach improved vision.

   (a) What is a stem cell? *(2 marks)*

   In another study scientists transplanted precursor cells for light sensitive cells, taken from normal three- to five-day-old mice. Precursor cells are cells that have already differentiated so that they can only go on to develop into a very limited range of cell types. After the transplant the blind mice were able to react to bright lights.

   (b) Further research may show that transplanting suitable precursor cells is likely to restore human sight in some conditions. What issues would you expect members of an Ethics Committee to consider in deciding whether to approve research on humans? (3 marks)

Answers

1. (a) Because the recipients body recognises the tissue as foreign/ antigenic;
   Lymphocytes;
   Produce antibodies which attack the new tissue;
   Leads to rejection. (max 3)

   (b) Transplantation from one species to another e.g. pig to human.

2. (a) cells that can divide indefinitely;
   cells are undifferentiated/not specialized;
   cells that can develop into any type of specialised cell
   (b) source of cells;
   problems of xenotransplants;
   opt-in, opt-out argument
   dangers/possible side effects;
   cost;

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