06 & 07 -Practical 2023/2024

Organ transplantation. Reproductive ethics

Kostadin Kostadinov, MD, MPH, MEcon

ORGAN TRANSPLANTATION

Determining Death

In most patients, death is determined without any special diagnostics. Determining death becomes important in comatose patients sustained by mechanical ventilation and other auxiliary intensive care. If a **radioisotope examination** confirms the complete loss of blood supply to the brain, there is no doubt: the patient has died. We do not refer to **brain death**, but **death**. *The patient is dead even if the heart will remain active for some time*. Even with appropriate levels of compassion, it is not always easy to explain the situation to the relatives; many find it hard to reconcile themselves to the death of their loved one whose appearance is the same as the day before and whose heart is still beating. **Only after death has been confirmed, can we open discussion on possible organ donation.**

Brain death

Medicine and society continue to struggle thoughtfully with the definition of death, particularly with the progression of sophisticated life-support systems that challenge traditional concepts. The questions of when a disease is irreversible, when further treatment is ineffective, or when death has occurred are of great consequence. These questions are independent of, and galvanized by, the practice of **organ donation**.

Brain death is defined as the **absence of all brain function demonstrated by profound coma with the irreversible loss of capacity for consciousness, loss of the ability to breathe and absence of all brain stem reflexes**. Analogous to a cardiac arrest, it is better understood as **brain arrest** – the loss of all clinical brain function. If a proximate cause is known and there are no reversible conditions present, death is determined by documenting the absence of brain function by clinical examination. In most cases, brain death can be diagnosed at the bedside. *Common causes* include trauma, intracranial hemorrhage, cerebrovascular accidents, hypoxia owing to resuscitation after cardiac arrest, drug overdose or near drowning, primary brain tumor, meningitis, homicide, and suicide.

The concept of brain death was influenced by two major health care advances in the 1960s: the development of *intensive care units*, with artificial airways and mechanical ventilators to treat irreversible apnea, thus interrupting the natural evolution from brain failure to cardiac arrest, and **the emergence of organ donation** arising from the new discipline of transplant surgery. An ethical consensus existed that the donation itself must not cause the death of the donor, commonly referred to as the "dead donor" rule. Advanced technologies also revealed the existing limitations in the lexicon of death. The word *death* may be inadequate to describe the event or process in the various domains in which it can be defined, including medical–biological, legal, social, bioethical, philosophical, religious, spiritual, and existential. Brain death as a criterion for determining the death of a person is a medicolegal and social formulation. It implies a notion of irreversible loss of personhood and integrative functions of the brain. The diagnosis uncovers cultural and religious diversity in a pluralistic society.

Brain death is a detailed clinical examination that documents the complete and irreversible loss of consciousness and absence of brainstem function, including the capacity to breathe. The following criteria apply

1. Established etiology capable of causing brain death in the absence of reversible conditions capable of mimicking brain death
2. Deep unresponsive coma
3. Absent brainstem reflexes as defined by absent gag and cough reflexes, corneal responses, pupillary responses to light with pupils at mid size or greater and vestibulo-ocular responses
4. Bilateral absence of motor responses, excluding spinal reflexes
5. Absent respiratory effort based on the apnea test
6. Absent confounding factors.

Definition of organ transplantation

Medical and other activities of obtaining organs, tissues and cells from human cadaver or living person and their implantation to other person for treatment, as well as obtaining organs, tissues and cells from animals and their implantation in human body

Organ transplantation is both a **life-extending and a life-saving medical procedure** in which a whole or partial organ (or cells in cell therapy) from a deceased or living person is transplanted into another individual, replacing the recipient's non-functioning organ with the donor's functioning organ. Advances in the science of organ transplantation since the 1980's have significantly broadened the range of transplantable organs and improved transplant outcomes. Transplant centers in different parts of the world successfully transplant kidneys, livers, lungs, hearts, pancreases, and intestinal organs, and the procedure is considered the preferred treatment for several indications.

