# NOTE TO USERS

# Small hearts - grand matters.
# The ethics of neonatal treatment with unknown long-term outcome:
# The case of hypoplastic left heart syndrome.

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To all my Children

*"The problem is not in finding exception*
*but in defining harm."*
*Brody, 1981.*

**Abstract**

Ethical decisions about medical care of infants is based on the by proxy evaluation of the infants' best interests. Since parents and physicians may have different points of reference, conflicts may arise during the decision-making process. The decision about the infant's well being becomes even more complex when high risk treatment with an uncertain long-term outcome is considered. Surgical palliation of hypoplastic left heart syndrome (HLHS) is an example of such a treatment. I use this example in my discussion on the relevant ethical issues and possible roots of conflicts between the decision-makers.

I argue that as long as long-term survival rates are variable, and the survivors' quality of life remains uncertain, palliative surgery for HLHS should not be obligatory. Rather, the parents should be informed not only about the existing treatments but also about the non-treatment option, and what each option may imply for the infant, parents and the family.

## Résumé

Les décisions dordre éthique sur les soins à dispenser aux nouveau-nés sont fondées sur une appréciation indirecte de leurs intérêts. Comme les parents et les médecins nont pas nécessairement les mêmes repères, le processus de prise de décision peut donner lieu à des différends. Les décisions affectant le bien-être de l'enfant se compliquent encore davantage lorsqu'on envisage un traitement comportant des risques élevés dont l'issue à long terme est incertaine. L'intervention chirurgicale visant à corriger une hypoplasie du coeur gauche en offre un exemple. C'est d'ailleurs cet exemple que j'utilise pour discuter des différentes questions d'éthique pertinentes et examiner les sources de différends éventuels entre les décideurs.

Je soutiens que dans la mesure où les taux de survie à long terme varient et que le degré de qualité de vie des patients qui survivent reste incertain, la chirurgie palliative visant à corriger l'hypoplasie du coeur gauche ne devrait pas être obligatoire. Il faudrait plutôt informer les parents non seulement de l'existence du traitement, mais aussi de la possibilité de ne pas intervenir, en exposant clairement les avantages et les inconvénients de chaque option pour le nouveau-né, les parents et la famille.

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# I. Introduction

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The model of ethical decision-making explored in this thesis searches for a balance between burdens and benefits when a treatment with an unknown outcome is considered for infants. Ethical decisions for patients of all ages are based on either the principle of autonomy or an evaluation of the best interest standard, including quality of life judgments. Since infants are not autonomous and cannot express their wishes, a proxy must make judgments for them. The parents have a *prima facie* right to make decisions for their children, that can be overriden only in exceptional cases.

For infants, the evaluation of best interest depends on the life experiences of the decision-makers, namely the parents and the health care professionals. Therefore, the best interest standard for an infant has different perspectives that may introduce some conflicts during the discussion. In the case of a treatment with an unknown long-term outcome, the decision about the infants' well being becomes even more complex. To understand the process of decision-making in these cases, I searched for the possible roots of conflicts in the judgements of all involved.

I have chosen palliative surgery for hypoplastic left heart syndrome as an example of treatment with multiple inherent risks and an unknown long-term outcome. I examined how the infants' best interest and quality of life principles are evaluated in general and in particular for hypoplastic left heart syndrome patients. Finally, I have tried to answer the following questions:

1. Are the burdens inherent in the treatment of hypoplastic left heart syndrome in balance with the potential benefits for the child?
2. Should non-treatment be an option?

3. What information should be given to the parents and what should be the process of decision-making for infants with hypoplastic left heart syndrome?

To answer these questions, it was necessary to learn about hypoplastic left heart syndrome. I followed the development of the surgical palliation technique from inception, some 25 years ago. Then, I evaluated the benefits of this treatment and analyzed the risks inherent in this procedure. I reviewed available data on the long-term survival and outcomes over this period. The review showed that, shortly after the first trials, the surgery offered progressively increasing survival rates to infants who, otherwise, would die within the first month of life. Yet long-term survival rates remain low, and survivors often present physical and mental disabilities of different degrees. Therefore, palliative surgery for hypoplastic left heart syndrome bears the dilemma of uncertain benefits and requires an in-depth ethical evaluation of the infants' best interests before a decision may be reached for the individual infant. Below, I summarize the general ethical approach that I analysed in an attempt to resolve the dilemma. A full discussion of the best interest and quality of life standards of infants with hypoplastic left heart syndrome was only possible after the evaluation of the risks inherent in the palliative surgery as well as that of non-treatment.

## I.1. Deciding for others

One of the most important principles in medical ethics is that of autonomy of patients. Originally based on Kant's theory of self-determination, this theory states that those who can formulate and appreciate their duties, including avoiding harm to others, honesty, justice and autonomy, are moral agents. The principle of autonomy requires a respect for all individuals as moral agents.

In the North American context, the principle of autonomy requires full disclosure of the diagnosis and prognosis of a disease to patients. The patient has to be informed about the known and possible risks and benefits of a proposed treatment and of alternative therapies, if any exist. The timing of the conversation, language barriers, and other extraneous factors influence the quality and outcome of this communication.

The decision-making process becomes even more complicated in cases of incompetent patients. In the case of adults who used to be independent (e.g. stroke victims), a proxy may have some idea of what the particular patient would have wanted, had he been able to decide. A proxy would have evidence about the patient's values, religious beliefs, and lifestyle. Whenever such information is not available, a discussion of the patient's best interest is required, which is based on determination of the optimal balance of benefits and burdens for that patient. This discussion is of supreme importance. The aim of the best interest standard is to determine the direction of action so that benefits can be maximized and burdens reduced.

Infants present a unique case where medical decision-making is concerned. Unlike adult patients who are no longer competent, they have never been competent. Therefore, for the infant, such decisions can be made only on the basis of a judgment of their best interest by a proxy. It is generally accepted that parents are guardians of their children's well being. Only in instances of abuse or neglect will society, acting through the courts, suspend or revoke this trust. Since health professionals who are responsible for the care of infants are also social agents, they are expected to defend children whose best interests are jeopardized. When issues of children's rights and child abuse come into play, they are obliged to notify agents of the state such as child welfare agencies or the courts. The

treating physician will make a recommendation on which treatment, if any, should be pursued.

Physicians have a general duty to preserve life where possible. Nevertheless, I will explore how the duty of physicians to preserve the life of a newborn can be suspended when the chances for success are low, and the quality of life decreased, while personal costs to the patient of securing that life are high. This approach may reconcile selective non-treatment with a general commitment to save lives, while recognizing plausible exceptions.

### I.2. Possible conflicts between decision-makers

Parents and health care professionals evaluate the infants' best interest and quality of life, and the parental decision may be influenced by other members of the family. Parents' decision-making competence is not usually open to serious doubt in a legal sense. However, there may be a conflict between moral requirements of the parents and the law on the one hand, and protecting the physician's professional integrity on the other. Such a situation may arise when, for instance, the physician sees a clear obligation to treat an infant but the parents disagree with the treatment.

The understanding of pertinent information and the reaching of a quality decision may be complicated by several factors, including the communications skills of the clinician, the personal dynamics between those involved in the discussion, and the setting where the decision-making process takes place. The parents' decision-making capacity may be impaired because of anger or despair, disappointment or denial, or controversial opinions of other family members, so that a truly informed consent process may never be possible. Reaching the final decision is further complicated in cases when treatments with unknown outcomes are discussed.

## I.3. Discussion about treatment with unknown outcome

When a treatment with unknown outcome is proposed for an infant, the parents may not be offered satisfactory information, or the information may be too difficult to be adequately understood. Therefore, they may never fully understand the nature of the treatment, or the consequences of their choice. Physicians offering an innovative treatment or a treatment under development to parents should make it clear that the long-term outcomes of the treatment are not yet known. I will suggest possible ways how the process of decision-making could be optimized, proposing ways in which physicians could inform the parents about possible benefits, but also warn them of all known risks, and an existing possibility of other, yet unknown, risks.

The risks of mortality or abnormal survival are inherent to some innovative treatments. Yet without undertaking risks, the opportunity to potentially improve a child's outcome would never progress. In 1977, Doty and Knott took upon themselves risks of unknown magnitude when they first operated on five hypoplastic left heart syndrome patients. Despite the death of all these patients shortly after surgery, this first attempt opened the gate for the current hope of survival to such patients. I will discuss the ethical consideration that need to be examined for the individual cases involved in such technological advances.

# II. Hypoplastic left heart syndrome

## II. Hypoplastic left heart syndrome

Hypoplastic left heart syndrome accounts for 7.5% of congenital heart diseases, and, if not operated, it is responsible for 25% of cardiac deaths within the first week of life (Watson and Rowe 1962) and 40% of cardiac deaths within the first month of life (Fyler et al. 1980). There is only one case in the literature of a child with hypoplastic left heart syndrome who lived without surgery for 3.5 years (Moodie et al. 1972). The majority of these patients die shortly after birth as a result of ischemia-induced peripheral and cerebral lesions, and intracranial hemorrhage, metabolic acidosis, hepatic or renal dysfunction (Bove 1998; Morris et al. 1990).

Without effective techniques, clinical diagnosis of all cardiac defects included in the syndrome was once difficult, if not impossible. Continuous improvements in perinatal care, cardiac anesthesiology, surgical and perfusion techniques, and postoperative intensive care have led to the consideration of more complex cases of hypoplastic left heart syndrome for correctional surgery or cardiac transplantation. However, despite an improved surgical treatment, a large percentage of these infants die after successful operations, usually of unforeseen and undiagnosed pathologies in the pulmonary vasculature and lymphatics, or of heart failure (Lloyd and Marvin 1989; Rychik, et al. 1999). Survivors live with frequent hospital visits, the need for multiple cardiac catheterizations, and daily medication (Bando et al. 1996; Mahle et al. 2000a,b). Because the long-term outcome following surgical palliation is unknown for any individual patient, the treatment for infants with hypoplastic left heart syndrome continues to present a weighty moral dilemma for both parents and health care teams.

## II.1. Historical view

### II.1.a. Classification of the syndrome

In the early 1950s, Lev (1952) introduced the term "hypoplastic left aortic tract complex" to describe a group of congenital cardiovascular malformations having atresia or stenosis of the left heart as a common characteristic. In 1958, Noonan and Nadas grouped and described the pathophysiology of five cardiovascular lesions under the term of "the hypoplastic left heart syndrome" (HLHS): aortic valve atresia, mitral atresia, mitral stenosis, aortic arch atresia, and hypoplasia of the aortic arch. All have clinically similar symptoms. The lesions may be present in one patient in different combinations. However, infants with HLHS may appear to be normal at birth and clinical symptoms such as dyspnea, hypoxemia, hypotension, and low cardiac output may develop only after a few days after birth (Reis et al. 1998; Rogers et al. 1995). The etiology of the syndrome is unknown. It is possible that the syndrome is a developmental anomaly, possibly related to premature closure of the foramen ovale or to an abnormally large ductus arteriosus during fetal life (Noonan and Nadas 1958).

Because of its complexity, clear classification of the syndrome is difficult. Saied and Folger (1972) proposed to narrow the classification of the syndrome to atresia of the aortic and/or mitral valve with normal anatomical relationship of the great arteries, intact ventricular septum, and a left ventricle clearly incapable of creating systemic blood flow. Presently, the term "hypoplastic left heart syndrome" includes hypoplastic or absent left heart, stenosis and/or atresia of the mitral and aortic valves, hypoplasia of the ascending aorta and of the aortic arch, and atrial and ventricular septal defects (Bove 1998; Fyler 1980; Tchervenkov et al. 2000). Tchervenkov et al. (1998) proposed an additional term, "hypoplastic left heart complex," to describe hypoplasia of the left heart without intrinsic

valve stenosis or atresia, and with systemic circulation not always dependent exclusively on the right ventricle. More recently, Tchervenkov et al. (2000) presented the classification of four levels of hypoplastic left heart syndrome, each with different combinations of lesions of the heart-aortic complex.

### II.1.b. Development of surgical palliation

Since the early 1950s, surgical attempts were undertaken to correct single lesions included in the HLHS, but the post surgical survival of these infants was only occasional and never longer than 23 days (Noonan and Nadas 1958). In 1958 Noonan and Nadas wrote: "It seems unlikely that many of these infants will benefit by surgical intervention unless one is prepared to correct the associated defects. It is possible that in the not-too-distant future, by use of a cardiac bypass apparatus, surgical correction of all these defects at one time may be feasible."

Surgical treatment of the HLHS remained unthinkable until 1968 when, on the basis of their autopsy findings, Sinha and his collaborators (1968) suggested a procedure that would enable the right ventricle to supply a sufficient blood flow to the systemic and pulmonary circulations. However, after the first unsuccessful attempts, Cayler et al. (1970) concluded that "no specific surgical therapy can be recommended" for infants with classical HLHS. The authors suggested that the anatomy of the heart may be successfully corrected only in 10-20% of all infants with HLHS, and that only in these selected cases could palliation be a "curative procedure in a near future" (Cayler et al. 1970).

In the late 1970s, Doty and Knott (1977) attempted to treat infants with HLHS by creating a shunt between the pulmonary artery and the aortic arch with a rigid Dacron tubular prosthesis so that the right ventricle effectively became the systemic ventricle. This operation, performed in 5 newborns with HLHS, provided temporary clinical

improvement. However, the stability of the peripheral and pulmonary circulations was short-lived. All 5 infants died of inadequate right ventricular performance or compromised coronary blood flow within 2 hours and 45 min after surgery (Doty and Knott 1977). The closing remarks of Doty and Knott after this total failure are stunning: "This experience is presented to stimulate thought and some hope for babies with a uniformly fatal cardiac anomaly." Only those with a high level of perseverance could have continued further trials: others would not have considered undertaking them.

Despite the total failure of the operation, a few years later, after some modification to the technique, Doty et al. (1980) reported a 12-week survival in an infant who was discharged from the hospital, but died as a result of choking while being fed at home. Simultaneously, using a similar surgical approach, Mohri et al. (1979) and Norwood et al. (1980) reported short-term survival in about 30% of their patients. In 1981, Norwood and his colleagues replaced the rigid Dacron tubular prosthesis with an elastic one, but the survival rate did not improve. Eight out of sixteen newborns with HLHS died postoperatively of hemorrhage, hypoxemia, or cardiac ischemia; another three died 3-5 months later, and only five infants survived. Following this low rate of success, the authors concluded that "this lesion is universally fatal with no established surgical management" (Norwood et al. 1981).

Nevertheless, further trials were under way. Centers with a high number of operated patients started to observe an increase in survival rates. For example, at the Children's Hospital of the University of Michigan, where 57 patients with HLHS were operated between 1983 and 1989, the survival rate beyond 30 days after the surgery (i.e. hospital survival) was 46% (Meliones et al. 1990). In contrast, in the Children's Hospital of Philadelphia where 200 infants with HLHS were operated between 1985 and 1989 the

survival rate was 66% (Chang et al. 1991), showing the positive impact of accumulated experience and improvement of surgical skills and techniques. The large variation between institutions was confirmed by a University Hospital Consortium from 62 university hospitals in the Unites States during the 4-year period from 1989 to 1993, with the average hospital survival rate of 47% (Gutgesell and Massaro 1995). The most frequent causes of early death, within 24 hours after surgery, were low cardiac output and inadequate pulmonary and systemic blood flows (Meliones et al. 1990).

**II.1.b.i. Fontan procedure**

To increase cardiac output and to reduce the volume work of the right ventricle, Norwood and his coworkers (1981, 1983) introduced the Fontan procedure as an additional correctional step in the treatment of HLHS patients.

The Fontan procedure, described by Fontan and Baudet (1971), creates an "in series" circulation that allows the single ventricle to pump fully saturated blood only to the systemic circulation. The principle of this approach is that the systemic veins drain directly to the pulmonary circulation. However, in those infants who survived the first palliative surgery, the first attempts at the Fontan procedure failed. The first patient who survived first-stage palliation died two days after the Fontan procedure (Norwood et al. 1981). The results of the surgery by others were similarly disappointing. A 1986 symposium on HLHS gave a summary of the contemporary situation in the USA. At that time, 249 patients underwent the first-stage surgery and only 75 (30%) survived in different hospitals throughout the country (Sade et al. 1986).

