

Organ Transplantation

Last update: March 2010 Contact: Lisa Tambornino

I. Medical aspects

The medical use of the word transplantation refers to the replacement of organs, body parts, tissue and cells for therapeutic purposes. Two basic categories of transplantation can be defined: autologous and allogeneic. In the case of an autologous transplantation tissue or cell material is simply moved from one part of the patient's body to another – in other words, the donor and the recipient of the transplant are one and the same person. When organs, tissue or cells are transferred from one member of a given species (who may or may not still be alive) to another member of the same species, the transplantation is referred to as being allogeneic. Further qualifying terms include **syngeneic transplantation** (see module Syngeneic transplantation) , i.e. transplantation between identical twins, **xenotransplantation** (see module Xenotransplantation) , which refers, for instance, to transplantation between animals and humans, as well as **alloplastic transplantation** (see module Alloplastic Transplantation) , in which human organs are replaced by artificially manufactured ones.

The history of transplantation medicine

There are indications in some ancient myths that man may have attempted to perform transplantations in historic times, but the origins of scientifically sound transplantation practice can be traced back to the early twentieth century, when improvements in vascular surgery and operation techniques provided practitioners with the necessary technological basis. The first successful kidney transplantation was performed between identical twins in the USA in 1954. 1963 saw the first successful liver and also the first lung transplantation. In 1965, the pioneers managed to transplant a pancreas successfully. The first heart transplantation, carried out by Christiaan Barnard in South Africa in December 1967, caught the attention of people throughout the world. The first successful **multi-organ transplantation** (see module Multi-organ transplantation) took place in 1989. The problems which became evident during the initial stages, such as the difficulties encountered in preserving organs after removal or in dealing with the recipients' **immunological response** (see module Transplantation immunology and immunosuppression) , could be addressed and at least to some extent solved through the experience gained and the development of **immunosuppressive drugs** (see module Immunosuppressive medication) .

The present state of research

About two decades ago, transplantation medicine emerged from its phase as a field of experimental research and today its techniques are recognized as being part of standard professional practice in all developed countries. There is a long list of different cell and tissue types, organs or indeed entire organ systems for which the medical basis for transplantation is now secured. According to the **German Foundation for Organ Transplantation**

(Deutsche Stiftung Organtransplantation – DSO) (see module DSO) , an average of eleven organs are transplanted every day in Germany alone. In the great majority of cases this involves **kidney transplants** (see module Kidney transplantation and renal replacement techniques) , followed by **liver transplants** (see module Liver transplantation, living-donor liver donation and split liver transplantation) and **heart transplants** (see module Heart Transplantation) . Less common are transplantations of the **pancreas** (see module Transplantation of the pancreas) and **lungs** (see module Lung transplantation). Transplantation can only succeed when the transplanted material is not rejected by the receiving organism. Transplantation of foreign organs may trigger an **immunological defence reaction** (see module Transplantation immunology and immunosuppression) , with the result that the transplanted organ cannot fulfil its proper function. One differentiates between acute rejection and chronic rejection. Acute rejection refers to the period immediately following transplantation, and it may occur in varying degrees of severity. The chronic form of rejection is characterised by a long-term process in which the organ gradually fails. The defence mechanisms of the patient's own body must be kept permanently suppressed with the help of **immunosuppressive medication** (see module immunosuppressive medication) , and this requires a high degree of co-operation on the part of the patient. In addition to the phenomenon of failure or rejection of the transplanted organ or tissue, transplantations can also lead to a so-called **graft-versus-host reaction** (see module Graft-versus-host reaction) in which the immune system cells which are transferred with the transplant recognise the recipient's body as being 'foreign' and attack it.

Organ shortage

At present there is a large discrepancy between the number of patients who require a transplantation on the one hand and the number of available organs on the other. According to statistics gathered by the **German Foundation for Organ Transplantation (Deutsche Stiftung Organtransplantation – DSO)** (see module DSO) , in 2008 about 12,000 people were waiting for an organ to become available – over 8,000 of them for a kidney. Each year about 1,000 people die who could probably have been saved if a suitable organ had been available in time. This shortage is apparent throughout the world, but particularly so in Germany. Comparisons have shown that, in proportion to the total population, fewer organs are donated in Germany than in other European countries. As a means of dealing with the ongoing organ shortage, new techniques have been developed such as **split liver transplantation and living donor liver transplantation** (see module Liver transplantation, living-donor liver donation and split liver transplantation) . Also, research continues into alternatives such as **xenotransplantation** (see module Xenotransplantation) and **alloplastic transplantation** (see module Alloplastic transplantation) .

The procedure for post-mortal organ donation in Germany

The procedure to be adopted in Germany in a case of post-mortal organ donation is defined in the law on organ and tissue donation, removal and transplantation (“Gesetz zur Spende, Entnahme und Übertragung von Organen und Geweben” (**TPG**) (see module TPG) . The TPG stipulates that three agencies in particular must be involved in the organisation of a post-mortal organ donation: firstly the hospitals, secondly the **German**

Foundation for Organ Transplantation (DSO) (see module DSO) and thirdly the international allocation agency **Eurotransplant** (see module Eurotransplant) . It is the task of the hospital staff to diagnose brain death in accordance with the **Guidelines of the German Medical Association (Bundesärztekammer)** (see module Guidelines of the German Medical Association (Bundesärztekammer) for organ allocation) , to communicate with the next of kin and to inform the nearest operative centre of the DSO if approval for an organ donation has been obtained – either in the form of an **organ donor card** (see module organ donor card) or in that the next of kin have confirmed the will of the person who has died. It then devolves upon the DSO to coordinate the removal of the organ. For the protection of the organ recipient, the first step is to conduct appropriate laboratory investigations. If there are no signs of infections or tumour disease which could endanger the recipient, the DSO transmits all relevant data to Eurotransplant, which performs the selection of the recipient with the help of computer analysis. As soon as the recipient has been selected, Eurotransplant prepares the organ removal together with the DSO and the regional coordination staff of the donor hospital. At the same time, the (international) transport of the organ from the donor hospital to the respective transplantation clinic for the recipient is set in motion. The DSO reimburses the personnel and material costs which arise in the course of an organ donation. The costs incurred for the actual transplantation of the donated organ are carried by the recipient's health insurance. The name of the donor is never communicated to the recipient, and also the next of kin of the donor are not informed as to the identity of the donor. However, the transplantation centre will disclose whether it was possible to transplant the organ or organs successfully, if the next of kin wish to find out.

The procedure for living donor organ transplantation in Germany

A living donor transplant represents a possible alternative to post-mortal donation. According to German **transplantation law** (see module German transplantation law) a living donor transplantation involving a kidney, parts of a liver or any other organ which cannot regenerate is only allowed between close relatives and persons with very close personal ties. In order to ensure that a donation of this kind takes place on a voluntary basis and that medical risks for the donor are minimized as far as possible, and also to preclude any possibility of abuse or trading in organs, every potential case must be thoroughly investigated by an expert commission beforehand. As well as comprehensive laboratory tests to determine the respective blood groups and other medical factors such as **HLA compatibility** (see module Transplantation immunology and immunosuppression) , cardiopulmonary exercise tests and organ-specific function tests are to be carried out. Finally, investigations in the form of psychological interviews must be conducted with the aim of shedding light on the relationship between the donor and the recipient, the donor's motivation and the extent to which he or she is aware of the possible consequences of losing the organ in question. Living donor transplantations are increasing in number in Germany. According to the German Foundation for Organ Transplantation DSO, 565 kidney transplantations using organs from living donors were performed in 2008, and the transplantation of liver segments from living donors accounted for five percent of all liver transplantations. As it is possible to provide for an optimal donor- recipient matching, the prospects of success for transplantation from a living donor are generally significantly better than is the case with post-mortal organ donations. In some countries, such as **Switzerland** (see module Legal regulations in Switzerland) , so-called cross-over transplantations are allowed. In such cases suitable pairs are brought together which display matching, i.e. corresponding blood

group incompatibility. In one **specific case** (see module Admission of a cross-over living donation) cross-over transplantation has been declared to be permissible in Germany as well. In the view of the Federal Social Court (Bundessozialgericht) this was to be justified on the basis of the close personal relationship between the donor and the recipient.