Ethical considerations

Since the first kidney transplant in 1954, the increasing success of, and innovations in, transplantation have created a **demand for organs that greatly exceeds the supply in most coun-**

tries. The scarcity of organs is a major impetus behind the continuing search for, and development of, alternative ways to **expand the pool of organs and tissues available for transplantation**. A major development is the procurement of organs from family members, and most recently from friends and even from strangers. We are also witnessing desperate patients soliciting organs on the Internet, the compensation of living donors for related expenses or even the bestowing of **financial rewards** for donation, and the experimental use of organs from animals (i.e., xenotransplantation). These recent trends are at the forefront of current ethical debate on transplantation, and they are gaining varying levels of acceptance in different countries by both the public and the transplant community. The sale of organs is another highly complex subject that has received much attention

Types of organ transplantation

There are two different types of living donor transplants. In the first, an organ becomes available as a result of a procedure carried out **primarily for the benefit of the donor**. The most common scenario is what is known as a **'domino' transplant**, in which a patient needing new lungs has his or her heart and lungs removed and replaced by organs from a **cadaveric donor**. The patient's own heart **is then available for transplantation to another person**. Recipients are asked to consent both to the clinical procedure itself and to the donation of other organs removed in the course of the treatment. The second type of live donation – **altruistic donation** from healthy donors – raises more issues around consent.

The main concern about living donation from healthy volunteers is that **it exposes donors to the small but significant risks of major surgery for no personal physical benefit**. Living donation does, however, carry significant advantages for recipients. Donation from a healthy volunteer – both related and unrelated – carries a higher chance of success for the recipient compared with cadaveric donors. Living donation has other advantages:

- it facilitates pre-emptive transplantation for someone with progressive renal failure, so avoiding the need for dialysis;
- it allows the transplant to proceed at the optimal time for the recipient;
- and it allows those with end-stage renal failure to escape the long wait for a kidney from a cadaveric donor.

Although the physical benefit is all for the recipient, **those who donate to people close to them may achieve psychological and practical benefits** from the recipient's recovery, such as their ability to return to work or participate more in everyday activities. Many medical interventions carry a risk of harm, **but this is outweighed by the anticipated benefit for the individual**. Nevertheless, it has long been accepted that, **with limited exceptions, adults with capacity are entitled to put themselves at risk to help other people**. Bone marrow and oocyte donation, for example, are accepted even though they put the donor at some degree of risk with no personal physical benefit.

Paired and pooled donation

Under this system, where someone needs a donor organ and has a friend or relative willing to donate but the two are not compatible with each other, they can pair up with one or more other incompatible donor and recipient pairs in an organ exchange.

- In **paired donation**, donor *A* gives an organ to recipient *B* and donor *B* gives to recipient *A*.
- In **pooled** donation, more **than two donor–recipient pairs** take part in an organ exchange, coordinated by the medical agencies (so, for example, donor A's kidney goes to recipient B, donor B's kidney goes to recipient C and donor C's kidney goes to recipient A).

Altruistic non-directed donation

Donation of **blood, gametes or bone marrow** by strangers is commonplace and accepted as a autuistic act. However, organ donation is under strict regulation. Medical commission is entitled to **evaluate donor wishes** in such cases.

According to the source of the organ

Organ donation can be categorized based on the source of the organ, and there are various types of organ transplantation methods.

1. Heterotransplantation, or xenotransplantation, is the practice of transplanting organs or tissues from one species to another.
    1. *Cross-Species Organ Transplants*: Xenotransplantation involves transplanting organs or tissues from animals (e.g., pigs) into humans to address the shortage of human organ donors.
    2. *Risks of Disease Transmission*: Critics argue that xenotransplantation may lead to the transmission of new viral diseases from animals to humans, posing ethical and public health concerns.
    3. *Loss of Human Identity*: Concerns exist about the psychological impact on recipients, as they may struggle with the idea of having animal organs. Pre- and post-operation counseling is seen as important to address these concerns.
    4. *Informed Consent Challenges*: Patients facing life-threatening situations may feel pressured to consent to xenotransplantation, raising questions about the validity of their consent.
    5. *Resource Allocation Dilemma*: Xenotransplantation is expensive, and the allocation of resources in healthcare becomes an ethical issue, as it affects overall healthcare distribution.
    6. *Instrumental Use of Animals*: Using animals for organ transplantation should be justified based on aspects where humans are superior to animals. This raises questions about the ethics of using animals for the benefit of humans.