Following a study of Freed et al. (1981), preoperative medication with prostaglandin $E_1$ had become a routine and effective management of infants with HLHS (Norwood and Pigott 1985; Sade et al. 1986). A greater precision in the diagnosis was

also achieved by the introduction of color-Doppler and echocardiography. Regardless, the survival rate after first-stage surgery combined with the Fontan procedure across the United States remained low throughout the 1980s (40%). The main reason was that the best timing for carrying out the Fontan procedure had not yet been defined. Because of the poor outcome of surgical palliation, cardiac transplantation was recommended as a preferred option for the HLHS treatment. In the face of the shortage of human donors, one group suggested xenograft transplantation as a promising area of investigation and application (Sade et al. 1986). In fact, several institutions, discouraged by the low survival rates of first-stage palliation, selected cardiac transplantation as an alternative option to the HLHS treatment (Gutgesell and Massaro 1995; Razzouk et al. 1996).[1]

The Fontan procedure is based on the principle that the left ventricle is not essential and that right atrial pressure is adequate to channel systemic venous blood flow directly to the pulmonary circulation. However, a direct systemic venous blood flow into the pulmonary arteries may occur only if the pulmonary vascular resistance is low enough to accept this flow. When pulmonary vascular resistance is high (and infants with HLHS have a high pulmonary vascular resistance), the procedure is bound to fail. Therefore, survival rates after the Fontan were discouragingly low when it was performed in infants at an age before maturational changes in the pulmonary vasculature have occurred (Norwood et al. 1981; Norwood and Pigott 1985; Pigott et al. 1988). The majority of deaths took place during the first day after surgery, due to acute cardiovascular failure (Murdison et al. 1990) or hypoventilation (Pigott et al. 1988). It became clear that the Fontan surgery could not be successful in infants with a high pulmonary vascular resistance. To improve survival rates, an intermediate stage surgery was introduced before the Fontan procedure.

### II.1.b.ii. Intermediate stage

Two intermediate approaches, similar in purpose, were recommended and tried as the pre-Fontan step: the Glenn procedure and a modified Fontan, the hemi-Fontan (Hopkins et al. 1985; Norwood and Jacobs 1993). Both procedures decrease the right ventricle volume load imposed by the systemic shunt created during the first-stage surgery. The Glenn approach was first proposed by Carlon and co-workers in 1951, and in 1958 Glenn demonstrated its clinical effectiveness in cyanotic congenital heart diseases (in Zeller and Sade 1996). In 1985, the Glenn procedure was introduced as an intermediate step in high-risk HLHS patients before the Fontan procedure (Hopkins et al. 1985), and accepted later as a routine pre-Fontan intervention by others (Bando et al. 1996; Pridjian et al., 1993; Starnes et al., 1992). Norwood and Jacobs (1993) modified the Fontan procedure so that it could be performed in two steps, which were adapted in timing to the physiological maturation changes taking place in the pulmonary circulation of the newborns. In some centers, hospital survival rates following Glenn and hemi-Fontan procedures exceeded 80% (Norwood and Jacobs 1993; Starnes et al. 1992), and after the of completion the Fontan, they became similarly high (Douglas et al. 1999; Jacobs and Norwood 1996).

Some centers prefer the hemi-Fontan procedure to the Glenn for a variety of reasons including the complexity of the latter procedure and a lower hospital survival rate following it. In addition, the hemi-Fontan allows for the correction of some cardiovascular risks that may have evolved after the first-stage. For example, central pulmonary artery hypoplasia or distortion, which is common after the first-stage surgery, can be effectively corrected during the hemi-Fontan procedure, thus improving the overall outcome (Douglas et al. 1999). The Glenn procedure does not offer this possibility (Bove

1998, 1999). Furthermore, the duration of cardiopulmonary bypass for the Glenn is about twice as long as that for hemi-Fontan (Bove 1998), and a prolonged time of cardiopulmonary bypass increases the mortality risk (Starnes et al. 1992).

## II.2. HLHS in the 1990s

In 1990, Morris et al concluded: "Hypoplastic left heart syndrome is a lethal congenital heart defect in children and poses management and ethical dilemmas." The increasing hospital survival rates of patients with HLHS during the last 10 years reflect a progress in the perioperative management of these infants. Nevertheless, the palliative surgery continues to pose management and ethical dilemmas.

### II.2.a. Hospital survival rates

Between 1990 and 2000, hospital survival rates after the first-stage palliation varied from 37% to 91% (Allan et al. 1998; Bando et al. 1996; Bove 1998, 1999; Brackley et al. 2000; Breymann et al. 1999; Daebritz et al. 2000; Gutgessell and Massaro 1997; Kern et al. 1997; Mahle et al. 2000b; McElhinney et al. 2000a; Nicolson et al. 1995; Starnes et al. 1992; Tworetzky et al. 2000; Williams et al. 2000). Although it seems that there has been no obvious improvement in the survival rates with time, these data come from centers with different levels of expertise. After hemi-Fontan the hospital survival rates could be as high as 98% (Bove 1999; Douglas et al. 1999), and after completion of the Fontan, the hospital survival rates varied from 83% to 100% in different centers (Bove 1998, 1999; Breymann et al. 1999; Douglas et al. 1999; Kern et al. 1997; Mahle et al. 2000b; Mosca et al. 2000; Nicolson et al. 1995; Poirier et al. 2000; Seliem et al. 1997; Williams et al. 2000). The survival rates after each stage further increased with the reduction of cardiopulmonary bypass and hypothermic circulatory arrest times (Kern et al. 1997; Starnes, et al. 1992). Yet newer modifications of the

developed techniques are still taking place. For example, at one center the first-stage surgery for HLHS patients was performed without using graft material, with a positive outcome in the first 4 operated patients (Nagy et al. 2000). Weinstein et al. (1999) performed the first stage surgery in premature newborns with a body weight below 2 kg, but with only 50% hospital survival. Nevertheless, the authors claim, in contrast to other reports (Bove 1998; Mahle et al. 2000b), that low weight alone should not be considered an obstacle to staged reconstructive surgery.

### II.2.b. Today's options

The decision about the management of patients with HLHS is complicated by the lack of well-documented long-term follow-up after surgery. In different centers, either staged correctional surgery or cardiac transplantation, or both, have been practiced for the treatment of HLHS. A prompt intervention is advocated, before a general deterioration of the clinical condition of the patient may develop (Bove 1999; Iannattoni et al. 1994). Different centers have different management tactics for patients with HLHS.[2] Some centers offer, in addition to the surgical treatment, an option of comfort measures, allowing the infant to die (Brackley et al. 2000; Chiavarelli et al. 1993; O'Kelly and Bove 1997; Osiovich et al. 2000; Storch 1992; Zahka et al. 1993). In these centers a substantial percentage of parents opt for basic comfort care alone.

## II.3. Procedures today

### II.3.a. Perinatal care

The incidence of HLHS diagnosed after birth constitutes about 5% of congenital heart disease. Using prenatal tests, HLHS has been determined at 16-41 weeks' gestation by echocardiography as one of the most frequently diagnosed fetal heart defects (Allan 1989; Allan et al. 1991, 1998, Busken et al. 1997).

Prenatal detection of cardiac abnormalities gives a new option to the parents and affects obstetric management. The prenatal diagnosis is important because the majority of newborns with HLHS appear normal at birth (Bove 1998, 1999; Reis et al. 1998; Rogers et al. 1995) and, therefore, postnatal diagnosis may be delayed. In the past, the mother often opted to terminate the pregnancy after the prognosis and risks of the HLHS treatment were explained (Allan et al. 1991; Crawford et al. 1988; Davis et al. 1990; Johnston and Sakala 1990). As a consequence, the frequency of HLHS in newborns decreased. However, most recently, because better chances for survival exist with the three-stage palliation, parents increasingly elect to continue with the pregnancy (Allan et al. 1998; Osiovich et al. 2000).

If the decision is to continue the pregnancy, the delivery can be planned according to the parental decision. When the parents opt for the surgical treatment the delivery may take place at a center practicing the preferred treatment. In this way, the hazardous consequences of neonatal transport can be eliminated and the patient's management can be planned in advance thereby reducing the period of hypoxia and acidosis, which is detrimental to the newborn's central nervous system (Allan et al. 1998; du Plessis 1997).

Nevertheless, in practice, the utilization of prenatal screening for HLHS on the health of newborn infants showed limited benefits (Busken et al. 1997; Johnston and Sakala 1990). The preoperative mortality among infants managed aggressively, and the prenatal diagnosis itself did not improve postoperative stability, and the early mortality rate was similar for the prenatal and postnatal diagnosis groups (Kumar et al. 1999).

**II.3.b. Preoperative care**

In the intensive care unit, the patients receive a continuous intravenous infusion of prostaglandin $E_1$; hemoglobin oxygen saturation and acid-base status are measured in the

arterial blood; metabolic acidosis is corrected with intravenous infusions of bicarbonate and intravascular volume expansion. Mechanical ventilation with air enriched in oxygen and carbon dioxide is required to optimize the pulmonary vascular resistance and to ameliorate blood gas levels (Nicolson et al. 1995). Sedation, cardiac catheterization, angiography, a perfusion lung scan, and two-dimensional Doppler echocardiography, often followed by a Magnetic Resonance Imagining, are performed as routine preoperative procedures (Byrne et al. 1996; Jacobs and Norwood 1996; Nicolson et al. 1995). In some centers, ultrasonography of the head and abdomen, and karyotype study are performed to exclude associated defects. If a defect is confirmed, some centers do not encourage surgical treatment for the HLHS patients (Bove 1998; Starnes et al. 1992).

**II.3.c. Surgery**

The staged palliation, an open heart surgical procedure, requires general anesthesia, muscle paralysis, the administration of heparin, artificial ventilation, a mid-line sternotomy, cardiopulmonary bypass, circulatory arrest, deep hypothermia (18-20° C)[3] and infusion of intraoperative inotropic drugs (Bailey et al., 1993; Razzouk et al., 1996; Starnes et al. 1992).

All infants require postoperative analgesia, as postoperative pain is related to the worst outcomes in neonatal cardiac surgery (Anand and Hickey 1992). Relief of pain for infants in the intensive care unit is achieved by intravenous narcotics given as a bolus or as a continuous infusion. However, control of pain in infants is extremely difficult. The pain may be mistaken for discomfort from restraints or, if ventilated, from an endotracheal tube, in addition to the pain caused by numerous incisions. The additional difficulties in the management of pain in newborns and infants are often non-specific symptoms, which may be taken for hemodynamic alterations secondary to the surgery or

hypoxemia (Baum and Sangwan 1995). With the recently developed specific scales for the evaluation of postoperative pain in infants, the control of pain in this group of patients may be improved (van Dijk et al. 2000). Evaluation of pain in critically ill newborns constitutes an additional difficulty because of their inherent physical weakness and ineffective protests (Larsson 1999). Therefore, there is still a possibility that some pediatric patients could be undermedicated (Higgins et al. 1999; Larson 1999).

There is some evidence that integrated emotional and behavioral responses to pain are retained in long-term memory. The memory of pain modifies subsequent behavioral patterns and neurological development (Anand and Hickey 1987; Larsson 1999). Therefore, the evaluation of the risk of anesthesia and analgesia during painful procedures requires thoughtful evaluation, especially in HLHS patients who are assigned for palliation and are submitted to three consecutive surgeries.

**II.3.c.i. The first-stage**

The aim of the first-stage palliation is to make a permanent communication between the right ventricle and aorta, to optimize the pulmonary blood flow, and to ensure a satisfactory intra-atrial communication (Norwood et al., 1980). At this stage, an entire aortic arch complex is created with a gusset of cryopreserved pulmonary artery homograph. A connection is made between a pulmonary aorta and the systemic arteries so that the right ventricle may provide both the systemic and pulmonary blood flows (Jacobs and Norwood, 1996).

Following the surgery, the infant returns to the intensive care unit with pressure monitoring catheters placed in the right atrium and open sternotomy. The sternal incision is left open up to a week after the surgery and the infant remains on artificial ventilation.[4] The patients are ventilated with a mixture of air enriched in oxygen and with moderately

increased carbon dioxide concentrations in order to maintain a balance between systemic and pulmonary vascular resistance.[5] The patients stay in the intensive care unit for about 2 weeks after the operation.

**II.3.c.ii. The second-stage**

Either a Glenn or hemi-Fontan procedure is undertaken approximately six months after the first-stage surgery (Jonas 1991; Nicolson et al. 1995). Both procedures are similar in purpose; they direct systemic blood to the pulmonary artery from the superior vena cava (Bando et al. 1996; Starnes et al. 1992; Zellner and Sade 1996). A small group of infants with HLHS whose left ventricle is able to support systemic circulation may undergo a biventricular repair, an option offered to infants "at the mild end of the spectrum of HLHS" at the Montreal Children's' Hospital (Tchervenko et al. 2000).

Usually no cardiac medication is necessary for the management of infants after the hemi-Fontan procedure. After approximately a 2-week recovery period in the intensive care unit, if there are no complications, the infant may go home, and the final stage of the correctional surgery, the completion Fontan, is usually scheduled 6 to 12 months later (Jacobs and Norwood 1996; Nicolson et al. 1995).

**II.3.c.iii. The third-stage**

At the time of the third stage, the completion Fontan, the infant undergoes full hemodynamic evaluation. The aim of this procedure is to separate the pulmonary and systemic circulations. The separation is accomplished by directing all systemic venous return to the pulmonary vasculature (Nicolson et al. 1995). The graft implanted during the first-stage is open longitudinally to create a lateral atrial tunnel for the blood flow from the inferior vena cava to the pulmonary arteries. A portion of the tunnel is comprised of the free wall of the right atrium and therefore has the potential for growth. The infant

returns to the intensive care unit equipped with necessary catheters to control the pressures within the atrium and the systemic venous pathway.

## II.4. Risks involved

### II.4.a. Inherent risks

It has been reported that a high pulmonary artery pressure (Mosca et al. 2000), a birth body weight of less than 2.5 kg, and an age at the time of the first-stage palliation of more than 14 days, diminish the chance for survival of infants with HLHS (Iannettoni et al. 1994; Mahle et al. 2000b). The survival potential decreases further if closing of the ductus arteriosus during the first-stage produces ischemic organ injury (Nicolson et al. 1995). Low levels of arterial oxygen saturation may lead to necrotizing enterocolitis and interstitial ischemia (McElhinney et al. 2000b) and may have harmful effects on neuronal development (Limperopoulos et al. 2000).

Bove (1998) defined two risk groups of infants with HLHS. The standard risk group was composed of infants with a 'classic' HLHS who underwent first-stage surgery within the first month of life. This group represents the majority of cases. The high risk group were infants whose age at the first surgical intervention was over one month, and those who had a severe obstruction to the pulmonary venous return causing severe hypoxemia, and pulmonary edema, or with noncardiac congenital conditions such as prematurity (<35 weeks, <2.5 kg), chromosomal anomalies, or diaphragmatic hernia. These high risk newborns have significantly compromised survival rates (Bove 1998; Brackey et al. 2000).

#### II.4.a.i. Coexisting abnormalities

The majority of infants with HLHS are probably free of other congenital malformations (Morris et al. 1990). However, the literature reports some differences. For

example, Natowicz et al. (1988) found a genetic disorder or major extracardiac anomaly in 28% of HLHS non-survivors of the first-stage palliation. Glauser et al. (1990b) reported that 41% of patients with HLHS show some dysmorphic features (abnormal karyotype, craniofacial abnormalities, or major organ system malformations). Other studies found congenital hernia in about 12% of infants with HLHS (Fauza and Wilson 1994). Abnormal karyotype, including Turner's syndrome, duplication of the short arm of chromosome 12, trisomy 18, chromosomy 21, and malformation of the central nervous system were reported by others in about 12% of HLHS patients (Allan et al. 1998; Bove 1998; Brackeley et al. 2000; Glauser et al. 1990b; Reis et al. 1998, 1999). On autopsy, about one third of infants who died of HLHS showed holoprosencephaly or absence of the corpus callosum, dysplasia of the cerebral gyri, of the cerebellum, and of the brainstem (Glauser et al. 1990b).

Roughly 2.5% of HLHS patients are born with Turner's syndrome. Their surgical survival rate is significantly lower than that of infants in the standard HLHS risk group. One study reported that only 2 out of 10 (20%) infants with both HLHS and Turner syndrome survived first-stage palliation and underwent the second-stage. Both infants were alive two years after the surgery but with significant medical problems (Reis et al. 1999). For comparison, in the same institution, the survival rate of infants in the standard risk group (infants without accompanying anomalies) after the first-stage palliation exceeded 80% (Bove 1999). Hospital survival rates after the third stage in infants in the standard risk group are twice as high as those of the high risk group (86% as compared with 42%; Bove 1998).

According to Bove (1998), 5% of infants with HLHS are born prematurely or with a body weight below 2.5 kg; noncardiac malformations coexist in 12% and are major in

3% of these patients. Noonan and Nadas (1958) reported that, in fact, over one third of infants diagnosed with HLHS had one or more accompanying noncardiac anomalies including those of the digestive (25%), genitourinary (10%), skeletal (7%), and central nervous systems (6%), multiple spleens (7%), harelip and cleft palate (8%), diaphragmatic hernia (5%) and Down's syndrome (1%).