II. Legal aspects

1. Germany

The German Transplantation Act (TPG)

In Germany, transplantation of human organs is governed by the Act on “organ and tissue donation, removal and transplantation” (Gesetz über die „Spende, Entnahme und Übertragung von Organen und Gewebe“ or: **Transplantation Act – TPG**) (see module German transplantation law) .

The Act was passed by the German Bundestag on 5th November 1997 and came into force on 1st December 1997; an amended version was published on 4th September 2007.

The legal provisions governing post-mortal organ donation under the TPG

The TPG stipulates the so-called **extended consent solution** (see module Narrow and extended consent solution) , and i.e. the organs of a deceased person may only be retrieved if the person in question gave permission for organ donation (§ 3 para. 1 no. 1 TPG), e.g. in the form of an **organ donor card** (see modul organ donor card) , or if the next of kin consent to the donation (§ 4 TPG). Furthermore, the removal of organs or tissue from a deceased donor is only allowed if the donor’s death has been determined according to the rules that are in accordance with the state of knowledge of medical science (§ 3 para. 1 no. 2 TPG) by two independently acting, qualified physicians, who must not be involved in the process of either organ removal or transplantation (§ 5 TPG). Besides, the operation itself must be carried out by a physician (§ 3 para. 1 no. 3 TPG). Likewise, the removal of organs or tissue from a dead embryo or foetus is only permitted after death has been determined by a qualified person. Moreover, the woman who was pregnant with the embryo or foetus in question, must consent to the donation (§ 4a para. 1 TPG).

The legal provisions governing living donation under the TPG

Living donation is only permissible in Germany if the donor is of full age and capable of consent, has been adequately informed and has consented to the removal (informed consent), and is considered suitable as a donor according to medical judgment; furthermore, it has to be ensured that the person is exposed to no foreseeable risk beyond that of the operation (§ 8 para. 1 TPG). Whereas self-renewing organs or tissue may also be donated to unknown persons, the donation of non-regenerative organs (e.g. kidney, parts of the liver) is only permissible for the purpose of transplanting to relatives of the first or second degree, spouses, registered life partners, fiancé(e)s or other persons with whom the donor obviously has a very close personal relationship (§ 8 para. 1 no. 4 TPG).

General provisions of the TPG

Apart from the detailed prerequisites for organ removal from both deceased and living donors (§§ 3 8 TPG) the TPG sets out some general principles and procedural requirements. Accordingly, transplantation of organs that are subject to allocation (“vermittlungspflichtige Organe”), such as hearts, kidneys, liver, pancreas and intestines (§§ 3, 4 TPG) may only be performed in authorised hospitals (so-called transplantation centres) (§§ 9, 10 TPG); the respective organs have to be allocated by the allocation agency (§ 11 TPG). The TPG also provides that the transplantation centres must keep waiting lists for the transplantation of such organs. However, not all

patients in need of a new organ can be included in the waiting list: Where the risks related to transplantation and the necessary follow-up treatment are too high and the prospects of success are poor, transplantation is not considered an option. Doctors are bound to observe the **German Medical Association's Guidelines for waiting list inclusion** (see module Guidelines of the German Medical Association (Bundesärztekammer) for waiting list inclusion) ; furthermore, they must document the reasons for waiting list inclusion/exclusion and inform the patient accordingly (§ 16 TPG). Pursuant to § 12 TPG, the donated organs must be allocated at national level in accordance with the **Guidelines of the Federal Medical Association (Bundesärztekammer)** (see module Guidelines of the German Medical Association (Bundesärztekammer) for organ allocation) . The TPG further stipulates that underage persons may declare their willingness to donate organs donation from the age of 16 and their objection to organ donation from the age of 14 without consent of a parent or legal guardian. The TPG also makes provision for criminal and summary offences. Trading in organs is prohibited, as is the transplantation of traded organs, and may be punished with a prison sentence of up to five years (§ 17 TPG). Moreover, the TPG stipulates that the federal authorities, in particular the Federal Centre for Health Education (Bundeszentrale für gesundheitliche Aufklärung) and the health insurance funds shall inform the population on the possibilities of organ and tissue donation and make organ donor cards available (§ 2 TPG). Health insurance funds shall further invite the persons insured with them at regular intervals to make a personal decision regarding organ donation.

Guidelines and opinions of the German Medical Association

The Transplantation Act (TPG) commits the Bundesärztekammer (German Medical Association) to establish Guidelines for specific areas of transplantation medicine, which must account for the current state of medical science (§ 16 TPG). These Guidelines have been elaborated by the “Permanent Committee on Organ Transplantation of the Bundesärztekammer” (Ständige Kommission Organtransplantation der Bundesärztekammer) and have been updated at regular intervals to account for new findings in medical science. The interdisciplinary Committee includes experts from the fields of medicine, law and philosophy, but also patients as well as relatives of organ donors. Pursuant to the provisions of the TPG the Bundesärztekammer has issued the following Guidelines:

- **Guidelines for the determination of brain death** (see module Guidelines of the German Medical Association (Bundesärztekammer) for the determination of brain death)
- **Guidelines for waiting list inclusion** (see module Guidelines of the German Medical Association (Bundesärztekammer) for waiting list inclusion)
- **Guidelines for organ allocation** (see module Guidelines of the German Medical Association (Bundesärztekammer) for organ allocation)
- **Guidelines regarding essential measures for the protection of organ recipients** (see module Guidelines of the German Medical Association (Bundesärztekammer) regarding essential measures for the protection of organ recipients)
- **Guidelines regarding quality assurance measures** (see module Guidelines of the German Medical Association (Bundesärztekammer) regarding quality assurance measures)

In addition to these Guidelines, which are legally binding for all actors involved in the transplantation process pursuant as defined by § 16 TPG, the Bundesärztekammer has published **recommendations and opinions on the issue of organ transplantation** (see module Recommendations and Opinions of the German Medical Association (Bundesärztekammer) with regard to organ transplantation) .

Legal regulations pertaining to xenotransplantation in Germany

The German Transplantation Act does not cover xenotransplantation, as (pursuant to § 1 TPG) it only governs the removal and donation of human organs, parts of organs and tissue. In its 1999 **opinion on xenotransplantation** (see module Opinion of the German Medical Association (Bundesärztekammer) on xenotransplantation) the Bundesärztekammer decided that the prerequisites for performing xenotransplantations in a reasonably low-risk way were not yet met. For lack of an individual regulation, the provisions of the Medicinal Products Act (Arzneimittelgesetz – AMG) are relevant when it comes to xenotransplantation. Pursuant to § 2 para. 1 no. 1 AMG medicinal products are substances and preparations made from substance which, by application on or in the human body, are intended to cure, alleviate, prevent or identify diseases, suffering, injuries or medical conditions. The prevailing opinion is that a xenograft represents a medicinal product in accordance with the AMG. Pursuant to § 5 para. 1 medicinal products must not be placed or made available on the market if they are unsafe. According to § 5 para. 2 AMG medicinal products are to be considered unsafe if, according to the current state of scientific knowledge, there is reason to suspect that, when used in accordance with their intended purpose, they have harmful effects which exceed the limits considered tolerable in the light of current medical knowledge. Whether this is the case when animal organs are transplanted to humans is subject to controversy.

Regulations in other countries

In many countries, the basic principles governing organ donation and transplantation are quite similar. Now and then, the **brain death criterion** (see module The criterion of brain death) may give rise to lively debate – particularly in **Japan** (see module Legal regulations in Japan) – but in general, the irreversible and total loss of the cerebral functions is legally accepted as being the point in time from which post-mortal organ donation may take place. Organ trade is a punishable offence in most countries, transplantation may only be performed by qualified physicians, and the allocation of donor organs is incumbent on specific institutions. As to the question of whether – and in which form – the potential donor must consent to post-mortal organ donation, regulations vary from one country to another. Depending on the respective legislation, some countries apply the “ **dissent solution** ” (see module Dissent solution) , the “narrow” or the “ **extended consent solution** ” (see module Narrow and extended consent solution) or the “ **information solution** ” (see modul Information solution) . The dissent solution, according to which organs may be removed if the donor has not explicitly objected to post-mortal organ donation during his or her lifetime, is applied, for example, in Italy, Luxemburg, **Austria** (see modul Legal regulations in Austria) . Portugal, Slovenia, Spain, the Czech Republic, and Hungary. In Belgium, Finland and Norway, the extended dissent solution is applied, i.e. the next of kin can also object to organ donation. Denmark, Greece, Great Britain, the Netherlands, Switzerland, as well as Germany apply the extended consent solution which provides that the deceased person must have consented to organ donation during their lifetime, e.g. in the form of an **organ donor card** (see module Organ donor card) . Where this is not the case, the extended consent solution allows the next of kin to decide whether organ donation should take place; this decision must be based on the wish expressed by the deceased prior to death or on their presumed

wish. In Japan, a specific form of the consent solution is applied: Post-mortal organ donation may only take place if the next of kin of the potential donor have declared their consent. In France and Sweden, the so-called information solution is applied: Organs may be removed unless the deceased person objected to post-mortal organ donation during their lifetime. While the next of kin must always be informed about the intended organ removal, they have no right to object to it.

