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## Case Report

### To Treat or Not To Treat: The Case of Methylmalonic Acidemia

Peter A Clark\* and Andrew T Myers

Department of Medical Ethics, Saint Joseph's University, Philadelphia, USA

#### Abstract

In a time when medical technology is advancing more rapidly than corresponding policy, additional neonates are the recipients of complex surgeries and other aggressive treatments in an attempt to extend life; nevertheless, in some cases, these treatments may not be in the neonates "best interests". Despite extensive literature detailing the complex pathophysiology of the recessive genetic condition Methylmalonic acidemia, no workable policy has been proposed to standardize treatment guidelines or offer recommendations to categorize who should receive aggressive treatment. In conjunction with the quality-of-life criteria proposed by Richard McCormick SJ, five diagnostic treatment categories have been developed by Peter Clark SJ, as a framework for complex decision-making in neonatal care. These two criteria will be used to categorize a case of a Palestinian neonate with isolated Methylmalonic Acidemia. After medical, legal, and cultural analyses are offered, it will be ultimately concluded that, in this specific case, should the medical staff and parents decide that aggressive treatment would not offer any medical benefit to their child, then it is not morally obligatory to pursue any additional treatments as they would cause excessive hardship to the neonate as extraordinary means of life-prolongation.

**Keywords:** Methylmalonic acidemia; Palestine; Quality-of-life; Tubulointerstitial nephritis

#### Introduction

Across the globe, neonatal medical care is becoming more accessible to mothers and their infants while advances in care technologies continue to extend the range of treatment options for medical professionals. For this reason, many newborns whose families can afford treatment are treated aggressively with new medical regimens, dynamic surgeries, and other life-prolonging measures. Among these neonates are many that, in the past, would not have survived past infancy due to complex medical complications such as genetic defects, premature births, low birth-weights, and other disadvantageous abnormalities. Judgments on who is to receive aggressive treatments have yet to be standardized with a widely accessible moral criterion, and as a result, many neonates with potentially lethal genetic disorders

\*Corresponding author: Peter A Clark, Department of Medical Ethics, Saint Joseph's University, Philadelphia, USA, Tel +610-660-3425; E-mail: pclark@sju.edu

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have been the recipients of such treatments. Previously, some of these neonates would have been allowed to die without aggressive treatment, but for some, to whom aggressive treatment has been given, success has been seen. For many others, however, the life-prolonging outcomes are in opposition to ethical, cultural, and moral analyses of the best interests of the neonates.

For this reason, there are conflicts when decisions need to be made about specific newborns with genetic disorders such as Methylmalonic Acidemia (MMA). Methylmalonic acidemia is a recessive genetic disorder in which there is a complete or partial deficiency of the enzyme Methylmalonyl-CoA mutase or a defect in the transport or synthesis of its cofactors which results in an increase of organic acids in the body when proteins are ingested. The organic acids overwhelm the neonate causing severe ketoacidosis, hypotonia, hyperammonemia, neutropenia, and thrombocytopenia [1]. MMA is a major concern in countries such as Palestine where immediate family members often marry and have children that inherit MMA at a much higher prevalence than neonates in western countries. The size of the local gene pool in countries such as Palestine is decreased when familial marriage occurs, which results in a higher inheritance rate of recessive disorders. Much research has been completed on MMA; however, literature is lacking a consensus on treatment protocols and has only fabricated recommendations specific to the condition but these do not account for cultural issues in Palestine.

Richard McCormick SJ a revised natural-law ethicist has developed a quality-of-life criterion that can be used to evaluate treatment options for neonates born with MMA. This criterion assumes a middle position that accounts for the best interests of the patients. Evolving from McCormick's criterion are Peter Clark's SJ five diagnostic treatment categories for neonates. These five categories along with McCormick's breakthrough moral criteria will be central to this article. Because MMA can manifest within the first days of life but also not present itself for months after birth, terminology surrounding patients must be clarified. The term neonate is applied to newborns for the first thirty days of life, and infant is used to describe young children typically under the age of one. Both terms will be used in this article although McCormick and Clark's criteria are specific to neonates. The aims of this article are to present the case of a Palestinian infant born with acute Methylmalonic acidemia, provide a medical analysis of this genetic anomaly along with legal, cultural, and ethical analyses, apply McCormick's criterion and Peter Clark's SJ five diagnostic treatment categories to this specific case of MMA, and consider cultural dispositions in order to generate a concise conclusion to aid decision-makers whether to treat or not to treat similar cases. Once McCormick's guidelines for determining the "best-interests" of never-competent patients are established, and the specific case of isolated MMA is classified into Peter Clark's fourth category, it will be reasoned that it is morally justifiable to forgo aggressive treatments in this specific case of MMA because they offer no benefit to the patient once she is integrally and adequately considered.

## Case Study

AH was a 2.5-kilogram infant born to Palestinian parents at Caritas Baby Hospital in Bethlehem. AH was delivered by cesarean section; her head circumference was 33 cm, length 46 cm, and Apgar score 7/9. As part of the normal newborn screening protocol at this state-of-the-art hospital, AH was tested for a variety of genetic disorders through a simple blood test. The lab report came back normal with no flags for any life-threatening conditions. The flag for Methylmalonic acidemia is the proportion of propionylcarnitine (C3) to acetylcarnitine (C2) in the blood. When over 0.40, results are abnormal and further testing must be conducted to affirm a positive MMA screening [2]. Baby AH's C3 ratio was 0.38, so she was at risk, but was not initially diagnosed with any inherited genetic abnormalities. Neither of AH's parents had previously undergone genetic counseling.