### II.4.b. Acquired risks

#### II.4.b.i. Artificial ventilation

Many infants need artificial ventilation before open-heart surgery and all infants require it after the surgery. Following the operation, the infants have low lung compliance and high airway resistance due to an accumulation of interstitial fluid in the lungs (DiCarlo et al. 1992). Since decreased lung compliance increases the work of breathing, these infants need artificial ventilation to improve blood gas levels. But artificial ventilation is not free of risks, as cases of overinflation of the lung, air trapping, and flat diaphragm were found to be related to a prolonged need of artificial ventilation in the HLHS patients (Nicolson et al. 1995).

#### II.4.b.ii. Anesthesia

Fentanyl anesthesia may have long-term effects. Given to newborns as a sedative, fentanyl was associated with significantly lower behavioral states scores at the age of 1 year than those infants who received a placebo (Orsini et al. 1996). In fact, emotional trauma resulting from neonatal pain extends into childhood, and the survivors of multiple surgeries have an increased tendency for somatization (Grunau et al. 1994). The surgery and the weaning periods from anesthesia are continuous challenges, while the best method of anesthesia has not yet been standardized (Zickmann et al. 1992).

### III.4.b.iii. Sternotomy

The open midline sternotomy increases risks of infection. Since the immune system is fragile after open-heart surgery in newborns (Hauser et al. 1991), mediastinal and superficial infections may become chronic and they may delay repair of congenital lesions (Kearns et al. 1999).

### III.4.b.iv. Cardiopulmonary bypass

The development of a low-flow cardiopulmonary bypass system (CPB) accompanied by deep hypothermic circulatory arrest, was a turning point for open-heart surgery. Although some authors have described no postoperative complications in survivors (Nicolas et al., 1994; Subramanian, 1978), others reported fatal consequences resulting from open-heart surgery (Terplan, 1976). At present, it is well recognized that the technique has a number of inherent risk factors. The duration of CPB is significantly correlated with the subsequent duration of endotracheal intubation and the length of the infant's stay in the intensive care unit (Mosca et al. 2000), and has been considered a risk factor for hospital mortality (Kern et al. 1997) and abnormal neurological status (Limperopoulos et al. 2000).

Despite the recent development of techniques (e.g. finer suturing, administration of vitamin K and platelets to promote homeostasis), bleeding is the most common complication related to cannulation of large vessels (Aeba et al. 2000). Aortic cannulation may not only cause postoperative bleeding but may also produce tears in the wall of the right atrium, which are sometimes difficult to repair. Cannulation of the superior vena cava may partially obstruct venous return and decrease cardiac output. If pericardial tamponade develops, it may cause a decrease in cardiac output and an increase in the right

atrial pressure (Edmunds 1995). Finally, cardiopulmonary bypass may affect the mechanical properties of the blood, the heart and the blood vessels in diverse ways:

a/ During CPB, blood is exposed to non-physiological conditions such as a high shear stress, turbulence, and decreased oncotic pressure. These factors lead to both immediate and delayed hemolysis, and to a decrease in the compliance of red blood cells. The increased rigidity of red blood cells may contribute to the impaired microcirculation and oxygen supply to tissues (Kameneva et al. 1999). Ischemic-hypoxemia may lead to a temporary dysfunction of nearly every organ, and may trigger a massive defense reaction - the so-called "whole body inflammatory response" - which may have fatal consequences (Edmunds 1995).

b/ Perfusion of heparinized blood may result in the formation of microemboli responsible for much of the morbidity associated with CPB. Multiple treatments with heparin increases the risk of bleeding associated with platelet activation and fibrinolysis during and after surgery (Edmunds 1995). On the other hand, inadequate systemic heparinization may cause extensive activation of the coagulation cascade and generate microthromboses leading to organ ischemia, coagulopathy and fibrolysis (Hartz and Hanafy 1996). For example, hypoxic-ischemic or embolic brain lesions, and intracranial hemorrhage are observed in 45% of the infants with HLHS who underwent first-stage surgery (Glauser et al. 1990a). Similarly high rates of incidence of stroke and other neurologic problems are observed in all patients who undergo open-heart surgery. In some patients, deficits are temporary, but in over 30% of patients they are still present one year after the surgery (Edmunds 1995).

c/ Cerebral blood flow is impaired for some time after termination of CPB, which may lead to brain injury (Pua et al. 1998).

d/ During CPB, the coronary arteries constrict and the heart contractility is reduced due to cardioplegic edema and the distention of the flaccid cardioplegic heart. Thus, the high afterload produced by CPB during the weaning process increases cardiac stress (Edmunds 1995).

e/ CPB causes massive fluid retention and increased capillary permeability, which consequently give rise to edema. Pulmonary edema and CPB-related changes in surfactant decrease alveolar stability. Atelectasis develops and continues to be a problem during the first 48 hours after CPB ends. In some cases, acute respiratory distress syndrome can develop (Edmunds 1995).

Most recent modifications in CPB, such as enhanced removal of carbon dioxide (Aeba et al. 2000), lower priming volume, the use of smaller cannulae, and vacuum-assisted venous return (Berryessa et al. 2000), may contribute to improved hemodynamics and reduced the adverse effects of CPB in newborn infants.

**II.4.b.v. Deep hypothermia and circulatory arrest**

The degree and the duration of hypothermia contribute to mortality and neurologic morbidity in infants (Miller et al. 1995; Starnes et al. 1992). Moderate hypothermia (28° C) resulted in lower survival rates compared to those whose body temperature was lowered to 20° C (Mosca et al. 2000). If cooling is not homogeneous or if the duration of arrest is markedly prolonged, the risk for a brain injury increases (Nicolson et al. 1995). Although the majority of strokes are embolic or ischemic, hypothermia may also contribute to the damage (Edmunds 1995).

A circulatory arrest time of over 50 minutes is an important risk factor for early mortality (Bando et al. 1996). The circulatory arrest time during palliation for HLHS may be substantially longer (Staners et al. 1992). In fact, the risk for neurobehavioral

abnormalities increases with each additional minute of circulatory arrest and hypothermia after 26.4 minutes (Limperopoulos et al. 2000), while the most recent literature reports hypothermia and circulatory arrest period of 15-64 minutes (median 37 minutes) necessary for a modified first stage procedure (Poirier et al. 2000). In infants with circulatory arrest lasting longer than 30 minutes, spectrum analyses of the EEG show abnormalities at least until the end of surgery (Massaut et al. 1984). In fact, when the duration of circulatory arrest exceeds 36 min, infants, due to brain injury, may experience early postoperative seizures with neurological and developmental sequelae (Eke et al. 1996; Nicolson et al. 1995).

Transient postoperative clinical and EEG seizures were associated with worse neurodevelopmental outcome at ages 1 and 2.5 years. Like other children with neonatal seizures from various causes (Holmes 1991), those who develop seizures after open heart surgery have lower motor function and mental development scores, abnormal neurological examinations, and lower scores in several areas of function as compared to a reference population (Goldberg et al. 2000; Rappaport et al. 1998).

Circulatory arrest in newborns is associated with a high risk of delayed motor development and neurological abnormalities at one year of age (Bellinger et al. 1995). Adverse neurological consequences of open heart surgery correlate positively with the duration of circulatory arrest, and the longer the duration, the more severe are the long term consequences. Low developmental, motor, problem-solving, and IQ scores are present at the age of 4 months to 4 years in children who were operated during their infancy (Williams et al. 2000). Data on older survivors confirm the above findings (Goldberg et al. 2000).

### II.4.b.vi. Inotropic drug infusion

Inotropic agents can act to increase systemic vascular resistance and further exacerbate the flow imbalance in the pulmonary and systemic circulations (Nicolson et al. 1995).

## II.5. Postoperative period

Infants who survived open heart surgery may develop a predisposition to either a hypercoagulable state or bleeding complications (Jaggers et al. 1999), and single or multiple organ failures accompanied by high fever, thrombocytopenia and neurological involvement (Book et al. 1982; Seghaye et al. 1993). The most important factors responsible for organ failure are hypotension, poor tissue perfusion, and hypoglycemia (Chesney et al. 1975). Recent use of vasodilators in combination with catecholamines seems to have preventive effects on postoperative renal insufficiency (Asfour et al. 1996). Low perfusion during the perioperative period may lead to heart block, necrotizing enterocolitis, or mensenteric ischemia, all having potentially fatal consequences (Douglas et al. 1999; Fatica et al. 2000; Hebra et al. 1993). Hyperglycemia, developed a few hours after the open-heart surgery, may have an unfavorable effect on the cardiac muscle (Benzing et al. 1983).

Patients may experience post-surgery feeding difficulties (Jonas et al. 1986) or pancreatitis (Tikanoja et al. 1996). During the early postoperative period following first-stage palliation, cardiac tamponade may occur, and this must be treated with a continuous aspiration of blood from the mediastinum (Nicolson et al. 1995). Some patients may need reoperation for cardiovascular problems, and others may develop an often fatal abnormal physiology of the coronary blood flow (Forbess et al. 1995).

About 20% of infants who underwent first-stage surgery are diagnosed with obstruction of the aortic arch about 5 months later (Tworetzky et al. 2000). Aortic arch obstruction, coarctation of the aorta, restrictive atrial defects, tricuspid valve regurgitation, and pulmonary artery distortion may develop in survivors of first-stage palliation. Limited blood flow through the systemic-to-pulmonary artery shunt, a restrictive interatrial communication, or high pulmonary vascular resistance results in cyanosis. These incidents require an immediate intervention to minimize their harmful effects on the already volume-loaded ventricle and decrease the mortality risk (Jacobs and Norwood 1996; Jonas et al. 1986; Meliones et al. 1990; Vincent et al. 2000). Cases of aortic arch obstruction and coarctation of the aorta can be managed by coarctation balloon arterioplasty (Starnes et al. 1992; Tworetzky et al. 2000). But this procedure also has inherent risks. The arterioplasty may cause death or bradycardia requiring cardiopulmonary resuscitation (Tworetzky et al. 2000).

About 25% of all survivors of the first-stage palliation require an intervention between first and second-stage palliation represent. These infants may need several additional palliative surgical procedures, including arch reconstructions, additional shunts, repeated atrial septectomies, Glenn shunts, coarctation balloon angioplasties, or pulmonary artery reconstruction and reshunting. All these post-operative risks may decrease the long-term survival rates of the HLHS patients to about 20% (Kern et al. 1997; Meliones et al. 1990).

For several days after second-stage palliation, the cardiopulmonary physiology is very unstable because of the changes in the heart and blood flow. At this stage, some infants develop ventricular dysfunction combined with swelling of the upper body and the airways, excessive irritability or lethargy lasting over several days (Nicolson et al. 1995).

Pulmonary blood flow remains non-uniform (Seliem et al. 1997) and about 20% of survivors show pulmonary artery trombosis, cardiac dysrhythmias, tachycardia, left pulmonary artery occlusion, pulmonary artery hypertension, necrotizing enterocolitis, heart block, and hemidiaphragmatic paralysis, all associated with considerable morbidity and mortality (Bove 1998; Douglass et al. 1999). Infants with cardiac and phrenic nerve complications often require surgical intervention (implantation of a permanent pacemaker, plication), others may be treated with medication, oxygen therapy or mechanical ventilation (Bove 1998). The patients may need reoperation for bleeding, or treatment with extracorporeal membrane oxygenation (ECMO) to improve oxygen saturation; both interventions increase the risks for the infants' survival (Douglas et al. 1999).

Following the third-stage, the completion Fontan, survivors are often hospitalized for cardiac operations, pacemaker insertion or replacement, arrhythmia, heart failure, or infections. There is always a possibility that the right ventricle may fail as a single pump for both the systemic and pulmonary circulations. The most frequently acquired post-Fontan problems are atrial arrhythmias, thromboembolic complications, and protein-losing enterophathy (Dr. S.W., personal communication).

In summary, the full impact of these complications has been clouded by the presence of a marked decrease in postoperative mortality of infants with previously lethal heart conditions. However, it is evident that open heart surgery presents significant life threatening risks and possible morbid consequences for survivors, including brain lesions, intracranial hemorrhage, neurobehavioral abnormalities, early postoperative seizures with neurological and developmental sequelae such as lowered motor function and mental development scores later in life (du Plessis 1999). The HLHS patients must undergo three

open heart surgeries before the required palliation is achieved, and survivors of the first stage may require additional interventions between the next stages that drastically diminish their chances for survival.

### II.6. Long-term survival

The long-term survival of operated HLHS patients depends on a variety of inherent factors. For example, the survival rate was better when an experienced surgeon operated, and was affected by the physiological state of the newborns before the first-stage operation (Williams et al. 2000). When the surgery was performed during the first month of life, the chances for a long-term survival increased as compared to older infants (Chiavarelli et al. 1993; Iannettoni et al. 1994). Nevertheless, the long-term survival rate remains significantly lower than the 30-day hospital survival rate, and decreases with each year of life.

The survival rate of patients considered at standard risk for palliation is 85%, 80% and 69% at 1 month, 1 year and 5 years of age. By comparison, the survival rate for high risk patients is 61%, 20%, and 20% at 1 month, 1 year and 2 years (Bove 1998). In this group of infants, data for 5-year survival are not available. A review article by Cohen and Allen (1997) reports a 58% 5-year survival rate following the three stages of palliation, excluding from the calculations infants who were designated for palliation but died before surgery. A study of Breymann et al. (1999) reported a 4-year survival rate, including hospital mortality and deaths at subsequent stages, to be 28% between 1989 and 1994, and 58% between 1994 and 1997. Survivors often have significant harmful cardiorespiratory conditions, which in some cases need a permanent pacemaker. In cases with hemidiaphragm paralysis, plication is needed (Bove 1998). The majority of

survivors have to return for postoperative cardiac catheterization about 1 year after the Fontan procedure (Farrell et al. 1992).

A recent paper by Mahle et al. (2000b) describes the long-term survival of patients who underwent reconstructive surgery in the Children's Hospital in Philadelphia between 1984 and 1999. Determination of patient status was carried out during the first five months of 1999. During the fifteen years under study, 840 HLHS patients underwent the first stage surgery, and during the follow-up period, about 36.8% (309 out of 840) survived. After the Fontan procedure, performed on 337 patients, the 1-, 5-, and 10-year survival was 52% (175 out of 337), 40% (135 out of 337) and 39% (131 out of 337), respectively. The above data suggest that the accumulative 1- and 10-year survival rates of the entire study cohort after the Fontan procedure were about 21% and 16%, respectively. However, the long-term survival rates after the first-stage surgery almost doubled between the late 1980s and the late 1990s in this institution (Mahle et al. 2000b). A large variability in the survival rates remains between different centers. Williams et al. (2000) reported 58% and 54%, the 1- and 5-year survival rates, after the staged surgery in his institution, while in the other, Jenkins et al. (2000) reported 42% and 38% for the same two periods of survival.

### II.7. Long-term outcome

The long-term outcome of patients with HLHS may depend on the infants' preoperation conditions (Bove 1998), but the relationship between the preoperative status and the long-term outcome is not well documented. On the one hand, following the first stage procedure, no correlation was found between the preoperative condition and the outcome in one set of patients (Iannattoni et al. 1994), and on the other, severe

preoperative obstruction to pulmonary venous return was found to be associated with their poor survival (Bove 1999).

Rogers et al. (1995) described the developmental outcome of 11 survivors among the HLHS patients, at ages from 11 months to 5.5 years. The authors included infants who underwent only the first-stage, and others who survived the second and the third stages of palliation. All these children were underweight, had microcephaly (in 8), various degrees of mental retardation (in 7), cerebral palsy (in 2), substantial functional disabilities (in 8), and gross motor delays (in 5). Their head growth was closely related to their cognitive development. Occasionally, neuroimaging showed diffused cerebral atrophy. Several children had more than one of these malformations.

In another study, survivors of the three stage palliation, between the ages of 3-8 years, who were considered at standard risk, had slightly reduced motor skills, verbal performance, and intelligence test scores, and in 50% of these children, the scores were significantly lower (Bove 1998). In a more recent study, HLHS survivors of the three-stage palliation who, at 3-7 years of age, underwent imaging of the brain with MRI or CT scan had a brain abnormality (in 50%), an evidence of previous ischemia or infarction (in 39%), and a congenital abnormality (in 10%). The HLHS survivors had significantly lower verbal performance and overall scores than children who underwent the Fontan surgery for other single ventricle lesions. Nevertheless, in this study, most of the HLHS survivors demonstrated intelligence scores within or above the normal range (Goldberg et al. 2000).

A study of Williams et al. (2000) shows delayed development, especially in communication and gross motor skills, at ages of 4 months to 4 years in all infants after the first-stage procedure. After the second-stage, a low developmental status was

observed in 60% of operated children. After the third-stage, the lower developmental status was observed in 50% of the children. In 25% and 12% of these children the lower developmental status was accompanied with low gross and fine motor function, respectively.