III. Ethical aspects

The new paths which have been opened up by transplantation medicine raise not only medical and legal, but especially ethical questions. Looking at the situation from an ethical point of view, this involves issues such as the definition and time of death, the rights of those who have died, the fair allocation of organs, the extent to which organs are donated voluntarily and the implementation of xenotransplantation. Generally, the ethical questions fall into the categories of post-mortal organ removal, the allocation of organs, living donor donation and those concerning **xenotransplantation** (see module Xenotransplantation) .

Ethical questions arising in connection with post-mortally donated organs

The main issue to be addressed in cases of post-mortal donation is concerned with the point in time at which it becomes ethically justifiable to remove organs from human bodies.

Reliable determination of death

Where organs are to be donated post-mortally, the central debate revolves around the question as to when exactly the donor may be considered to be dead. More specifically, the concept of death needs to be addressed from a philosophical rather than medical point of view. In addition to an irreversible cardiac arrest (**'cardiac death'**) (see module Cardiac death) a certain sign of death is to be seen in the irreversible and complete functional failure of the entire brain (**'brain death'**) (see module Criterion of Brain death) . This criterion applies in Germany and in most other countries. The term brain death may be applied where the brain has ceased to 'operate', so that its ability to function has permanently disappeared, even though it may be possible to maintain the cardiac and circulatory functions in the rest of the body by means of intensive medical care. The **Guidelines of the Federal Medical Association (Bundesärztekammer)** (see module Guidelines of the German Medical Association (Bundesärztekammer) for organ allocation) contain exact descriptions of the procedures and processes involved in the diagnosis of brain death. The debate on the definition of brain death reached a climax in connection with several drafts of the Transplantation Law and with its being passed in June 1997, but still today it remains the subject of heated discussion. The argument put forward in favour of using brain death as a sure sign of death maintains that when the brain functions have failed permanently the physical-mental unity which makes up the human being is irretrievably destroyed. As soon as brain death has occurred, the human being is no longer able to think, recognize, decide, plan, feel or perceive. He or she can no longer experience consciousness, nor self-awareness, so that other persons can, at the most, have a relationship to him/her, but it is no longer possible to establish a relationship with him/her. Those who oppose the use of brain death as a general criterion for death consider brain death as merely a stage encountered on the path leading to death, a phase which must still be associated with the life which is in the process of being extinguished. As many patients for whom brain death has been diagnosed still display physiological reactions – from bodily warmth and skin hue through spontaneous embraces up to erections and ejaculations on the part of male patients and even the continuation of a pregnancy for a certain time in a brain dead mother – they maintain that those affected cannot be regarded as actually being dead in a fully comprehensive sense of the word.

Consent to post-mortal organ extraction

The question arises as to whether a physician is authorised to remove tissue or organs from a dead body for the purpose of healing another person without either the approval of the next of kin or evidence of approval having been given by the dead person during their lifetime. If the person who has died gave such approval either in writing or verbally, the doctors are required to investigate the medical feasibility of carrying out the organ donation and, if possible, to implement it. Opinion remains divided as to how to deal with cases in which the dead person has left neither a statement of consent nor of objection. This gives rise to a condition of uncertainty between public interest in obtaining a sufficient number of organs for transplantation and the interests of the dead person and their next of kin in respect of maintaining the dead body's integrity. Proponents of the **dissent solution** (see module Dissent solution) recommend a compromise: There should be no obligation to remove organs, but the potential donor should carry the burden of decision.

Questions of fair allocation of organs when the supply is limited

A further ethical problem in current transplantation medicine can be seen in the equitable distribution of post-mortally donated organs. It is necessary to establish a fair means of allocating organs when the number of donors fails to meet the demand. The question becomes acute in cases where two or more patients meet the medical criteria for one and the same donor organ. The allocation of organs is then based on the fundamental ethical principles of equal treatment and the achievement of the greatest possible (medical) benefit. However, these two principles can easily collide. Thus a relatively young and otherwise healthy person may be expected to receive the greatest benefit from a transplantation, but this could be at the expense of somebody else for whom the organ in question represents the last chance for survival. It is not possible, from an ethical point of view, to lay down hard and fast rules for applying these two principles – their relationship to each other must be tested again and again in an ongoing and transparent process of social discussion. In Germany, the organs subject to allocation (heart, lungs, liver, kidney, pancreas and intestines) are distributed by the allocation Eurotransplant, according to the **Guidelines of the German Medical Association (Bundesärztekammer)** (see module Guidelines of the German Medical Association (Bundesärztekammer) for organ allocation) . In view of the difficulties inherent in allocating organs, suggestions have been put forward to limit the distribution of donor organs to people who themselves have agreed to allow their organs to be used in the event of their death. Critics of this model point out that its practical implementation could lead to undesired discrimination. There is a broad degree of agreement that social criteria such as a person's standing in society should not play a role in the distribution of organs.

Ethical questions concerning organ donation by living donors

The progress being made in transplantation medicine, together with the present shortage of organs, adds fuel to the discussion concerning the legitimacy of donation by living donors. Where an organ donor is still living, the ethical issues revolve around the donor and the recipient, as well as the physician in his or her role as mediator between them. Free-will decision on the part of a living donor The donation of an organ by a living donor presupposes his or her informed consent. According to the stipulations of the German Transplantation Act it is permissible only between first and second degree relatives or between people who have a “close personal relationship”. The aim of this ruling is to prevent the possibility of trade in organs, to ensure that the donation

is, indeed, voluntary, and also to protect donors against making over-hasty decisions which they may regret later if complications arise. In view of the fact that in such cases a healthy person undergoes an operation which does not directly benefit himself or herself and which involves a health risk which could even result in the donor's death, most countries require that the number of such donations be limited to what is absolutely necessary in order to supply the demand for transplants. In Germany, this requirement is implemented by means of the "principle of subsidiarity of post-mortal donation against donation by living persons". This means that a donation from a living donor is only permissible when no suitable organ from a dead person is available at the time of organ extraction. A surgeon may only remove organs from living donors when these criteria of urgency and lack of alternatives are fulfilled. Further, physiological tests must be performed to confirm that the operation will not endanger the potential donor more than is normally to be expected. Finally, psychological tests must be carried out in order to establish whether the donor's decision is truly made of his or her own free will and that he or she is adequately informed. As far as the responsible medical practitioners are concerned, the ethical discussion focuses on the extent to which an operation which does not benefit the person being operated on can be reconciled with the classical principle of medical ethics known as 'nihil nocere' – 'do no harm'.

Extension of the group of potential donors

It is a matter of debate as to whether those people who donate organs or parts of organs while they are still living should receive a remuneration in order to increase the number of people willing to donate. There is a body of opinion which regards such 'acknowledgement payments' as being appropriate in view of the considerable risks and disadvantages which the donor takes upon himself or herself. As they are prepared to make a positive contribution towards reducing the shortage of organs for donation, this deserves recompense. Further, it may be a psychological aid for the recipient if they know that the donor at least receives some sort of financial compensation. Feelings of guilt are common, and could in this way be somewhat relieved. However, many experts from the fields of medicine, law and ethics reject any form of organ sale out of hand. In their view, donation of organs against payment of money is not compatible with human dignity and the constitutionally defined code of ethics, and therefore unacceptable. There is grave concern that such a practice would lead to the exploitation of poorer members of society, because such people would be more likely to agree to organ removal while they are still living. In addition to the idea of providing financial incentives to encourage more people to become living donors there are several other possibilities which have been put forward with the aim of increasing the donor pool. For instance, discussion of cross-over donation has increased in recent years. This could prove to be a life-saving solution for patients who cannot benefit from a donation from close relatives on account of blood group and HLA incompatibility. Another way of increasing the number of donors would be to introduce a so-called pooling system of anonymous living donors. These donors provide organs for persons whom they have not themselves designated and who remain unknown to them.

