



*Presidenza del Consiglio dei Ministri*

**NATIONAL BIOETHICS COMMITTEE**

**ORGAN TRANSPLANTS IN CHILDHOOD**

21st January 1994

## CONTENTS

<b>Preface</b>	p. 3
<b>Abstract</b>	p. 4
<b>Paper</b>	p. 6
<b>1. Organ Transplants in Children</b>	p. 7
1.1. Kidney Transplants	p. 7
1.2. Liver Transplants	p. 8
1.3. Heart Transplants	p. 9
1.4. The Conditions of Children who have Received Transplants	p. 10
<b>2. Problems Common to Various Kinds of Transplants</b>	p. 10
2.1. Brain Death	p. 11
2.2. The Availability of Organs	p. 15
2.3. Legal Aspects	p. 18
2.4. The Special Features of Paediatric Transplantology	p. 20
<b>3. Ethical Reflections</b>	p. 22
<b>Bibliographical Notes</b>	p. 28

## PREFACE

In agreeing to the publication in October 1991 of the document 'Organ Donations for the Purposes of Transplants', this Committee observed how the question of the donation of organs for the purposes of therapeutic transplants had for a long time been the subject of doctrinal formulations in the legal field as well, as it had been in the specifically medical field; how it had consequences of an ethical character of very great importance; and how it was the subject of impassioned debates in public opinion. In addition, it had to be observed how in all countries that were advanced in health-care terms the question of the removal of organs for the purposes of transplants was rigidly regulated and how the laws that had been drawn up were rather divergent, although in each case they addressed the question of consent to donation. On that occasion the basic questions of the donation of organs for the purposes of transplants were addressed. The question of consent in general, and of information, was addressed in a specific document entitled 'Information and Consent to the Medical Act', which the National Bioethics Committee agreed to publish on 20 June 1992. In particular, in it was stressed the complexity and the importance of information and consent to the medical act in childhood and adolescence. This document considers the specific aspects of organ transplants in children and adolescents. In summarising fashion, data of medical-scientific relevance and the results that are being obtained in paediatric transplantology are presented; the legal norms that apply to the juvenile age of patients are analysed; and attention is paid to the interaction between transplant services, patients and family relatives. This document was drawn up by Prof. Nordio, who coordinated a group of 'experts' made up of Prof. Caccia, Prof. Defanti, Prof. Farrazi, Prof. Grevame, Prof. Marcelletti, Prof. Mazza, Prof. Parenzan, Prof. Parisi, Prof. Sereni and Prof. Torrioli. Prof. Cendon of the University of Trieste contributed to the legal part. It is to all of them that I and the Committee express our gratitude for the valuable contributions made. The document was widely discussed, and in some parts modified, with the contributions of Prof. Barni, Prof. Berlinguer, Prof. Cattorini, Prof. Farrando, Prof. Leocata, Prof. Manni, Prof. Merli, Prof. Rescigno and Prof. Sgreccia, and then in plenary meetings of the National Bioethics Committee. Within the limits of the tasks of this Committee, which are to provide indications at the level of bioethics connected to a precise scientific analysis at all possible interdisciplinary levels, the greatest effort has been made to offer elements that are useful and coherent for a reflection on this delicate matter, for which is always required an open dialogue and all possible contributions to which are always to be welcomed.

Rome,  
21 January 1994

The Chairman,  
*Adriano Ossicini*

## ABSTRACT

Organ transplants constitute a great advance for medical science and because of the successes that have been statistically recorded it is seen as a consolidated therapy for all age bands, including children. Obviously, it cannot take the place of other therapies wherever these are possible. In addition, it is necessary to place more emphasis on work of prevention in order to avoid resort to transplants.

Transplantology in general, and paediatric transplantology which has special features, raises questions of what is termed frontier bioethics, because it represents one of the most advanced frontiers of the scientific-technical progress of medicine, and of what is called daily bioethics, because in the general system of health care it creates situations that are very demanding at human level and technical-organisational levels.

This document belongs to frontier bioethics in the parts that present the documented statistical data of the successes of transplantology, and it belongs to daily bioethics in the parts in which are considered the application of the methodologies and the technologies understood in a broad sense; the experiences undergone in the therapeutic event by parents, children, adolescents, health-care personnel; and the relationships that are established between them, above all at the humanly most demanding moment of informed consent.

This document seeks to be an appeal to reflections that are held to be essential, which concern the whole of medicine, with its scientific, technological and technical advances and with the ethical and social questions that derive from them; an appeal which has a special value in transplantology, especially transplantology in children; it seeks to be an appeal to scientific thought that is quantitative, statistical and technical, but also qualitative, and which in the need to be scientific-technical should not sacrifice thought and reflection.

The reflections that are proposed can be summarised as follows:

Assessed over a period of several years, the successes of transplants that are most frequently carried out on children are undoubted, but one cannot yet speak about definitive cures. There are the side effects of immunosuppressive therapy; it is not yet known what these side effects are in the long-term and how such therapy will control, over time, chronic rejection; and trust is placed in advances in immunology and in an improvement in drugs at the level of efficacy and toxicity. It is argued that a service must be organised in transplant centres that has a character that is not only medical in a strict sense but also multidisciplinary, where there is a complete approach to the problems that people find themselves facing both as regards the operation and afterwards, and for all the time that is required.

The criteria of the ascertainment of brain death in children, above all in neonates, are different from those in the case of adults, and they must be adopted in intensive care units leaving to one side the question of the donation of organs. The workers in these units should thus know and apply these criteria, which are differentiated according to age.

The availability of organs is not as great as the demand created by the spread of the practice of transplantation, and for this reason waiting for an operation is prolonged and the ratio of clinical recommendations for a transplant to the availability of organs is high – in our country even more than in others. For transplants in general, and not only for paediatric transplants, this imbalance is not necessarily due to a low readiness to engage in donation. Rather, it could be the consequence of organisational failings that obstruct the use of organs where there is a wish to donate in a spirit of solidarity. Thus initiatives and regulations are required to achieve a sound organisation which, with a correct assessment of needs, and always respecting the principle of the rational allocation of resources, defines the ways in which organs are collected, the distribution of centres, and the programmes of these centres.

The transplantation of the organs of deceased anencephalic infants raises questions regarding treatment to maintain the vitality of the organs and special problems regarding the ascertainment of brain death, the need for which is incontestable for these infants as well, even if they are inescapably destined to die within a short period of time.

Informed consent to a transplant, in which older children are also involved, first of all adolescents, involves a particularly arduous role at the level of communication because of the symbolic representations and the experiences that parents and patients have, and because of the prognosis, which can be envisaged only in terms of percentages of survival after a number of years and in terms of trust in scientific progress. Informed consent involves a role at the level of communication of a unique delicacy when the transplant is proposed for an infant who has just been born with malformations that are incompatible with life, that is, at a moment which even in normal conditions the affective tie between the parents and the child is at a stage of consolidation, when the feelings of the parents are complex, opposing and contradictory, ones of acceptance and readiness to suffer and to engage in sacrifice, of incredulity, pain, anger and rejection. For this reason, the appeal is still, as was stressed in a previous document of the National Bioethics Committee, for the need for practical initiatives, in hospitals themselves, to promote a system of training of health-care personnel that aims at the maturation and strengthening of a culture of communication as well.

The context of transplantology at the present time may be described – apart from the legal aspects which, as they deal with minors, are, as has been said, special in paediatric transplantology – as clinical successes with confidence in future successes; as enthusiasm as regards the scientific and technical advances by transplantologists; and as confidence, hope and anxiety as regards expectations and suffering as regards hopes which, given a lack of organs, leave parents disappointed.

Transplantology is a reality that has established itself and which raises, together with other approaches and like other activities on the frontier of medical-scientific progress, the question of responsibility, in particular the responsibility of the education of young people. This will benefit the cultural transmission of technologies; the adaptation of the value systems in which people are educated to the criteria produced by scientific technological knowledge; and to the creation of technologies that are in agreement with historical values and values that are undergoing evolution in society.

# PAPER

# 1. ORGAN TRANSPLANTS IN CHILDREN

The history of organ transplants in children began in 1957 with the first transplant of a kidney from an identical twin which was carried out at the Peter Bent Brigham Hospital. In 1959, at the same time in Boston and Paris, the first kidney transplant between non-identical twins was performed. In 1963 Starlz carried out the first liver transplant and in 1967 Kantrowitz performed the first heart transplant. For years failures were frequent, above all because of the difficulty of impeding rejection. Immunosuppressive therapy with high doses of steroid hormones provoked severe secondary effects and to such an extent that there was much opposition to transplants in the paediatric age. The situation changed in 1980. With cyclosporine for anti-rejection treatment, the successes notably increased, the armoury of immunosuppressive pharmaceuticals broadened, and organ transplants became a consolidated therapy. But these major scientific-technical advances also raised great question connected with the typology and organisation of services, the use of services in the context of the needs of all the service of health care, the promotion of donation, the spread of a 'culture of transplants', and the effects that this produces in the culture of people – all fundamentally ethical questions.

This document is organised into three parts:

- Organ transplants that are most common in the paediatric age and the conditions of children who have received transplants.
- The problems common to various types of transplants.
- Ethical reflections.

The most frequent transplants are kidney, liver and heart transplants.