In the above study, Williams et al. (2000) evaluated parental perception of the quality of life of infants who survived the three stage palliative surgery. Their data show that after first stage palliation, the children seemed not to be different from the normal population. In contrast, following the second stage, children scored significantly worse on scales measuring physical ability, growth and development, discomfort and pain, temperament and mood, general health perception, and on the emotional parental impact. After the third stage, children were better on the discomfort and pain scale than the reference population, but they were worse on the general health perception scale. Some of these unfavorable characteristics remained in pre-school children, and were related to perioperative conditions. Williams admits that the perception of quality of life by the parents may reflect the modest expectation held by most of them after the first stage.

The quality of life of older survivors, as measured by the summary psychosocial score, lagged behind that of healthy children. Five- to seven-year-old HLHS patients scored significantly lower in emotional, behavioral, self-esteem, global health, and family activity items. On the other hand, physical summary scores were similar to those of healthy children. Gestational age and the duration of circulatory arrest were predictive of the physical health summary score. The shorter the circulatory arrest time during surgery, the better the performance in growth and development, the less pronounced discomfort and pain, and better overall temperament, moods, and behavior (Williams et al. 2000). Therefore, improved quality of life of the survivors could be achieved by centralization of

centers offering palliation where greater experience allows a shorter circulatory arrest time (Mosca et al. 2000). However, because Williams examined different infants at different ages, the longitudinal data allowing evaluation of the time course of postoperative development in HLHS patients are not yet available.

Finally, Mahle et al. (2000a) reported that at school age, children with HLHS, in many respects, did not differ dramatically from their peers. The majority of them were in good or excellent health; their academic performance was about average. Nevertheless, over 60% of patients had to use chronic medication, and although intelligence tests showed scores within the normal range, the mean performance of these survivors was lower than that in the general population; about 20% of these children presented mental retardation.

When the developmental delays are detected in the HLHS infants during their first years of life, it does not necessarily mean that they will remain behind the other children later in life. On the other hand, it is possible that some developmental delays will become more evident in older survivors; unfortunately, the long-term analyses of neurological development of this group of children are missing.

## II.8. Summary

The life of infants who underwent three staged palliation depends on the performance of a single ventricle. Following palliative surgery, unfavorable survival is associated with pre-operative factors such as noncardiac congenital conditions, obstruction of pulmonary circulation and hypoxemia, and during surgery, prolonged hypothermia and a circulatory arrest period (Bove 1999; Clancy et al. 2000).

Summarizing the recent achievements in the management of the HLHS patients Freedom (2000) stated: "[any] number of challenges, including definition of particular treatment strategies, remain to be confronted in these difficult-to-treat cohorts of patients." The history of the three-stage palliation for HLHS is not very long and, therefore, data on long-term outcome after this treatment are not yet available. There are data on a 5- to 10-year survival after the three stage palliation (Bove 1998; Mahle et al. 2000b), but the medical state of these children has not been systematically documented. On the other hand, in adult patients, cognitive decline has been recognized as a complication after cardiac surgery with cardiopulmonary bypass. The decline of cognitive function was still present five years after the surgery (Newman et al. 2001).

More importantly, to estimate the long-term outcome of infants who were operated during their infancy, not a few years but several ten-year follow-up periods must be evaluated. It is impossible to foretell the HLHS patients' future well being on the basis of the existing but scanty data on the first 10 years of their lives. Growth of the surgically created new vascular pathways has not yet been examined and urgently needs to be evaluated (Jacobs, 2000). More systematic study of the psychophysiological status of these infants is still missing.

The considerable mortality rate, unknown long-term outcomes, and the fact that a large percentage of parents choose comfort care alone when this option is offered, suggest that palliative surgery is still in its developmental stage. Revisions of the surgical palliation of HLHS continue (Mahle et al., 2000b). One of the most recent modifications of the first stage described by Poirier et al (2000) is aimed at ensuring sufficient coronary blood flow and, therefore, at eliminating one of the most important risk factors of this stage of palliative surgery. Further modifications are focused on the improvement of the long term outcomes by reducing the potential adverse effects not only of the surgery itself, but also of the accompanying deep hyporthermia, circulatory arrest, and cardiopulmonary bypass. Nevertheless, until the mortality rates become less variable and while the long-term outcome is more clearly defined, palliative surgery remains an 'experimental' procedure; the management of newborns with HLHS will remain controversial, since the future benefits for the patients cannot be clearly judged.

## II.9. Footnotes

1. The advantage of cardiac transplantation is the replacement of an abnormal circulation with a normal one in only one operation. The most important disadvantages of this approach is a low availability of donors, the time constraints dictated by the physiological fragility of newborns with HLHS, the lifelong need of immunosuppressive therapy, and management of sometimes multiple rejection episodes in addition to the late complications of infection, graft atherosclerosis, and a lymphoproliferative disease (Bove 1999; Braunlin 1990; Chiavarelli et al. 1992). During the waiting period, infusion of prostaglandin $E_1$ causes cortical hyperostosis in infants if the infusion lasts longer than 60 days (Woo et al. 1997), and the waiting period for a heart donor may well exceed this limit (Bando et al. 1996; Boucek et al. 1990). Up to 84% of infants may die while waiting for transplant (Backer et al. 1991; Bove 1991, 1999; Starnes et al. 1992; Williams et al. 2000). The overall 5-year survival is 61% when all infants who have been designated for cardiac transplantation are included in calculations (Razzouk et al. 1996). When immunosuppressive therapy is ineffective, a final approach to refractory rejection is total lymphoid irradiation (Byrne et al. 1995). Systemic and pulmonary hypertension and coronary artery disease are frequent complications in the graft recipients (Starnes et al. 1989, 1992). Some recipients may need retransplantation, or additional surgeries for repairs of aortic coarctation, or pacemaker insertion (Chiavarelli et al. 1993; Razzouk et al. 1996). The recipients are prone to nephrotoxicity or immunosupression-induced malignant disease (Backer et al. 1991). The therapy may have various side effects (excessive body hair growth, hypertension, tremors, impaired renal and liver function, gartrointestinal disturbances and bone marrow toxicity, leukocytosis, thrombocytopenia, and anemia, Cushing's syndrome, excessive weight gain, gastrointestinal disturbances, and mood swings). Data on long-term outcome are conflicting. One study reported that the majority of graft recipients have normal psychological and mental development (Backer et al. 1991), while the other reported neurological complications (Lynch et al. 1994). West et al. (2001) described a successful ABO-incompatible cardiac transplantation in 10 infants performed in the Hospital for Sick Children in Toronto, 2 of these infants died within 29 days after surgery. However, these are only preliminary data with a follow-up of the survivors lasting 11 months to 5 years, and need to be confirmed.

2. Some institutions have chosen only palliation (Pigott et al. 1998). Others focus on cardiac transplantation as the only therapy for HLHS (Backer et al. 1991; Razzouk et al. 1996). Still other institutions have a flexible program and offer both procedures as equally valued treatment (Meliones et al. 1990; Starnes et al. 1992; Gutgesell and Massaro 1995; Bando et al. 1996). For example, the Colombia-Presbyterian Medical Center and the University of Michigan offer staged palliative surgery for all patients as the preferred option, and transplantation is reserved only for those who are unsuitable for surgery (Bove 1999; Williams et al. 2000). At the Loma Linda University Medical Center cardiac transplantation has been the preferred treatment of HLHS for the last 15 years (Razzouk et al. 1996).

3. Hyporthermic circulatory arrest at as low as 14° C was used for reconstruction of the interrupted aortic arch in neonates with 77% long-term survival rate (Tlaskal et al. 1997).

4. Open sternotomy has become an elective procedure for the first-stage surgery. The clinical practice shows that it may help to improve respiratory and hemostatic stability sooner after cardiac surgery (Kay et al. 1989; Starnes et al. 1992; McElhinney et al. 2000). However, since randomization to this treatment has never been done, there is no data on the effect of open sternotomy on postoperative mortality (McElhinney et al. 2000).

5. Increased levels of carbon dioxide in inspired air reduce pulmonary vascular resistance and result in a marked stabilization of the early postoperative physiology and reduce significantly the early postoperative mortality (Gullquist et al. 1992; Nicolson et al. 1995).

# III. Ethical considerations

## III. Ethical considerations

"The goal of ethical decision-making is an emotionally grounded reflective equilibrium in which all systems are integrated, all tests are satisfied, and a wholehearted decision can be made" (Spence 2000). When a standard treatment is discussed, a sound ethical decision may be relatively easy to achieve. Potential risks and benefits of this treatment for a patient are well establish. If fatal consequences of a standard treatment may be expected, the rate of their occurence is also well determined. Therefore, in this case, weighing the burdens against benefits may not offer unexpected constraints. However, in other cases, the decision cannot be so easily reached. The difficulty escalates drastically when a treatment under development and with unknown long-term outcome is discussed.

Ethical decisions in medical care require the process of informed consent given by the patient before any treatment can be undertaken. The concept of informed consent is based on several key elements, including competence of the patient, his or her autonomy, and adequate disclosure of relevant information. In the process, the patient must gain a full understanding of the disclosed information and must be aware of the potential risks and benefits of a suggested treatment. In the case of infants, the above guidelines apply to parents or guardians. Therefore, as Lynch (1991) indicated, it is more appropriate to speak of authorization or permission for any interventions that involve children rather than to use the term 'consent.' Brody (1981) holds a similar opinion. He says that since an infant is not able to exercise autonomy, it is it impossible for a proxy to consent on a child's behalf in a real sense. In his opinion, the parents' consent to their child's

treatment, and "we hope that they think about their commitment toward this child as its guardians."

John Rawl's moral theory maintains that parents have duties to their children, despite an inherent paradox: "In choosing for a child as if he were myself, I am choosing for the child to be independent of myself" (in Blustein 1988). This contradiction cannot be avoided because judgments about immature children are made from the adults' perspective. Nevertheless, in general, only the parents may reach a decision about their duties to children, trying to predict from their own viewpoint what kind of life their children will value, and what kind of persons they may become (Blustein 1988; Brody 1988).

### III.1. The best interest standard

Ethical decision-making for children and incompetent patients of all ages is based on the best interest standard that respects the individual's self-determination, concern for the individual's well being, and distributive justice. The standard finds its reflection in the Canadian Charter of Rights and Freedoms[1] in protecting individuals from unnecessary harm. The best interest standard has been an important tool, both in ethics and law, in the evaluation of such basic ethical principles as preservation of life, beneficence and non-maleficence for individual patients.

The best interest standard guides the decision-makers to establish the net benefits for the patient of a given treatment option, and to weigh those benefits against burdens of the option for the patient, so that the burdens-to-benefits ratio is favorable to the patient. The standard is patient-centered, because it focuses primarily on the current and future interests of the incompetent patient. Consequently, it takes into account a quality of life judgment inasmuch as a treatment will be in a patient's best interest only when life after a

treatment is worth living for the patient (Ahronheim et al. 2000; Buchanan and Brock 1989; Lynch 1991; Pearlman and Speer 1986). I will discuss the quality of life judgments separately below.

Although the best interest standard applies to both infants and incompetent adult patients, there are important differences in the decision-making process for these two age groups.

In the case of an incompetent patient who used to be self-governed, the proxy making the decision may have some indications, based on the patient's past, of what the patient would choose in these circumstances were he competent, and what the patient would understand by his best interests. The proxy, in his decision, would be able to substitute his judgement for that of the patient, relying on what was known about the patient's preferences. Accordingly, all these patients have the same rights as competent persons, including the right to refuse medical treatment. Not using substituted judgment in these cases would mean a loss of this fundamental right of the patient.

In contrast, surrogate decision-making for infants does not involve a once-autonomous person. Newborns have never been autonomous and their preferences are unknowable. They have no wish or will as agents.[2] They are not yet developed as individuals with complex interests, nor have they developed social and intimate bonds with others. Thus, ethical decisions concerning children are made for them in a state of relative ignorance about the children's own wishes; this ignorance can possibly be reduced, but never eliminated (Brody 1988). The parents have the *prima facie* right to consent for their children, which may be overruled by legal authorities only when the fundamental rights of a child are not respected.

For children, predictions are made regarding their future potential for development as human beings with opportunities for relationships, experiences and awareness. Both the immediate and the future benefits depend on the consequences of the chosen action and existing knowledge about a treatment. In some cases, and especially when a new treatment is selected, only the future may tell if the predictions were accurate and the undertaken action was favorable. The best decisions based on the best information available at the time may turn out to be wrong in the future (e.g. past treatment of respiratory distress syndrome in newborns with oxygen led to retinopathy).

Standard treatments decrease the probability of future unfavorable outcomes. The benefits of a standard treatment with known outcomes are relatively easy to predict; efficacy of a treatment and its risks are usually well established, so the benefits-to-risks ratio can be estimated for an individual infant. In contrast, when the treatment is experimental and/or its outcome is uncertain, the infant's best interest may be jeopardized; with uncertain outcomes, benefits are obscure. However, there is no general agreement on which neonatal outcomes should be considered good and which harmful. Certain outcomes may be regarded as sufficient for their child's well-being by some and unacceptable by others (Kraybill 1998). For instance, some parents may accept a one-year survival of their child as beneficial. Others may reject it as an unacceptable outcome. Uncertain benefits of a treatment can increase the controversy.

Lack of adequate information or variable outcomes elicit uncertainty about the balance between burdens and benefits. It is generally accepted, that inasmuch as the long-term harm of a treatment is unknown, it is not permissible for the infant to be subjected to pain or discomfort. Before the initiation of a new treatment, potential risks should be identified, and within the context of good clinical practice, minimized so that they would

not be greater than those of a standard treatment, if such exists (Emanuel et al. 2000; Freedman et al. 1993). For children, the risks of a treatment may be established in comparison with the potential risks of everyday life (Lynch 1991).

Any modifications of a treatment with uncertain outcome can be justified only if potential burdens to individual patients are minimized, and potential benefits to these patients are maximized. Modifications of a technique should aim to eliminate, if possible, or at least to minimize, risks that were identified in the previous trials, so that the burden-benefit ratio may become more favorable for future patients. Therefore, the potential benefits to an individual patient should be proportional to or outweigh the burdens (Emanuel et al. 2000). With the gain of experience and knowledge, the recognition of risks helps further modifications of a treatment to increase benefits for the patients. There would be no progress in medical technology if moderate risks were not undertaken.

For example, decisions concerning the management of HLHS patients today are based on variable survival rates and limited data on their long-term outcomes. However, if the immediate outcome of these first attempts was considered exclusively, the palliative surgery would have never been developed.

After the first published attempts of surgical correction of HLHS in infants, Doty and Knott (1977) wrote: "the ethical considerations of surgery in patients with hypoplastic left heart syndrome also are difficult. Even if surgery were successful by the procedure described, a second, or even multiple operations would be required to allow growth." They concluded: "Many argue that nothing should be done for hypoplastic left heart syndrome because of extreme cardiac deformity. This experience in these five patients is presented to stimulate thought and perhaps some hope for these helpless babies with a uniformly fatal cardiac anomaly." All five patients died shortly after the surgery.

Now, twenty-five years later, we do not know who those children were and what the process of ethical decision-making was, if such a process did take place. We do not know if there were ethical considerations of the risks involved, to what extent the parents were involved in the decision-making, or how well they were informed. Nevertheless, in the line of reasoning of Doty and Knott, the deaths of these five infants stimulated thought and offered hope for HLHS patients today. Thus, from a utilitarian viewpoint, these first attempts at HLHS treatment might be considered morally sound, but viewed with hindsight, did not serve the patients' best interest.

The surgery described by Doty and Knott in 1977 involved an infinite risk-to-benefit ratio.[3] Since the 1970s, great progress has been achieved in the surgical treatment of HLHS patients. Nevertheless, the long-term outcomes are not well defined, and the one-year survival rates after palliative surgery may vary from 20 to 58% (Bove, 1998; Kern et al. 1997; Mahle et al., 2000b; Williams et al., 2000). Therefore, as in all cases of treatments under development, physicians who propose a treatment for a HLHS patient are responsible for giving full information on the nature of these treatments, including all uncertainties implicated in the long-term outcome. In this way, parents may make a well informed decision in choosing a treatment that will best protect the child's best interests.

Ethical issues arising at times when new treatments are offered are associated not only with uncertain outcomes of these treatments, but also with difficulties in communicating the early and late risks in plain and comprehensible language. Another problem in communication between physicians and parents may arise from "the various ways of expressing 'current' mortality that may give different estimates, when mortality is changing rapidly over time" (Bull et al., 2000). Additional problems may arise when there are uncertainties about the parent's capacity to decide, or when it is unclear what

could be the legal implications of a particular decision, when the importance of certain moral principles is not fully appreciated, or when it is uncertain how to weigh one principle against the other (Anhronheim, et al., 2000).

