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The Fetus as Our Patient:
The Confluence of Faith and Science in
The Care of the Unborn

by

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And it came to pass, that, when Elisabeth heard the salutation of Mary, the babe leaped in her womb; and Elisabeth was filled with the Holy Ghost:

And she spake out with a loud voice and said, "Blessed art thou among women and blessed is the fruit of thy womb.

"And whence is this to me, that the mother of my Lord should come to me?

"For, lo, as soon as the voice of thy salutation sounded in mine ears, the babe leaped in my womb for joy."

–Luke 1:41-44[1]

Introduction

Elisabeth and Mary bear witness in the first chapter of the gospel of Luke to the overwhelming evidence, available for many centuries, of the humanity of the fetus. The very idea that a baby in utero will respond to external stimuli no longer remains in doubt. Parents rush out to buy Mozart, Bach, and other "brain-building" music thought to enhance the prenatal development and future intellectual development of their preborn little one.[2] The purpose of this paper will entail the meshing of our Christian faith with the latest in care of the preborn baby: the unseen human in our care.

The paper will address the fetus as our patient by addressing five areas: basic Christian ethical framework for the discussion, Christian

medical history, a brief description of fact-value distinction, the medical development of the fetus as our patient, and a description of care of the terminal perinate.

Basic Christian Ethics

This paper does not suppose to be an exhaustive discussion of moral theology or the Bible. The paper approaches the Bible and the elaboration of the Christian ethic from the perspective of Cornelius Van Til and his ethic of presuppositions.[3] Van Til argued that the presuppositions or basic beliefs brought to scripture will drive the interpretation and application of Biblical truth. Thus, this paper presupposes that: God's word is inerrant (without error as written), God does exist as His word says He does, He is present and operational in our everyday lives, and that His word is clear enough for us to understand and formulate a Biblical ethic. The Bible addresses the pre-delivery personality of the unborn child,

> Psalm 139:14 "I will praise thee; for I am fearfully and wonderfully made: marvelous are they works; and that my soul knoweth right well"

> Luke 1:39-41 "And it came to pass that, when Elisabeth heard the salutation of Mary, the babe leaped in her womb;"[1]

From these two brief examples in scripture, the humanity of the unborn are affirmed and the basis for the ethical treatment of babies validated.

Christian Medical History

Science has been described as "thinking God's thoughts after him". From the earliest days of its inception, Christianity took a great interest in the physical human body since Christ deigned to come in the flesh to dwell amongst men (John 1:14-15).[1]

Numerous examples in history demonstrate the profound influence of Christianity on medicine and give us a proud heritage to emulate. A few salient examples follow. The first is "Fabiola of the Fabians" (c 395 A.D.). Fabiola was a wealthy Roman matron of the patrician Fabian family, burdened with a profligate husband. She established the first Western hospital in Rome.[4] She was an avid patron and supporter of Jerome (translator of Scriptures from Greek to Latin Vulgate Bible) Jerome wrote of Fabiola,

First of all she founded an infirmary and gathered into it sufferers from the streets, giving their poor bodies worn with sickness and hunger all a nurse's care… How often did she carry on her own shoulders poor filthy wretches tortured by epilepsy. How often did she wash away the purulent matter from wounds which others would not even endure to look upon! She gave food with her own hand, and even when a man was but a breathing corpse, she would moisten his lips with drops of water… Rome was not large enough for her compassionate kindness. She went from island to island and traveled round the Etruscan Sea, and through the Volscian province, with its lonely curving bays, where bands of monks have taken up their home, bestowing her bounty either in person or by the agency of men of holy faith.[5]

Her efforts led to the establishment of one of the first hospices ever known in Portus, Italy in roughly 395 A.D. This hospice was so successful that it became famous from Parthia (the Eastern Roman empire) to Britain (the Western Roman empire) for its loving care of dying patients.