According to the model presently under discussion the organs donated in this way are to be 'pooled' so as to ensure that mutual anonymity is maintained and the possibility of trading in organs is excluded. The pooled organs are then to be allocated according to criteria similar to those which are applied to post-mortal donation.

Ethical questions relating to xenotransplantation

The central ethical concern here is the question as to whether man has the moral right to kill animals for the purpose of using their organs. There are various schools of thought which have led to differing **ethical assessments of xenotransplantation** (see module Ethical assessment of xenotransplantation) : Advocates of **anthropocentrism** (see module Anthropocentrism) see the human race as being the decisive factor influencing ethical considerations; non-human nature, which includes the animal kingdom, is only of value insofar as there is a relationship between it and man and it serves his needs. In contrast, the proponents of **biocentrism** (see module Biocentrism) clearly oppose the establishment of a value gradient which places humans above animals.

The majority of professionally concerned people in Germany adopt an integrative stance which acknowledges both lines of argument. In practice, this means that animals are accorded certain rights, but they are not necessarily to be regarded as being coequal partners on the same footing as humans. Consequently, supporters of this view are in favour of xenotransplantation where it may enable the preservation, saving, promotion and protection of human life.

Another aspect of xenotransplantation which provokes discussion concerns the assessment of its risks and benefits. Its advocates stress its value, for instance in helping a seriously ill patient. The critics point out that the risks involved in using transplants of animal origin remain obscure. In the main, these risks concern the rejection reactions, which so far remain beyond satisfactory medical control, and the possibility of transferring infectious pathogens to the transplant recipient and other persons. There are also differences of opinion in respect of the ways in which xenotransplantation may effect changes in the recipient's identity.

Authors

Organ Transplantation

-

Medical aspects

Written by Lisa Tambornino (September 2009).

-

Legal aspects

Written by Lisa Tambornino (September 2009), revised von Lisa Tambornino and Philipp Kölgen (January 2010).

-

Ethical aspects

Written by Lisa Tambornino (September 2009).

Modules

Modules of Organ Transplantation



Admission of a cross-over living donation

Judgment of the Federal Social Court on the admission of a cross-over living donation

In a judgment dated 10th December 2003, the Federal Social Court (Bundessozialgericht – BSG) ruled that cross-over living donation shall be, in principle, inadmissible, but that it may be performed in exceptional cases. An exceptional case may occur if donor and recipient stand in a particular personal relationship to each other; these personal ties must be that strong that there is reason to expect the relationship to last for an unlimited period beyond the operation. In the judges' view, the personal relationship at the time of the operation, as stipulated in § 8 para. 1 clause 2 Transplantation Act (TPG), must be interpreted in a broad sense in the context of cross-over living donations. It shall suffice that the psychologist or physician attending to the patient before transplantation certifies the existence of an adequately intense and firm relationship. However, the mere fact that two couples have only met on the occasion of an intended cross-over transplantation or that a relationship has only been existing for a relatively short period of time, need not a priori represent an argument against the existence of a close relationship. The shared experience of illness may suggest that there is a correspondence of living conditions which may result in the establishment of strong emotional ties. However, since the existence of such a close relationship cannot be taken for granted either, judgment must be made on a case by case basis. Bundessozialgericht (BSG) (2004): Urteil vom 10.12.2003. Az. B9 VS 1/01 R. In: Juristenzeitung 2004, 464-469.



Alloplastic transplantation

Alloplastic transplantation

Alloplastic transplantation refers to the implantation of foreign material into the human body, such as artificial hips, pacemakers, teeth or dental roots, cartilage tissue, skin, and even hearts. Medical and technological progress has made it possible to implant even microchips or electrodes directly into the human brain. One example is the use of deep brain stimulation in the treatment of neurodegenerative diseases.



Anthropocentrism

Anthropocentrism

Anthropocentric (Greek anthropos: human being) approaches can often be traced back to the Kantian tradition and Kant's ethics of autonomy. Due to their capacity to reason, human beings possess unconditional value: they are ends in themselves. Hence, every human being must respect his own value and that of other human beings, and has obligations to other human beings.

- Patzig, Günther (1996): Der wissenschaftliche Tierversuch unter ethischen Aspekten. In: Hardegg, Wolfgang / Preiser, Gert (Hg.): Tierversuche und medizinische Ethik. Beiträge zu einem Heidelberger Symposium. Hildesheim: Olms, 68-84.
- Patzig, Günther (1993): Ökologische Ethik - innerhalb der Grenzen bloßer Vernunft. In: Elster, H. J. / Studienzentrums Weikersheim et al. (Hg.): Umweltschutz - Herausforderung unserer Generation. Mainz: v. Hase & Kochler, 63-81.
- Singer, Peter (1991): Animal Liberation. London: Thorsons.
- Singer, Peter (1994): Praktische Ethik. 2. Auflage. Stuttgart: Reclam.
- Wolf, Ursula (1990): Das Tier in der Moral. Frankfurt a.M.: Klostermann.
- Wolf, Ursula (1997): Haben wir moralische Verpflichtungen gegen Tiere? In: Krebs, Angelika: Naturethik. Grundtexte zur gegenwärtigen Tier- und ökoethischen Diskussion. Frankfurt a.M.: Suhrkamp, 47-75.



Biocentrism

Biocentrism

Biocentrism (Greek bios: life) is represented, for example, by Paul W. Taylor and Hans Jonas. Both adopt a teleological (goal-oriented) approach, claiming that all living organisms strive for self-preservation and reproduction, i.e. to achieve their natural aims in life. According to Jonas, every living organism is an end in itself and thus valuable. Human beings must therefore do justice to the responsibility they have towards all living beings and act in a way that is conducive to the thriving of every species in accordance with the goals that it pursues. Jonas, Hans (1988): Das Prinzip Verantwortung. Versuch einer Ethik für die technologische Zivilisation. Frankfurt a.M.: Suhrkamp. (English title: The imperative of responsibility. In search of an ethics for the technological age.)

Taylor, Paul W. (1986): Respect for Nature. Princeton: Princeton University Press.

Taylor, Paul W. (1996): The ethics of respect for nature. In: Olen, J. / Barry, V. (Eds.): Applying Ethics. Belmont: Wadsworth, 465-475.



Cardiac death

Cardiac death (Non heart-beating donor)

Besides the brain death criterion, some countries, including Great-Britain, Austria, Switzerland, the Netherlands, Spain, Belgium, and the USA, also apply so-called NHBD (non heart-beating donor) criteria. According to this procedure, it is permissible to remove organs before the determination of brain death, as soon as a ten minutes' cardiovascular arrest at normal body temperature has been diagnosed. In Germany, the NHBD procedure may not be used as a criterion for the determination of death. According to a communication of the German Medical Association Bundesärztekammer, a ten minutes' cardiovascular arrest at normal body temperature does not represent a valid equivalent to brain death, as each successful reanimation (even if it is only temporary) demonstrates that cardiac arrest is not a safe criterion of death. On the other hand, proponents of the NHBD procedure argue that the cerebral functions are irreversibly lost after a ten minutes' cardiovascular

arrest. In the light of persistent organ shortage, they support early organ removal, as the organs cease their functions shortly after the onset of cardiovascular arrest.

Communication of the Bundesärztekammer on the NHBD procedure



Dissent solution

Dissent solution

According to the so-called dissent solution organs may only be removed for transplantation if the deceased person did not explicitly object to organ removal during their lifetime. Some countries, such as Austria, keep so-called dissent registries for this purpose. The dissent solution applies e.g. in Italy, Luxemburg, Austria, Portugal, Slovenia, Spain, the Czech Republic, and Hungary. In some countries, including Belgium, Finland, and Norway, the next of kin can also object to post-mortal organ donation; this method is referred to as “extended dissent solution”.