The complexity of the best interest judgment for infants and uncertainty regarding prognosis of survival and long-term outcomes following a given treatment are among the most compelling issues of medical ethics. These issues are relevant to the decisions made for the HLHS patients and need careful discussion concerning the best interest standard among all involved.

**III.1.a. The best interest of the infant**

The best-interest standard implies that the patient has some capacity to experience pleasure and pain, and infants definitely may experience both. But infants are not conscious of the existence of interests. The infants' interests are held in trust primarily by the parents, and then by family, nurses and physicians involved in the infants' treatment (Kennedy 1988), or in particular cases, as mentioned above, a legal authority.

Like those of other individuals, infants' interests are present and future oriented. The present interests include achieving pleasure, being warm, being well-fed, and the avoidance of pain and discomfort (Buchanan and Brock 1989). The future interests include developmental interests, opportunity interests, and human relationship interests. In some cases, the primary importance of the developmental interests may outweigh an infant's current best interests. For instance, pain caused by a treatment during infancy may guarantee the infant's development in the future. In contrast, when a treatment alleviates a patient's pain, it improves his or her short-term well being, but it does not necessarily mean that lasting effects of this treatment will also be beneficial (Spence 2000). The developmental interests are especially important since they influence an

infant's possibilities during the rest of his or her life. Thus, a newborn who has a *potential* for development of the capacities necessary for being a moral agent has an *interest* in developing these capacities. Because human thriving is dependent on the success of human life, infants have an interest in having opportunities to be successful. Finally, human thriving requires human relationships, thus infants have an interest in developing the capacities for such relationships (Buchanan and Brock 1989). Therefore, where there is a possibility of a short term survival after a painful treatment combined with a severe handicap, nontreatment could be considered as an option toward the infant's best interest (see *Re J* case below).

The present and future interests of infants are evaluated for them by the decision-makers. Despite their best intentions, there are many cases where the standard of the child's best interest does not give clear-cut guidelines (Kraybill 1998). More importantly, judgment of best interests may differ depending on who is making the judgment: lawyer or philosopher, obstetrician or pediatrician, parents or special interest advocacy groups (Doyal and Wilsher 1994). Although all these parties aim to act with the best intentions, only the future can prove whether or not the infant, had he or she been competent at this particular moment of his life, would have undertaken the same decision.

Pellegrino (1987) suggested three ways for considering the best interests of the infant. Firstly, when there is an uncertainty and a treatment can have some medical benefit, then the treatment should be used. However, because this course of action does not concentrate on the individual infant, in some cases, it may jeopardize a particular infant's well-being. Secondly, Pellegrino implied that discussion of the infant's best interests should be based on a projected quality of life judgment, so that an operation which meets only the infant's short-term interest should not be considered. A difficulty in

accepting this way of reasoning is that 'interest' has no absolute value. For some parents, short-term survival of their infant would meet their perception of the best interest standard. Thirdly, Pellegrino argued, consideration of best interests should examine the burden of life for the neonate understood as 'disability that will affect the infant's potential happiness.' He stated that when the potential burden of continuation of life seems too great as compared to potential benefits, then a decision of non-treatment should be undertaken. However, the definition of 'burden' is unclear; a tolerable burden for one person, can be intolerable for another.

Spence (2000) promotes a caring, rather than a curing approach, as the preferred way of action toward the infant's well being. The caring approach focuses on infants as individuals with feelings, relationships and families. It takes into account both short-term and long-term interests, evaluated as the infants' potential to develop into quality survivors. The caring approach reflects Duff's concept of "close-up ethics," emphasizing the ethics of good (Duff 1979). In contrast, the curing approach is based on the availability of a treatment and aims to cure the illness, ignoring other needs of individual patients. The patient could be seen only as a problem requiring a solution. Therefore, it favors only the short-term interests by treating the immediate problem, while not considering the type of survival, or what happens when the cure is not complete. Duff refers to the curing approach as "distant ethics." Considering the use of a treatment from the distant ethics viewpoint, the treatment may not be in the infants' short-term and long-term best interests, while the caring approach always is (Duff 1979).

The caring approach allows one to recognize that it may not always be in the best interest of the infant to continue his or her life. In some cases, suffering and pain may be recognized as being too great to risk a treatment, even if there may be some possibility of

a good outcome. In other cases, infants who are in continuous pain or are kept alive but have no prospect of normal development and ability to form a relationship with their parents, may be "better off" if they die without a treatment. In all these cases, to treat them, or to keep these newborns alive could do them terrible harm, which could be known only in retrospect (McCormick 1974). However, it is difficult to compare the advantages of life, even with disabilities, against nonexistence following death. Such a comparison can be made only on the basis of what we accept as being 'good.' In general we believe that life is good. In contrast, a life with elements of 'bad' (e.g. constant pain and suffering) might lose this value. Again, a decision on what is 'good' and what is 'bad' may be influenced by who is making the judgment, and the evaluation of 'bad' in infants may represent an obstacle in itself.

Suffering and pain of infants is unavoidably evaluated from the adult point of view, and the existing tools of 'measuring' the infants' pain are often criticized. Arras (1984) suggests that we should ask "not whether a normal adult would rather die than suffer...but rather whether this child, who has never known the satisfactions and aspirations of the normal world, would prefer nothing to what he or she has." He continues that adopting "the child's viewpoint would be difficult in practice, but it would conform more closely to the spirit of the best interest standard." However, in practice, this way of action may not only be difficult but impossible. If one follows the suggestion of Arras, the value that is given to the quality of prolonged life would be rejected because newborns have no perception of their future life. Nevertheless, I agree with Arras that by focusing directly on the infant, the well being of that infant would not be confused with the best interests of others involved in the decision-making (Arras 1984).

However, focusing on the infants' well being does not guarantee that decision-makers may free themselves of their personal preferences while evaluating the infants' well being, and interpretation of the standard depends on who is involved and when the judgment is made. For instance, parents may consent to a treatment because they may be unable emotionally to undertake any other decision at this particular time (Avery 1998). Physicians may occasionally disagree with the parental judgment, and the disagreement may lead to a conflict between the physician's obligation to the patient and the parents' wishes. Alternately, a physician might find it difficult to let a baby die. Therefore, the best interest standard for an infant has different perspectives, and in particular cases, the court is involved in protecting the infants' well being.

### III.2. The parents' perspective

It seems to be generally accepted that any decision concerning an infant's treatment and its consequences cannot take place without parental contribution (Kraybill 1998). Parental judgment must be respected by physicians, because it is the parents who are responsible for creating a bond with their child. They take upon themselves a burden that cannot be shared by anyone else, and from which they cannot escape – no matter what parental decisions are made (Stevenson and Goldworth 1998). Only in exceptional cases may parental decisions expose their children to risks against the general understanding of the best interests of the child. In these cases, a third party (e.g. the courts) may intervene on behalf of the child, acting in agreement with the ethical view that medically reasonable efforts must be undertaken to preserve a child's life, even against strong, or religiously based objections by the parents (Ahronheim et al. 2000). The courts recognize the best interest standard only as a regulative ideal and not as a strict requirement, because parents' obligations toward the other children and their own self-

interests can conflict with what maximizes the child's well being. The case for legal deviation from the standard as a directive in decision-making depends on the fact that optimizing for the ill infant may conflict with the legitimate interests of other family members (Buchanan and Brock 1989).

Parents not only wish to give life and to nurture their children, but they may also expect emotional gratification in return. This self-centered consideration is intertwined in the parental understanding of the well being of their children. Therefore, the best interests of their children, reflect the parents' own perceptions of those interests, as influenced by their own status. In a diverse society, different parents facing similar dilemmas will reach different conclusions, based on their differing personal, cultural, and religious values.

For example, the concept of 'sanctity of life' may become the main decisional standard when the balance between burden and benefit and outcomes is uncertain (Shewchuk 1995). Whatever their motivations, such decisions relate to parents' beliefs about the meaning of life, suffering and death. Those who believe in the sanctity of human life will choose to sustain life, even at the cost of the infant's and family's suffering (Kraybill 1998). Others may recognize that life is good only when it can support higher values, including the development of human relationships.

The parents' identification of moral issues is defined in terms of their relationships with other people and their commitments to those people, especially individuals in their family (Pinch and Spielman 1989). Often, the best interests of the parents are satisfied if the best interests of the child do not conflict with achieving their own goals. For example, the parents may decide for non-treatment of their newborn who, because of his or her handicap, would require special care and sacrifices on their part in the future. Nevertheless, such decisions would be in contrast to the child-based best interest

standard, and may have to be resolved in the court. An example of a similar court case (*Re B)* is given in a separate section below that reviews relevant court judgments.

There may be a variety of factors that could hinder the expected role of parents as the decision-makers. I discuss some of these factors below.

**III.2.a. Compelling influences**

The recognition of the best interests of a child may not be free of compelling influences that parents may be unaware of, or do not wish to recognize. Mothers given increasing responsibility for the well being of their newborn children may be afraid of societal judgment when the pregnancy outcome is disappointing. Interviewed parents whose infants were diagnosed with congenital heart diseases described their feelings of disappointment combined with sadness, anger, and guilt (Cohn 1996). Even more minor malformations in newborns bring about shock and disappointment in many parents. This psychological state may influence their decisions regarding the child's treatment. For example, about 75% of mothers described the birth of a child with a facial cleft as a mental shock, which was often followed by depression. The parental attitude of rejection, if persistent, may interfere with the child's best interests, or have negative effects on his or her self-esteem, mental development or social interactions (Dytrych et al. 1991). In some cultures, society may reject a 'defective' child and social humiliation may increase the parents' stress.

**III.2.a.i. Guilt**

An interesting statement by a mother of an infant with HLHS who was deciding between treatment and non-treatment illustrates her feeling of guilt and vulnerability. The mother said: " In a crisis after birth you are very sensitive and easy to influence. You feel that you have to do everything possible to save your child. As a parent you are egoistic....

You don't consider the kind of life your child will have, or that he may suffer during surgery and then die." Interestingly, the mother opted for basic comfort care only (Vandvil and Forde 2000).

Parents could subconsciously project their guilt onto physicians, expecting them to "do everything to save the baby." In contrast, they may unconditionally rely on a doctor's opinion. Either of these reactions has a deeply imprinted social background, namely the social responsibility granted to parents to safeguard the well-being of their children, or the general belief that "the doctor knows best." In these situations, the majority of parents would cling desperately to any hope the doctors may offer them. However, offering this hope can be misleading in some cases, especially when the long-term effects of a treatment are not yet well established. Parents may agree to a new treatment because its outcome is not clear to them. Because an unclear prognosis introduces additional difficulty for the parents in end-of-life decisions, the parents may become more submissive in accepting a suggested treatment, especially when religious beliefs play a role (Spence 2000). The ease with which physicians may influence parents could create a conflict between the interests of the parents and the interests of the person who the child would become (Kuhse and Singer 1985).

**III.2.a.ii. Stress**

While under stress, parents might be unable to make a clear decision that may lead, in some cases, to life-prolonging treatment in children, disregarding how ill or impaired they are and will be if life is preserved. On one extreme, there are infants with birth defects such as anencephaly, or Trisomy 18. On the other extreme, are infants who have a good potential for recovery and full mental development, but whose parents refuse treatment. Between these two extremes there are children who are markedly retarded or

physically handicapped. The development of these children would depend on the ability of their families to give them the special care and emotional support that they might require (Pinch and Spielman 1989).

Parents may be unaware of their role in ethical decision-making involving their high-risk children. They may recognize the communication regarding a treatment as simply informative, believing that it is one of the requirements on their part to fulfill a legal necessity. In the parents' perception, their contribution in the decision-making may not seem important, since in their opinion, a treatment would not be offered if it were not in the best interest of their child to receive such treatment (Pinch and Spielman 1989).

An interview of 32 families has shown that, in general, whenever negative outcomes were likely, parents adopted a passive role in the decision-making responsibility (Pinch and Spielman 1990). The parents justified their behavior as resulting from stress, not understanding the technological details of the offered treatments, or by their submission to the health professionals' expertise. While their children were in the neonatal intensive care units, most parents found themselves distant from the child and perceived the physicians as being paternalistic. They expressed feelings of emptiness, lack of fulfillment and depression. When asked specifically about their role in treatment decisions, they stated either that no decision-making was necessary, or that they were not involved in the process. Some parents felt intimidated by the professional staff and confessed that, because of the intimidation and their own lack of medical knowledge, they depended fully on the judgments made by physicians (Pinch and Spielman 1990).

Especially during the early days in the intensive care unit, parents may be vulnerable if left alone to face a reality drastically different from their expectations. If the father alone is expected to become a primary caregiver, he may be in an especially

vulnerable position if unprepared for this role (Shellabarger and Thompson 1993). In such cases, others, especially physicians, can easily influence either of the parents in their decision-making.

**III.2.a.iii. Possible conflicts**

When there is a conflict between the parents and the physicians in their judgments of the infant's best interest, the majority of parents focus on their own emotional state during the conflict, and that is what they want to discuss (Pinch and Spielman 1990). In one report, they mentioned their physical and mental status as factors limiting their ability to make reasonable choices. Parents of chronically ill and handicapped infants often expressed shock at the implications of a proposed treatment plan when they fully recognized the depth and magnitude of subsequent childcare required (Pinch and Spielman 1990).

Parents may become reluctant to accept the physicians' rationale when conflicts arise between them and the health professionals in understanding the best interest of a child. Parents' reluctance may reflect ignorance about the disease and/or the treatment, or misunderstanding of the clinical situation. Reluctance frequently arises from the parents' inability to cope emotionally with the stresses related to their ill child and a recommended treatment. Under stress, parents may be vulnerable to psychological reactions which lessen their abilities for constructing a decision (Callahan 1988).

Extreme parental non-compliance may represent a special form of child abuse where, due to the presence of psychopathology, parents are unable to consider the child's best interest (e.g. Munchausen syndrome by proxy).

### III.2.a.iv. Parental background

The parents' decisions about the best interest of their infant can depend on their socio-economic status. Parents with higher education show the adaptive character of thoughts and better understanding of given information that facilitates the decision-making process. Nevertheless, when both the predispositional and situational distresses are increased, the ability of decision-making for all parents decreases (Hollen and Brickle, 1998).

However, the decision process may depend on whether a treatment, non-treatment, or both are considered. A Norwegian study by Vandvik and Forde (2000), which compared the decision-making process for treatment and non-treatment of infants with HLHS, reported that those parents who opted for comfort care (non-treatment) took longer time to reach their decision. The motive for their decision was to prevent the child's suffering. Mothers who chose surgical treatment for their infants, were of the opinion that when there was technology it should be used. Mothers in 'the basic medical care group' had a higher educational level and better childhood experiences than those who chose surgical treatment. Interestingly, more mothers in 'the comfort care group' had been working in healthcare, suggesting that some medical knowledge may create greater opposition to a complicated treatment with an unknown outcome.

### III.2.a.v. Communication

The parental decision may depend on how the diagnosis and prognosis have been presented to them. For instance, De Wet and Cywes (1985) reported that when the attitude of a physician was sympathetic, parents responded positively to an offer of corrective surgery. The offered hope also changed their perception of how the diagnosis was revealed to them. When there was no element of hope, as for example in the case of

cystic fibrosis, the largest percentage of parents were dissatisfied with how a physician presented the child's diagnosis to them (De Wet and Cywes, 1985).

**III.2.b. Long-term consequences of a decision**

There are unpredictable consequences of an infant's stay in an intensive care unit. A review by Shellabarger and Thompson (1993) indicated that months and years into the child's development, the parental stress caused by the experience with the intensive care unit may create problems in the parent-child relationship, leading to difficulty in bonding or parenting, and a possibility of child neglect or abuse.

The evaluation of the infants' best interests by physicians relies on the standards of their profession. On the basis of the risks-to-benefits ratio, they may recommend or disapprove of a treatment, and the parents choose between existing options, unless in particular cases, legal authorities remove their *prima facie* right. The decisions must be approached with extreme caution in individual cases because a treatment that would benefit the patient in the short term may not necessarily be in his or her future best interests; other options may have greater benefits, with less cost to the patient from suffering and disability.

A series of interviews with parents of children with Down's syndrome carried out by Shepperdson (1983) showed that about 50% of those parents accepted the idea that not all handicapped children should be kept alive at all costs. Some of these parents objected to active euthanasia, others objected to the cruelty of a lingering death, but all accepted an "allow to die" approach. Interestingly, the strongest support for active euthanasia came from the mothers of older children, suggesting their psychological burnout (Shepperdson 1983).