Edward Jenner (1749-1823), the conqueror of smallpox, possessed a vital faith. He spent over 20 years investigating the linkage between cowpox and smallpox. Jenner found that milkmaids infected with smallpox did not become ill with smallpox. His final test included Phipps, a young boy with cowpox, waiting two months and then infecting him with smallpox. The boy proved immune to smallpox, definitively proving that vaccination would prevent a disease (smallpox). He noted about God (with regard to smallpox), "I do not wonder that men are grateful to me, but I am surprised that they do not feel gratitude to God for thus making me a *medium of good*." (my emphasis)[5] Thomas Hodgkin (1798-1866) was a devout Quaker and discoverer of Hodgkin's Lymphoma. His kindness, charity, and lack of recognition marked his life.[5] He died in Jaffa of dysentery while on a mission to assist persecuted Jews in the Holy Land.[5] James Young Simpson (1811-1870) discovered chloroform for anesthesia/ child-birth as part of his never-ending search for improved methods of accomplishing surgery.[5] His tenacity of purpose, coupled with his great faith, allowed Simpson to become successful. Simpson provided millions of women and patients a freedom from the pain of childbirth and surgery. Joseph Lister (1827-1912), the originator of antiseptic surgery, blended his devout faith with his keen scientific mind to save thousands of lives by perfecting surgical techniques to decrease infections from operations. Lister made the observation of the Christian physician's task, "It is our proud office to tend the fleshly tabernacle of the immortal spirit, and our path, if rightly followed, will be guided by unfettered truth and love unfeigned."[5]

Fact-Value Distinction

The process of the growth of science led to a "fact-value" distinction in society. The belief became dominant that the only things knowable were scientific and since moral values were not scientific, they were not knowable. As the explosive growth of science began in the Renaissance, it continued into the Enlightenment and promptly "lost" God. In the Enlightenment, autonomous man became the measure of all things. Religious faith was denigrated and made somehow incongruous with science. Thus, there was made a "fact-value distinction" in that which is knowable, is science, and that which is moral, is not knowable and relative. The philosophy took root that only science is repeatable, observable, and knowable.

However; it is known that specific moral actions (i.e. sexual promiscuity resulting in venereal disease/cervical dysplasia for women) will lead to certain outcomes much as jumping off a bridge leads to gravity taking you down to meet the water (science).

Coupled with this new moral relativism came the onslaught of Darwin's theory of evolution regarding the origin of man. Darwin, in his hatred of God, needed to remove the divine from the scientific realm. His clever answer was to remove God from science. To validate evolution, Darwin postulated a series of random events over eons of time causing multiple evolutionary changes and resulting in "man the accident". Unfortunately, scientists like Darwin and the higher critics had it all wrong. Organisms did not evolve and life is not random. It is now known that life is "irreducibly complex", necessitating the simultaneous appearance of multiple organs, biochemical pathways, and processes at precisely the appropriate time. This complexity may be demonstrated in just a few examples:

a) Problem of the eye: How and why would such an organ develop? All the elements must appear at the same time, including the necessary biochemical reactions present in the rods/cones to make us "see" as well as neural pathways in brain. The pathways need to be intact with the neurochemicals in the brain matter itself to transmit the inverted images to the frontal lobes, which would then "know" how to invert the image so it is "right-side" up!

b) Closer to the fetal world would be the formation of a placenta with the literally hundreds of chemical/hormonal/receptor interactions necessary to support a human life. All of these pathways, hormones, and biochemical cascades must be present from the beginning, able to follow in a complex order in the proper

sequence, and not miss a step, or we see a miscarriage or fetal malformation.

c) Embryologically, the formation of a single fetal heart outstrips the most fantastic science fiction ever written. The choreography of the folding, bending, rotating of the fetal heart all takes place almost before the mother knows she is with child (about 5 weeks from the first day of the last menstrual cycle).

Development of the Fetus as Our Second Patient

There have been fantastic advances in human embryology since the 19th century. Scientific inquiry discovered how the human fetus grew from a single cell into the complete baby ready for delivery. The moral theory of personhood from the scripture in Psalm 139 dovetails with scientific theory. As the Psalmist notes in verses 139:14-16,

". . . for I am fearfully and wonderfully made: marvelous are thy works; and that my soul knoweth right well. My substance was not hid from thee, when I was made in secret, and curiously wrought in the lowest parts of the earth. Thine eyes did see my substance, yet being unperfect; and in thy book all my members were written, which in continuance were fashioned, when as yet there was none of them.[1]

The discovery by the deeply pious, Christian physician Dr. Jerome LeJeune in 1959 of the etiology of Trisomy 21, or Down Syndrome, as an extra chromosome 21 signaled the birth of modern genetics. Dr. LeJeune was the first physician to characterize an abnormal chromosomal complement as the etiology for a specific syndrome: Trisomy 21 as the source of the diagnosis of Down syndrome. Unfortunately, due to Dr. LeJeune's outspoken pro-life views and passion for children with chromosomal defects, he was denied a Nobel Prize in medicine for his ground-breaking discovery.