DSO

German Foundation for Organ Transplantation (DSO)

The German Foundation for Organ Transplantation (Deutsche Stiftung Organtransplantation – DSO) is the national coordination agency for organ donations. Its task is to promote organ donation and transplantation in Germany. The DSO was founded in Neu-Isenburg on 7th October 1984. § 11 of the German Transplantation Act, which came into force in 1997, stipulates that there must be an institution that is responsible for the preparation and organisation of organ donation at national level. This responsibility was assigned to the DSO on 27th June 2000. Its tasks as coordination agency are specified in a contract with the German Medical Association (Bundesärztekammer), the central association of health insurance funds (Spitzenverband Bund der Krankenkassen) and the German hospitals association (Deutsche Krankenhausgesellschaft). The DSO makes sure that organ donation is possible throughout the national territory and at any time. The Foundation closely cooperates with 1,400 hospitals, with the nearly 50 transplantation centres in Germany, and with Eurotransplant, the organ allocation agency in Leiden, the Netherlands. Funding of the DSO as coordination agency is secured by a budget that is prospectively negotiated for a period of three years – on the basis of the expected number of organ transplantations. Hospitals that were involved in an organ donation procedure receive lump-sum payments from the DSO to cover their expenses.

Website of the German Foundation for Organ Transplantation (DSO)



Ethical assessment of xenotransplantation

Ethical assessment of xenotransplantation

Ach, J.S. / Anderheiden, M. / Quante, M. (2000): Ethik der Organtransplantation (Ethics of organ transplantation). Fischer: Erlangen.

For an introduction to the ethical discussion on animal rights, see “In Focus: Animal Experiments in Research” (DRZE publication).



Eurotransplant

Eurotransplant

The allocation agency Eurotransplant is based in Leiden, the Netherlands, and coordinates the international exchange of donor organs across a region with 124 million inhabitants. Transplantation centres and tissue typing laboratories as well as hospitals with intensive care units in Belgium, Germany, Luxemburg, the Netherlands, Austria, Croatia, and Slovenia take a share in this international co-operation. Acting as mediator between donors and recipients, Eurotransplant plays a key role in receiving and allocating donor organs for transplantation. On the one hand, Eurotransplant stores data of all potential recipients – such as blood group, tissue type (HLA groups), cause of illness, and urgency – in a central database and includes the patients on a waiting list. On the other hand, Eurotransplant is being informed as soon as organs from a deceased donor become available anywhere in the Eurotransplant catchment area. The regional tissue typing laboratory determines the donor’s blood group and tissue characteristics in order to find a suitable recipient. Following a computer-assisted selection procedure Eurotransplant immediately communicates the relevant medical donor information to the doctors at the respective recipient’s transplantation hospital. The doctors then decide whether they accept or refuse the donor organ in question. If the organ is accepted, the attending physician will inform the selected recipient without delay. If there is no suitable recipient within the Eurotransplant region, Eurotransplant will contact one of its sister organisations, e.g. UK Transplant or Scandiatransplant. As a general rule, the entire process from removal of the donor organ until transplantation must not exceed a few hours.

Website of Eurotransplant



German transplantation law

German transplantation law

Gesetz über die Spende, Entnahme und Übertragung von Organen und Gewebe (Transplantationsgesetz – TPG)
Höfling, W. (Ed.) (2003): Transplantationsgesetz. Kommentar. Berlin: Schmidt.

Schroth, U. / König, P. / Gutmann, T. (Eds.) (2005): Transplantationsgesetz. Kommentar. München: Beck.

Schreiber, H.-L. (2008): Rechtliche Aspekte der Organtransplantation. (Legal aspects of organ transplantation.)
In: Beckmann, J.P. / Kirtse, G. / Schreiber, H.-L.: Organtransplantation. Series “Ethics in the life sciences – DRZE expert reports”, vol. 7. Freiburg i.B.: Alber.



Graft-versus-host reaction

Graft-versus-host reaction

Not only can the immunological reaction after organ or tissue transplantation result in the rejection of the transplant by the receiving organism (so-called host-versus-graft reaction); it may also happen – and is particularly frequent after bone marrow or stem cell transplantations – that the immune cells of the transplant from a donor recognise the recipient's body as being foreign and attack it. This phenomenon is referred to as graft-versus-host reaction or disease, according to the ICD-10, the system for the classification of diseases, developed by the WHO. The graft-versus-host reaction is characterised by severe infections and changes in the mucous membranes of the gastrointestinal tract, the skin and the liver and may possibly be life-threatening.

The severity of graft-versus-host disease can be attenuated to some extent by treating the transplant recipient with immunosuppressive drugs.



Guidelines of the German Medical Association (Bundesärztekammer) for organ allocation

Guidelines of the German Medical Association (Bundesärztekammer) for organ allocation

The Bundesärztekammer has defined several criteria for organ allocation. The most important criteria are: prospect of success, urgency, lack of alternatives, and equality of opportunity. The allocation agency Eurotransplant must distribute organs and tissue in accordance with the Guidelines of the Bundesärztekammer. Richtlinien zur Organtransplantation gemäß § 16 Abs. 1 Nr. 2 und 5 TPG



Guidelines of the German Medical Association (Bundesärztekammer) for the determination of brain death

Guidelines of the German Medical Association (Bundesärztekammer) for the determination of brain death

In 1982, the Scientific Committee of the Bundesärztekammer defined standardised criteria for the determination and documentation of brain death, which have legal status in Germany. In 1998, the Guidelines were adapted to meet the formal requirements of the Transplantation Act.

Richtlinien zur Feststellung des Hirntodes, 3. Fortschreibung 1997 mit Ergänzungen gemäß Transplantationsgesetz (TPG)



Guidelines of the German Medical Association (Bundesärztekammer) for waiting list inclusion

Guidelines of the German Medical Association (Bundesärztekammer) for waiting list inclusion

The Bundesärztekammer has established Guidelines for inclusion in the waiting list for donor organs. These Guidelines stipulate that a patient may only be included in the waiting list if

- 1 no other treatment is likely to be effective,

- 2 the disease of the patient's organ is certain to induce serious, life-threatening illness, or if such a stage of disease has already been reached, and
- 3 if there is a substantial likelihood of the patient having a longer and better life after successful transplantation than without this intervention.

Arguments against waiting list inclusion include several diseases that are likely to negatively affect the short- or long-term success of transplantation, such as malignant diseases which have not been cured, clinically manifest infectious diseases, HIV infections, and serious diseases of other organs. Other possible contraindications for waiting list inclusion include heavy consumption of nicotine, alcohol or other drugs; still, the physical and mental condition of each patient must be appreciated and assessed as a whole. Another prerequisite for the allocation of a donor organ is that the recipient's general state of health must be stable enough for an operation and that he/she has consented to undergo long-term follow-up drug therapy (compliance). Especially the latter is subject to controversy in an ethical context: Although it is undisputed that the regular intake of immunosuppressants following organ transplantation is a prerequisite for long-term success of the intervention, it could be considered disproportionate, from an ethical point of view, to classify non-compliance as a contraindication. Pursuant to § 16 TPG physicians have a duty to observe the Guidelines of the Bundesärztekammer for waiting list inclusion.

Richtlinien zur Organtransplantation gemäß § 16 Abs. 1 Nr. 2 und 5 TPG



Guidelines of the German Medical Association (Bundesärztekammer) regarding essential measures for the protection of organ recipients

Guidelines of the German Medical Association (Bundesärztekammer) regarding essential measures for the protection of organ recipients

Richtlinie zur medizinischen Beurteilung von Organspendern und zur Konservierung von Spenderorganen gemäß § 16 Abs. 1 S. 1 Nr. 4 a) und b) TPG



Guidelines of the German Medical Association (Bundesärztekammer) regarding quality assurance measures

Guidelines of the German Medical Association (Bundesärztekammer) regarding quality assurance measures



Heart transplantation

Heart transplantation

Heart transplantation is being considered when a patient suffers from advanced cardiac failure and the condition cannot be improved by other therapeutic interventions. Cardiac damage can result from coronary heart diseases (narrowing or blockage of the blood vessels in the heart, infarcts), advanced cardiac insufficiency following an infection, or heart defects in children and newborns which cannot be 'fixed' by an operation. Many heart

diseases also induce damage to the lungs, making combined heart-lung transplantation necessary. Even today, heart surgeons only consider transplantation at the end-stage of a disease process, because the intervention bears considerable risks for the organ recipient; besides, very few donor hearts are available. The waiting time for a donor heart may sometimes be bridged with the aid of an artificial heart pump, which means that the patient must stay in hospital and can hardly be subjected to exercise stress during that period. About 800 patients are waiting for a heart transplant each year; however, there are only approx. 400 donor hearts available on average. Due to the seriousness of the underlying disease, a lot of patients die while they are waiting for a suitable donor organ. On the other hand, the results after heart transplantations are now very good. According to the German Foundation for Organ Transplantation DSO, 72% of transplanted hearts continue to function one year after the operation, and 62% still work well after five years.