## 1.1 Kidney Transplants

These are carried out on dialysis patients because of irreversible renal insufficiency and it is hoped that this will become the first therapeutic intervention, that is to say that it can avoid the dialysis stage of treatment, with its problems of organisation at the level of care, and the disturbances, malaise and sufferings of a physical, psychological and psycho-social nature that it involves.

According to data presented in the international literature in the field over recent years (EDTA 1990; Nephrol. Dial. Transplant. 1991), one can calculate that 4.6 out of every million children are afflicted by terminal renal insufficiency ever year. Extrapolated for the population of Italy, one can affirm that every year 50 of our children should be helped by the dialysis/transplant programme. According to the North America Pediatric Renal Transplant Cooperative Study and the European Dialysis and Transplant Association (EDTA), the illnesses that lead to irreversible renal insufficiency, and thus prior to, or after, a transplant, are the following in order of frequency:

- Interstitial pyelonephritis/nephritis 24%-26.6%;
- Glomerulonephritis 24.2%-25.2%;
- Hereditary nephroses 15.1%-15.8%;
- Congenital renal hypoplasias 7.5%-18.1%;
- Systemic illnesses 4.7%-13.3%;
- Others of known or unknown causes: 9.6%-15.8%.

There are possibilities of preventing renal insufficiency and delaying its onset and development. These take the form of early diagnosis in the womb through ultrasonography; the early surgical correction of certain congenital anomalies of the urinary pathways; the early and correct treatment of infections; and, when insufficiency has nonetheless been installed, diet therapy and medical therapies, amongst which the administration of the growth hormone.

The hope of making transplants the fundamental therapeutic objective of irreversible renal insufficiency in order to reduce to the minimum the duration of dialysis treatment has found positive confirmation and is also seen as a primary therapy. In the North America Pediatric Renal Transplant Cooperative Study and in the study of the EDTA early transplants were carried out in 20% and 18% of cases respectively.

According to the *Associazione Nazionale Emodializzati* (ANED), 100 Italian children are in dialysis awaiting a transplant. From an informal survey of paediatric blood dialysis centres in Genoa, Padua, Milan and Rome, it emerged that in these centres there were 90 children waiting for a transplant. In the years 1977-1988 the EDTA, referring to data from various European countries, reported that 30-60% of young people under the age of 25 awaiting a transplant had done so for less than a year and 8-28% had done so for more than three years. With respect to the data of Nord Italia Transplant (NITp), it has been calculated that the median waiting time is 1 year and the average waiting time  $1.6 \pm 3.2$  years. The request for a transplant is thus not matched by the possibility of carrying it out suitably quickly. The need to respond as quickly as possible to the request for a transplant concerns above all the smallest infants of less than one year of age. In the NITp programme, 80% of children on the waiting list are of this age. In Italy, as in other European countries, attention has been drawn to the increase in cases of terminal insufficiency in children of less than two years of age. Within the context of the NITp programme, the number of transplants in children increased during the two-year period of 1988-1989 and decreased over the subsequent two years. It should, however, be noted that in North Italy there are centres which work outside this programme and that a non-specifiable number of children receive transplants abroad. The data of the EDTA demonstrate that the ratio between children in dialysis and children who have received transplants varies in European countries. It is 1.09 in Italy, 1.6 and 1.9 respectively in Greece and Portugal, 0.89 in Holland and 0.19 in Norway and Sweden. This testifies to the varying capacities of European countries to meet the demand for transplants in children.

The survival of children who have received transplants is high. It is 80% at 30 months according to the North America Pediatric Transplant, a figure which matches that recorded by our NITp. The need for a repeat transplant is not rare. In the literature in the field frequencies of a repeat transplant of 22.6%-28% are registered and of 5%-9.3% of two or even three repeat transplants. As emerges from numerous American case studies, survival is longer by 10% if the transplant comes from a living person. In Italy, transplants from a living person are less frequent than in other countries, in Belgium, in the USA and above all in Sweden and Norway. Initiatives are to be welcomed that will foster a readiness on the part of parents to engage in donation. Survival rates two years after a transplant from a living person of 81%-85% of 2-17 years of age and of 71% in less than 1 year of age (North America Pediatric Transplant 1992) have been observed.

## **1.2 Liver Transplants**

Differently from transplants of other organs, there is a lack of data on a broad population of children which could specify the demand for liver transplants. The list of hepatic illnesses where a transplant is recommended is continually growing and in the case of many of these illnesses their real incidence is not known. One may consider as being certain the epidemiological statistic on atresia of the extra-hepatic biliary pathways which has an incidence of 1 case in every 10-15.00 children born alive. For this illness, an alternative intervention is, according to Kasai, portoenterostomy, which provides definitive and satisfactory results in only 25% of cases. One can transplant the whole of the organ or only a part of it. In this case a single liver allows the carrying

out of two transplants. The transplantation of a part of a liver of a living person has been successful and the promotion of this practice is to be hoped for.

Liver transplants at the present time are recommended for three groups of illnesses:

- the colostatic: atresia of the biliary pathways, ductular paucity, sclerosing cholangitis;
- the metabolic: Wilson's disease, Byler's disease, and Crigler-Najjar's disease in grave form, alpha-antitrypsin deficit, tyrosinosis, glycogenosis types I and IV, fructosemia, oxalosis, hypercholesteremia type II, defects of the urea cycle, protoporphyria;
- others: cryptogenetic cirrhosis, fulminant hepatitis, tumours, congenital hepatic fibrosis, auto-immune chronic hepatitis.

The transplant prevalently takes place in young infants. At the present time it is calculated that 65%-70% are carried out in children under the age of 3; 20%-25% in children between the age of 3 and 6; and 10%-15% in children over the age of 6.

Survival generally depends on the type of illness, on general conditions, and on the age and the weight of the infant. Overall, it can be estimated at 75%-90% at the age of 1 and 65%-79% at the age of 5. It is lower if the transplant is carried out in conditions of urgency, that is to say 50%-70% at the age of 1. It is higher, being 90% at the age of 5, in the case of metabolic illnesses. For the same illness the survival is not different if the transplant involves the whole organ or only a part of it.

The need for a repeat transplant is not rare. Up to four transplants have been carried out in the same individual. Overall, from the literature in the field a frequency of repeat transplants of 17%-25% is recorded. The duration of survival is inverse to the number of repeat transplants required.

From the data of European paediatric centres, we see a relationship between the time of waiting for a transplant, because of the availability of organs, and the blood group of the recipient, with a median of about 3 months, and 6-12 months and 12-15 months for children with, respectively, blood groups A, B, and O.

For our country, a need for 50-60 new transplants every year is calculated, which corresponds to 25 transplants carried out annually, of which 40% in children under the age of 6 (report 1986-1991 of Nord Italia Transplant). The results are different from those that are obtained in other countries, above all in the smallest infants, a fact which can probably be attributed to a lack of centres with specific paediatric, surgical and hepatological, capacities.

### **1.3. Heart Transplants**

These are carried out in children with complex congenital heart disease involving malformation and with myocardial affections that are grave and resistant to medical therapies. It is held that there is an incidence of congenital heart anomalies in 4 out of every 1,000 neonates, excluding those associated with chromosome aberrations. The advances in surgical techniques have been very great, with a notable fall in mortality rates. Mortality as a result of the surgical correction of a defect in the interventricular septum, the most common form of congenital heart disease, has become very low. The current tendency is to anticipate the correction and to eliminate palliative interventions as bridge-interventions towards definitive ones, both for reasons connected with the functionality of the heart and circulation and to solve first the psychological problems, the worries that afflict families. Transplantation in the place of other surgical techniques when these, because of the complexity of the heart disease involve high risks and provide less satisfactory results, is becoming increasingly recommended. The utility of transplantation as the chosen therapy, as the first early and definitive intervention, in the neonatal age, is already coming into view. In neonates there are theoretical assumptions to believe that there is less risk of rejection. Reference is made to the 'unique newborn response', thus to a unique opportunity that is offered to the surgeon carrying out a transplant. A less intense immunosuppressive therapy is required, with the possibility of a more rapid move to the use of a single drug (cyclosporine), with, therefore, a possible reduction of side effects. The International Registry Heart Transplantation reported that in 1991 in the world

500 children under the age of 5 had received transplants. The survival of these children 2 years after the operation was 70%. 36 children of the same age who received transplants in Italy had a similar survival rate at 6 years after the operation. The survival rate could be higher if the transplant was carried out at a very young age.

70% of heart diseases for which transplantation is recommended take the following forms:

- severe congenital or acquired cardiomyopathy;
- hypoplasia of the left heart;
- Ebstein's anomaly with normal pulmonary arteries;
- obstructive multiple rhabdomyosarcomas;
- atresia of the pulmonary artery with integral interventricular septum
- equivalents of hypoplasia of the left heart;
- transposition D of the great arteries with hypoplasia of the right ventricle and the aorta;
- single ventricle with hypoplasia of the aorta;
- transposition L of the great arteries with single ventricle and heart blockage;
- atrioventricular canal with hypoplasia of the left ventricle and mitral valve (frequently associated with coarctation);
- single ventricle with sub-aortic obstruction (bulb-ventricular foramen).

Given these recommendations, it has been calculated that in Italy, given the present birth rates, 300 heart transplants would be required every year, half of which for infants in their first year of life. With the optimisation of techniques, and because heart diseases involving malformation traditional techniques have less satisfactory results, an increase in the number of transplants is foreseeable.