At the 48h mark, AH's metabolic parameters were measured. Urinary methylmalonic acid was determined to be 23 mmol/mol of creatine (n.v. 0-25), C3 concentration was 3.12  $\mu\text{mol/L}$  n.v.0.04-3.18 and C14 level was 0.43  $\mu\text{mol/L}$  n.v.0.05-0.53. AH's parents were elated at the birth of their first child. She was taken home and began breastfeeding. Although AH initially struggled with latching, she improved within the second week and began to show progressed weight gain at 14 days but still had low muscle tone. At day 22, however, AH woke up in the night vomiting, with limbs weak and a blue hue to her skin. At the hospital, AH was immediately put on a ventilator. Doctors ran a myriad of tests and the C3/C2 ratio came back at 0.98, a definite indicator of vitamin B12 deficiency and Methylmalonic acidemia. This crisis was severe; AH continued to seize, was hypoxic and her blood pH fell to 7.07, well below the normal level. AH's Glomerular Filtration Rate (GFR) was 45 mL/min per 1.73 m<sup>2</sup>, which was a strong indicator of renal failure [3].

Despite attempts to reverse the episode by administering intravenous L-Carnitine, Baby AH continued to require mechanical ventilation and 100% oxygen support at day 32. Her doctors diagnosed her with chronic tubulointerstitial nephritis caused by Methylmalonic acidemia and said she would require a kidney transplant to attempt to reverse the acidosis episode; they could not comment much on the benefits such treatment would have on improving AH's prognosis but said it may only add a relatively brief period to AH's life. They did explain that an alternative to aggressive treatment was removing AH from the ventilator and allowing natural death.

A difficult discussion considering aggressive medical treatment ensued between AH's parents, her pediatricians, and surgeons. Overwhelmed, AH's parents were confused during the discussion surrounding medical futility, prolongation of the dying process and ethical responsibilities. They were uncomfortable in the hospital and thought it was a place of dying. They wished there was some moral criteria to advance their knowledge so they could act in the best-interest of their daughter but were heard speaking to relatives saying: "If this is the will of Allah, we must not interfere". Doctors tried to explain that the struggle for AH's survival was entangled in medically futile treatments and that her potential for human relationships was compromised by her condition. Still, AH's parents struggled to come to any decisions and AH remained on the ventilator for an additional 25 days until she passed away at day 57.

## Medical Analysis

The isolated form of Methylmalonic Acidemia (MMA) is caused by mutations in vitamin B12-dependent Methylmalonyl-CoA mutase enzyme (MCM). This enzyme is encoded by the MUT gene in humans; over half of the mutations causing this disease are missense mutations meaning that the replacement of one nucleotide results in a codon that codes for the wrong amino acid. A complete or partial deficiency in apoenzyme MCM or diminished synthesis of its cofactor 5'-deoxyadenosylcobalamin causes an accumulation of metabolic amino acids originally destined for the Krebs cycle [1]. Pathophysiologically, valine, isoleucine, threonine, methionine, odd chain fatty acids, and cholesterol side chains enter the pathway and are typically broken down by a set of enzymes into succinyl-CoA, but when MCM or its cofactor are mutated, a buildup of esterified methionine occurs and methylmalonic acid is seen in the urine and blood of the individual [4]. In the event of acute MMA, this manifests itself as metabolic acidosis. The prevalence of MMA caused by MCM deficiency in Middle Eastern countries is 6 neonates per 10,000 births [5]. Compared to Western statistics, countries like Palestine see an estimated 60% more cases of MMA per 100,000 births [6]. Clinical symptoms and severity range from mild to life-threatening depending on the degree to which the pathway is inhibited. The earliest signs of MMA appear during the first week of life as the neonate presents with lethargy that progress to obtundation. Despite such early onset in most cases, it is possible for the infantile form of MMA to not display itself for up to a month [7]. Conditions secondary to MMA include intellectual disability, tubulointerstitial nephritis, pancreatitis, ketoacidosis, hypoglycemia, hepatomegaly, failure to thrive, seizures and spasticity [1].

The diagnosis of MMA is based on clinical assessment and newborn screening. However, in developing nations, the technology for newborn screenings is not widely available. A new approach to diagnosing MMA is analyzing organic acids in blood plasma and urine using mass spectrometry. An increase in blood propionylcarnitine (C3) indicates MMA in newborns [1]. Other assessments such as ammonia screenings, blood glucose and levels, cardiac stability, plasma amino acid tests, and increased cranial pressure and CT scans are more commonly used in hospitals outside of the United States since the technology necessary for these tests is more readily available than the newer approaches. Newborn screening results commonly are not returned fast enough, so clinical assessment is the primary tool for diagnosis.

The prognosis of MMA is varied and fluid. Depending on severity, life-expectancy and quality-of-life range from days to years. Overall mortality for isolated MMA has been reported at 50% with a median age of death of 2 years [1]. Upon diagnosis, the newborn's condition is immediately managed with high-glucose fluids, eliminating protein intake, administration of insulin, and stabilizing the acid imbalance in the blood. However, beyond severe decompensation episodes, treatment guidelines falter, and there is no consensus surrounding mandatory protocols. Early screening and aggressive treatment have improved the outlook for some patients; from data in the 1970s, survival rate past one year has increased from 65% to 90% in the 1990s [1]. Less severe forms of isolated MMA permit patients to grow into adulthood and lead relatively normal lives unaffected by MMA if symptoms are managed properly. Nonetheless, small missteps can still lead to significant acidosis episodes and possible death.