Schmid, C. / Hirt, S. / Scheld, H.-H. (2009): *Leidfaden Herztransplantation*. 3 Aufl. Darmstadt: Steinkopff-Verlag.



Immunosuppressive medication

Immunosuppressive medication

Whenever transplantations are carried out, the treatment does not end with the performance of the operation. Where it proves necessary to suppress the body's defence mechanisms, the rejection of the transplant can only be prevented by providing a permanent supply of immunosuppressive drugs. These are agents which suppress the immune system's natural defence mechanisms, at least to some extent. They are used not only for transplantations, but also to treat inflammation and autoimmune diseases. The development of immunosuppressive drugs began in the 1960s and it is continually being improved. There are many different substances which have immunosuppressive effects, the best known of which are Ciclosporin, Methotrexat, Azathioprin and calcineurin inhibitors. The recipient of a transplant is given a high dosage of immunosuppressive drugs immediately after the operation, which is then reduced over the following weeks and months. As immunosuppressive agents not only reduce the body's attempts to reject the new organ, but also suppress its defence against infections etc., the risk of the transplant recipient contracting an infection is very high. In addition, other disorders such as diabetes mellitus, high blood pressure or reduced kidney function can be triggered as well.

Kirste, G. (2008): *Medizinische Aspekte der Organtransplantation. (Medical aspects of organ transplantation.)* In: Beckmann, J.P. / Kirtse, G. / Schreiber, H.-L.: *Organtransplantation* . Series "Ethics in the life sciences – DRZE expert reports", vol. 7. Freiburg i.B.: Alber.



Information solution

Information solution

In countries where the so-called information solution applies, the legislator assumes that – like in the case of the dissent solution – there is a general willingness to donate organs after death unless a person has objected to organ removal during their lifetime. The relatives of the deceased person must always be informed about

the intended organ removal, even though they have no right to object to it. The information solution is applied, for example, in France and Sweden.



Kidney transplantation and renal replacement techniques

Kidney transplantation and renal replacement techniques

The kidneys are those organs of the body with the highest throughput of blood. They fulfil very important functions: They conduct metabolic end products which can no longer be used as well as substances which have not originated in the body (such as medicines) out of the body, they regulate the body's hydrological balance and release various hormones which are involved in blood formation and affect blood pressure and bone metabolism. Causes for kidney disorders can be diabetes, long-term intake of large doses of certain medicaments, but also genetic diseases such as cystic kidney condition and renal shrinkage. In addition, secondary damage can be caused to the kidneys, for instance when high blood pressure is not treated adequately over a long period of time. Kidney insufficiency or pyelonephritis can also have serious consequences for the kidneys. Untreated failure of both kidneys is fatal. One way of treating insufficient kidney function is with the aid of so-called dialysis techniques. Two different dialysis techniques are used: haemodialysis and peritoneal dialysis. In the first case a dialysis device is used as an external, artificial kidney which filters the blood. The dialysis takes four to five hours and is carried out three times a week. The patient must follow a strict and permanent diet so that certain toxic substances which the device cannot filter out do not accumulate in the blood. Also, the patient must not drink more than a certain amount, because the malfunctioning kidneys are not able to remove enough fluids from the body. Peritoneal dialysis, which is only very rarely practised in Germany, does not involve a device. In this technique the peritoneum is used as a natural filter organ. As the body normally has two kidneys, it is, in principal, possible for a living person to donate a kidney. According to information released by the German Foundation for Organ Transplantation DSO, 2,188 kidneys were transplanted by post-mortal donation in 2008, whereas in the same period 565 were provided by living donors.

Verband Deutsche Nierenzentren (DN) e.V. – Fachverband der vertragsärztlich tätigen Fachärzte für Hochdruck- und Nierenkrankheiten in Deutschland

Kuratorium für Dialyse und Nierentransplantation e.V. (KfH)



Legal regulations in Austria

Legal regulations in Austria

In contrast to Germany and Switzerland, transplantations in Austria are not governed by a specific law, but under the Federal Law on Hospitals and Health Clinics (Bundesgesetz über Krankenanstalten und Kuranstalten – KAKug), section 7, §§ 62a to 62c. Austria applies the dissent solution, i.e. organs, parts of organs or tissue may be removed from a potential donor if they did not object to organ donation during their lifetime. In order to ensure the effective documentation of objections against organ donation, Austria has established a dissent registry („Widerspruchregister gegen Organspende“). Besides objections documented in this registry, any other form of declaration of a deceased person's will regarding post-mortal organ donation, such as an informal

document found among the identity papers of the deceased, or an oral declaration made in the presence of family members, is being respected. The dissent registry was primarily established for persons who have their permanent residence in Austria. As the retrieval of data from the registry is mainly effected via the Austrian Social Security Number, it is recommended that persons who only stays in Austria for a limited period carry their personal written declaration of will regarding post-mortal organ donation among their identity papers to ensure that their wish is respected in the event of death.

Bundesgesetz über Krankenanstalten und Kuranstalten (KAKug)(Federal Law on Hospitals and Health Clinics)

Österreichisches Bundesinstitut für Gesundheitswesen (ÖBIG) mit Informationen zum Widerspruchsregister gegen Organspende (Austrian Federal Institute for Health Care with information on the organ donation dissent registry)

Austrotransplant – Österreichische Gesellschaft für Transplantation, Transfusion und Genetik (Austrian Society for Transplantation, Transfusion and Genetics)

Novartis Transplant Österreich –Austrian information website



Legal regulations in Japan

Legal regulations in Japan

In Japan, brain death only became accepted as a legally valid criterion for the end of human life when the “Law on organ transplantation” came into force in October 1997. The Japanese law stipulates a particularly narrow form of the consent solution, according to which organs may only be removed after death if both the donor during their lifetime and the family members consent to organ donation. Since many Japanese think that a human being is only dead when the heart and the lungs have ceased to function, they are frequently opposed to organ removal from brain-dead patients. Another striking aspect of Japanese organ transplantation legislation is the regulation pertaining to underage persons. In its version from 1997, the law prohibits organ donation and transplantation for children below the age of 15. According to critics of this prohibition, many children, whose families could not afford to pay for an expensive operation abroad, consequently died. Over the past 12 years – i.e. since the adoption of the transplantation law until today – only 81 organs have been transplanted in Japan, whereas hundreds of transplantations are performed in Europe each year. In July 2009, the aforementioned regulation was finally amended. Following years of controversy, transplantations are now also permissible for children.



Legal regulations in Switzerland

Legal regulations in Switzerland

In Switzerland, the Federal Act on the Transplantation of Organs, Tissues and Cells (Bundesgesetz über die Transplantation von Organen, Geweben und Zellen (Transplantationsgesetz)) came into force on 1st July 2007. The Act put an end to the legal fragmentation that had until then prevailed in the area of transplantation medicine, by providing a uniform and comprehensive legal framework. Like Germany, Switzerland applies

the extended consent solution, i.e. legal removal of organs, cells or tissue requires consent of the donor prior to their death. In cases where the person has not made a declaration regarding organ donation, the next of kin shall be asked to give consent (Art. 8). Another prerequisite is the determination of brain death (Art. 8). It is prohibited to grant or to derive financial profit or any other advantage from the donation of human organs, tissue or cells (Art. 6), to trade in human organs, tissue or cells, or to remove or to transplant human organs, tissue or cells which have been obtained in exchange for payment or by granting advantages (Art. 7). The main differences between German and Swiss transplantation legislation concern living donation: the Swiss Transplantation Act does not stipulate that the donor and the recipient must be relatives or have a very close emotional relationship. Hence, cross-over living donation, for instance, is permissible in Switzerland (Art. 6). Transplantation of embryonic or foetal cells is only permitted with an authorisation of the Federal Office of Public Health (Bundesamt für Gesundheit – BAG). Certain procedures, e.g. donation to a designated person or the use of embryonic or foetal tissue or cells from women who are incapable of exercising sound judgment, are prohibited. The performance of xenotransplantations must be authorised by the BAG.