Parental burnout could be the reason for a tragedy documented recently daily Montreal press, where a mother killed her 14-year-old daughter before attempting to kill herself (Kalogerakis 2001). The daughter was not in chronic pain, but was mentally handicapped, suffered seizures, walked with difficulty, and could not feed herself. Like the Robert Latimer case (*R. v. Latimer*), this event inspired social reaction from many parents who "have spoken out about the lack of resources available to alleviate the stress and crushing workload that comes with raising disabled children" (Kalogerakis 2001).

Parents of HLHS patients are not free of stress, especially when they care for these children between surgical bouts and in the intensive care units. In recognition of this unavoidable stress, and of the need of a support system for these parents, a national parent group, called "Left Heart Matters," has been set up in Britain. The organization supports parents with individual requests, organizes annual get-togethers and publishes information booklets (Brawn et al. 1997).

In summary, the expressed parental decision about treatment may not reflect the real choices they would make if they were free of conflicting feelings and stress. It may not always be true that parents know or are able to clearly establish the best interest of their children, and this is an important constraint in their expected role as the decision-makers.

### III.3. The family's perspective

Although it is generally accepted that the best interest standard of infants bears a paramount value, others believe that, because the life of the newborn is intertwined with the lives of its family members, parents cannot choose for the infant without choosing for the family (Benfield et al. 1978; Downie and Randall 1997; Hackler and Hiller 1990; Kraybill 1998). The future best interests of the infant, and its role as a member of the

family cannot be easily separated. Therefore, parents' actions in the infant's best interest might be limited by the interests of other members of the family. According to this train of thought, long-term decisions concerning the infant could be justified in terms of the importance of preserving intimate family relationships, rather than only in terms of the best interests of the child, although ideally, best interests will be common for the child and the family (Downie and Randall 1997). However, in situations in which the benefit to the infant is questionable, and where treatment may impose grave burdens on the family, the family's interests may become more important and the best interest standard may be expanded to include the best interests of the family as a whole (Brody 1988; Kraybill 1998; Lynch 1991).

When the long-term outcomes of a treatment are contrary to expectations, difficult and demanding adjustments may have to be made by the immediate family of a handicapped child. The parents and siblings may react to the burdens such care imposes with resentment, guilt, and hostility, which may explain why families with handicapped children have an increased rate of marital break-up (Kuhse and Singer, 1985). Siblings of a handicapped child may feel rejected or neglected. Consequently, they may be delayed in their development of speech, language, and in their education. They are likely to suffer socially, or they might even decide not to have children of their own (Kew, in Kuhse and Singer, 1985). However, these burdens alone do not justify non-treatment, even though the parents cannot be forced, even by law, to raise a child they are not psychologically and financially fit to care for (Blustein, 1988). Thus, although the burdens placed on the family are considered in the decision-making process, they cannot be the primary reason for withholding treatment.

Regardless, it may be expected that the survival of a handicapped child may have long lasting consequences for the whole family. Families with a disabled child may decide not to have any more children. Stinson and Stinson, (1979), whose child was kept alive for five months against their wishes, described their emotional costs during this period and their concern about how the infant's survival in a damaged state destroyed their plans to have another child. In contrast, if a newborn dies shortly after birth, a decision by the parents to have another child could be more likely. For example, in a study by Vandvik and Forde (2000), nine out of ten mothers who opted for the basic medical care for their infants with HLHS had given birth after their losses. Although none of the mothers who chose palliative surgery expressed regrets, one said: "If I think about the future of my child I may become mad."

In summary, in some cases, a handicapped child who may be a joy for one family may destroy another, and there is a 50% probability that survivors of the palliative surgery for HLHS will have physical or mental handicaps of varying degree that would require special care (Bove 1998; Mahle et al. 2000a; Rogers et al. 1995; Williams et al. 2000). Therefore, the burden placed on the families of children with HLHS should be considered in the decision-making process, although it cannot be the primary reason for withholding the treatment.

### III.4. The health care team's perspective

For physicians or nurses, to act in the immediate best interest of an infant is relatively easy when this action is to alleviate pain and discomfort. However, to evaluate the child's future interests may be more difficult, or sometimes even impossible. The main difficulties arise when the health professionals do not share the value outlook of the parents, and do not know what the consequences of a treatment will actually mean in

terms of the infant's and the family's life (Brody 1981). Disagreement is most likely to occur in cases of severely ill infants, who may survive with a very poor quality of life (Spence 2000) and a court may be asked to resolve the dilemma (see cases of Baby K and *Re Eve*, below).

Several factors may influence the physicians' judgment of the best interest of their patients. I discuss some of them below.

**III.4.a. Compelling influences**

Agreement between the physicians caring for a patient is the crucial condition for the initiation of discussion with the parents. Only when all the parties agree upon the goal to be achieved can there be an agreement about the beneficial or nonbeneficial nature of a medical intervention. As I mentioned above, when the judgment of the physicians differs from that of the parents, the parents' *prima facie* right prevails. Nonetheless, in particular cases, physicians may initiate an action to override the parental decision. These can be cases of infants who are "irreversibly comatose" or born dying, or when the pain and suffering does not balance with a likelihood of success, and the ratio between burdens and benefits approaches infinity, yet parents wish full life-prolonging measures. In these and other (e.g. refusal of blood by Jehovah Witnesses) exceptional cases, physicians are expected to use their "reasonable medical judgment." Such a judgment precludes aggressive treatment of babies afflicted with conditions that are both incompatible with life and for which treatment might entail considerable suffering, (e.g., in cases of trisomy 13 and 18) (Ahronheim et al. 2000; Stevenson and Goldworth 1998).

When a physician decides that non-treatment is in the best interest of an infant, he or she has to explain the motives of the decision and communicate clearly the consequences of this option to the parents, who may or may not agree. However, in some cases, where

the prognosis is ambiguous and benefits of a treatment are unclear, physicians have to comply to parental wishes to initiate a treatment (Ahronheim et al. 2000; Churchill 1985) – and the prognosis for HLHS patients is often ambiguous. Therefore, a physician can face a conflict between preserving his or her professional integrity, on the one hand, and meeting the parental requirements on the other.

There are limited data in the literature on the effects that the parents' decisions have on physicians, when parents and physicians do not agree. If the court decides in favor of the parents, this too is an act of coercion that compels the physician to treat or not to treat against their professional judgment (Morreim 1994).

An example of the coercive influence of political trends on the physicians' decision is illustrated by the treatment of spina bifida in the 1960s in England. At that time, physicians felt morally forced to refer all infants born with this malformation for surgery, and many surgeons who did not agree with this policy felt that they had to operate for fear of public criticism. It would seem that the policy of universal treatment was initiated as the easiest way out of a dilemma rather than as the result of careful consideration of the infants' well being (Kuhse and Singer 1985).

Sometimes, the physician under legal, political, societal, cultural, and family influences may feel compelled to suggest a treatment against his or her own moral values. Thus, for example, the easiest decision for the physician could be to operate on all HLHS patients, independently of their physiological state, for fear of public criticism, or because of the physician's own compassion.

### III.4.a.i. Compassion

Medicine is based on compassion. But compassion, in Kant's theory, belongs to "imperfect duties" as opposed to "perfect duties" that are strict and determined. Thus, it is not sufficient in medicine to be compassionate. The "perfect duty" of physicians is to care for the patients' well being and to prevent unnecessary suffering. This means that physicians should not use life-sustaining technology to prolong life without thoughtful consideration of its other effects (Avery 1998). However, this principle may be difficult to apply in practice, resulting in over-extensive treatments with risks surpassing the benefits to the patient.

Dr. Nuland (1996) in his book 'How We Die' writes that the death of one of his patients would have been easier "without the added devastation of futile treatment and misguided concepts of "hope" that I had been reluctant to deny him and his family, as well as myself." Thus, it seems easy to hypothesize that life-sustaining technology should not be used to prolong life without thoughtful consideration of its other effects. It may be heart breaking for the physicians, the nurses, and the family, to give up on infants who seemed normal at birth. On the other hand, some caregivers could recognize the application of a treatment with unknown long-term outcome as inappropriate and inhumane.

### III.4.a.ii. Physician-researcher

On occasion, when a physician is also a researcher, his or her interest in the study may be a source of a conflict. The need for observation and data may push a physician, even subconsciously, to extend a course of care beyond the reasonable limits of benefit to the patient (Brody 1981). A dramatic example of the bias of a physician-researcher is the story of Dr. Steinschneider who in 1972, while carrying out a study on infants with sudden infant death syndrome (SIDS), did nothing to prevent the deaths of their siblings.

Twenty-two years later, his paper describing the theory on the origin of SIDS and its genetic nature was used as exhibit A in a murder case. During his studies, Dr. Steinschneider was insensitive to remarks made by nurses expressing their concerns about the mother-infant relationship. The mother [4] was convicted of smothering five of her children; two of them were Dr. Steinschneider's research subjects. On the witness stand, Dr. Steinschneider continued to promote his discredited theory, saying: "I wrote it, therefore, it's true." Before the trial, his theory received the recognition of *Science* (Marx 1975), "the bible of the American research establishment." Ironically, this case also marked the first time *Science* ever covered a murder case (Pinholster 1994, 1995).

**III.4.a.iii. Treatment under modification**

When a treatment is under modification and the physician in charge of the case is involved in the development of this treatment, there is a likelihood of conflicts of interests. Therefore, the infant's parents must be informed about the physician's dual role. In this situation, physicians must remember that the parents' decisions could be easily influenced by limiting or manipulating the disclosure of information on the infant's diagnosis and prognosis (Kimura 1986). To avoid bias, a physician who is not involved in the study should communicate the information about all expected risks, and possible benefits of the treatment under examination. The physician should compare all risks and benefits to those of other existing options or standard therapies, respecting the best interest of the child and the family (Lynch 1991). The physicians' obligation is to talk to the parents about the uncertainty of outcomes, and, if such exists, the possibility of impaired physical and psychological development, social isolation, or the child's dependence on others in the future.

It is the physician's role to assess the value of a treatment on the basis of his or her personal experience, the existing literature, or the experience of others. He or she has to determine whether it is appropriate to recommend a not yet fully proven therapy for a particular patient. On the basis of this knowledge, he or she must establish a favorable balance between risks and benefits to justify the discussion of the treatment with the parents.

When existing experience does not offer firm guidance, there is a significant potential for disagreement concerning the treatment strategy between physicians managing the patient. When such disagreement exists, it evokes additional ethical issues in the relationships among the physicians and in their relationships with the parents. For example, in the case of treatment of HLHS patients, an interview of a group of American neonatologists and pediatric cardiologists showed that more neonatologists recommended palliative surgery than did pediatric cardiologists, despite the fact that the latter were more optimistic than the neonatologists were in their perceptions of the patients' quality of life after the treatment. On the other hand, both groups of specialists agreed that exclusive comfort care is not usually discussed, whereas both surgical options (palliative surgery and cardiac transplantation) are discussed nearly always (Cooper et al., 1999).

### III.5. Summary

The best interest standard is patient-centered, focusing on the present and future interests of the infant. The standard allows comparison of the benefits of existing options for the infant, weighing the relative importance of the various interests they fulfill or ignore. The caring approach reduces the significance of the interests of other parties involved in the decision making. The growing experience and legal authorities emphasize the central value of the child-focused best interest and dictate moral standards for all those involved in the decision-making.

The evaluation of the infants' best interests by physicians relies on the standards of their profession. On the bases of the risks-to-benefits ratio, they may recommend or disapprove of a treatment, and the parents may choose between existing options, unless in particular cases, legal authorities expel their *prima facie* right. The decisions must be approached with extreme caution in individual cases because a treatment that would benefit the patient in the short term may not necessarily be in his or her future best interests; other options may have greater benefits, with less cost to the patient in suffering and disability.

### III.6. Quality of life

When difficulties arise in determining the objectives of care for incompetent patients, a quality of life judgment follows the best interest judgment as an important component of the ethical analyses. This judgment is particularly important when new and innovative techniques, or non-treatment are discussed. According to Campbell and McHaffie (1995), the quality of life judgment allows the consideration of "the least detrimental of several burdensome treatments when it becomes apparent that none will be of real benefit."

There is no simple method for evaluating the quality of life of incompetent adult patients and infants, and perceptions of quality of life change with personal background and with the standard of living of a given individual. It is a person's own sense of well being as derived from the whole life experience (Campbell 1976).

Because of the existence of these potential conflicts in the evaluation of the quality of life, Ramsey (1978) supported decisions made on the basis of quality of life only for competent patients. He argued that the only way to be sure of protecting the rights of incompetent patients is to use life-prolonging therapy, unless the patient would die with or without the therapy. However, this argument introduces an additional judgment, that is, the futility of a treatment, and the definition of futility is vague.[5]

To make the interpretation of the quality of life judgment simpler, Singer (1987) has tried to introduce the principle of a quality-adjusted year of life (QAYL), which compares the quality of life that is maintained by a treatment with a possibility of life in normal health. The aim of this method was to establish how much it costs a patient in pain and suffering to gain one year of life for this patient, using a given treatment. If the outcome of the treatment is so unfavorable that a patient would like to exchange one year

of life after the treatment for just six months of life in normal health, the prolongation of the patient's life is rated as 0.5 QAYL. Thus, probability of a bad outcome decreases the QAYL ratio. This test may be more sensitive than the "simple" quality-of-life test, but it has not been used frequently in practice.

Pearlman and Jonsen (1985) stated that a "quality of life judgment represents an evaluation by an onlooker of another's life situation." Being unable to make a proper evaluation of the quality of life of an infant, the infant may be forced to endure a treatment which, if competent, he would boldly reject (Brody 1981). Still, it is unavoidable to consider quality of life judgments in the absence of the patient's directives. Even a decision to extend the life of a dying person, based on the belief of sanctity of life, does not escape from quality of life judgments. In contrast, focusing on the patients' basic interests respects the continuing of human life, though it does not go as far as the sanctity of life notion requires (Ahronheim et al. 2000). Therefore, in individual cases, the quality of life judgment may bear a lesser value than the best interest standard has.

Fox (1987), discussing the status of elderly patients, makes a distinction between "quality of life" and "life." Quality of life, means living, and involves the ability to reason, to choose, to communicate and to interact with others. If a patient is deprived of some of these attributes, it is not sufficient reason for not protecting his rights. The ability to 'live' must be supported, regardless of the age and circumstances. In contrast, "life" implies a vegetative existence, and in these patients, there is no justification for artificially maintaining life. A similar meaning of "quality of life" and "life" can apply to newborns, when we recognize their potential to develop into an interacting and reasoning entity.

For infants, parents have the *prima facie* right and are in the best position to make judgments about their child's quality of life. Their judgment is based on standards they have accepted for themselves (Blustein 1988). Decisions made by others may not be child-centered decisions. Instead, children could be used to serve a larger political agenda, as in the Baby Doe debate, in which activists felt morally justified to override parental decisions for their political interests (Groding et al. 1990; Marcia et al. 1986).

In Canada's heterogeneous society, the tendency to measure quality of life in terms of the values of health professionals may be seriously misleading. For example, suffering for a devout Christian patient could have an important meaning of martyrdom, the reward of which is union with God in Heaven. For the advocates of active euthanasia, physical pain, existential or spiritual suffering have no other meaning than pain that can justifiably be terminated by killing the patient. Therefore, prior to making any decision for the patient, a physician has to deeply understand and appreciate the patient's cultural background, and personal circumstances (Evans 1987). Before this understanding can be achieved, no treatment should be denied because others may decide that the patient has a poor quality of life (Fox 1987).

Given the difficulties encountered in making accurate predictions about the future development of infants, decisions based on quality of life should be extremely cautious, and must be based on each individual case. The long-term perspective for the infants further complicates evaluation of their quality of life. For some parents, the infant's potential capacity to interact with its surroundings and people in a way that is more than merely vegetative, could be a suitable criterion (Spence 2000). For other parents, this limited interaction would be unbearable. The assessment of quality of life to which a patient, if competent, may look forward to has been a difficult issue in medical ethics.

The issue may be further complicated by the difficulty in making a distinction between comparative and noncomparative quality of life judgments (Ahronheim et al. 2000).

The comparative judgment assesses the subjective character of one person's life against that of another; it reflects social worth or interpersonal values, and takes into account the interests of the patient's society, including his family, health care team, or society on the larger scale. For instance, a physician may impose his understanding of quality of life on the parents if he suggests a treatment that could offer the kind of life that he would want for himself or his family (Spence 2000).[6] Differences between the physician's and the parents' assessment of quality of life may represent a significant barrier in their communication. The bias and discrimination present when the social worth criteria are introduced may negatively affect the physician's dedication to the patient's welfare.

The comparative judgment employs a utilitarian criterion in considering a person's potential future contribution to society. In the extreme, a morally unacceptable conclusion could be that a poor child has less social worth than a wealthy one. In relation to a rational potential, McCormick wrote (1974), "life is a value to be preserved only insofar as it contains some potentiality for human relationships."