## Legal/Procedural Issues

With a broadened range of treatments available for previously incurable conditions comes a better chance of preserving neonatal life. More opportunities for maintaining life in the NICU inherently bring about more difficult decisions regarding which neonates should be treated. Before analyzing this dilemma, it first must be explained who will be making these decisions on behalf of the neonates. As never-competent human beings, neonates obviously can neither make judgments in their own best interest nor consent to any medical intervention. Legally, the neonates' parents are their health care representatives. The child's mother and father share equal responsibility and have equal decision-making power. Most bioethicists and medical professionals agree that it is the parents' responsibility to ultimately decide which medical treatment to pursue in the best-interest of their child, but this is almost impossible to do without a health care professional's assistance considering the high stakes and uncertainty involved [8]. Here, McCormick acknowledges ethicist Robert Weir's four criteria that a decision-maker should meet. These criteria have been outlined by Peter Clark, but will be further summarized for the sake of brevity in this article.

The four criteria are:

1. The proxy should have relevant knowledge and information [and] should be knowledgeable regarding the family setting.
2. The proxy should be impartial [and] should determine cases as objectively as possible.
3. The proxy should be emotionally well-equipped to make such treatment decisions.
4. There should be consistency in moral decision-making from case to case.

It appears difficult, if not impossible, for a single decision-maker to possess all four of these qualities. While parents may have relevant knowledge about their family setting, they most likely do not understand the prognosis to the extent of a pediatrician. Familial emotions are strained during situations such as these, and most parents have no experience with similar cases with which to compare or upon which to base decisions, so support must be provided by a third party to aid parents toward the morally-appropriate decision.

To assist in the legal and ethical decisions surrounding cases such as Methylmalonic acidemia, McCormick nominates four potential candidates. They are the neonate's parents, health care professionals, ethics or infant care review committees, and the courts. While each unit alone has its benefits and weaknesses, McCormick ultimately decides that it is the child's parents, partnered with the guidance and expertise of health care professionals, who are the appropriate decision-makers in most cases [8]. It is the role of the parents to protect their child; Peter Clark explains that parents and physicians alike are legally bound to pursue "what their child ought to want, that is, what is in their "best interest", normatively understood" [8]. Similar to the Christian tradition of the family being tightly bound and a fundamental unit of society, the Islamic faith holds that the family is the "cornerstone of a healthy and balanced society" [9]. Accordingly, only when there are doubts concerning the best-interests of the neonates or a conflict between parental wishes and physicians' medical advice should a review committee or the courts be called upon to intervene. It should be assumed that the parents' motives are always in the best-interest of the never-competent neonate; it is a last resort to

remove parents from a case and have the courts appoint a guardian *adli temas* an advocate. Now that the appropriate decision-makers have been described, cultural aspects will be appraised before applying an ethical analysis to the decision-making process.

## Cultural Issues in Palestine

The State of Palestine is located on the eastern side of the Mediterranean Sea and claims jurisdiction over the Gaza Strip and the West Bank of Israel. Palestine, like most of the Middle East, has been subject to war, conflict, geographical, and political disputes for the majority of its existence as a state. Without digressing into the religious and political conflicts, it should be noted that these disputes have taken their toll on the State of Palestine's health infrastructure. President Jimmy Carter addressed this issue in 1977 saying, "The health situation in the Occupied Palestinian Territories shows the urgency of finding a political solution, as restraints and insecurities continue to undermine the creation of a health infrastructure able to address the dire public-health needs of Palestinians" [10]. Due to the instability that continues in the year 2017, many neonatal medical conditions are left undiagnosed, misdiagnosed, or untreated. In addition to the barrier to healthcare posed by on-going conflict in the Middle East, the religious practices of many Palestinians obscure the typical approach a western physician may take towards medicine. 93% of Palestinians identify as Sunni Muslim [11]. The Sunni branch of Islam makes up 80% of the worldwide Muslim population [12]; special considerations during childbirth must be made to respect every religion.

Thus, care must be taken when applying a Catholic bioethic to cases of MMA in Palestine. Most Muslims strongly believe that their lives, and intrinsically their health, are controlled by the will of Allah; often, the phrase "Inshallah" is spoken meaning that the circumstance is "in Allah's hands" [13]. The hospital is commonly viewed with fear and negativity because there is a preconceived notion that it is a place of misfortune where people's lives end. Preventative care is infrequent in Palestine because society associates being healthy with being able to perform daily duties without complaint [14]; translating this to neonates, genetic testing is almost never pursued, and if the neonate does not appear abnormal, families typically continue life as normal.

When doctors are presented with a case similar to the aforementioned, they must consider the structural and familial roles in Palestine in order to avoid harming the neonate. Children in Palestinian culture are valued because they are a means to higher social status and provide security for familial heritage [14]. Fathers commonly value sons more so than daughters because they perpetuate the family name. Though no one would want to admit it, these social factors might play a role in determining aggressive treatment of newborns. The Islamic faith and culture in Palestine present some variables to the characteristic application of McCormick's moral criteria and Clark's treatment categories but none so confounding that the framework's model approach deteriorates. Next, the case study will be examined ethically using these two diagnostic tools to provide decision-makers a platform upon which they may standardize future decisions.