7. *Animal Suffering*: Donor animals may undergo increased suffering due to isolation and rigorous testing to prevent disease transmission. Genetic modifications are made to increase compatibility, further raising ethical concerns.
8. *Blurred Boundaries*: Genetic alterations could make the boundary between humans and animals less distinct, challenging our understanding of species distinctions.
9. *Differences Among Animals*: Ethical perspectives differ on which animals are suitable donors. Some consider all animals equally acceptable, while others base acceptability on genetic similarity to humans.

2. Homotransplantation / Allotransplantation:
    - Homotransplantation, or allotransplantation, is the most common type of organ transplantation. It involves transplanting organs or tissues **from one human to another** of the same species.
    - For instance, a kidney transplant from a living or deceased human donor to a recipient is a common example of allotransplantation.
3. Isotransplantation:
    - Isotransplantation is a hypothetical term used to describe a situation where an organ or tissue is transplanted from one individual to another **who is genetically identical**.
    - This could occur, for example, in the case of an identical twin donating an organ to their sibling.
4. Autotransplantation:
    - Autotransplantation involves transplanting tissues or organs **from one part of an individual's body to another part of their own body**.
    - An example of autotransplantation is a *skin graft*, where skin is taken from one area of a person's body and transplanted to another area, often to treat burn injuries.
5. Biotransplantation:
    - Biotransplantation is a relatively uncommon term that can refer to any transplantation involving **technologically modified tissues or organs** or entirely artificial organs.
    - For example, a biotransplantation could involve transplanting a tissue or organ that has been modified using genetic engineering techniques or 3D bio-printing.

REPRODUCTIVE ETHICS

Contraception, abortion and birth

The increasing ability of people to exercise control over fertility and reproduction has led to major changes in the way people live their lives. Women are now able to exercise choice over whether and when to have children to a greater extent than ever before. Although emphasis is often placed on the provision of contraception to young women, **boys and men also**

need advice about contraception and sexual health. Similarly, although decisions about the progress of a pregnancy ultimately rest with the woman carrying the fetus, fathers also have a role in decision making, particularly when they intend to take an active part in bringing up the child. Reproduction differs from many other areas of medical practice because of its complexity and because tension can sometimes arise between the **rights of women** to make decisions about their own bodies and the **moral duties owed to embryos and fetuses**. It is this aspect of reproduction that is at the root of many of the ethical, legal, social and psychological questions that continue to be of concern to society. Control over one's body, abortion, reproduction and parenthood are matters about which most people hold strong views. For many, such views are based on moral, religious or cultural convictions. Given the existence of such diversity of opinion, it is clear that some of these questions can never be resolved to the satisfaction of all sections of society, but will be the subject of continuing ethical debate. Broad areas of moral consensus can, however, be sketched out after wide ranging consultation and public debate, and these form the basis of legislation, guidance and practice in this area.

General principles

When considering questions about contraception, abortion and birth, the following general principles should apply.

1. The confidentiality of all patients, including those aged under 16, should be respected except in exceptional cases.
2. Young people who are sufficiently mature to understand the nature and implications of the treatment requested are able to give valid consent, but parental involvement should be encouraged.
3. No treatment may be provided to an adult who has capacity without valid consent.
4. Adults are presumed to have capacity unless there is clear evidence to the contrary. (Being in labour does not, in itself, affect decision-making capacity.)
5. Women should be encouraged to participate to the greatest possible extent in decisions about their pregnancy.
6. A woman who plans to carry her fetus to term has special moral responsibilities towards the unborn child, but neither health professionals nor society can force her to fulfil those duties.
7. Discussion about reproduction inevitably focuses primarily on women, but the role of men should not be undermined. Contraception and sexual health are the responsibility of both sexes.