#### **1.4. The Conditions of Children who have Received Transplants**

The duration of controls, of the follow-up for children who have received transplants, corresponds to the lengths of the survivals indicated. Thus for the moment the assessment of the conditions of health of these children is medium-term. Limiting ourselves to the period of observations, we can without doubt declare the success of paediatric transplantology.

The growth of these children is regular and if previously compromised improves even to the point of normalisation. Reference is made to a good psychological adaptation of children to their new condition and of their families as well. The immunosuppressive therapy is, overall, well tolerated. Side effects such as renal damage caused by cyclosporine and arterial hypertension caused by cyclosporine and steroid hormones seem less frequent than in adults. As regards heart transplants, it is observed that when these are carried out at an early age renal damage and hypertension, tumours and coronary arteriosclerosis seem less present. Obviously, we can know nothing about the frequency of tumours and the development of arteriosclerosis over the long term. Or about chronic rejection caused by immunosuppressive drugs. Improvements in the treatment are envisaged in terms both of efficacy and of lower toxicity with the use of new drugs.

## **2. PROBLEMS COMMON TO VARIOUS KINDS OF TRANSPLANTS**

These are fundamentally two in number: that of the ascertainment of death for the removal of transplantable organs, that is to say still living organs, and that of the donation of organs.

## 2.1. Brain Death

The transplantation of organs from a cadaver is allowed by the law and pre-supposes the ascertainment of 'brain death'. For transplantation organs are used which thanks to the most advanced techniques of resuscitation are able up to the moment of removal to receive oxygen and nutrition for the maintenance of the metabolic activities. One may say that the advances in the techniques of resuscitation have produced the reality of a 'new kind of cadaver', of a person who is already dead because they have lost the encephalic centre of coordination of the functional unity of their organism, conserving, however, some living organs and thus ones that are transplantable.

In agreement with what has already been recommended by the National Bioethics Committee, a net distinction should be made between ascertainment of brain death and the donation of organs. The ascertainment of death is always a due act and one that is independent of a possible removal of organs for the purposes of transplantation. Only in this way is it possible to avoid an erroneous interpretation of the relationship that exists between the diagnosis of brain death and transplants.

As regards the definition of death and the ethical debate that has taken place on the subject, the National Bioethics Committee has adopted the notion of total brain death, according to which the human person can be said to be dead when the whole brain (the cortex and the brain stem) is dead.

Once brain death has been established, by whatever cause, it is the responsibility of the medical team to decide on the basis of the available parameters – including the cause of death – the usability of the organs and to request informed consent. To this end some call attention to Law 614 of 2 December 1975 in which are indicated as donors individuals affected by primitive cerebral lesions, where the word 'primitive' would appear to exclude the possibility of using the organs of children who have died because of various causes, amongst which perinatal asphyxia.

For the ascertainment of brain death a shared definition of precise criteria is required.

The ascertainment of brain death, always understood as death of the entire encephalon, presents particular problems as regards the paediatric age. In the USA there are said to be 400 cases a year of the ascertainment of brain death in children. By extrapolation one could think that in Italy there are 100 annually. From the international literature in the field it emerges that 1/5 children who die in intensive care units have an ascertainment of brain death.

Certain conditions specific to children should be borne in mind. Their brain is more resistant to the reduction in the haematic flow and the input of oxygen. In neonates the minimum threshold of flow beneath which brain death takes place is not known. As long as the sutures are open, the increase in intra-cranial pressure – which in adults is the principal mechanism of brain death because it impedes the circulation of the blood in the brain – is lower. The examinations carried out with equipment, which complete clinical ascertainment, are not always applicable, or they are applicable with greater difficulty, for reasons connected with the availability of equipment in the intensive care units as well.

The most cited criteria are those of the Ad Hoc Committee on Brain Death which deliberated in response to an initiative of the Children's Hospital of Boston, of the Task Force for the Determination of Brain Death in Children, and of the President's Commission of the USA. To these are added the Loma Linda Protocol proposed for the use of the cadavers of anencephalic infants for organ donation.

To the official proposals are added the results of joint studies and numerous publications which comment on them or criticise them. For example, the Loma Linda Protocol for the keeping alive of anencephalic children by mechanical ventilation until the moment of the removal of organs is seen as having failed. Criteria are being developed in Italy by various scientific societies. The proposals, comments and criticisms do not always give rise to contributions marked by clarity. However, they are stimuli to reflection and to what can never be sufficient prudence, and

agreements are not absent. It is certain that the criteria that are used for adults are not applicable to children of all ages. The American President's Commission considered these to be valid until the age of 5. This is a recommendation that should be seen as a principal reference point, even though some people think that the criteria for adults can be extended until the age of 2, more or less when the cranial box closes. Specific protocols for neonates are absent. There are the recommendations of the Task Force for the Determination of Brain Death in Children for children over the age of 7 days.

The neurological assessment of neonates, especially pre-term neonates, is more uncertain. The reflexes of the brain stem appear between the twenty-eighth and thirty-fourth week of gestation. The neurological reactivity of a neonate can be modified by the presence of congenital cerebral anomalies and in a pre-term neonate in intensive therapy by encephalic suffering caused by illnesses and haemorrhages which can be the cause of permanent damage but not death. In a neonate the cerebral hemispheres are less developed; the possibility of exploring the set of supratentorial functions is lower; and the functional relationships between the high structures and the brain stem are evidently different. Many factors can make the ascertainment of brain death difficult 24-48 hours after death, amongst these, in premature births, increased arterial hypertension. Infants in intensive therapy, above all neonates, are frequently treated with anticonvulsive, barbituric and diazepinic drugs that depress the nervous system, including the respiration centres, with an easier consequent outbreak of apnoea, which is one of the criteria for the ascertainment of brain death.

In substance, the ascertainment of brain death in infants is different from that in adults. A set of clinical signs has to be identified which include the absence of reflexes of the brain stem – an absence which must be detected but which is not a sufficient index. The reflexes of the brain stem may be absent or modified because of incomplete maturation and other factors which are more frequently at work in infants, above all the youngest.

There is no agreement on the need to use an electroencephalograph (EEG) test, even though everyone recognises its utility in confirming clinically ascertained brain death. It is certainly to be recommended in infants, given the greater difficulties that exist in their case connected with the clinical ascertainment of death. However, the problems at the level of interpretation of the tracings due, as well, to the positioning of the electrodes on a cranial surface of small dimensions and more frequent artefacts, should be remembered. It is said that the clinical picture of brain death can be accompanied by the persistence of a certain electrical activity and vice versa that an electric silence is detectable in the absence of the clinical criteria of brain death. In reality, neither of these are conditions for brain death if by brain death is meant the death of the entire encephalon. That is to say they take place if the criteria that are used are not those for the ascertainment of overall brain death. The orientation, however, is to engage in an EEG with an infant and to repeat it after twenty-four hours. In children who are being treated with anticonvulsive drugs, which also have myorelaxing effects, an electromyographic assessment of the activity of the neuromuscular plaque is recommended. The study of evoked potentials is promising because of its non-invasiveness, the objectivity of the findings, and resistance to the effects of neurodepressive drugs. But in children the results seem to be still controversial. Of importance is the ascertainment of the pCO<sub>2</sub> in order to assess the threshold level of the appearance of apnoea which is a clinical criterion of great significance in the ascertainment of brain death – a level that should never be lower than 60 mm Flg. In adults, rheological tests, digital angiography, angioscintigraphy with Tc99, Doppler, tomography with Xe133 and HM-Pao, and tomography with the emission of positrons, are held to be of value. If they are positive they demonstrate a blocking of the blood flow because of an increase in endocrinal pressure. In children the results should be assessed taking into account that blockage is less frequent because the cranium is more expandable. In addition, it should be remembered that the minimum threshold of cerebral flow is lower. Flows of 7-10 ml/minute/100gr.

are compatible with survival, and these are lower than those registered, for example, by tests with angioscintigraphy with Tc99 whose threshold of sensitivity is 15ml./minute/100gr. Panangiography and tomography with the emission of positrons have a great diagnostic value. They document with certainty the compromising of the blood flow and of the metabolic activities of the brain, and thus in a more certain way the destruction of the brain. But there are more difficulties in carrying out these tests on children in intensive care units, especially if one is dealing with small neonates, and because of the availability of the relevant equipment. Angioscintigraphy and Doppler are more easily carried out but they explore in a reliable way only the anterior and carotid blood flow. However a positive angioscintigraphic finding and a registering by the Doppler of a reduction and then disappearance of the diastolic component of the blood flow, of subsequent evidence of a retrograde flow, and of a reduction and finally the disappearance of the systolic component, are very significant signs of a severe alteration in the circulation. It is important to observe that these tests can have falsely negative findings but never false positive findings.

To summarise: the clinical and instrumental ascertainment of brain death in children is more difficult than is the case in adults and should be carried out with prudence, above all in infants beneath the age of 2, with great prudence during the first year of age, and with the utmost prudence in neonates, especially pre-term neonates of 34 or less weeks of pregnancy age. The age of 5 is always seen as the age limit for the complete extension of the criteria that are adopted with adults.