## Ethical Analysis

### McCormick's Criteria

McCormick will determine how treatment decisions are made for handicapped newborns by proposing his normative understanding of

best interests which evolves gradually into his quality-of-life criterion. This is a patient-centered, teleological assessment, which is based on a normative understanding of what reasonable persons ought to choose in a particular situation for the never-competent patient [15]<sup>1</sup>. It appears that McCormick's quality-of-life criterion is nothing more than a further specification of his normative understanding of "best interests" [16]<sup>2</sup>. McCormick has a normative understanding of "best interests" because, "as social beings, our good, our flourishing (therefore, our best interests) is inextricably bound up with the well-being of others" [15]<sup>3</sup>. The "best interests" category is a composite category that involves quality-of-life considerations, benefit-burden considerations, and the use of proportionate reason as a tool for establishing what is promotive or destructive for the good of the person integrally and adequately considered [17]<sup>4</sup>. McCormick understands "quality of life" to be an elusive term whose meaning varies according to context. However, at a more profound level, when the issue is preserving human life, the term assumes a more basic meaning. "Just as life itself is a condition for any other value or achievement, so certain characteristics of life are the conditions for the achievement of other values. We must distinguish between two sets of conditions: those that allow us to do things well, easily, comfortably, and efficiently, and those that allow us to do them at all" [18]. The quality-of-life criterion is ethically significant for parents and health care professionals because it represents not only the value of the whole person, but it affirms that respect for the human person entails considering all the relevant factors and circumstances that are involved in any situation.

There are real difficulties in trying to establish a perfectly rational criterion for making quality-of-life judgments. To make his quality-of-life criterion more concrete, McCormick will establish two guidelines and four norms that will further specify his criterion. The first guideline developed for dealing with never-competent patients focuses on the potential for human relationships associated with the infant's condition. By relational potential McCormick means "the hope that the infant will, in relative comfort, be able to experience our caring and love" [15]. Specifically, he proposes that "if a newborn baby had no potential for such relationships or if the potential would be totally submerged in the mere struggle to survive, then that baby had achieved its potential and further life-prolonging efforts were not mandatory, that is, would no longer be in the best interests of the baby" [19]. Therefore, according to this guideline, when a never-competent patient, even with treatment, will have no potential for human relationships, the appropriate decision-makers can decide to withhold treatment and allow the patient to die<sup>5</sup>. McCormick claims this quality-of-life approach has its foundation in the traditional ordinary-extraordinary means distinction that was later clarified by Pius XII [20]<sup>6</sup>. This is not an easy guideline to apply, especially in the case of never-competent patients. In essence, this guideline requires that the appropriate decision-makers must be able to determine if a minimally accepted "quality of life" can be expected. This determination ought to be made on the basis of the never-competent's "best interests" understood normatively. This guideline does not depreciate the value of the never-competent individual but affirms that a genuine respect for the person demands attention to the prospects held out by continued life [21]<sup>7</sup>.

This guideline of the potential for human relationships has been criticized for being too general and open to possible abuse [20,22]<sup>8</sup>. McCormick himself stated when he advanced this guideline that it was "general and rather vague. But this is the way it is with all moral

norms" [23]<sup>9</sup>. Despite being convinced that this guideline is fundamentally sound, McCormick understood that he must further concretize it. Specifically, there are those circumstances when the never-competent patient has the potential for human relationships, but the underlying medical condition is critical and will result in imminent death, or after treatment has been initiated it becomes apparent that the treatment is medically futile [24]<sup>10</sup>. In these two situations it is clear that, besides the potential for human relationships, McCormick must incorporate an additional guideline that can weigh the benefits and burdens of certain treatments.

The second guideline of McCormick's quality-of-life criterion is the benefit-burden evaluation. "Where medical procedures are in question, it is generally admitted that the criterion to be used is a benefits-burdens estimate . . . The question posed is: Will the burden of the treatment outweigh the benefits to the patient? The general answer: If the treatment is useless or futile, or it imposes burdens that outweigh the benefits, it may be omitted" [25]. As is the case with his first guideline, McCormick claims the benefit-burden evaluation emerges out of the "ordinary-extraordinary means" distinction.

McCormick believes that his notion of benefit-burden evaluation within his quality-of-life criterion is a logical development of the "ordinary-extraordinary means" distinction or what he refers to as an extension of the tradition into new problem areas [18]<sup>11</sup>. McCormick believes that the "ordinary-extraordinary means" distinction has an honorable history and an enduring validity. However, he argues that these terms "summarize and promulgate judgments drawn on other grounds. It is these 'other grounds' that cry out for explication" [18, 19]<sup>12</sup>.

To further explain these "other grounds," McCormick reformulates the "ordinary-extraordinary means" distinction by advancing his benefit-burden evaluation. An extraordinary means is one that offers the patient no real benefit, or offers it at a disproportionate cost. For McCormick, one is called to make a moral judgment: Does the benefit of a proposed medical intervention really outweigh the harm it will inevitably produce? This is a quality-of-life judgment. The benefit-burden interpretation is not a departure from the Catholic tradition. It is a reformulation of the tradition in order to deal with contemporary bioethical problem areas [25]<sup>13</sup>.