The autonomy of pregnant women

It is an accepted principle of medical law and ethics that adults with capacity have the right to refuse any treatment or medical intervention, even if that refusal results in their avoidable death. The courts have held that this rule applies equally to a woman who is pregnant even if she is carrying a viable fetus capable of being born alive. **The fetus, up to the moment of birth, does not have any separate legal interests capable of being taken into account by**

a court, and therefore the legal position is that the woman's right to refuse treatment overrides all other legal considerations.

Is there a right to reproduce?

A woman's right to refuse life-prolonging treatment is one of a number of 'rights' that are frequently appealed to in relation to reproduction. A distinction is often made between negative and positive rights or between a liberty and a right. **Negative rights simply involve being free from interference and are based on the notion that the state should not interfere with essentially private decisions**. In terms of reproduction, this confers the right not to be prevented from procreation, for example by non-consensual sterilisation. **Positive rights, however, would include the right to demand appropriate healthcare**. In terms of reproduction, this would include a positive obligation on the state and health professionals to support the individual's reproductive choices, including providing reproductive technology for every person who requires it. Claims to positive rights are often seen as problematic in that they suppose that there is a corresponding obligation on other people to supply what the right holder claims.

Contraception

The continuing high number of unwanted or unintended pregnancies demonstrates a clear need for better access to, and uptake of, contraceptive information and services. Cooperation has been encouraged for many years between various agencies, including health and education services, the voluntary sector, and service users to try to improve family planning services. This includes recognition of the need for specific training to enable providers to assess, and explain to patients, the range of contraceptive methods available and to provide general advice about sexual health to accompany the provision of contraceptives. Most women who seek contraceptive advice and services do so from their GP practice, although many younger women tend to prefer the anonymity of specialist clinic

Before providing **contraception to young people**, health professionals must:

1. Consider whether the patient **understands the potential risks and benefits** of the treatment
2. Consider whether the patient understands the **advice given**
3. Discuss with the patient the value of **parental support**(doctors must encourage young people to inform parents of the consultation and explore the reasons if the patientis unwilling to do so) – it is important for persons aged under 16 who are seeking contraceptive advice to be aware that, although the doctor is obliged to discuss the value of parental support, he or she will respect their confidentiality
4. Take into account whether the patient is **likely to have sexual intercourse without contraception**
5. Assess whether the patient's **physical or mental health** or both are likely to suffer if the patient does not receive contraceptive advice or treatment

6. Consider whether the patient's best interests would require the provision of contraceptive advice or treatment or both without parental consent.

Even if the doctor is unwilling to supply contraception on the grounds of the patient's immaturity, he or she still maintains a general duty of confidentiality unless there are exceptional reasons for disclosing information without consent. Such reasons could occur when, for example, the request for contraception arises in the context of sexual exploitation, incest or other sexual abuse. In such exceptional cases the doctor has a duty to protect the patient and this may eventually involve a breach of confidentiality, although with counselling and support the patient may feel able to agree to disclosure. Nevertheless, it is important that doctors avoid making completely unconditional promises about secrecy to individual young people, while at the same time making it clear that confidentiality as a general principle extends to all consultations.

Sterilisation

Depending on national legislation, men or women above certain age may apply for sterilization. For men, the procedure (vasectomy) is simpler than for women (tubectomy or the blocking of Fallopian tubes). From the point of view of ethics, it is important that the person understands that after successful sterilization, fertility can be recovered only in exceptional cases. **Sterilization without consent or even under coercion is illegal and represents a grave ethical offense.**

Male or female sterilisation is usually expected to produce **permanent sterility** (although this is not necessarily the outcome). Although some people have conscientious objections to sterilisation for contraceptive purposes, within society as a whole it appears to be viewed as an acceptable form of family planning, as long as individuals are adequately informed of the implications of the procedure and no pressure is exerted upon them. Reliance on sterilisation for contraceptive purposes is highest amongst older women. Non-consensual sterilisation of those who are unable to give valid consent has, however, been the subject of intense debate Sterilisation (unless for therapeutic reasons) is one of a small number of procedures that must not be carried out without applying for a court declaration. This is because of its intended irreversible nature, which deprives the individual of what is, according to one judge, 'widely and rightly regarded as one of the fundamental rights of a woman, the right to bear a child'.