The advent and progress of diagnostic obstetrical ultrasound over the last 30 years gives us a fantastic window to the womb. Ultrasound depiction of fetal anatomy replicates the embryological development of the human fetus almost exactly as previous gross pathologic studies had discovered. The most recent real-time 3D/4D ultrasounds now produce scans so life-like and human-like that no one can mistake them for anything but a baby. Once again, the Biblical view is vindicated as science follows scripture.

The technological advances in therapies for newborns have accelerated from relatively modest beginnings to very sophisticated and high technology therapies. These developments have led to the new science of invasive "in utero therapy". All of these new therapies owe their impetus to the creative genius of Dr. (Sir) William Liley (1929-1983). He is truly the "father of modern in utero therapy" with his discovery of in utero blood transfusions for hemolytic Rh disease in the fetus. Dr. Liley knew the Rh affected neonate was severely anemic at birth. He reasoned he could use packed red cells to transfuse a premature anemic Rh positive affected fetus in utero much as an anemic adult would be transfused. Dr. Liley began by transfusing radioactively tagged O negative red cells into the fetal abdomen in 1963.[6] Liley chose the radioactively tagged red cells so fluoroscopy could be used to guide placement of the packed cells into the fetal abdomen since obstetrical ultrasound was not yet available.

In Utero Anomalies Amenable to Therapy

The list of in utero anomalies that are amenable to therapy has risen steadily since Dr. Liley's first transfusions. One of the major triumphs of in utero therapies has been the advent of vitamin therapy with the addition of extra folic acid to the diet of women to prevent NTDs or to decrease the recurrence of NTDs in patients with either a previously affected child or family history of neural tube defects (NTD). This simple vitamin therapy has decreased the recurrence risk of NTD in a previously affected woman by more than 70%.[7] In utero therapy is now available for multiple conditions. They include: bladder outlet obstructions, immune or infectious hydrops, diaphragmatic hernia, fetal immunity (SCIDS) defects, neural tube defects, fetal teratomas, fetal cardiac arrhythmias, and fetal cardiac anomalies.

Bladder outlet obstruction results usually from incomplete cannulization between the pelvic and distal urogenital sinus. The incidence is 1/5000-1/8000 male fetuses and the babies usually die from pulmonary hypoplasia secondary to incomplete lung development with anhydramnios. Fetal urinalysis provides prognostic projections of anticipated neonatal outcomes.

The fetal bladder is sampled via an amniocentesis needle. Using the values in the table below results in a good prognosis:

Urine sodium < 100 Meq/liter[8]
Urine chloride < 90Meq/liter[8]
Urine osmolality < 200 milliosmo/liter[8]
Beta-2 microglobulin < 4 mg/liter[9]

The algorithm for evaluation for possible fetal bladder shunt placement requires three sequential urine samples 48-72 hours apart.[10] After ascertainment of the fetal bladder urine with good prognosis biochemical results, a double pig-tail vesicoamniotic shunt to drain the bladder is placed. The placement of the shunt does not necessarily solve the possible problem of renal dysplasia that may follow the therapy. The shunt does, however, allow amniotic fluid to accumulate and prevents pulmonary hypoplasia with relatively normal lung function. There is still a 33-50% risk of renal failure in childhood after shunting.[11] Some researchers believe there is a possible role for renal biopsy of the fetus prior to shunt placement to look for histologic evidence of intact renal function.

The next triumph of science came in treating immune hydrops for Rh sensitization. The incidence of Rh negative blood in the various ethnic groups is 15% caucasian of European descent, 8% African-Americans, 8% Hispanics from Mexico/Central America, and <1% in Eskimo, Native American, Chinese, and Japanese descent.

Prior to the advent of Rhogam the rate of Rh sensitization was 43.3/ 1000 samples in 1967 and dropped to 2.6/1000 samples in 1996 after Rh immune globulin injections at 28 weeks and post-partum.[12] The management of Rh disease involves testing for Rh antibody titers and looking for a critical titer of at least 1:16 or a 4-fold rise from base (i.e from 1:8 to 1:32). The maternal titers are tested monthly and must be done at the same laboratory for consistency and to prevent variation. Part of the antepartum testing involves paternal Rh status and zygosity testing. New advances allow us to check the father of the baby for possible Rh negative gene status. If the father of the baby is heterozygous (one Rh negative gene), it is possible to do fetal Rh typing on an amniocentesis sample with a 98+% accuracy[13] and fetal RhD testing on the fetal DNA in maternal serum with virtually 100% accuracy.[14] An RhD negative fetus would require no further antepartum follow up or testing.