To increase the number of potential organ donors the use of paediatricians in intensive care units and emergency services in general to ascertain brain death, before the heart stops, is recommended. But there are justifiable doubts about the real efficacy of this. It is, however, to be hoped that in Italy a task force will be created that will promote among the workers in this field the spread of consolidated and shared criteria of ascertainment.

### **Criteria for the Ascertainment of Brain Death of the *Ad Hoc* Committee on Brain Damage**

A). Brain death has occurred when the functions of the brain and the brain stem are irreversibly absent.

1). The absence of cerebral functions is clinically manifested as the absence of a capacity for perception and responsiveness, that is to say no somatic response or response of the autonomous nervous system to any external stimulus that passes through the brain stem.

2) The absence of the functions of the brain stem is clinically demonstrated when photomotor, cornea, oculocephalic, oculovestibular, oropharyngeal and respiratory reflexes are irreversibly absent.

3) Especially in the case of children, the activity of the peripheral nervous system, including the spinal reflexes, can persist after brain death.

4) Irreversibility is ascertained:

a) if the cause of death has been identified and it is sufficient to determine the loss of cerebral functions:

b) if the possibility of revival is excluded by observation for an appropriate period of time;

c) if, when the cause of death cannot be identified, the reversible conditions are excluded through specific laboratory tests such as:

— blood and urine analyses to identify clinically significant concentrations of toxic substances that produce coma, such as sedatives, hypnotics and anaesthetic agents;

— measurement of the central corporeal temperature which must be greater than 32°C; measurement of the peripheral neuromuscular function (to exclude neuromuscular blockage);

d) as regards the duration of the period of observation, when the cause has been identified

B) Confirmation tests can be useful for the ascertainment, accelerating it as well, of the irreversibility of death. However, if the cause and the irreversibility have both already been established, and if the clinical examination demonstrates unmistakable signs, confirmation tests are not necessary. The tests that can be useful, when they are recommended, are:

1) Angiography with Tc-99m. In the case of brain death this demonstrates:

- a) bilateral absence of the arterial phase in the territory of the middle and anterior brain;
- b) absence of visualisation of the sagittal sinus in the venous stage;
- c) absence of the arterial peak in cerebral activity-time curves;
- d) perfusion of the soli extra-cerebral tissues.

2) EEG. The tracing must be 'flat' and when there is no reaction it should be repeated 24 hours later when:

a) the first isoelectric EEG was obtained in conditions of intoxication by drugs and/or hypothermia (in this case at the time of the second EEG the concentrations of drugs must be below toxic levels and the temperature of the body must be above 36C);

b) despite a persistent positive clinical objectivity of brain death, the first EEG is not isoelectric but demonstrates a basic low voltage basic activity or a burst-suppression pattern which can indicate agonic phenomena;

e) the first EEG is isoelectric but at the moment of the clinical examination the patient displays a persistence of reflexes of the brain stem or spinal reflexes;

d) the interpretation of the first EEG is controversial because of the presence of artefacts.

In the absence of these conditions a repetition of the EEG is neither necessary nor advisable.

3) (Acoustic) potentials evoked by the brain stem. The tracing must demonstrate the presence of the first wave, which corresponds to the cochlear nerve, with the absence of subsequent waves. If the first wave is also absent, one cannot exclude peripheral damage and thus the examination should be supported by somatosensory evoked potentials.

The carrying out of the evoked potentials of the brain stem is recommended when:

a) the interpretation of the EEG is controversial;

b) the EEG is not completely isoelectric;

c) the EEG is isoelectric but there is intoxication by substances which depress the central nervous system or hypothermia.

### **Criteria for the Ascertainment of Brian Death of the Task Force for the Determination of Brain Death in Children**

A) Clinical history: identify the cause of the coma in order to exclude treatable or reversible conditions.

B) Objective examination:

1) coma and apnoea;

2) the absence of the function of the brain stem:

a) pupils in media mydriasis or completely dilated;

b) the absence of oculocephalic reflexes ('doll's eyes') and ocular movements induced by heat;

c) the absence of movements of the musculature (of the face and the oropharynx) controlled by the bulb;

- d) the absence of reflex of the cornea, of deglutition, of coughing, of sucking and of fixation;
- e) the absence of respiratory activity *evocable* by a standard apnoea test;
- 3) exclusion of hypothermia or hypotension;
- 4) muscular flaccidity and the absence of spontaneous or induced movements, excluding mediated (by centres) activity at a spinal level;
- 5) stability of neurological objectivity for the whole of the period of observation.

C) The period of observation varies with age:

- from 7 days to 2 months: two clinical examinations and EEG at a distance of 48 hours;
- from 2 months to 1 year: two clinical examinations and EEG at a distance of 24 hours and/or a clinical examination and an isoelectric initial EEG together with an angioscintigraph which demonstrates an absence of cerebral blood flow;
- above the age of one: two clinical examinations at a distance of 12-24 hours (the EEG and the angioscintigraph are optional).

### **Criteria for the Assessment of Brain Death of the President's Commission of the USA**

A) Ending of all cerebral functions, including:

- a) clinically assessed brain functions;
- b) functions of the brain stem, based upon apnoea and the absence of reflexes of the brain stem;

B) Irreversibility of this ending of all cerebral functions is demonstrated by all the following conditions:

- a) the cause of coma has been established and is sufficient to consolidate the loss of the functions of the brain;
- b) various conditions that can mimic brain death have been excluded;
- c) the ending of the functions of the whole of the brain persist for an appropriate period of observation;
  - of 6 hours, if for the confirmation an EEG or a blood flow test is used;
  - of 24 hours, if for the confirmation an EEG or a blood flow test is not used.

### **2.2. The Availability of Organs**

The demand for organs for transplants is considered to be higher than their real availability.

In the USA it has been calculated with reference to deaths between the ages of 4 months and 19 years in 1984 that the potential heart donors were 280 in number, the potential kidney donors were 480 in number and the potential liver donors were 610 in number. Real donors were of the order of 9%-30%/x. In Italy was observed that in the period November 1985-August 1991, of 74 children on the waiting list for a heart transplant, 32 received transplants and 38 died before being able to have the operation. A recent study in the USA demonstrates that 17.1% of children between the ages of 1 and 16 who died in a university hospital over the space of 13 months had organs removed for the purposes of transplantation. The authors of this study believe that a high percentage of the 20,000 people of this age band who die each year could be used for donation and that if only a half of these cases were used there would be an availability of organs greater than the need: 6 times greater for kidney transplants, 7 times for liver transplants and 36 times for heart

transplants. It has already been observed that in Italy the ratio between children receiving transplants and children in dialysis awaiting a transplant is lower than in other European countries, higher only than Greece and Portugal.

The problem is therefore the ability to obtain organs, the promotion of donation, and the organisation of services and of a 'culture of donation' amongst health-care workers and the general public.

Medical doctors who work in paediatric intensive care units should certainly be sensitised to the ascertainment of 'brain death'. A careful and constant commitment to this ascertainment is first of all a diagnostic requirement. It would also allow the use of equipment and machinery for other patients who need them.

But the problem of the promotion of donation and the spread of a 'culture of donation' is complex and cannot be solved with overly simple proposals which could become ineffective. Certainly, prudence should not be forgotten in the use of the criteria of the ascertainment of brain death under a specific age; the uncertainties of staff for reasons of different kinds, and not only technical ones, in deciding on the interruption of therapy; and the response of parents, with their families, to the request for the removal of organs. As regards the use of organs of neonates who die because of perinatal causes, it should be remembered that with the advances in forms of therapy over recent years mortality rates have greatly diminished in the bands of the lowest gestational age and the lowest birth weight. Today, up to 80% of neonates with a weight lower than 1.5kg survive. In recent years the trend has been registered of a reduction of mortality rates in children because of road accidents and this may cause a reduction in the availability of organs for transplantation.

Given this lack of donors, people think of the promotion of transplantation from living donors and the use of the cadavers of anencephalic infants, xenotransplantation and xenotransplantation are also posited.

Transplantation from a living person, apart from that involving kidneys, a dual organ, is considered a new prospect in hepatology. A segment of the liver is transplanted, and the first experiences in Australia, Belgium, Brazil, Japan and the USA are held to be positive. The most numerous set of cases is at the University of Kyoto: 17 to 18 children who have received transplants of a section of the liver of one of their parents are alive after 1-13 months, with a survival rate calculated at 87.7% at 6 months.

In Europe, the average incidence of anencephaly, apart from Ireland where it is higher, is 1 case for every 1,000 births. An Italian assessment indicates this incidence to be 1 case in every 3,900 births. We do not have evidence on the effects of pulse-echo diagnosis *in utero* with a consequent voluntary interruption of pregnancy. It is known that about 40% of anencephalic infants are born alive and that those born alive on average die within 3 weeks. Different forms of anencephaly exist but amongst teratologists there is not complete agreement on their classification. The most common form is the so-termed mesocranial form, with the absence of cranial bones, a structure of the brain stem present, and an absence of the endbrain. Given the working of the brain stem, numerous activities are present, from sucking to swallowing, from facial reactions to taste stimuli, to crying, and to the withdrawal of limbs in response to painful stimuli. Apart from the cranial anomaly, the child appears normal. The parents are not always fully aware of the gravity of the conditions until they witness the first clinical manifestations: difficulties in sucking, apnoeas, and crises of brachycardia. They also try to form a relationship with their child; the rejection of physical appearance appears to be less frequent than in with other malformations.