Bundesgesetz über die Transplantation von Organen, Geweben und Zellen (Transplantationsgesetz) (Federal Act on the Transplantation of Organs, Tissues and Cells)



Liver transplantation, living-donor liver donation and split liver transplantation

Liver transplantation, living-donor liver donation and split liver transplantation

The tasks of the liver, which is the most important and the largest metabolic organ of the human body, encompass, among others, the decomposition and elimination of substances, the production of vital proteins, and the absorption of nutrients. The most frequent liver diseases – where liver transplantation is often the only option for patients – include malignant tumours, infectious hepatitis, intoxications, diseases of the biliary tract, metabolic disorders, scarring of the entire liver (liver cirrhosis), or alcohol-induced liver damage (alcohol cirrhosis). As with kidney diseases, the time until transplantation can be bridged by means of a dialysis procedure. In a few cases, the liver regenerates itself and transplantation can be avoided. The world's first human liver transplantation was performed on a three-year-old child in the USA on 1st March 1963. Besides post-mortal donation of a whole liver, living-donor liver donation and split liver transplantation are other techniques used in modern medicine. Split liver transplantation involves the division of a donor organ into a left and a right segment in such a way that preserves the essential structures of the hepatic hilum with the liver artery, portal vein and bile ducts on both sides and allows an anatomically exact separation of the draining veins. Provided that the relation between size of the liver and body height is taken into account, one donor organ may benefit two patients. However, since the rate of complications following split liver transplantation is high – even in cases where very good donor organs (age factor) are used – the procedure has not yet become standard practice. The technique of split liver transplantation has led to the development of living-donor liver donation and transplantation where the right or left part of a healthy liver is removed from a living organ donor and transplanted into a recipient. This procedure is mainly used with paediatric patients who suffer from hereditary enzyme deficiency or bile duct atresia and for whom transplantation of the left lobe of a parent's liver often represents the only therapeutic option when a suitable donor organ from a deceased donor cannot be supplied

in time. According to figures published by the German Foundation for Organ Transplantation DSO, 1,067 liver transplantations were performed following post-mortal organ donation in Germany in 2008, whereas in 55 cases the transplants were obtained from living donors. In the same period, slightly more than 1,600 new patients were entered on the waiting list for a donor liver.

Informationen zur Lebertransplantation bereitgestellt von der Klinik für Allgemein-, Visceral- und Transplantationschirurgie an der Charité in Berlin. (Information on liver transplantation provided by the Charité hospital in Berlin)

Lebertransplantierte Deutschland e.V.



Lung transplantation

Lung transplantation

Lung transplantation is a form of treatment for patients suffering from advanced lung disease and is being considered when the possibilities of drug therapy are exhausted and remaining life expectancy has dropped to two or three years due to the illness. The underlying diseases, which in most cases gradually induce severe breathing difficulties, frequent infections, and induration of the lung, are either congenital (such as cystic fibrosis – a congenital disease characterised by very viscous body secretions that block the airways of the lung) or are caused by increased blood-vessel resistance and increased blood pressure in the pulmonary circulation (pulmonary hypertension). Depending on the underlying disease, one lung, both lungs, or one or more pulmonary lobes are being transplanted. Lung transplantation results have improved significantly over the past ten years. At the end-stage of the disease process, lung transplantation is the only option for patients. For a few years, children with lung diseases have had the possibility of so-called living-donor lung transplantation. This procedure consists of transplanting one pulmonary lobe each from two living donors into a – in the majority of cases – very young recipient. According to the German Foundation for Organ Transplantation DSO, 270 lung transplantations were performed in 13 German transplantation centres 2008; in 18 cases, heart transplantation was performed simultaneously. 442 new patients were entered on the waiting list in 2008.



Multi-organ transplantation

Multi-organ transplantation

The term multi-organ transplantation embraces both combined transplantation and multiple transplantation. Combined transplantation is defined as the simultaneous transplantation of two organs into the same person; examples include pancreas-kidney transplantation (performed for the first time in Minneapolis, USA in 1966), heart-lungs transplantation (performed for the first time in Houston, USA in 1968), and liver-intestine transplantation (performed for the first time in Toronto, Canada in 1989). Multiple transplantation refers to the transplantation of three or more organs. The en-bloc transplantation of three or more abdominal organs is called multivisceral transplantation.



Narrow and extended consent solution

Narrow and extended consent solution

The narrow consent solution provides that the deceased person must have declared their consent to organ removal during their lifetime, e.g. by carrying an organ donor card. Where this is not the case, the extended consent solution allows the next of kin to decide whether organ donation should take place; this decision must be based on the wish expressed by the deceased prior to death or on their presumed wish. The extended consent solution applies e.g. in Germany, Denmark, Greece, Great Britain, the Netherlands, and Switzerland.



Opinion of the German Medical Association (Bundesärztekammer) on xenotransplantation

Opinion of the German Medical Association (Bundesärztekammer) on xenotransplantation

Stellungnahme des Wissenschaftlichen Beirates der Bundesärztekammer zur Xenotransplantation



Organ donor card

Organ donor card

In Germany, there is no central registry of persons willing to donate their organs after death. The Federal Centre for Health Education (Bundeszentrale für gesundheitliche Aufklärung – BZgA) provides an organ donation form which is available in many doctor's practices and chemist's shops and can also be downloaded via the BZgA's website. It is also possible to document one's willingness to donate all organs or particular organs without using a specific form. Underage persons can also fill in an organ donor card. Pursuant to § 2 of the German Transplantation Act, federal authorities as well as health insurance funds shall make organ and tissue donor cards available and provide adequate information material. Another objective is to create a standardised European organ donor card. Some countries where the so-called dissent solution applies keep a "dissent registry" of persons who have explicitly decided against post-mortal organ donation.

Organ donor form provided by the BZgA



Recommendations and Opinions of the German Medical Association (Bundesärztekammer) with regard to organ transplantation

Recommendations and Opinions of the German Medical Association (Bundesärztekammer) with regard to organ transplantation

Empfehlungen zur Lebendorganspende (Recommendations on living-donor organ donation)

Empfehlungen für die Zusammenarbeit zwischen Krankenhäusern und Transplantationszentren bei der postmortalen Organentnahme (Recommendations for the co-operation between hospitals and transplantation centres in post-mortal organ removal procedures)



Syngeneic transplantation

Syngeneic transplantation

Syngeneic transplantation (also referred to as isogeneic or isologous transplantation) is the transplantation of cells, tissue or organs between genetically identical individuals. The recipient of a syngeneic graft needs no immunosuppressive therapy, as there usually is no transplant rejection due to the genetic identity of donor and recipient.



The criterion of brain death

The criterion of brain death

Organs may only be removed from a potential organ donor when death has been definitely determined. Until the mid-twentieth century, the standstill of respiration and heartbeat was considered a valid criterion of death (cardiac death). However, patients with cardiovascular failure may sometimes be reanimated by means of modern methods of intensive care, and can recover. It hence became necessary to establish an additional criterion for the determination of death. The Ad-Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death took the lead in the establishment of such a criterion. The results of the Committee's work were published in the so-called Harvard Report in 1968. According to the definition of the German Medical Association (Bundesärztekammer – BÄK), brain death is a state of irreversible cessation of the total function of the cerebrum (upper brain), the cerebellum (little brain) and the brain stem while the cardiovascular function is artificially maintained by controlled ventilation. The cerebral functions are irreversibly lost when the brain lacks blood and oxygen supply for a few (at most 10) minutes. After this time, the brain is cut off from the blood circulation and its cells degenerate and die, even if the rest of the body is still being supplied with blood by means of artificially maintained ventilation and cardiac action. Hence it is possible to remove still intact organs for transplantation purposes from a brain-dead patient. The BÄK has established Guidelines for the determination of brain death. Pursuant to these Guidelines, brain death must be diagnosed beyond doubt by two independently acting physicians who are not part of the transplantation team and who have several years of professional experience in intensive care medicine or neurology. In addition, the cessation of all reflexes of the brain stem and of spontaneous breathing must be demonstrated in a clinical examination. While brain stem reflexes can still be triggered in unconscious patients, they are absent in brain-dead patients. These reflexes include:

- Pupillary reflex: In healthy persons, both pupils are normally equally wide; they narrow when exposed to light. Brain-dead patients lack this reflex; their pupils are no longer reactive to light.
- Doll's eye reflex (oculocephalic reflex): If a patient is unconscious but not brain-dead they react to brisk turning or tipping of their head with slow eye movement in the opposite direction. The eyes of a brain dead patient however do not react to this test and remain in their initial position.
- Corneal reflex: When the outer layer of the eye (cornea) comes in contact with a foreign object, the eyes close as an automatic reflex. When the physician tests this reaction by touching the cornea of a brain-dead patient with a cotton swab, this reflex is absent.