In the recent past (5 years), serial amniocentesis would be performed for titers beginning at approximately 18-22 weeks and use the Liley curves for determining if a fetus was at risk for being affected. Liley developed the curves using the delta optical density or OD450 for hemoglobin breakdown to assess how much fetal blood was being hemolyzed. The OD450 values would reflect fetal status in utero with regard to anemia. The Liley curves use 3 simple zones based on delta OD450 compared to gestational age to determine critical values.

If the fetus was found to be in a critical range on the delta OD450 curve, a fetal cord blood sampling at the cord insertion site with a 22 gauge spinal needle would be done to determine if the hematocrit was less than 30% or 2 standard deviations below mean for the gestational age. An opening hematocrit is obtained, and if anemic, the fetus transfused to a

hematocrit of 35-40%. The transfused RBCs degrade their hematocrit about 1%/day, so, multiple intravascular transfusion procedures are often necessary. Most sensitized babies deliver between 35-37 weeks with the last transfusions at 30-32 weeks.[15] Transfusions for a hematocrit < 30% may be done as early as 18 weeks.

Doppler ultrasound is now used at less than 35 weeks with the measurement of a peak middle cerebral artery velocity (MCA) to determine the need for cord sampling or delivery. It is over 98% accurate at >1.5 MoM (multiples of median for gestational age) for predicting fetal anemia.[16] The MCA also seems to be accurate for clinical management for the non-Rh isoimmune disorders of Kell, Kidd, or Duffy isoimmunization.[17]

Infectious etiologies related to fetal hydrops include the two most common etiologies: toxoplasmosis and Parvo-B19. Toxoplasmosis is a protozoan parasite that is commonly found in cat feces as a result of exposure to rodents who carry the disorder or by eating poorly cooked red meat. Seroconversion in toxoplasmosis may take 1-4 months and carries a risk of infection in fetus of 15% in the first trimester, 25% in the second trimester and 65% in the third trimester.[18] Diagnosis of toxoplasmosis is by maternal blood testing for immune globulins: IgM (acute infection) and IgG (previous infection). Generally serial titers are performed 6-8 weeks apart to determine if there is a four-fold rise in titers. Fetal infection may be documented with the obstetrical ultrasound findings of: hydrops, cerebral calcifications, and liver calcifications. Diagnosis in the fetus may be done with amniocentesis with DNA-PCR on amniotic fluid (specificity of 95% and sensitivity-64%) to demonstrate evidence of infection.[19] Treatment in utero for toxoplasmosis with antibiotics (spectinimcyin and sulfa) has been successful in at least one case of fetal infectious hydrops.[20]

Parvo-B19 infection as a cause of non-immune hydrops is more common than thought and has been seen in 10-15% of previously undiagnosed cases of infectious hydrops.[21, 22] Viral transmission rate to the fetus is about 30% and risk for fetal death, if infected, is 5-10%.[21, 22] Therefore, the risk of death for the fetus is < 1%.[21, 22] The fetus most likely develops hydrops as a result of suppression of bone marrow red cell production by the virus or possibly due to fetal viral myocarditis.[23] Diagnosis is made by a positive IgM titer (acute infection) in maternal serum. The fetus is followed with serial weekly ultrasounds for 8-12 weeks after acute infection to rule out hydrops and evidence of failure. If the ultrasound demonstrates hydropic changes, evidence of failure (ascites or pleural/pericardial effusions), or increased Dopplers (MCA), it will necessitate fetal cord blood sampling and possible intravascular transfusion (IVT) via the umbilical cord. Data shows that fetal IVT survival after hydrops diagnosis is over 84% where observational survival for hydrops was only 70%.[24]

Diaphragmatic hernia affects roughly in 1-4.5/10,000 live births and affects males/females equally. Left side hernias comprise 75-90% of hernias, right side hernias are 10%, and bilateral hernias are less than 5%.[25] The etiology is unknown but failure of closure of the pleuroperitoneal canals in the fetal abdominothoracic cavity is thought to be the cause. Hernias are diagnosed in the antepartum most commonly by ultrasound with a fluid collection in fetal chest. Fetal mortality in unselected cases is about 80%.[26] Prognosis for the fetal survival postpartum is related to: large size, diagnosis at < 24 weeks, liver above diaphragm (liver above the diaphragm survival 43%/ECMO 53% and liver below the diaphragm survival 93%/ECMO 19%), small contralateral lung, associated anomalies, and bilateral hernias.[27] Originally, open repairs in utero were attempted with varied success. Hernias with the liver above the diaphragm often "kinked" the umbilical/portal vein when the hernia was reduced and the abdominal contents pushed from the chest. There is an ongoing NIH trial at the University of San Francisco to try fetoscopic tracheal occlusion. A videofetoscopic technique is used to occlude the fetal trachea with a clip. The theory is to occlude the trachea to make the lung grow and gradually push the abdominal contents out of the chest back into the abdomen. To remove the clip at term, they use ex-utero intrapartum treatment (EXIT) procedure to partially deliver baby head/neck by c-section, the tracheal clip is identified by its string and removed, and the fetus intubated prior to delivery.[28] The success rates in the 8 fetuses treated so far are 75% success rates versus traditional surgery post-delivery.[29]