It is a current opinion that a congenital anencephalic infant is like an adult whose endbrain has been destroyed. But such may not be the case. The functional relationships between the

existing structures could be different in an individual who has developed without an endbrain compared to an individual whose endbrain has been destroyed. Some degree of sensorial perception cannot be excluded. The infant certainly reacts to stimuli. Certainly, one cannot speak about a complete relational life. The forms of treatment are limited to protection against cold and alimentation. If one waits for inescapable death to occur spontaneously, the organs are compromised and cannot be used for the purposes of transplantation. Intensive therapy is thus proposed, with mechanical ventilation, to assure, together with nutrition, a supply of oxygen to the organs. The greatest experience with this programme of keeping anencephalic infants alive has been at the University of Loma Linda, whose protocol seems, however, to have been abandoned. On the question of the ascertainment of death in anencephalic infants, a question that is closely connected with the question of the possibility of using their organs, a Medical Task Force on Anencephaly, made up of representatives of all the most prestigious scientific academies and societies in the USA, drew up a special document. Given the intrinsic anatomical conditions of an anencephalic infant, both an EEG and ascertainment of the blood flow in the brain are held to be superfluous. With respect to testing the working of the brain stem, it is observed that it is not always possible to explore this given that anomalies of the cranial nerves are often associated with this condition and thus it is not possible to evoke reflexes that indicate its activity. The ascertainment of the death of the brain stem can, therefore, be carried out only with the disappearance of reflexes that have been previously evoked. If these have never been demonstrated, their absence *ab initio* does not necessarily indicate the death of the brain stem. There thus remains the concrete difficulty of defining the death of an anencephalic infant above all when he or she is subjected to intensive therapy and to mechanical ventilation. And a great deal of perplexity remains as regards what these forms of treatment mean for the child, prior to the perplexity that is felt as regards the possibility of conserving his or her organs. There is, and this cannot be denied, the risk that in the case of a child in such grave conditions who is destined irremediably to die, one will end up – pushed forwards by an impetus to engage in transplants – by accepting an exaggerated treatment that is to be deprecated.

Heart surgeons above all think of xenotransplantation and xenotransplantation. The current orientation is use the hearts of baboons as a pump for temporary ventricular assistance and as a bridge-transplant while waiting for the transplantation of a human heart in the more remote prospect that this can be a permanent replacement. For the moment this operation is confined to small children aged under 3 months. It is said that the bridge-transplant does not compromise the success of a definitive transplant. The possibility should however be borne in mind of the production of cross-reacting anti-bodies in the transplantation against the heart of the primate and then, provoking a rejection, against the human heart. We are therefore in a completely experimental stage, with many reflections on the limits that can be bestowed on experimentation on humans.

To summarise: the question of increasing the availability of organs to such an extent as to meet the needs of transplantology, which is developing, involves many factors and is open to many reflections, as is the case with very many questions in medicine, but with human and ethical implications of special relevance. This is also the question of ‘induced needs’ which can be induced by scientific and technical progress itself, the interplay of the comparison between the ‘needs’ of institutions and those who work in them with a variety of scientific and professional motivations and the ‘requests’ of people which are the expressions of complex needs – it is difficult to control this interplay given the number of factors which influence the working of the health-care system.

### 2.3. Legal Aspects

In relation to these, the specific legislation on transplantation and that on the power of parents in the decisions regarding health-care treatment in general should be mentioned.

The legislation in force on transplants governs transplants both from cadavers and from living humans.

As regards transplants from cadavers, it should be borne in mind that whereas art 11. of the Law of 3 April 1957, n. 235, lays down that ‘the removal of parts of cadavers is allowed for the purposes of therapeutic transplants if the individual has authorised it’, by subsequent laws the possibility has been conceded of removing parts from a cadaver where ‘the dead person has not laid down the opposite when in life, in an unequivocal way and in writing’ (see art. 1 Law of 2 April 1968, n. 519 and art. 6 the Law of 2 December 1975, n. 644).

Particular questions arise, however, as regards the legitimacy attributed to a specific category of individuals – connected to the dead person by a kinship tie – of opposing a removal in the absence of provisions by the dead person on the subject. And it should be observed how at a parliamentary level we are still waiting for a final approval of the law that limits the power of opposition of relatives, and that Law n. 301/93 on cornea transplants displays in this sense a step backwards.

Within the sphere of existing legislation, there emerges however a clear indication regarding the favourable view that the legislature has of the removal of organs from cadavers for therapeutic purposes.

As regards the interruption of treatment at the moment of the ascertainment of brain death, the legislature laid down the conditions for this in arts. 3, 4, 5 of the Law of 2 December 1957, n. 644 and in arts. 2 and 9 of the DPR of 16 June 1977, n. 409 and recently in the Law of 29 December 1993, n. 578.

In none of these laws is mention made of the hypothesis of the transplanting of organs removed from minors or of the transplanting of organs to minors.

The regulation of transplants from living people finds its fundamental legislative reference in art. 5 c.c. which prohibits acts in the using of one’s body that lead to a permanent reduction in physical integrity (or which are anyway against the law, public order or public decency). The limitations imposed by this article appeared to the legislature to be too rigid and not in line with the concrete requirements for the defence of the primary interests of the individual. As a result, pushed forward by pressing requests that came above all from those who worked in the medical sector, by the Law of 26 July 1967, n. 458 (‘Kidney Transplants between Living People’) it regulated the hypothesis of transplants from living people. The subsequent art. 4 of Law 458/1967 laid down that ‘a kidney transplant legitimately removed and destined for a specific patient cannot take place without the consent of that patient or in the absence of a state of need’. Whereas the subsequent art. 5 established as a condition that the donor of the kidney had to be of adult age.

When a transplant involves a minor the question arises of identifying the individuals who are legitimised to express consent. Here one should distinguish between a case where a minor is the recipient of the donation, and thus the individual receiving a transplant, and a case where a minor has the role of being a (potential) donor. In the first case it is common opinion that the transplant should be considered on a par with all other forms of health-care treatment and thus the rules relative to the power of parents should apply. The duty to instruct, educate and maintain one’s children (art. 30, e. 1 Const.) should be performed by parents ‘taking into account the capacities, the natural inclination and the aspiration of their children’ (art. 147 c.c.). If the parents are married, this power should be exercised by ‘common agreement’ (art. 316 c.c.). This rule on agreement, introduced by the reform of 1975 which actuated the principle of parity between the spouses, raises the legal question of the resolution of conflicts that may arise over decisions regarding children. If the contrast concerns questions of ‘particular importance’, recourse to a Tribunal for Minors is allowed. This tribunal, ‘after hearing the parents and the child, if over the age of fourteen, suggests

the measures that it believes most useful in the interests of the child and the family unit'. If this so to speak 'reconciling' intervention does not go well and the contrast remains, powers of decision are attributed to the judge. However, these decisions do not concern the merits of the question but rather the choice of the parent who must take the decision, inasmuch as he or she is held 'in the individual case more suited to take care of the interests of the child' (art. 316 u.c. c.c.). Only when there exists the danger of an impending prejudice for the child (as in the case of an emergency surgical operation), is there recognised the prevalence of wishes of the father, given that he is able to 'adopt urgent measures and ones that cannot be postponed' (art. 316, e. 4). These rules are also applied in the case of parents who have adopted and of unmarried parents as long as they live together and have both recognised the child (art. 317 bis).

Naturally, the rule of agreement, and the intervention of the judge when there is disagreement, cannot be applied when the parents do not live together. For married parents it is envisaged that 'in the case of distance, incapacity, or another impediment of one of the parents', this power is exercised exclusively by the other parent (art. 317). When, instead, the absence of living together is the result of personal separation, divorce or the annulment of the marriage, the power is in the hands of the parent who is entrusted with the custody of the child, with the other parent having the power of surveillance over the exercise of this power and of taking, in agreement with the other parent, 'decisions of greater interest to the children' (art. 155 c.c.).

Partially different rules apply to natural parents who do not live together. In this case the power is in the hands of the parent who has recognised the child, or (in the case of recognition by both parents) to the parent with whom the child lives, with the other parent retaining, however, a 'power of surveillance' over the instruction, the upbringing and the maintenance of the child (art. 317 bis).

According to the rules cited above, it is thus the task of the parents, and more in general of those who exercise power, to give or deny consent to the transplant. Always according to the general rules (art. 333 c.c.), the judge has powers of control every time that the behaviour of the parents (or the decisions taken by them) are 'prejudicial' to the child. As regards transplants, the question presents itself of whether recourse to the judge in line with art. 333 c.c. is allowable and how this 'prejudice' which could be caused to the child by a rejection expressed by the parents to the transplant should be assessed if the question arises. In other cases of a lack of consent by parents to medical treatment, recourse to a judge has been held to be admissible. However a transplant raises special questions and issues because of the risks to which the patient is exposed, the probability of success, and the expected quality of life. The probabilities of success, life expectations, vary from one type of transplant to another; they depend on the age of the child and his or her physical conditions: these are assessments that have to take into account the quality of life after the transplant and not only the probabilities of survival. For that matter, the notion of 'prejudice' in art. 333 c.c. constitutes a 'general clause', that is to say an elastic and flexible principle that should be applied taking into account the special features of the concrete case, which the judge can assess in a suitable way with the help of a technical consultant.