The reason for this reformulation of the tradition is that over the centuries the "ordinary-extraordinary means" distinction has become less objective and more relative because medicine and technology have become more sophisticated. The medical profession is committed to curing disease and preserving life. Today, we have the medical technology to make this commitment a reality. However, McCormick argues that "this commitment must be implemented within a healthy and realistic acknowledgment that we are mortal" [26]. Therefore, there is a need to reformulate the basic value of human life under new circumstances. For many contemporary ethicists the traditional terminology of ordinary-extraordinary means has outlived its usefulness and could take us only so far, especially in the case of handicapped newborns [27]<sup>14</sup>. Focusing on the value of human life, McCormick sought to reformulate the "ordinary-extraordinary means" distinction without abandoning the tradition. Contemporary medical problems no longer only concern newborns for whom biological death is imminent. Modern medicine and technology have the ability to keep almost anyone biologically alive. Therefore, a gradual shift has occurred from the means to reverse the dying process to the quality of life sustained

and preserved as the result of the application of medical technology [15]. Today, because of the advancements in medicine and technology, the focus is on the quality of life thus saved that establishes a means as extraordinary.

To address this shift in the problem from means to quality of life preserved, McCormick has reformulated the “ordinary-extraordinary means” distinction to mean the “benefit-burden evaluation” [28-30]<sup>15</sup>. For McCormick, “it is clear that the judgments of burden and benefit are value judgments, moral choices. They are judgments in which, all things considered, the continuance of life is either called for or not worthwhile to the patient” [31]. In making these moral judgments one can see how proportionate reason is used as a tool for determining whether a particular life-sustaining treatment is a benefit or a burden, that is, in the “best interests” of the never-competent patient and those involved in the decision-making process.

The benefit-burden evaluation was also proposed by the Sacred Congregation for the Doctrine of the Faith in its *Declaration on Euthanasia* and by the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research in its *Deciding to Forego Life-Sustaining Treatment* [32]. The issuance of the *Declaration on Euthanasia* in 1980 by the Magisterium gave McCormick further justification for incorporating the benefit-burden evaluation into his quality-of-life criterion [33]<sup>16</sup>. It also gave him further proof to anchor his guideline and thus his criterion for treatment decisions in the benefit-burden evaluation. Medical treatments are not morally mandatory if they are either gravely burdensome or useless for the patient [20,34-37]<sup>17</sup>. McCormick has a normative understanding of medical futility, which considers whether the agreed on potential effect is of any value and benefit to the newborn, that is, in the newborn’s “best interests” normatively understood. For McCormick, a medical treatment might be successful in achieving an effect (physiologically effective), but the effect might not be beneficial to the patient (qualitatively effective). Since the goal of medical treatment is to benefit the patient, it follows that nonbeneficial treatment is medically futile [38-40]<sup>18</sup>. This entails making a value judgment and the evaluation of whether a treatment is a benefit or a burden can be open to personal interpretation. That means these evaluations can be “borderline and controversial” [31].

The two guidelines of McCormick’s quality-of-life criterion, even though he argued they were both reformulations of the “ordinary-extraordinary means” distinction, continued to be criticized by ethicists Leonard Weber, John Connery and Warren Reich for being too relative, subjective and consequential in nature. To address this criticism McCormick, along with ethicist John Paris, S.J., proposed the following norms that would further specify the capacity for human relationships and the benefit-burden evaluation:

1. Life-saving intervention ought not to be omitted for institutional or managerial reasons. Included in this specification is the ability of this particular family to cope with a badly disabled baby.
2. Life-sustaining interventions may not be omitted simply because the baby is retarded. There may be further complications associated with retardation that justify withholding life-sustaining treatment.
3. Life-sustaining intervention may be omitted or withdrawn when there is excessive hardship on the patient, especially when this combines with poor prognosis.
4. Life-sustaining interventions may be omitted or withdrawn at a

point when it becomes clear that expected life can be only for a relatively brief time and only with continued use of artificial feeding [31].

These norms or rules do not mandate certain decisions, nor do they replace the role of prudence and eliminate conflicts and decisions. They are simply attempts to provide outlines of the areas in which prudence should operate [31].

McCormick further specified his quality-of-life criterion to help enlighten medical situations for the appropriate decision-makers. However, guidelines, even specified by concrete norms, cannot cover all circumstances and every possible situation. McCormick’s quality-of-life criterion assists the appropriate decision-makers by giving them a range of choices. As rational persons, it is up to the appropriate decision-makers to examine each situation using proportionate reason, and the guidelines advanced by McCormick in his quality-of-life criterion, to determine what is in the “best interests” of the never-competent patient and those involved in the decision-making process. McCormick makes clear that no criterion can cover every instance where human discretion must intervene to decide. There is always the possibility of human error because we are finite and sinful people. For McCormick, “the margin of error tolerable should reflect not only the utter finality of the decision (which tends to narrow it), but also the unavoidable uncertainty and doubt (which tends to broaden it)” [31]. With the assistance of these guidelines and norms, McCormick believes that the appropriate decision-makers will be given the necessary guidance to act responsibly.

To assist parents and health care professionals further in medical decision-making for handicapped newborns five specific diagnostic treatment categories of handicapped newborns have been established. These categories attempt to encompass, as far as possible, the entire spectrum of handicapped newborns. They are based on McCormick’s moral criterion of the potential for human relationships.