Abortion

In order to understand the very contentious background to the abortion debate, it may be helpful to mention briefly the main strands of the argument. People generally give one of three common types of response to abortion: prochoice, anti-abortion and the middle ground that abortion is acceptable in some circumstances. The main arguments in support of each of these positions is set out below.

Arguments in support of abortion being made widely available

Those who support the wide availability of abortion consider the matter to be primarily one of a woman's right to choose and to exercise control over her own body. These arguments tend not to consider the fetus to be a person, deserving of any rights or owed any duties. Those who judge actions by their consequences alone could argue that abortion is equivalent to a deliberate failure to conceive a child and, because contraception is widely available, abortion should be too. Others take a slightly different approach, believing that, even if the fetus has rights and entitlements, these are very limited and do not weigh significantly against the interests of people who have already been born, such as parents or existing children of the family. Most people believe it is right for couples to be able to plan their families and for women to have control over when they become pregnant. Although contraception is understood to be the appropriate means to avoid unwanted pregnancy, all methods have a failure rate. When contraception fails, or when couples fail to use it effectively, many people accept that abortion is preferable to forcing a woman to continue with an unwanted pregnancy.

Arguments against abortion

Some people consider that abortion is wrong in any circumstance because it fails to recognise the rights of the fetus or because it challenges the notion of the sanctity of all human life. They argue that permitting abortion diminishes the respect society feels for other vulnerable humans, possibly leading to their involuntary euthanasia. Those who consider that an embryo is a human being with full moral status from the moment of conception see abortion as intentional killing in the same sense as the murder of any other person. Those who take this view cannot accept that women should be allowed to obtain abortions, however difficult the lives of those women or their existing families are made as a result. Such views may be based on religious or moral convictions that each human life has unassailable intrinsic value, which is not diminished by any impairment or suffering that may be involved for the individual living that life. Many worry that the availability of abortion on grounds of fetal abnormality encourages prejudice towards any person with a handicap and insidiously creates the impression that the only valuable people are those who conform to some ill-defined stereotype of 'normality'. More recently, some have shifted the arguments on to the pregnant woman and have argued that abortion is wrong because of the psychological and health consequences for a woman, although evidence in support of this is elusive and controversial. Some of those who oppose abortion in general nevertheless concede that it may be justifiable in very exceptional cases when termination is seen as the lesser moral offence. This could include cases such as where the pregnancy is the result of rape, or the consequence of the exploitation of a young girl or a woman lacking capacity. Risk to the mother's life may be another justifiable exception, but only when abortion is the only option. It would thus not be seen as justifiable to abort a fetus if the life of both fetus and mother could be saved by implementing any other solution.

Types of abortion

1. Medical Abortion:

- Medical abortion is a type of abortion that is conducted for **medical reasons**, typically when the continuation of a pregnancy poses a **threat to the health or life of the pregnant person**. It may also be performed in cases of severe fetal abnormalities where the baby is not expected to survive after birth
- This type of abortion is typically carried out with the guidance of healthcare professionals, using medication or surgical procedures to ensure the safety of the patient.

2. Social Abortion:

   - Social abortion, also known as **elective abortion**, is the termination of a pregnancy **for non-medical reasons**. It is a personal choice made by the pregnant person due to various factors, such as their life circumstances, financial situation, or personal beliefs.
   - The legality and availability of social abortions **can vary widely** from one region or country to another. Some places may have strict regulations or restrictions on elective abortions, while others may have more permissive laws.

3. Criminal Abortion:

   - Criminal abortion refers to an abortion that is performed **in violation of the laws of a particular jurisdiction**. This can encompass a wide range of circumstances, such as performing an abortion **without proper medical training or in a setting that doesn't meet legal standards**.
   - Criminal abortion may also refer to cases where abortion is **considered illegal**, regardless of the circumstances. The legality of abortion varies widely across the world, with some countries allowing it under certain conditions and others prohibiting it entirely.