Nor should one neglect the complexity of the questions that the judge has to address when the child, a mature adolescent, is able to formulate his or her choice.

In this case, indeed, the minor as well has to give his or her assent. The ethical option in favour of a free and informed consent expressed personally by the adolescent has already been formulated by this Committee in the document on consent to medical treatment and will be further discussed in the final part of this document.

When, following the communication of information suited to his or her sensitivity and culture, and respectful of his or her overall personality, an adolescent has expressed his or her wish, the question arises of establishing its juridical value. Is the consent given by a minor valid or invalid? This question brings into play the question of the relationship between not being of age and incapacity, the admissibility and the limits of an 'anticipated capacity of the minor' which already finds partial recognition in the Civil Code and in special laws but whose meaning, breadth and limits are all still to be explored.

With regard to transplants, the question becomes particularly delicate when there is disagreement between parents and their child. Dissent, indeed, opens the question, which today has not been expressly resolved by law, of the legal instruments by which to overcome it and reach a decision that guarantees, from every point of view, the achievement of the best interests of the child.

Another order of questions is raised when one considers the minor not in the form of a recipient of an organ but as a potential donor. Here one should further distinguish the case of a transplant from a cadaver from the case of a transplant from a living person.

In the case of a transplant from a cadaver it is problematic to establish what value should be attributed to a wish that may have been expressed by a minor when alive, whether favourable or contrary to a donation. Today the law reserves to relatives the power of opposing the removal of an organ, even when the donor when alive has expressed a different wish. In the case of a donor who is a minor, the power of opposition which parents are recognised as possessing does not constitute power over their children, but is, rather, an expression of their own prerogative attributed to them by the value of family feelings.

The autonomy of the minor is thereby sacrificed: value should instead be given to the decision of the child, a mature adolescent, expressed as well through membership of voluntary work associations. However, the legislature even recently has not demonstrated itself to be sensitive to these subjects as is demonstrated by the recent Law on cornea transplants (n. 301/1993) where the wish of the minor is not taken into consideration.

As regards a transplant from a living person, the donation of a kidney is expressly forbidden as regards minors, whereas the donation of cells or tissues – within the limits indicated by Law n. 107/90 – is allowed where there is the prior consent of those who exercise the power of the child. On this front as well existing law does not seem to consider in an adequate way the question of the relevance of the wish of the minor, a mature adolescent, which may be in contrast with that of his or her parents; nor that of a possible abuse by the parents of their own power to consent to a donation.

Hence the need for further reflection which in the field of transplants as well should achieve the right balance between the prerogatives of the parents and the autonomous decision-making capacities of a child in his or her personal choices.

## **2.4. The Special Features of Paediatric Transplantology**

The special features of paediatric transplantology do not relate only to the organisational aspects of services; the ascertainment of brain death, the availability of organs; donation involving anencephalic infants; the search for other kinds of implants and transplants; and the laws that govern its practice. Paediatric transplantology, which is also becoming neonatological, a therapy that is proposed to the parents of infants who are born with severe anomalies and with anomalies that are at times incompatible with life, raises questions that transcend the medical, scientific, technical and legal domains. They are questions that affect the complexity of the relationships between the world of adults and the world of childhood and the responsibility that scientists and medical doctors adopt in relation to children and these relationships when spreading the knowledge about, and the use of, technologies which are increasing in number. Bioethics committees certainly also have the task of having a 'pedagogic' role so as to make the meaning of the scientific and technological advances of medicine enter the culture of the community, in order, as well, to protect, as far as necessary, man from increasing technologies and examples of the technical. This is a role that has a special relevance in the case of children, adolescents and their families. The question of paediatric transplantology also emerges, especially in the case of neonatological transplantology, within the context of the contemporary culture of childhood, from the anthropological-cultural reality of the welcoming and rejection of infants.

For centuries little children, and above all neonates, were perceived as provisional beings, they did not find a ready welcome and a welcome that was affectively full in human society. This

was a reality correlated with the high levels of infant mortality, and persisted in areas of poverty where such mortality rates were even higher. There was a multiplicity of social and individual factors that influenced the welcoming and the rejection of infants, which in the case of rejection brought about their abandonment, various forms of abuse, and violence. With the improvement in socio-economic and cultural conditions, awareness of the autonomous reality of childhood was consolidated, responsibility towards it was strengthened, the principle of the rights of children from birth was upheld in international declarations, and a new culture of childhood matured. It was in this context, and also remembering the 'pedagogic' importance, above all for parents, of the scientific proof of the capacity of children to establish early relations with the environment – and today the observations that lead people to believe that already in intrauterine life there are incipient elements of a mental life – that the idea of the welcoming of children found new support. In this new vision of children which entered the world should also be located the culture of paediatric transplants which are even becoming neonatological transplants.

The perception that a child is a provisional individual, which everywhere and completely has not yet disappeared, can become accentuated when a child is born abnormal, malformed, and severely compromised at the level of his or her vital functions, and in this way rejection can also be accentuated. The propensity to recognise as a human person a being with abnormal physical features, as in the case of a neonate with malformations or who is very premature, is different. This different propensity can be seen in the infant's parents themselves and also in health-care workers who have the task of having the responsibility of establishing the proportionality of treatment and of whether to engage or not in therapies that are technically and scientifically advanced and perhaps still at the experimental stage. It is the highest responsibility of these workers to find a suitable way of informing the parents, of involving them in decisions, and in obtaining their consent with an understanding of their experiences, their feelings, their ambivalences and their contradictory stances, the ordeal that they feel over scruples regarding a difficult acceptance if not an impulse to rejection, to abandonment. With an adequate culture and with attitudes and forms of behaviour marked by a special sensitivity, health-care workers must know how to involve as soon as this is possible the children as well, and always adolescents, above all those most advanced in years.

Health-care workers possess the clinical and statistical data for a prediction based on probability of the outcome of the therapy, for a medical prognosis, but for them the prediction of the quality of life, in the family and of the family, the human prognosis on which they also have a duty to reflect, must be something else.

### 3. ETHICAL REFLECTIONS

The 'new type of cadaver' produced by advances in intensive therapy, the removal from it of organs for transplants, the donation of an organ, or of a piece of an organ or of a tissue, of a healthy living person to another person who is ineluctably destined to die, constitute a reality that one can never know enough about as regards how it is experienced in the world of medicine and above all outside that world in the culture of the community. This new reality generates very many reflections and it is an ethical duty to multiply them. They may be referred to two concepts that are emerging today from the development of medical culture in general and which are acquiring a special significance in transplantology: that of methodology and technologies and that of the cultural transmission of technologies.

Medical methodology is based on the multiple forms of knowledge of the various disciplines that converge in the field of medicine: scientific, epidemiological and clinical knowledge and the knowledge of the organisation of services, of monitoring and of assessment, of communication, and of the medical humanities. As is suggested in medical teaching, it is advisable not to confuse this with the knowledge of methods, when by this is meant not only instrumental techniques. Medical technologies, in the meaning that is attributed to them by the World Health Organisation, involve a set of necessary procedures, which are not only instrumental techniques: that is to say various types of 'care' (because they provide care), approaches to the needs of patients which are not only biological or organicist. And it is of fundamental importance to define their appropriateness ('appropriate technologies').

A first reflection is on the transplant centres, on the capacities and skills that should characterise them, which in the case of paediatric centres are special. These centres are a reality of the health-care system and their capacities and skills must correspond to precise recommendations:

- they should function together closely with paediatric structures;
- they should form a part of a multidisciplinary departmental system;
- the activity connected with transplants of a centre should not be limited to a single organ;
- as they perform a number of different transplants they should be distributed correctly within the national territory;
- capacity and skill at the level of surgery should be matched by a corresponding capacity and skill at the level of specialist nursing;
- the greatest attention to the psychological aspects of care and treatment should be assured;
- a complete multidisciplinary follow-up should be organised;
- from this follow-up should be obtained and pointed out the causes of failure as well as the conditions of health of the children involved at the physical, psychological and relational levels;
- research activity should be assured to optimise the diagnostic and curative interventions.

One can add the recommendation for a national centre of reference to which should be assigned the task of supervising the obtaining and the distribution of organs, the constant updating of epidemiological data connected with requests for transplants, the availability of organs and the duration of waiting for a transplant, and informing the public on the results that are being obtained.

As regards the reflection whose subject is transplantology in children, of essential importance is taking into account the idea that individuals – including children and above all adolescents – have of organ transplants, which is certainly not like the idea that is had about other operations, even though they are technically more difficult. One may think that it is the symbolic meaning of a transplant which determines this, the giving and receiving of a piece of the body of another person, a person who has just died or who is alive granting it, and that this symbolic

meaning is special when it is a child, in likelihood above all a young child, a neonate, who receives the transplant. The success of the operation can be experienced as healing, in the hope that it is such, by the patients and their family relatives. It is not healing for those who carry out transplants who prescribe treatment and subject patients to controls. They define as good the quality of life of the person who has received a transplant. But defining the quality of life of a person in his or her existential context is always difficult. The child appears, and may feel physically, normal. But his or her parents, the child himself or herself if of sufficient age, above all else an adolescent, know that the risk of a rejection is there, that to avoid this continuous therapies are needs, and that their duration cannot be specified. The parents learn about the survival data and the children can also learn about them; adolescents can do so more easily. They, and first of all the parents, know that a long-term prognosis is not definable and they can feel that the future is threatening and live it with anxiety. The culture that is lived in the transplant centres must be up to the special complexity of the needs of the patients and their families, and in the paediatric centres this must be a paediatric culture which should also be up to a suitable level in the broadest sense and not based on organicism alone.