- Response to pain in the face: Even patients who are in deep coma respond to painful stimuli that are applied to the face with distinguishable twitching of the muscles and defence reactions of the head and neck muscles. Brain-dead patients lack these reflexes.
- Gag- and cough reflex (tracheal and pharyngeal reflex): Touching the back of the pharynx induces a gag reflex in healthy and unconscious persons. This reflex is absent in brain-dead patients.

If all five reflex tests are suggestive of brain death, the physician will perform a spontaneous breathing trial. Automatic breathing is a vital reflex. When mechanical ventilation is stopped the carbon dioxide level in the blood increases due to the consumption of oxygen. This immediately activates the respiratory centre in the brain, which triggers a breath. The absence of spontaneous breathing is characteristic of the complete failure of the respiratory centre. Shortly after the publication of the Harvard Report, critics raised their voices against the introduction of the brain death criterion. In Germany the debate reached its climax before the adoption of the Transplantation Act in 1997.

A definition of irreversible coma. Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death. In: *Journal of the American Medical Association (JAMA)* Aug. 1968, vol. 205, no. 6, 337-340.

The President's Council on Bioethics (2008): *Controversies in the Determination of Death. A White Paper by the President's Council on Bioethics.* Washington, D.C.

Ach, J.S. / Quante M. (Ed.) (1999): *Hirntod und Organverpflanzung. Ethische, medizinische, psychologische und rechtliche Aspekte der Transplantationsmedizin.* (Brain death and organ transplantation. Ethical, medical, psychological and legal aspects of transplantation medicine.) Stuttgart/Bad Cannstatt.

Angstwurm, H. (2003): *Der Hirntod als sicheres Todeszeichen.* (Brain death – a certain sign of death.) In: Düwell, M. / Steigleder, K. (Eds.): *Bioethik. Eine Einführung.* Frankfurt/M.

Frewer, A. (1999): *30 Jahre Hirntod-Definition. Historische und ethische Aspekte.* (30 years of brain death definition. Historical and ethical aspects.) In: *Ethik in der Medizin* 11(2), 114-118.

Honnefelder, L. (1998): *Hirntod und Todesverständnis: Das Todeskriterium als anthropologisches und ethisches Problem.* (Brain death and the understanding of death. The death criterion as an anthropological and ethical problem.) In: *Jahrbuch für Wissenschaft und Ethik* 3, 65-78.

Beckmann, J.P. / Kirtse, G. / Schreiber, H.-L.: *Organtransplantation.* (Organ transplantation.) Series "Ethics in the life sciences – DRZE expert reports", vol. 7. Freiburg i.B.: Alber.



Transplantation immunology and immunosuppression

Transplantation immunology and immunosuppression

The most important function of the immune system is to provide protection against infection. An essential part of this defence system consists in the mechanism which allows it to distinguish between 'friend and foe', i.e. between what belongs to the body and what is foreign to it. Transplants are frequently recognised as being, in the most literal sense of the term, foreign bodies, and as a result the recipient organism rejects them. The so-called human leukocyte antigen (HLA) system plays a decisive role in determining whether a transplant is accepted as belonging to the organism or regarded as being foreign to it. HLAs are to be found on practically

all body cells. In preparing the transplantation of an organ or foreign tissue, donors are sought whose HLA systems are similar to the potential recipient's, i.e. who are HLA compatible. This minimises the severity of immunological defence reactions. Where the HLA parameters for the recipient and the donor are especially well matched, e.g. as is the case with identical twins, the reactions are mild or do not even occur at all, which means that the transplant is permanently accepted by the patient's organism. Today it is possible to perform organ transplants even when the HLA parameters are less compatible, because the reactions against the foreign organ can be controlled by means of immunosuppressive drugs.

Kirste, G. (2008): Medizinische Aspekte der Organtransplantation. (Medical aspects of organ transplantation.) In: Beckmann, J.P. / Kirtse, G. / Schreiber, H.-L.: Organtransplantation . Series "Ethics in the life sciences – DRZE expert reports", vol. 7. Freiburg i.B.: Alber.



Transplantation of the pancreas

Transplantation of the pancreas

The pancreas produces enzymes essential for the digestion of food in the intestines, as well as the hormones insulin and glucagon, which regulate the blood sugar level. A pancreas transplant may be an option for diabetics whose pancreas does not produce enough insulin. For some years, doctors have been attempting to transplant only the insulin-producing cells (islet cells) instead of the whole organ. For this procedure, two to three pancreases are needed per patient. According to the German Foundation for Organ Transplantation, 138 pancreas transplantations (including combined pancreas-kidney transplantations) were performed in Germany in 2008. In the same period, nearly 200 new patients were registered on the waiting list for a donor organ.



Xenotransplantation

Xenotransplantation

Xenotransplantation refers to the transplantation of functioning cells, tissue or organs between different species in general, and more specifically to animal-to-human transplantation. This term is in contrast to allogeneic transplantation (transplantation where donor and recipient belong to the same species). First attempts to replace human organs with animal organs were made as early as in the beginning of the 20th century. The first successful xenotransplantation was finally performed in 1963 when the surgeon Reemtsma transplanted kidneys from chimpanzees into six patients; however, none of these kidneys continued to function for more than nine months. Since 1990, there has been an increasing number of transplantations of pig cells and tissues. Due to their anatomical and physiological characteristics, pigs are particularly suitable donors, since their organs are similar to human organs in size and function; moreover, the husbandry and breeding of pigs is relatively easy. Pig brain cells are used in the treatment of Parkinson's disease, pig islet cells are used to treat diabetes, and pig liver cells are transplanted into human patients with liver failure. However, like any experimental therapy, xenotransplantation involves a number of problems and risks. Due to the phylogenetic distance between humans and animals, the transplanted material is usually rejected more rapidly and more violently than is the case with allogeneic transplants. The immunosuppressive agents which are available at

present do not yet allow to suppress xenograft rejection in the long term. There are attempts to increase the chances of success of xenotransplantations by targeted genetic modification, e.g. of the tissue factors of pigs. Nonetheless, it is still uncertain whether pig organs and other animal transplants can reliably substitute for the functions of human organs in the long term. Among other things, the upright posture of man could have an unforeseeable effect on the transplanted pig organs.

The issue of xenotransplantation raises many legal and ethical questions. In an opinion published in 1999, the German Medical Association (Bundesärztekammer – BÄK) came to the conclusion that the prerequisites for performing xenotransplantations in a reasonably low-risk way were not yet met. Nonetheless, the BÄK declared it would support any research activities and efforts aimed at clarifying open questions and at further assessing, and minimising, the risks associated with xenotransplantation.

Stellungnahme des Wissenschaftlichen Beirates der Bundesärztekammer zur Xenotransplantation. (Opinion of the Scientific Committee of the Bundesärztekammer on xenotransplantation.)

Beckmann, J.P. (2000): Xenotransplantation von Zellen, Geweben oder Organen: wissenschaftliche Entwicklungen und ethisch-rechtliche Implikationen. (Xenotransplantation of cells, tissue or organs: scientific developments and ethical and legal implications.) Wissenschaftsethik und Technikfolgenbeurteilung. Berlin: Springer.

Grimm, H. (Ed.) (2003): Xenotransplantation. Grundlagen Chancen Risiken. (Xenotransplantation. Principles, chances, risks.) Stuttgart: Schattauer.

Schicktanz, S. (2002): Organlieferant Tier? (Organ supplier: animal?) Medizin- und tierethische Probleme der Xenotransplantation. Frankfurt am Main: Campus.

Straßburger, J. (2008): Rechtliche Probleme der Xenotransplantation. (Legal problems of xenotransplantation.) Internationale Regelungen und nationaler Regelungsbedarf unter besonderer Berücksichtigung des Infektionsrisikos. Medizinrecht in Forschung und Praxis 11. Kovac: Hamburg.