McCormick has plotted the two extreme positions on this spectrum of handicapped newborns, but has left the “conflictual middle,” to be filled in by health care professionals and bioethicists [30]<sup>19</sup>. These diagnostic categories will attempt to complete the “conflictual middle.” The “conflictual middle” pertains to those neonatal anomalies that fall into the “gray area” of treatment decisions<sup>20</sup>. These diagnostic treatment categories have been arranged in a way that demonstrates the application of McCormick’s “best interests” category. There is a logical progression on the spectrum from the newborn who does not warrant medical treatment to the newborn who does warrant medical treatment.

The five diagnostic treatment categories are:

1. The handicapped newborns whose potential for human relationships is completely nonexistent.
2. The handicapped newborn who has a potential for human relationships but whose potential is utterly submerged in the mere struggle for survival.
3. The handicapped newborn who has a potential for human relationships but the underlying medical condition will result in imminent death.
4. The handicapped newborn who has the potential for human relationships but after medical treatment has been initiated, it becomes apparent that the treatment may be medically futile.

5. The handicapped newborn who has the potential for human relationships and has a correctable or treatable condition [8]<sup>21</sup>.

Establishing a full set of diagnostic treatment categories is not a panacea for determining treatment decisions for handicapped newborns. Not all medical conditions can be placed in specific categories; there is a marked difference in the severity of conditions within each category. Not all health care professionals or even bioethicists could or would agree to these specific categories. Nevertheless as McCormick argues, “we ought to attempt, as far as possible to approach neonatal disabilities through diagnostic categories, always realizing that such categories cannot deflate important differences and that there will always remain gray areas” [19]. The establishment of these five diagnostic treatment categories is an attempt to meet the challenge set before health care professionals and bioethicists to assist parents and medical professionals in making treatment decisions for handicapped newborns.

### Ethical Evaluation

In the case of Baby AH, the medical professionals have ascertained after 22 days Baby AH was placed on a ventilator and the medical tests revealed that the C3/C2 ratio to be 0.98, a definite indicator of a vitamin B12 deficiency and Methylmalonic academia. After day 32, she was diagnosed with chronic tubulointerstitial nephritis and would require a kidney transplant to attempt to reverse the acidosis episode. The prognosis was very uncertain, possibly adding only a few weeks to her life. It would appear that Baby AH would fit under diagnostic category four.

In this fourth diagnostic treatment category, since the potential for human relationships is present, McCormick’s second guideline of his quality-of-life criterion--the benefit-burden evaluation--would be applied to determine whether Baby AH ought to be treated. What is to be determined is whether the benefit of the treatment will outweigh the burden to the newborn. If the parents in consultation with the health care professionals determine that further medical treatment would not improve the newborn’s prognosis, or benefit the overall well-being of the newborn, then, all things considered, parents should decide that further treatment would not be in the “best interests” of the newborn. A newborn diagnosed with Methylmalonic academia with all her comorbidities appears to be in the dying process. Any aggressive treatment would be medically futile. To support this position McCormick’s third norm, that further specifies the burden-benefit evaluation, can be applied. “Life sustaining interventions may be omitted or withdrawn when there is excessive hardship, especially when this combines with poor prognosis”. Therefore, it appears that further treatment for Baby AH is not morally obligatory, because it is a disproportionate means.

The notion of a normative understanding of “best interests” considers not only the relevant medical facts but also the relevant social and familial factors. Financial and emotional costs ought to be considered. That means, if the social factors are excessive, then the newborn should not and would not want to be treated, because it would place excessive burdens on those who must care for the newborn’s existence. What the newborn “ought” to want should encompass the needs of those who will care for this child. Baby AH is in a terminal state and further aggressive treatments will only prolong the dying process. Both social and familial factors, especially being in Palestine with limited medical resources, ought to play a proportionate role in

determining the benefit/burden evaluation<sup>22</sup>.

In conclusion, when a handicapped newborn has the potential for human relationships but after initiating treatment, it becomes apparent that the treatment is medically futile, parents in consultation with health care professionals are not morally obliged to continue medical treatment. This is a value judgment that is based on McCormick’s guidelines of relational potential and benefit/burden evaluation. McCormick’s moral criterion sets basic parameters and enlightens the particular medical situation. Ultimately, the parents will use prudence to examine the medical facts and to weigh, all things considered, whether the burdens of treatment outweigh the benefits to the newborn. In this diagnostic treatment category, the burdens and benefits need to be weighed carefully. However, with the severity of this particular medical anomaly the burdens clearly outweigh the benefits to the newborn. Therefore, in the “best interests” of the newborn, and all concerned, parents in consultation with health care professionals have the moral obligation to forgo or withdraw treatment for a newborn in these circumstances.

McCormick argues that his moral criterion is appropriate for decision-makers because it considers not only the relevant medical facts and the pertinent circumstances of the situation, but also familial and social factors, such as, religious, cultural, emotional, and financial factors. Parents in consultation with health care professionals can best determine what the handicapped newborn ought to want and protect his or her “best interests” by using McCormick’s quality-of-life moral criterion. As reasonable people, parents are most knowledgeable about the family situation into which the newborn is born. This includes knowing the financial, emotional, and social factors. Parents can also weigh and balance the religious and cultural values that inform their decision-making. Health care professionals have the specialized medical knowledge and clinical expertise that can assist parents in the decision-making process. They also have a level of objectivity that parents may lack because of the overwhelming emotional stress of the situation. Together, parents and health care professionals are able to determine what are the appropriate needs of this newborn to assess these needs and to determine whether medical treatment is in the “best interests” of the newborn “integrally and adequately considered”.