If, as seems advisable, one wants to think that methodology is not synonymous with methods, it should be recognised that at times, pushed forward by the impetus of methods and above all by the successes of instrumental techniques, reflection on methodology, which is scientific and philosophical in character, is not suitably dwelt upon. This thought, which in situations charged with complex experiences, which is what a situation involving organ transplants is, should be enriched with special feelings of comprehension and participation. An organ transplant may be defined as a methodology that has the task of saving a life that is irremediably threatened, where given the current state of knowledge it is not known whether it has been definitively saved or only for a time whose possible length is still unknown; which uses surgery and requires other methodologies and methods for the completeness of care and treatment; and which uses techniques that have been consolidated through experience with a search for their optimisation. Ethical reflection, for transplants as for every frontier investigation of man, is on agreement on what must be done and on what must not be allowed, before being on what one could do, on what one would like to do, and on what it would be useful to progress to do. On the following points agreement can be seen to be incontestable:

- wanting to contribute to scientific-technical progress should not distract from the attention due to the experiences of each individual person who has a transplant;
- the proposal of this therapy should not be disassociated from a careful consideration, case by case and situation by situation, of the culture that people express in relation to it, and to death as well;
- the decision to engage in the removal of an organ must take place after an ascertainment of ‘brain death’ agreed upon by a number of people;
- the promotion of donation should not ignore the level of assimilation of the culture of transplantation by individuals:

The success of kidney, liver and heart transplants in children certainly meets the requirements of the ethics of methods. In optimal situations of the culture, of the structuring and the working of centres, one may believe that it meets the requirements of the ethics of methodology.

An ethically-based methodological role requires, always with a recognition of the absolute value of the life of each person, which is priceless, an assessment of the cost/benefit ratio in addition to the risk/benefit ratio. This is the question of the correct allocation of resources in the ‘overall system of health care’. There are very many conditions that threaten the lives of people and all of them require adequate resources. And there are also conditions and situations in which it is a social duty to promote health and prevent illnesses and where people need effective care and treatment and efficient services. The use and the distribution of available resources takes into account the entire gamut of needs. The health of a person, too, is priceless.

Reflection on methodology is certainly and greatly also reflection on the quality of the proposal of a transplant. In addition to being interpretable in its communicable technical aspects, the proposal should transmit the meaning of the event, of the adventure that the medical doctors, the patients and their family relatives live together. The patients, the sick and their family relatives, live with inevitable torment the duty to give an answer; they do not find in the communicated statistical data elements that help them to bear the existential moment that they are going through; they would like the answers to the questions they address to the medical doctor to be precise and definitive: a calculation of likelihood is not in line with the feelings that they experience. The communication of the prognosis in a situation in which one can speak about the duration of survival solely in terms of a few years, and about the future in terms of trust in scientific progress, is an undertaking which in human terms is very arduous. In making the proposal the thoughts of the medical doctor are about the persistent uncertainty of a chronic rejection, the duration of the immunosuppressive therapy and its secondary effects. Confidence in the benefits of the operation is determined by very many factors, which vary from patient to patient and from family to family. They are different if the patient is a child. For an adult who is fated to die, the importance of managing to obtain a prolongation of life, even though perhaps not long, can be great. For a child, in addition to his or her life, which one would want to be happy and long, there come into play the meaning and awareness that he or she has of death. It is known that a child experiences this meaning early on and that in his or her development he or she acquires this awareness – certainly first as mourning than as death – always less dramatically than an adult. The feelings of parents have roots in the relationship which, beginning with his or her birth, they have had with their child, with the person that he or she is, with his or her own mental capacities, which now we know to be very early, prior even to being born. They are feelings of attachment, but a new born person is still much to be discovered by the parents themselves. The symbolic meaning of a transplant in a neonate cannot but be different from that in a grown child. It has been said that the perception that a little child, above all a neonate, is a provisional being belongs to human history. With the great diminution in infant and neonatal mortality and the spread of the culture of childhood this perception has grown weaker. When a child is born the affective bond is not always well consolidated in the parents, it can still be labile, but with varying degrees of rapidity it becomes stronger with the deepening of this relationship. It is the process of ‘attachment’ in the interaction with the infant that makes it a stable relationship. The labile character of the bond is undoubtedly greater if the infant is born abnormal; it is of the highest level if the abnormality is incompatible with survival. The parents experience mourning for the ghostly, imagined, hoped for, and awaited, baby. Debate takes place between complex, opposing and contradictory feelings. Parents feel feelings of guilt about what they experience as a procreative failure; react with anger to the event; reject it; do not accept the reality of their baby and are beset by scruples. They can also tend to be led to give up. This is a suffering in the stage of extension – planned to varying degrees – of the life cycle of the family; it throws into imbalance the relational system of the family. The stage of extension has always had a component of crisis but in such a situation the crisis is deep, it is not always borne. With the passing of time it is not always overcome. The system does not always manage to find an equilibrium. In the feelings of the medical doctor who makes the proposal there is also the problem of creating hopes and causing disappointments. The hope of those who accept the proposal tends to go beyond the statistical reality that authorises the medical doctor to make it. The medical doctor has the obligation to control the wish to nourish hope. Disappointment arises from a failure, which is given as possible when the proposal is accepted, but it also arises from the prolonged wait for the operation, from not being able to have it because of a lack of organs.

The consent that the medical doctor requests with information also belongs to reflection on methodology. It must be asked for as soon as possible from the children as well, together with the parents; in general, one may believe, near the age of seven and always when the child becomes an adolescent, and with all the understanding, sensitivity and prudence that are needed. Certainly, precise suggestions do not exist for speaking about consent with children. However, Piagetan

concepts on their cognitive development can also be useful, a subject referred to in another document of the National Bioethics Committee. Consent is obtained with information; there are different ways of providing it; and the wish of the person carrying out the transplant to obtain consent is human. The information that is given to a child is more on the care aspects of the operation than on its technical aspects. The technical aspects, if requested, are presented only to adolescents; generally, one may believe, not before the age of 14. One can never place enough emphasis on the idea of informed consent as a basic principle of medicine, as a way of thinking about the relationship between the medical doctor, his or her patients and their family relatives, and not only in order to carry out specific actions. Informed consent is not certain rule, as perhaps some would have it, one of the very much wanted guidelines for behaviour, a legal reassurance, a sort of protocol by which to reduce one's responsibility, to feel authorised to engage in audacious experiments. It raises questions that are never the same. Consent is to be thought about with enthusiasm about scientific research, technologies and treatment, with the impetus of scientific and technical competitiveness and the desire for prestige, but it should also be thought about as a taking of responsibility for the set of problems of people, as participation in their expectations, hopes, and suffering caused by dashed hopes. It is thought with very many consequences, all of which are human, but one which requires a great deal of discipline, criticism, logic, and many feelings.

The concept of the cultural transmission of technologies is epistemological and cultural-anthropological in character; it certainly belongs to bioethical reflection on the advances of medical science; and it deserves a great deal of attention when speaking about transplantology, and even more attention when speaking about paediatric transplantology.

Technology is not only, as is often thought, that set of instruments and machines which is very much growing. Distinguishing technology from techniques, from instruments and machines, is like distinguishing reflective, qualitative thought from calculating, quantitative thought. It is always useful for those who work in medicine and in transplantology in particular to remember that quantitative thought is the thought of science, but it is not the only thought, and to remember that if such thought prevails excessively over reflective, qualitative thought then science becomes the technical. The tendency is certainly not rare to identify the progress of science with technical progress, to speak separately about science and culture, almost as if science was not an expression of human culture, as if scientific knowledge were detached from and not enriched by other forms of knowledge. Perhaps this is a tendency that expresses an increase in quantitative thought to the detriment of being reflective, an increase in computing with precision to the detriment of asking oneself questions with necessary uncertainties, a loss of pleasure in being reflective. The prevailing of quantitative, calculating thought over qualitative, reflective thought in the working of the system of health care can even be dangerous. The knowledge of different disciplines are flowing into this system and they expand the cultural horizons of medicine. Specialisations and super-specialisations are indispensable but this should not mean blindness in relation to the needs created by this expansion which, seen from the perspective of the greatest good for people, for patients, and for the whole system, should be brought back to the bioethical principle of being beneficial. More than was the case during the epoch when, within the framework of modern scientific traditions, great emphasis was placed on the distinction between the so-called soft sciences and the so-called hard sciences, and the view was that medicine was decidedly a hard science. Methodological pluralism is thus growing in medicine, and with this emerge forms of incomprehension, if not conflicts, about the very systems of values of medicine. The disciplines that flow into the field of treatment are very many in number: the scientific, epidemiological and clinical disciplines and the disciplines of the most advanced and sophisticated technologies and techniques, of planning, of management and of monitoring, of taking decisions and of communication. Finding a synthesis, balancing the hard and the soft aspects of medical science to advantage the overall character of the needs of man for health and wellbeing, is an ethical commitment. Man is the object of knowledge, of investigations for scientific progress and for improvement in treatment, but he is also a subject of knowledge, and the criteria of being scientific in exploring man are necessarily more extensive. The quality of the