The noncomparative judgment allows one to consider the infant's pain and to focus on the well being of the child as an individual with his own interests, rather than what the child will be able to do for society (Blustein 1988). The noncomparative judgment rates the value of that person's life to that person only, and is directed toward determining what kind of life the patient would choose, were he competent. The noncomparative judgment is the most ethically relevant consideration: it judges the value of life for the patient himself and not for society (Arras 1984).

The noncomparative quality of life judgment is of great importance because an infant is incapable of understanding what pain might be worth bearing for what possible benefits. On the other hand, if a decision on a treatment is made, the patient's inability to realize what was being done to him may cause more significant pain and suffering than for a capable patient in the same situation (Buchanan and Brock 1989). Therefore, in some cases, a noncomparative analysis, based on the ethical principle of nonmaleficence, may lead to a conclusion that non-treatment should be considered as an option (Ahronheim et al. 2000).

Despite the difficulties involved, quality of life judgments are unavoidable, although they might be concealed, because whether life would be worth living for the patient depends upon the length and the nature of an extended life (Buchanan and Brock 1989). For instance, a treatment that prolongs a patient's life could be harmful unless a favorable balance exists between simple pleasures, and pain and discomfort in the prolonged life. The evaluation of the quality of prolonged life bears greater importance for infants than for adults. Infants have their whole lives ahead of them, while adults may be approaching their physiological life span maximum. In general, children's well being depends less on their current individual preferences and more on the objective conditions necessary to foster their development and opportunities than does the well-being of adults (Buchanan and Brock 1989).

Alhtough it is recognized that the judgment is an important element of the decisions on non-treatment, in practice, a quality of life judgment is not necessarily always included in the decisions about nontreatment of infants. A survey of physicians showed that it was discussed only in 51% of nontreatment, and only in 23% of these cases was quality of life considered to be the major issue (Wall and Partridge 1997). The

results of the survey may reflect that quality of life judgments are often hidden under consideration of the best interests of the child or the family (Kuhse and Singer 1985). For example, the conclusion that prolongation of the dying process is not beneficial for an infant contains a judgment that a treatment would not benefit the infant. Thus, this decision also incorporates the nature and quality of the patient's life (Rhoden 1985). Furthermore, physicians often avoid the quality of life judgment and replace it by "reasonable medical judgement" in discussions of whether or not to treat.

### III.7. Summary

A noncomparative judgment of the quality of life is a necessary and important factor in ethical decision-making for infants. However, when considering a new treatment, it may be difficult to make noncomparative judgments. For example, infants with HLHS undergo a complex course of three consecutive open-heart surgeries with unknown long-term survival and quality of life concerning their cognitive and physical potentials. With unknown long term outcomes and variable survival rates, it is difficult to determine whether or not the burden of surgical palliation outweighs the predictable benefits to the infant in his or her prolonged life. Therefore, the assessment of quality of life of HLHS patients cannot be in terms of its value to these patients without making a comparison to anyone else.[7]

### III. 8. Court decisions

In certain instances, it is a court that makes treatment decisions for children. The court decisions in the protection of the children's best interest and quality of life are illustrated by the following two cases.

In the first example, *Re B* case, parents refused consent to surgery for their infant with Downs' syndrome and a blockage of the intestine. The British High Court ruled that the parents' decision should be respected. The Court of Appeal reversed this ruling and ordered the surgery to be performed, on the basis that it was in the best interest of the child. Nonetheless, the court agreed that there might be other circumstances when "the life of [the] child is demonstrably going to be so awful that, in effect, the child must be condemned to die" (in Singer, 1996).

The second case, (*Re J*) - a prematurely born infant with brain damage, was a ward of the court. At five months of age his breathing still had to be supported with a ventilator, and he was paralyzed, blind and deaf. The British High Court decision was not to put the infant back on the ventilator if he stopped breathing. The case went to the Court of Appeal, which rejected the view of the caregivers that life must be preserved irrespective of its quality, upheld this ruling and agreed that the paramount consideration was the child's best interest (in Singer, 1996).

The rights of parents as their children's guardians were reinforced following the *Otis Bowen v American Hospital Association et al* case, in 1986. The US Supreme Court criticized the Baby Doe regulations which ignored the role of parental consent in the medical care of infants. The court decided that conditions such as multiple handicaps or extreme prematurity might legitimately be used as grounds for non-treatment. The court also allowed parents to choose non-treatment where that decision had been an informed

one and made in the best interest of the infant. Furthermore, the legislation specified conditions in which treatment was not required. These included infants in irreversible coma, treatment that would 'merely prolong dying', and treatment that 'would be virtually futile' in terms of the survival of the infant. The court stated that treatment itself under such circumstances would be inhumane (in Singer, 1996).

The importance of the parents' wishes in the decision to treat or not to treat is illustrated in several court cases. For example, in the American case of Baby K, an anencephalic born in 1992, was still alive four years later because her mother had insisted, against the recommendations by physicians, ethics committees, and even national professional bodies, that everything should be done to keep the baby alive (Annas, 1994; Avery, 1998). The hospital physicians regarded treatment (occasional mechanical ventilation) as inappropriate. The hospital ethics committee agreed that medical treatment was futile and should be terminated. The mother, acting on the basis of a firm Christian faith that all life should be protected, refused to give her consent to the withdrawal of treatment. The hospital looked for a court's help. However, the District Court and then the US Court of Appeal ordered that treatment must be continued. This ruling was met with the disagreement of many physicians who objected to the unlimited authority given to parents to demand care that is beyond the standards of their profession.

On the other hand, some court decisions may set some limitations on parental authority. For example, in *Re Eve* case, the Canadian Supreme court decided that the best interest of an incompetent individual must be protected, disregarding inconvenience and even the hardship for others. The court decided that, the parent's *prima facie* right must be exercised in accordance with its underlying best interest standard that protects those who cannot care for themselves, and not others.

## III.9. Footnotes

1. The Canadian Charter of Rigths and Freedoms:
12. Everyone has the right not to be subjected to any cruel and unusual treatment or punishment.
15.(1) Every individual is equal before and under the law and has the right to the equal protection and equal benefit of the law without discrimination based on race, national or ethnic origin, colour, religion, sex,age or mental or physical disability.

2. According to Kant's theory of autonomy, moral agents are those who can formulate and appreciate their duties, and can recognize the respect to which all moral agents are entitled as autonomous individual (in Ahronheim et al. 2000).

3. Their approach was based on a theory that a ventricle is not needed for pulmonary circulation. They first examined this hypothesis on experimental animals, which all died within 30-60 minutes after the procedure. Nevertheless, they concluded that "because of the desperate nature of the hypoplastic left heart syndrome and lack of useful palliative or corrective operation, clinical trial of this procedure seems warranted" (Knott and Doty 1977).

4. Firstman and Talan described the story in a book "The Death of Innocents, A True Story of Murder, Medicine, and High-Stake Science," Bantam Books 1998.

5. The concept of futile treatment is a source of controversy because of the many uses to which the term futility has been put, and different understanding of this term when used by physicians, judges, or parents. Only a few believe that futility can be determined objectively. Youngner (1988) proposed that a treatment is futile if it offers no physiological benefit to the patient, fails to postpone death or to extend life, does not improve quality of life, and if the probability of achieving a specific goal is below some statistical norm that is arbitrarily elected. However, what the physician judges to be of no benefit for the infant, might be perceived to be of value by the parents. Thus, the slightest probability of a success may trigger hope and can also provoke a disagreement based on differences in the perceived value of the outcome (Truog et al. 1992).

6. Interestingly, physicians' evaluations of the quality of life of their patients are often lower than those reported by their patients' (Spence 2000).

7. Mahle et al. (2000b) discussed long-term outcomes of HLHS patients in the light of those who had the Fontan procedure for other forms of single ventricle; there was a continuing risk for late death 10-20 years after surgery.

# IV. Coming to a decision

# IV. Coming to a Decision

The goal of my analysis was to find answers to three questions:

1. Are the burdens inherent to the treatments of hypoplastic left heart syndrome in balance with the potential benefits for the child?
2. Should non-treatment be an option?
3. What information should be given to the parents and what should be the process of the decision-making for infants with hypoplastic left heart syndrome?

## IV.1. Evaluation of the burdens-to-benefits ratio for HLHS patients

### IV.1.a. Treatment option

There is a long list of burdens inherent to open heart surgery, and the survival rates after each stage of palliation vary between institutions. However, in more recent years, in centers specializing in palliative surgery and with larger numbers of operated infants, the hospital survival rates may exceed 80% after each stage of palliation (e.g. Bove 1998, 1999). With increasing experience and modifications of surgical, anesthetic, and intensive care techniques, it can be expected that the survival rates will improve further over time.

The risks of open heart surgery include excessive bleeding, embolic brain lesions, intracranial hemorrhage, or incidents of stroke or brain injury. Infants may experience seizures during and after surgery. Postoperative seizures may be associated with unfavorable outcomes such as abnormal neurological examinations, diminished mental development, and lower scores in several areas of function as compared to a reference group (Goldberg et al. 2000; Williams et al. 2000).

A circulatory arrest and hypothermia period for over 50 minutes is an important risk factor for hospital mortality, and for survivors, the risk for neurobehavioral abnormalities increases with each additional minute after 26 minutes (Limperopoulos et al. 2000). However, a circulatory arrest and hypothermia period of up to 67 minutes may be necessary for a recently modified first stage procedure (Poirier et al. 2000).

The postoperative period after each stage of palliative surgery is challenging for the infants mostly because of their unstable cardiovascular physiology and sedation requirements. There are a number of additional concerns. Bleeding complications may develop. There may be heart and other organ failure, hemidiaphragmatic paralysis, necrotizing enterocolitis or mensenteric ischemia, all with possibly fatal consequences. Survivors of the first stage may need several additional palliative surgical procedures, or other surgeries, between the stages, neither of which are free of risks. Some infants may require implantation of a permanent pacemaker, or plication of the diaphragm, while others may need mechanical ventilation or ECMO - all interventions that increase the risks associated with the infants' survival.

The operative risks for HLHS patients increase with each stage of palliative surgery, and the first stage has the highest hospital mortality rate. Once surgery is initiated, the infants and their parents are committed to multiple procedures, and sometimes, invasive diagnostic examinations, before full palliation is completed.[1] The survivors may continue to be on medication and may be expected to require frequent hospital visits. The slow time course of palliation may impair the emotional and physical health of the patient and his or her parents, as well as the rest of the family.

Despite the numerous inherent risks and the need for three complex operations, the first stage palliation alone offers a chance for longer life, the most important gift, to

infants who otherwise would die during their first month after birth. From the perspective of decision makers, survival alone may not satisfy the infants' best interest standard. In contrast, for an infant, who has no means of comparison, life alone might be sufficient to satisfy his or her best interest (Arras 1984).

The first stage of palliation is usually performed within the first 14-30 days of the patients' life. At that age, infants are not aware of their future existence. The next two stages of palliation are usually completed during the first 2 years of life, and the chance for hospital survival increases with each stage. During this period of time, infants have an opportunity to experience love and compassion, and may become attached to their parents and the health care team. They are cared for, kept warm and fed, and hopefully free of pain. Finally, they have a possibility to grow and develop into an independent individual. Without the treatment, these chances would not exist.

Unfortunately, the chance of long-term survival decreases with each year of life. The cumulative rate for a 10-year survival could be as low as 16% (based on data presented by Mahle et al. 2000b). Fortunately, the survival rates may be higher for the majority of HLHS patients who are free of other accompanying vascular and non-cardiac anomalies, and who are operated upon during the first 2 to 4 weeks of life (standard risk group, Bove 1998). However, older infants, and those who present with other congenital diseases and unstable preoperative physiology, have a significantly decreased chance for survival (high risk group, Bove 1998). Finally, all survivors may develop atrial arrhythmia, thromboembolic complications or protein-losing enteropathy, all with possibility of fatal consequences.

Infants in the high risk group may have abnormal karyotype (Turner's syndrome, duplication of the short arm of chromosome 12, trisomy 18, and chromosomy 21), or

malformation of major organs and of the central nervous system. The great majority (80%) of these infants die within a year after the first stage surgery (Bove 1998). Those who survive, have significant medical problems that compromise their quality of life (Reis et al. 1999). Therefore, for these infants, the burdens of surgery and of the postoperative period, and the suffering caused by non-cardiac abnormalities may outweigh benefits of their short-lived life, and non-treatment might be the only option meeting their best interest. This choice will be justified on the basis of the principle, "do not do unnecessary harm." Thus, it would be permissible to let the infant die, while respecting the moral value of the infant and the duty of the physician, if the infant's continued life is expected to be brief and marked by pain and discomfort (Jonsen et al. 1975).

Some parents would accept a short-term survival as being in the best interest of their child. Others may expect a treatment to guarantee that their infant will live, not for months, but for years, or decades of years, so that he or she may become an adult with a sufficient quality of life that the parents assumed for themselves as adequate. From their perspective, a surgery that cannot meet their expectations may be too harmful for the child. Unfortunately, there are limited data on the length and quality of life of the survivors, and the existing reports are inconsistent.

There is a report on a small number of 15-year old survivors (39%) of staged palliation, but their physiological and mental health has not been described (Mahle et al. 2000b). Other data on long-term survival show that patients with HLHS may have a probability of survival to school age of less than 50%, and that at least 50% of the survivors may have mental or physical handicaps of varying degree, including mental retardation, microcephaly, cerebral palsy, functional disabilities, growth failure, and gross

motor delays (Bove 1998; Mahle et al. 2000a; Rogers et al. 1995; Williams, et al. 2000). In a group of infants with HLHS studied by Mahle et al. (2000a), 34% required some degree of special education.

A study of Williams et al. (2000) gave additional details on the development of survivors following each stage of palliation. However, they confess their study has an important flaw. Different patients were studied immediately after surgery and later in life, nor were the same children evaluated following each step of the three stage palliation; therefore, the longitudinal assessments of quality of life of these children is missing. Thus, at the present time, it is impossible to adequately explore time trends in HLHS patients after palliation. Nevertheless, on the basis of their observation, Williams et al. (2000) concluded, "HLHS patients have developmental setbacks that may be related to the circulatory compromise during the procedures. In the area of quality of life, patients achieved levels that are below standard normal populations."

The uncertainties and the wide variability on reported short- and long-term survival rates and outcomes do not provide a clear basis for ethical decisions regarding surgical treatment for HLHS patients. More data on survival, developmental status, and quality of life of the HLHS patients would diminish the presently existing controversy and uncertainty regarding optional treatment strategies (Williams et al. 2000). Nevertheless, the available information on survivors may encourage treatment of the infants who, on the basis of clinical evaluation, could be expected to have the best outcomes.

The surgical technique undergoes constant modifications offering the prospect of better outcomes. New knowledge is being gained allowing better evaluation of quality of life of the long-term survivors of palliative surgery. The new knowledge will, hopefully,

provide a basis for the recognition of palliation as a standard treatment for the HLHS patients in the future. Until then, the favorable balance between risks and benefits might be likely only for some infants in the standard risk group, who are operated early after birth, and who live in close proximity to medical centers with the well-established surgical technique and medical teams (Rogers 2000). Nevertheless, about 20% of these children still presented mental retardation (Mahle et al. 2000a). These patients have the best chance for long-term survival with a satisfactory quality of life. Therefore, only for these infants the three stage palliation might be morally justified. Treatment of other infants may merely delay death and prolong their suffering.

**IV.1.b. Non-treatment option**

As I discussed in Chapter III, the best interest standard would not always mean continued existence. If the burdens of surgery were insignificant, then survival free of pain would seem to be the morally relevant consideration even when the child has a prospect of a short life. However, an open heart surgery is a long-lasting and complex procedure with a high probability of various adverse consequences and, sometimes, a prolonged recovery in the intensive care unit. In fact, a HLHS patient is subjected to three open heart surgeries, with possible supplementary surgical interventions in-between, before palliation is accomplished. Therefore, evaluation of the quality of life of survivors is exceptionally important in balancing risks against benefits for these patients.

Despite the existence of data showing that infants in the standard risk group have better chances for a satisfactory outcome than those in the high risk group, the option of non-treatment should be open to all patients. Positive outcomes, which greatly depend on the duration of hypothermia and circulatory arrest, are difficult to predict before surgery is initiated (Limperopoulos et al., 2000). It is possible that even infants in the standard

risk group can have unfavorable outcomes, if the circulatory arrest exceeds a critical duration.

All patients are exposed to the same surgical risks and suffering related to the treatment. An important difference between these two groups of patients is their preoperative physiological condition. Patients who have mental or physical handicaps may be limited in their capacity to develop human relationships even when they survive surgery. Their suffering may be magnified by their non-cardiac disorders. Therefore, their future best interests may never be fulfilled; the complexity of their burdens may outweigh their benefits. Therefore, for those infants, palliative surgery might not be morally required.