### Conclusion

Methylmalonic Acidemia is initially an elusive genetic anomaly difficult to diagnose but can have varied outcomes. Depending on the level of deficiency in apoenzyme MCM or diminished synthesis of its cofactor 5’-deoxyadenosylcobalamin, prognosis can be poor with one extreme being only a few months to live, or the prognosis can be hesitantly optimistic with a managed diet. MMA is much more common in Middle Eastern countries including Palestine where the major religion is Sunni Islam. Previously, there has been no consensus surrounding aggressive treatment decisions for neonates afflicted with MMA, but this article attempted to apply Richard McCormick’s quality-of-life criteria and Peter Clark’s diagnostic treatment categories to provide a succinct analysis of viable options that are culturally sensitive to Palestinian traditions. Parents should collaborate with health care professionals to consider their child’s potential for human relations through an objective lens of the “best-interests” of the newborn. In doing so, parents can reach morally justified decisions to forgo or pursue life-sustaining interventions on a case-by-case basis.

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## End notes

<sup>1</sup>The structure and individual components that makeup McCormick's moral criterion for decision-making are normative; they center on what "ought" to be the case, not what "is" the case. By normative McCormick means what the never-competent patient would want because he or she "ought" to want it. The never-competent patient "ought" to make this choice because it is in his/her "best interests." For a more detailed analysis of McCormick's position on a normative understanding of his patient-centered approach.

<sup>2</sup>Ethicist Robert Weir disagrees with McCormick on this point. Weir argues that the quality-of-life criterion and best interests criterion are distinct and separate. McCormick responds to Weir by stating: I believe Weir is wrong when he asserts that for those who use quality-of-life assessment, >it is not necessary to consider the best interest of the neonate. It is precisely because one is focused on best interests that qualitative considerations cannot be ignored but indeed are central. Weir is clearly afraid that quality-of-life considerations will be unfair. But they need not be. It all depends on where the line is drawn. I am all the more convinced of the inseparable unity and general overlap of best interests and quality-of-life considerations when I study Weir's clinical applications of his ethical criteria".

<sup>3</sup>It should be noted that McCormick's understanding of "best interests" is grounded in his "revised" natural law position. I believe we do have reasons for assuming we know in many cases what an incompetent would want. We may assume that most people are reasonable, and that being such they would choose what is in their best interest. At least this is a safe and protective guideline to follow in structuring our conduct toward them when they cannot speak. The assumption may be factually and per accidens incorrect. But I am convinced that it will not often be. . . . I believe most of us want to act reasonably within parameters that are objective in character, even though we do not always do so. Or at least I think it good protective policy to assume this".

<sup>4</sup>It should be noted that when McCormick refers to benefits in his "best interests" category it is not restricted to medical benefits. Benefits also apply to social and familial benefits. This notion of "benefit" originates in Pellegrino's four components of "best interests" that

McCormick has incorporated into his “best interests” category. For a more detailed analysis of Pellegrino’s position.

<sup>5</sup>This does not mean that once a decision has been made to forego or discontinue treatment, that the dying person is not treated with dignity and respect. For McCormick, even though a person has reached his or her potential and no treatment is recommended, as members of society we still have a moral obligation to give comfort to the person while he or she is in the dying process. That comfort would consist in palliative care. Palliative care is aimed at controlling pain, relieving discomfort, and aiding dysfunction of various sorts.

<sup>6</sup>McCormick quotes Pius XII as saying that an obligation to use any means possible would be too burdensome for most men and would render the attainment of the higher, more important good too difficult.” Pius XII, (The Prolongation of Life,” *Acta Apostolicae Sedis* 49 (1957): 1,031-1,032. McCormick understands Pius XII to say that certain treatments may be refused because it would lead to a life that lacks the proper quality.

<sup>7</sup>The potential for human relationships is based in the Catholic tradition. McCormick bases this potential for human relationships in the Catholic tradition. The Christian story does not yield concrete answers and fixed rules, but it does yield various perspectives and insights that inform human reasoning. One such insight is that human life is a basic good but not an absolute good. Since human life is a relative good, and the duty to preserve it is a limited one, then it is not always morally obligatory to use all means to preserve human life if a person cannot attain the higher more important good. For McCormick, the higher more important good is the capacity for relationships of love. The core of this guideline is developed from the love commandment found in the New Testament.

<sup>8</sup>Both Leonard Weber and John Connery have criticized McCormick’s quality-of-life criterion.

<sup>9</sup>They really root in general assertions that must be fleshed out by experience, modified by discussion and consultation, propped up and strengthened by cautions and qualifications. It is in the process of their application that moral norms take on added concreteness.”

<sup>10</sup>It should be noted that the term “medically futile” is an elusive and ambiguous term. There are four major types of medical futility. First, physiological futility--an intervention cannot lead to the intended physiological effect. Second, imminent demise futility--an intervention may be futile if despite that intervention the patient will die in the very near future (this is sometimes expressed as the patient will not survive to discharge, although that is not really equivalent to dying in the near future). Third, lethal condition futility--an intervention may be futile if the patient has an underlying lethal condition which the intervention does not affect and which will result in death in the not too far future (weeks, perhaps months, but not in years) even if the intervention is employed. Fourth, qualitative futility--an intervention may be futile if it fails to lead to an acceptable quality of life.