functioning of the system of research and health care depends upon the sensitivity of those who work for this reality. In this system plans involving surveys, scientific research and treatment are carried out; technologies and techniques are implemented; and predictions and assessments of results are engaged in. The opportunities for predicting and assessing the effects of programmes and results on people's culture are less. There is an epistemology of the foundations of theories, of the methodology of approach, of the implementation of programmes, of the results obtained and their application. And there is an epistemology of the effects that investigation of man produces over and above the results. The results are objectified and the effects are subjective. The effects are the experiences that people and each individual family and person have, with their own culture, of the medical-scientific forms of knowledge that are being disseminated; they are the needs, the expectations and the hopes created by the spread of knowledge. In the system of research and human health care both these epistemologies are required. And when the problems, the requests that cannot be met, and the questions are too many in number, moratoria can also be considered. There are very many approaches employed in acting in the system of health care. They should be thought about together, they are reasons for thinking a number of ways of thinking together and not only that which is strictly scientific-technical in character. The culture of limits, which guides the investigation of man, is born from awareness of the multiplicity of approaches, from a rejection of ways of thinking that are overly linear, which are engaged in one by one, which are not sufficiently sensitive to feedback of various kinds, which do not know how to locate themselves in a communicative circularity. Epistemology of the foundations of theories, of research programmes and treatment, of results and assessment, and epistemology of effects, together, can influence, and it is to be hoped that they will influence, the paradigm itself – of a very linear character – which has been consolidated in medicine. It is evident that all of this has different effects when the object of investigation, of treatment and of research, and the subject of knowledge, is a child or an adolescent.

For many centuries nature was thought to be unchanging; the limits of the natural were accepted and man submitted himself to them. The scene has changed. With the technical, nature is influenced; there is a technological and technical pride and haughtiness. One ends up by impacting on the fundamental values that are in the innermost parts of people, to the point of even committing violence against the culture of life and of death that are co-present in people. Medicine, which is culture for life, for health in life, becomes culture against death at any cost. It proposes struggle against death but it does not always know how to be also help in bearing the natural fear of dying.

Responsibility in the cultural transmission of technologies is also educational responsibility. Knowledge about technologies that are spreading helps the development of awareness about their utility, but one should also consider that the system of values in which people are educated is fundamentally alien to accepting criteria analogous to those that produce technological and scientific knowledge. We do not know when, in what situations, in the depths of the thoughts and feelings of people, is created a place in which this analogy is realisable. We never know sufficiently to what extent the criteria of the welcoming of life and of the acceptance of death produced individually by people manage to be analogous to those of a science which has produced sophisticated techniques to achieve the survival, for example, of an infant that is born weighing 500 grams or with a malformation that is incompatible with life and that could be eliminated by means of a transplant.

Responsibility in the cultural transmission of technologies also concerns the feelings of solidarity and sacrifice. The parents of a child who is born weighing less than 500 grams or who is gravely malformed, and who feel inspired by solidarity with the destiny of being disabled which may await that child, are ready to make any sacrifice to help him or her, but their lives become loaded with sufferings which they not always able to bear well and thus they have to rely on the concrete support of society. Parents who accept the proposal of a transplant for a child who has anomalies that are incompatible with life opt for a life that is 'created' by expressions of the technical but they do not now how it will be in terms of duration and quality and this causes them

suffering. Responsibility in the cultural transmissions of technologies is at its greatest when the donation for a transplant comes from a living person. The adult who donates an organ or a tissue opts for solidarity and sacrifice but one never knows how the experience of the option will turn out and how it could be in the future, and the same may be said of the experience of the person who has received this benefit. Children and adolescents should be involved; it is educational to involve them in events that require solidarity and sacrifice. But for all ages the human diversity of the capacity to maintain over time a spirit of solidarity and sacrifice should be always thought about, and the need that this has for concrete support in the context of social solidarity should also be thought about. It has been observed that after the heroic moment the effects of the act of solidarity and sacrifice can be unpredictable; effects that are psychologically complex, even onerous, possibly negative, on the existence of those who engage in them and those who receive them, and on the very relationship that is formed by living together within the family. Society must thus feel committed to supporting these difficult and involving forms of solidarity.

Ethical reflections, when life, death and the technologies produced by man to influence them are involved, never finish Bioethics draws up principles and proposes modalities for their application, and it is a stimulus to being reflective and to analysing the questions involved. Transplantology is one of the most significant features of the scientific and technical progress of medicine and this, given the development that we may think awaits us, call us more than ever before to the obligation not to set limits to reflections.

## BIBLIOGRAPHICAL NOTES

Alberti D., Palchetti D., Bonetti F. *et al.*, 'Sorveglianza a medio e lungo termine del bambino sottoposto a trapianto epatico', *Atti I Convegno Internazionale su «Le epatopatie: dalla prevenzione al trapianto»*, Brescia, 30 September- 2 October 1993, 15993.

Aashwak S., 'Considerations of anencephalic infants as organ donors. A working document 12.18.1987. A protocol written by the Anencephalic Organ Donation Committee of Lorna Linda University Medical Center', in Ashwal S. and Schneider S., 'Brain death in children: current perspectives', Part I and Part II: 3, 1987.

Ashwal S. and Schneider S., 'Brain death in children: current perspectives', *Adv. Pediatr.*, 38:181-202, 1991.

Aashwal S. and Schenieder S., 'Brain death in the newborn', *Pediatrics*, 84:429 -137, 1989.

Ad Hoc Committee on Brain Death, 'The Children's Hospital, Boston. Determination of brain death', *J. Pediatr.*, 110:15-19, 1987.

Bailey L.L., *et al.* 'Orthotopic transplantation during early infancy as therapy of incurable congenital hearth disease', *Ann. Surg.*, single volume: 208, 1988.

Churchill B.A., Sheldon C.A., McLorie G.A., and Arbus G., 'Factors influencing patient and graft survival in 300 cadaveric paediatric renal transplants', *J.Urol.*, 140:1129-1133, 1988.

Ehrich J.H.H., Rizzoni G., Brumer P.P., Brynger H, Geerlings W., Fassbinder W., Maine A.E.G., Selwood N.H., and Tufveson G., 'Combined report on regular dialysis and transplantation of children in Europe, 1989', *Nephrol. Dial. Trasplant.*, 6 (Suppl. 1), 1991.

Fire R.W., 'Renal transplantation for children. The only realistic choice', *Kidney Int.*, 28 (Suppl. 17): 15-17. 1985.

Ghio L., Tarantino A., Edofonti A., Mocciano A., Giani M., Guerra L., Borardinelli L., and Vegeio A., 'Advantages of cyclosporine as a sole immunosuppressive agent in children with transplanted kidney', *Transplantation*, 51:834-838, 1992.

Grimm P.C. and Ettenge R., 'Pediatric renal transplantation', *Advances in Pediatrics*, n. 39, 1992.

Klaus M.H. and Kennel J.H., *Parent-infant Bonding* (Mosby Comp., 1982).

Klaus M.H. and Klaus P.H., *Venire al mondo* (Il Pensiero Scientifico, 1988).

Kriett S.M. and Keye M.P., 'The Registry of the International Society for Heart and Lung Transplantation: Eighth Official Report', *J. Heart and Lung Transplant*, 10:491, 1991.

Labrusse-Riou C., in Gerin (ed.), *Funzione e funzionamento dei comitati etici* (Cedam, 1991), pp. 105 and 127.

McEnery P.T., Stablein D.M., Arbus G., and Tejani A., 'Renal transplantation in children. A report of the North American Paediatric Renal Transplant Cooperative Study', *N.Engl. J. Med.*, 326:1727-1732, 1992.

Medical Task Force on Anencephaly (The), 'The infant with anencephaly', *New Engl. J. Med.*, 322:669. 1990.

Parisi F. *et al.*, 'Trapianto cardiaco nel bambino', *Cardiologia* 36:937, 1991.

Peaboy J.L. *et al.*, 'Experience with anencephalic infants as prospective organ donors', *N. Engl. J. Med.*, 321:344. 1989.

Report of the medical consultants on the diagnosis of death to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, 'Guidelines for the determination of death' *J. A.M. A.*, 246:2184-2186, 1981.

Report of Special Task Force, 'Guidelines for the determination of brain death in children', *Pediatrics*, 80:298-300, 1987.

Tajani E. and Gragnanello G., 'La comparsa delle competenze fetali', in Nordio S. (ed.) *O.d.G. Bambino* (Capelli, 1992).

Tanaka K. and Uemoto S., *Ann. Surg.*, 217:82, 1993.

Tufveson G., Geerlings W., Brumer F.P., Brynger H., Dykes S.K, Ehrich J.H.H., Fassbinder W., Rizzoni G., Selwood N.H., and Wing A.J., 'Combined report on regular dialysis and transplantation of children in Europe, 1988', *Nephrol. Dial. Transplant*, 4 (Suppl.4), 1989.

Tzakis A.G. and Reyes J., *Transplants Proc.*, 23-(6): 3010, 1991.

(Documents of the National Bioethics Committee: *Definizione ed accertamento della morte nell'uomo; Donazione d'organo a fini di trapianto; Informazione e consenso all'atto medico; Bioetica con l'infanzia*).