Assited reproduction

Assisted reproduction enables the deliberate manipulation of the processes and materials of human reproduction outside of sexual intercourse. In describing the practices that constitute assisted reproduction, it must be understood that all such practices are embedded with ethical issues, whether standard therapies such as ovulation induction, insemination with donor sperm, and in vitro fertilization (IVF) ; emerging practices such as pre-implantation genetic diagnosis (PGD) ; or practices prohibited under law in many countries, such as the purchase or bartering of oocytes. Ovulation induction through clomiphene citrate has been practiced for over 30 years.

This oral therapeutic strategy can assist 50–80% of women with ovulatory dysfunction become pregnant, depending on the etiology of their disorder (with the exception of premature ovarian failure). Aromatase inhibitors are new oral ovulation induction agents. When these are unsuccessful in inducing ovulation, menotropins (also referred to as gonadotropins) may be used . This is a much riskier strategy, with side eff- ects including ovarian hyperstimulation syndrome and the creation of high-order multiple pregnancies. Provision of sperm, by other than the woman's partner, was one of the earliest forms of assisted reproduction and has been encompassed in medical practice for 50 years. Sperm donation is a common practice when a woman's partner has sperm of low count or quality or carries a communicable disease, when

she is in a lesbian relationship, or if she is single. Oocytes may be provided to women who no longer have an *"ovarian reserve,"* because of their advanced age or having undergone cancer treatment

Insemination or Egg Cell Donation

In the case of infertility, insemination with donor sperm or donation of egg cells are nowadays routine procedures. The main legal and ethical issues concern the status of the donor. In Bulgaria and in many other countries, the donor remains anonymous. Only in cases of exceptional and justified health-related reasons can the court in a non-contentious procedure allow disclosure of the donor's identity. In several countries, however, donors are not guaranteed anonymity with the justification that the child upon coming out of age has the right to know who his or her biological parents are

In Vitro Fertilization

In recent years, a stark increase in age at which the future parents decide to have children has been seen, especially in developed countries. Because fertility decreases with age, it is understandable that many parents require medical assistance in conception. The procedures of in vitro fertilization are also used in cases when we need to select among the fetuses to avoid genetic diseases. Ethical considerations here are similar to those in prenatal diagnostics: medicine supports the wishes of the parents to have only healthy children. Obviously, in vitro fertilization is ethically not accept- able when it serves to choose the gender or physical or mental characteristics of the child.

Surrogate Motherhood

The most significant deviation from natural conception and pregnancy is **surrogate motherhood**. Surrogacy arrangement means that the fetus is implanted into the womb of another woman who gives birth to the child and then gives the child to the "biological parents". Surrogacy opens the door to severe abuse. The indication for surrogacy is often not a medical one, that is, the inability of the biological mother to carry a pregnancy and give birth, but rather the biological mother wants to avoid all the risks and dis- comforts of pregnancy and birth. In some parts of the world, for example, India, the so-called rent-a-womb is already a well-established source of income for poor women. This practice is illegal in many countries and is ethically very problematic. Few healthy women would accept the role of a surrogate mother purely for altruistic motives, and in the large majority of cases, it is the money that drives the decision. Surrogate motherhood is a clear case of disrespect of the ethical principle of justice. Ethically, it is hard to defend exploitation of the poor, who are forced to put their health and well-being at risk. The second problematic issue is that pregnancy is not merely a waiting time, but rather a precious period for both parents to prepare for their new role. Talking, or singing to a child before birth, is a most common and enriching experience. Likewise, the father also gradually adapts to his new role. Thus, all events during pregnancy prepare the family for the great change in family life and for the (often difficult) period of caring for a newborn baby. This role of pregnancy

as preparation for parenthood is missing if the only reminder of the new family member is a marked date on a calendar. Finally, we must also think of some unfortunate potential scenarios. What happens if the newborn child is not healthy? Would the "biological parents" return him or her as we do with malfunctioning washing machines in stores? If the surrogate mother during pregnancy or delivery gets a disease or even dies - who is responsible and who takes care of her other children?