<sup>11</sup>McCormick writes: “A basic human value is challenged by new circumstances, and these circumstances demand that imagination and creativity be employed to devise new formulations, a new understanding of this value in light of these new circumstances while retaining a basic grasp upon the value. For example, in-vitro fertilization poses questions about the meaning of sexuality, parenthood, and the family because it challenges their very biological roots”.

<sup>12</sup>McCormick further states: “We must admit that the terms ‘ordinary’ and ‘extraordinary’ are but code words. That is, they summarize and are vehicles for other judgments. They do not solve problems automatically. Rather they are emotional and mental preparations for very personal and circumstantial judgments that must take into account the patient’s attitudes and value perspectives, or ‘what the patient would have wanted.’ ‘Ordinary’ and ‘extraordinary’ merely summarize other underlying judgments. They say very little in and of themselves”.

<sup>13</sup>McCormick further states that: “It must be remembered that the abiding substance of the Church’s teaching, its rock bottom so to speak, is not found in the ordinary means-extraordinary means terminology. It is found in a basic value judgment about the meaning of life and death, one that refuses to absolutize either. It is that judgment that we must carry with us as we face the medical decisions that technology casts upon us”.

<sup>14</sup>McCormick argues there are two reasons for this: First, the terminology too easily hides the nature of the judgment being made. The major reference point in factoring out what is “reasonable” (benefit) and “excessive” (burden) is the patient--his or her condition, biography, prognosis, and values. The terminology, however, suggests that attention should fall on the means in an all too mechanical way. Second, many people misinterpret the terms to refer to “what physicians ordinarily do, what is customary.” This is not what the term means. In their ethical sense, they encompass many more dimensions of the situation.

<sup>15</sup>Besides McCormick’s benefit-burden evaluation, other ethicists have suggested various terms to reformulate the ordinary-extraordinary means distinction. Paul Ramsey suggests that the morally significant meaning of ordinary and extraordinary medical means can be reduced almost without remainder to two components--a comparison of treatments to determine if they are “medically indicated” and a patient’s right to refuse treatment [28]. Robert Veatch maintains that the terms “ordinary” and “extraordinary” are “extremely vague and are used inconsistently in the literature.” Beneath this confusion he finds three overlapping but fundamentally different uses of the terms: usual versus unusual, useful versus useless, imperative versus elective.

<sup>16</sup>The Congregation concludes that, “it will be possible to make a correct judgment as to the means by studying the type of treatment being used, its degree of complexity or risk, its cost and possibilities of using it, and comparing these elements with the result that can be expected, taking into account the state of the sick person and his or her physical and moral resources”.

<sup>17</sup>Ethicists Warren Reich, John Connery SJ, Leonard Weber, and Donald McCarthy disagree with McCormick’s interpretation of the tradition on the benefit-burden distinction. Ethicist Richard Sparks writes: For Reich, Weber, Connery, and McCarthy the limiting factor is the quality of life, which, if judged to be excessively burdensome, can make the presumably beneficial treatment extraordinary and optional, [sic] must be caused by or directly related to the use of the means contemplated. In other words, “the burden must be the burden of medical treatment, not the burden of handicapped existence”.

<sup>18</sup>For McCormick, medical futility is determined by the parents in consultation with the health care professionals, because a determination must be made of the patient’s medical status and an evaluation must be made of the medical intervention. The determination of medical futility entails balancing the values of patients, the values of medicine, and the fact that there is much uncertainty in making “predictive medical judgments.” McCormick’s notion of medical futility is also rooted in his understanding of the principles of beneficence and nonmaleficence--do no harm to the patient.

<sup>19</sup>McCormick writes: It is the task of physicians to provide some more concrete categories or presumptive biological symptoms for this human judgment. For instance, nearly all would likely agree that the anencephalic infant is without relational potential. On the other hand, the same cannot be said for the mongoloid infant. The task ahead is to attach relational potential to presumptive biological symptoms for the gray areas between such extremes.

<sup>20</sup>This would include anomalies in which the newborn has the potential for human relationships, but the potential is utterly submerged in the mere struggle for survival, or the medical condition will result in imminent death, or it has been determined that further treatment is medically futile. Certain anomalies that would fall within this category would be spina bifida, hypoplastic left heart syndrome, trisomy 13, trisomy 18, Lesch-Nyhan syndrome, etc.

<sup>21</sup>For a more complete analysis of these five diagnostic categories refer.

<sup>22</sup>It should be noted that McCormick’s position on social and familial factors has been criticized for being too restrictive and deviating from both the Catholic tradition and from his own normative understanding of “best interests.” McCormick claims that his restrictive notion of social and familial factors, as they pertain to treatment decisions for handicapped newborns, is due to the fact that a broader interpretation could lead to social utilitarianism. This caution is certainly relevant because the possibility of potential abuse is always present. However, the safeguards McCormick has built into his quality-of-life criterion--guidelines and norms--should help to alleviate the possibility of such abuse. In addition, health care professionals serve as a safeguard in that they can act as the newborn’s advocate should they suspect abuse.