The uncertainty of the outcomes on the one hand, and the well-known and multiple risks of palliative surgery on the other, does not allow one to conclude that the treatment of the HLHS should be obligatory, even for the standard risk patients. Therefore, the non-treatment option should be oferred to all HLHS patients, and the final decision should be cautiously considered on an individual basis.

## IV.2. Summary

An infant with HLHS will die within the first month of life if not surgically treated. Sometimes, the process of dying may unexpectedly take a longer time. Some may argue that letting a baby die is not different from killing this infant in that both omission and commission cause death, and both compromise the principle of the sanctity of human life (Harris 1981; Kuhse and Singer 1985; Orlowski et al. 1992). However, in some cases the burden-to-benefit ratio could be too low to justify the treatment. For this reason, despite the increasing pressure on physicians to recommend, and on parents to choose a treatment for HLHS, basic medical care remains an option in several centers (Brackley et al. 2000; Cohen and Allen 1997; O'Kelly and Bove 1997), including at least one in Edmonton, Alberta (Osiovich et al. 2000). However, in light of continued improvement of surgical palliation, some may consider non-treatment as an unjustified option for the HLHS patients. Such an opinion might be justified on the basis of high rates of survival in centers specialized in palliative surgery and better outcomes, where patients, or pregnant mothers who have opted for surgery, are sent from larger geographical areas. In these centers the majority of parents have previously decided on treatment. In other hospitals, parents should be free to decide on treatment, non-treatment, or a transfer to other centers with a well-established surgical technique and medical team. From a physician's perspective, in some cases the parents' decision may collide with the medical principle not to cause any unnecessary suffering for the infant. Sometimes, physicians may resolve this problem by referring the patient to another specialist; in other situations, the solution may not be so simple (e.g. geographical isolation).

For HLHS patients, existing technology cannot assure the expected long-term outcomes. These children live with a three chambered heart after the three stage palliative

surgery. Therefore, ethical decisions involve dilemmas related to long-term outcomes that are still unknown in many cases (Tong et al. 1998). Consequently, answering the second question of this thesis, the above analysis led me to conclude that non-treatment should be presented to the parents as an option for all infants with HLHS.

The answer to the third question requires a discussion of the decision-making process.

### IV.3. Decision-making process

#### IV.3.a. Determining the infant's best interest

The decision-making process may be facilitated when prenatal diagnosis of HLHS is available. The screening procedure has become a routine evaluation of the fetal heart at 16-24 weeks of gestation. Some centers perform basic karyotype studies and ultrasonography of the head and abdomen of newborns with suspected HLHS to exclude associated extracardiac and chromosomal defects; if any defects or abnormalities are present, palliative surgery is not encouraged, and parents most often agree (Bando et al. 1996).

The availability of prenatal diagnosis gives the parents an additional choice but also an additional dilemma. Firstly, the diagnosis determined on the basis of utrasonographic images may not always be confirmed after birth (Boyd et al. 1998). Secondly, there is a 30% probability for the infant to be stillborn (Crawford et al. 1988). Both possibilities should be clearly presented to the parents. Thirdly, prenatal diagnosis opens an option of abortion that the parents need to take under their consideration.[2] Some parents might decide to terminate the pregnancy before their friends and family become aware of the bad prognosis. Other parents would like to have all available information, but might decide against abortion and opt for basic medical care only.

When a mother decides against abortion, and comfort care is not her choice, she may be transferred before delivery to a center specializing in surgical treatment of HLHS to optimize chances of neonatal survival (Busken et al. 1997). However, the effects of such management of affected pregnancies on the newborn's survival are still unclear (Brackley et al. 2000; Kumar et al. 1999). Nevertheless, when diagnosis is made before the infant is born, the parents are allowed some time to adapt to the unfavorable

diagnosis. They may be able to assure themselves about the correctness of their choice of the newborn's management, having the time to carefully take into account information on the possible risks of surgery and its uncertain outcomes.

The long-term outcomes of the palliative surgery may include a lifetime of specialized cardiac care, frequent physician visits, daily medication, and multiple cardiac catheterizations. Risks involved in open heart surgery, and the uncertainties about the duration and quality of life of the HLHS patients, and the long-term prospect of specialized cardiac care, should be communicated to parents during the decision-making process. The health care professionals should keep in mind that many parents will gladly clutch at any offered treatment. They want to believe that their infant will be among those who develop normally. Therefore, all available information on outcomes after surgery for HLHS should be discussed between physicians and parents. Only then will parents be able to make informed decisions about the probability of benefits for their infants and their families. Physicians should make it clear that their information comes from the literature, and that published reports may be biased toward the reporting of favorable outcomes, because most of the data in the literature includes cases from university hospitals, large children's hospitals and centers specializing in many aspects of surgical treatments of different congenital heart defects, especially HLHS (Bove 1999; Gutgesell et al. 1995).

Parents should be informed clearly about treatment and non-treatment options, and the survival rates after palliative surgery in a particular hospital, as well as that in other centers with possibly better outcomes. The physician should be responsible for presenting the option of transferring the infant to another center, including the risks involved. On the basis of this information, the parents will be free to decide for or against the transfer. However, in some situations, there might be medical, psychological, or social

reasons against such a transfer. This difficulty may create a new dilemma, but the information should not be withheld. In all situations when a treatment is not given, the physician must consider the ethical principles of minimizing harm, and maximizing beneficence, justice, and the infants' best interest in particular, as they apply to the individual situations (Lynch 1991).

The choice of treatment strategy requires full information regarding the procedure, and recent modifications. Parents should be informed about the multifactorial etiology of neurologic morbidity that includes preoperative, intraoperative, and postoperative issues. Full disclosure of these issues will help parents to understand the severity of the HLHS, and they might not demand that physicians do everything in their power to save their baby's life (see study of Vandvik and Forde 2000). The ethics of such a decision is discussed further below.

A medical decision for infants born with HLHS has to be undertaken relatively quickly (during the first 2 to 4 weeks of life) after the diagnosis is made, because early surgery is essential to maximize survival and minimize long term adverse effects related to the disease (Bove 1998; Mahle et al. 2000b). However, it is fundamental that the parents be allowed some time before the decision-making process is initiated. They should have a chance to "live through" the bad news. Contemporary routine practice of prostaglandin $E_1$ infusion in neonatal intensive care units gives the parents this chance. Therefore, the parents may have the necessary time to reach an understanding and acceptance of the situation and they may initiate a discussion of the information given with the rest of the family.

Other family members and nurses, not just parents and physicians, should take part in the discussions regarding treatment. Everyone's judgments is based on their own

life experiences. The family's opinion incorporates the judgment of what is good for the neonate as part of the family. Perception of pain is very subjective, and what one person considers endurable, another may find overwhelming. Nurses who are caring for the infant in the intensive care unit can evaluate the infant's best interests from their perspective on the infant's behavior during the postoperative period. Their unique understanding of infants' reactions to pain and discomfort is crucial for maintaining the caring approach (i.e., do not cause unnecessary harm) rather than the curing approach in medical ethics.

Physicians involved in the decision-making process should evaluate each infant individually, as the most important factor affecting survival and outcome following surgical treatment is the newborn's developmental status and accompanying abnormalities. Possible differences in the survival rates of different patients should be explained to the parents. Surgical treatment of infants with HLHS may prolong their dying process if the concomitant unfavorable physiological condition of the infant is not clearly recognized at the critical moment of decision-making. For this reason, some centers do not recommend surgery to HLHS patients with diseases of the central nervous system and those whose renal or hepatic dysfunction cannot be, at least partially, alleviated before the first stage palliation (Bove 1999; Kern et al. 1997; Starnes et al. 1992). On the other hand, demographic factors do not influence the survival rate after palliation (Barber et al. 1989) and should not be determinants in decision-making.

**IV.3.b. The psychological needs of parents**

The decision making process cannot be rushed, especially when a decision for non-treatment might be an option. The process should be honest, informative and based less on medical paternalism and more on informed parental involvement and empathy (Yu 1997).

When parents hesitate, they should be encouraged to support continued intensive care within safety limits, in the expectation that, during this time, they will be able to clarify their doubts and understand the discussed issues more clearly. The process of reaching an understanding and recognition of the consequences of treatment may take a long time, after which there may not be a possibility of reversing the previously undertaken decision. During this essential period of time, if necessary, consultation by a pediatric bioethics committee may be of great importance. Conversations between the parents, physicians and the bioethics committee may help to resolve disagreements, if such exist.

Parents, who often respond to the diagnosis of a congenital heart disease with guilt, blame, grief, and sometimes anger, may initially have difficulty understanding the information given to them by physicians. Physicians involved in the decision-making should consider such parental anxieties, the parents' perception of parenting and their doubts, and support open family communication (Riesch et al. 1997). These anxieties could be best understood in terms of psychological constructs, including 'defenses' such as 'denial' and 'splitting', 'repetition compulsion' and the need to 'work through' psychological barriers, so that the child's best interest is ultimately served. Parental reluctance may be a protective strategy against overwhelming fears and anxieties, which, if addressed, may transform their defensiveness to cooperation.

Remembering the vulnerability of the parents and understanding the sources of over- or non-compliance on their part, health professionals must be attentive to the possible consequences of their communication, which ought to be adapted on individual grounds. In this way, parents should be informed about the consequences of non-treatment as well as about treatment options. The time given to parents before they are expected to undertake a decision may be spent on counselling initiated by the health care

professionals. During this time, the neonatologists and cardiologists could continue to explain the infant's condition. Their counselling may help avoid the development of unrealistic fears on the one hand, and an over-optimistic outlook on the other (Menahem 1998). When the parents come out of their initial shock, they may be provided with further details of diagnosis and prognosis. They should know that surgery may be life saving. However, they should also know that the quality of life of surgically treated HLHS patients is not well documented, and that the survival rates for longer than 10-15 years are very limited. Despite vulnerability and stress, these uncertainties should not be concealed from parents, as the majority of the parents expect their infants to develop into adult, independent persons.

Neonatal intensive care unit staff can help to minimize parental stress by providing information, support, and understanding to facilitate coping with uncertainty and fears. Support and information will help the parents to regain some of their confidence, which may be strengthened by involving the parents in the child's caregiving. The professionals should be alert to the questions and nonverbal communication of parents, to ascertain when communication may start and when it may be especially important (Shellabarger and Thompson 1993). Minimizing parental stress may have an important positive long term effects on the parent-child relationship.

Shellabarger and Thompson (1993) reported that, in the long run, negative experiences gained in the intensive care unit may create problems in the parent-child relationship, which may lead to subsequent difficulty in bonding or parenting, or may be related to child neglect and abuse. Parental frustration, guilt and disappointment may have similar consequences on the parent-child relationships (Arras 1984).

Parents' expectations as far as professional help in the decision-making is concerned may differ. Some parents wish the involvement of physicians and nurses and others do not. It is important for physicians and nurses to differentiate between these two groups of parents at an early stage and respect their wishes (Pinch and Spielman 1990).

Those who wished that health professionals be involved in the decision-making process reported that helpful courses of action were the encouragement of advanced planning, well-timed communication, clarification of the family's roles, facilitating family common consent, and accommodating the family's grief (Tilden et al. 1995). When discussions involved the family, a vast majority of parents were pleased with their decisions and "would do it again, if necessary" (Chiavarelli et al. 1993). In contrast, those parents who felt they were excluded from discussions and that the decision on their infant's treatment belonged to physicians only, or who felt that the burden of decision-making was placed on one parent, without family support, found decision making very stressful. When left alone, they were unable to cope with fear and uncertainty. Therefore, health care professionals should make it clear to the parents that they are ready to help, and endeavor not to force any opinion on them at this difficult time.

Physicians should not impose on the parents their own enthusiasm for palliative surgery despite their experience of success and witnessing of the joy of other parents whose children survived. Once surgical palliation is initiated, children are committed to multiple procedures and invasive diagnostic examinations. The decision for surgery, as well as the decision of no treatment, requires a substantial degree of emotional and physical stamina. Therefore, some families will cope better than others.

## IV.4. Summary

Infants with HLHS should be managed individually on the basis of cardiac morphology, physiological condition, and family wishes. Careful analysis of individual cases seems to be obligatory while physicians and parents act on their discretion. No legislation can determine action for all cases. Families who bear the consequences of their decisions should receive the necessary support from health care professionals, especially the physicians and nurses who participated in the decision-making process. Parents have to be assured that non-treatment is justifiable when those closely involved in the care of the infant unanimously judge the burdens to be excessive, without sufficient compensatory benefits for the child.

## IV.5. Footnotes

1. Parents have the right to withdraw from this commitment before the last stage surgery.

2. One may argue that if it is morally acceptable to perform abortions, it should be morally acceptable to kill newborn infants (Brody 1981). For instance, the diagnosis of HLHS in a 22-24 week old fetus often leads to abortion (Allan et al. 1998; Osiovich et al. 2000). Thus one may compare abortion that destroys an unwanted child with unknown or poor prospects of developing into a healthy adult to a decision of no treatment. The only difference is that abortion kills an unseen *fetus*, and withholding surgery allows an *infant* to die. Consequently, it may seem that birth in itself may not be of great moral importance as far as the status of fetus and newborn is concerned, but it does represent a transition from intrauterine to extrauterine life. Birth initiates a relationship between the mother and the rest of the family that is different from the relationship the mother had with her unborn child.

# V. Conclusions

## V. Conclusions

Since the initiation of the three stage palliative surgery in the late 1980s, the technique has sen constant modifications aimed at improving survival of the HLHS patients. Indeed, with each modification and with increasing experience, the hospital and long-term survival rates also started to increase. Only recently, some physicians began to evaluate the survivors' quality of life. However, during the last 10 years, about 25% of the papers on HLHS published in medical journals still concentrate on the survival rates after surgery, while less than 2% of these papers describe long term outcomes. Thus, presently, the emphasis on improving survival rates persists, while data on long term outcomes are still scanty, so that the risk-to-benefit ratio to HLHS patients remains uncertain. Nevertheless, staged palliation offers the benefit of life to infants who would otherwise die within one month after birth. The benefit of life may outweigh even severe potential risks of the surgery and of the postoperative period, at least for some patients. Nevertheless, uncertain outcomes of palliative surgery may explain why a considerable number of parents still choose to terminate the pregnancy, when HLHS is diagnosed prenatally, or, after birth, select basic medical care for these patients.

As long as the technique is being modified, long-term outcomes will not be well established, and as long as the mortality rates remain variable, palliative surgery should be considered as a treatment in the transition phase between a new, "hope for" innovative technique, and the standard of care.

Because the existing uncertainties about long-term outcomes prevent a carefull balancing of risks and benefits, management of HLHS patients may evoke a challenging decision-making process with parents and physicians. Ethical decisions for infants are

based on proxy evaluation of the best interest and quality of life principles. Both judgments reflect the life experiences of the decision makers. Therefore, when the parents decide, the physician may have to act against his or her own personal perception of the infant's best interest. However, they should never project onto the parents their enthusiasm about the treatment.

Parents in a state of shock, distressed and lost in grief, may not be able to immediately undertake an autonomous decision. Therefore, the discussion of the infant's management should not be rushed. The parents should be informed about the existing treatments as well as the non-treatment option, and what each option may imply for the infant, parents and the family. They should know the risks of open heart surgery and be aware of the limited data on long-term outcomes. When judging the future best interest of their child, parents should be informed about the possibility of both moderate and severe developmental disabilities in the survivors. They should also be informed about other centers with well-established surgical techniques and better survival rates and long-term outcomes, if such centers exist and the transfer is feasible.

For infants in the high risk group with a high probability of dying shortly after the first stage surgery, non-treatment could be the only option that can prevent their unnecessary pain and suffering. These are the HLHS patients with accompanying severe obstruction of pulmonary venous return, genetic syndromes, prematurity and low birth weight, or infants older than 1 month of age at the time of the first stage surgery. For these infants, non-treatment may be justified on the basis of a disproportionate burden-to-benefit ratio, and poor quality of prolonged life. On the contrary, non-treatment cannot be justified only on the basis of the burden imposed on the family, or that the care of an

infant after palliative surgery for HLHS will deprive other children in the family of parental love and attention.

For HLHS patients in the standard risk group, palliation offers a better chance for survival in a relatively good health. Nevertheless, because of the complexity of the procedure, three open heart surgeries, the risks, pain and discomfort during the postoperative periods on the one hand, and unkown long-term outcomes on the other, treatment should not be obligatory even for those infants.

Surgery in specialized centers may result in higher survival rates and better developmental and functional long-term outcomes. Therefore, treatment in these centers could help to achieve a more favorable risk-to-benefit ratio for the HLHS patients. However, it is impossible to create a general rule for treatment or non-treatment of these infants. Each case should be considered on an individual basis, and all factors that may affect the parental decision should be taken into account.

# VI. Bibliography

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