A further attempt to treat congenital diaphragmatic hernias (CDH) involves the use of general or combined spinal-epidural anesthesia with fetal position for access of the neck to place a balloon into the fetal trachea.[30] A flexible Teflon cannula containing a pyramidal trocar is used to enter the amniotic cavity through the maternal abdomen. The cannula is directed to the fetal mouth and the trocar is removed. Fetoscopic instruments are placed with a sheath loaded with the fiber endoscope and a catheter loaded with a detachable gold valve balloon. A side port is used for amnioinfusion with Hartmann solution. The endoscope is passed through the vocal cords to the trachea and the catheter is positioned to place the balloon above the vocal cords. The balloon is then inflated with isotonic Omniscan, a magnetic resonance imaging contrast agent. The balloon is removed at approximately 34 weeks either by fetal tracheoscopy or by puncturing the balloon with an ultrasound-guided needle.[30] A recent study involved 21 consecutive cases with occlusion. The lungs all became more echogenic within 48 hours and the lung area-to-head ratio improved from a median of 0.7 to 1.8 within 2 weeks. Nine of the twenty-one newborn infants died from complications of pulmonary hypoplasia. Ten of the 12 infants having surgical repair of CDH were doing well post-surgery

for a median of 18 months. Survival rates went from 30% in the first 10 cases done in the third trimester to 64% in the next 11 cases done in the second trimester. The control group without balloon surgery had only 1 of 11 infants survive to discharge.[30]

The congenital cystic adenomatoid malformation (CCAM) is a hamartomatous pulmonary lesion seen on ultrasound as a cystic mass. They usually are unilateral, may involve either lung and any lobe, but usually are isolated to one lobe or segment of lung in about 95% of cases.[31] CCAM's are bilateral in < 2% cases.[31] There are three types of CCAM: macrocystic (cysts 2-10 cm-60% include medium cysts), medium size cysts (cysts < 2 cm), and microcystic (cysts < 0.5 cm-40%).[32]

The lesions may appear as solid or mixed cystic/solid tumors on ultrasound. Usually CCAM's are diagnosed at 16-22 weeks and most regress by third trimester (100% fetuses with regression survive).[33] Fetal hydrops is a very poor prognostic sign (100% mortality if treated expectantly).[34] Mediastinal shift is an indication to attempt to tap a large mass in utero and may even result in the placement of an indwelling double pig-tail catheter. Some fetuses with large masses and hydrops may need to have in utero resection with an open surgical procedure (61% survival compared to 100% mortality with expectant management).[33]

Severe Combined Immunodeficiency Syndrome (SCIDS) may be inherited as an X-linked recessive, autosomal recessive, or even as a sporadic form.[35] It consists of the absence of both B-cell and T-cell immunity. These are the so-called "bubble children" who have been kept alive in a totally sterile environment within a plastic bubble room. If not kept in such a sterile environment, death comes to the neonate in the postpartum period by overwhelming viral or bacterial infection, usually within one year's time. The etiology of the disease is thought to be due to failure of hematopoietic stem cells to differentiate into the B and T lymphocytes.[35] The fetus affected with SCIDS is immune incompetent and therefore able to be transfused with maternal stem cells without having a graft-versus-host rejection (the healthy fetus is immune competent by 14 weeks).[35] Therapy consists of taking maternal stem cells from maternal bone marrow and infusing the cells via the fetal umbilical cord with an IVT into the fetus at approximately 18+ weeks.[35] The infant is born as a chimera with a mixture of maternal and fetal T and B lymphocytic cells with immune competence and normal ability to fight infection.[35] New developments in the stem therapy story may even allow for in utero therapy of complex protein disorders like muscular dystrophy. Muscular dystrophies (MD) are a group of congenital disorders notable for progressive muscle degeneration and fibrosis. The defect in many of the MDs are either in the dystrophin or other proteins in the dystrophin-associated protein (DAP) complexes. MDs are characterized by

progressive muscle destruction with focal regeneration with fibrosis in the affected muscles. This leads to a depletion of the satellite (muscle stem cells) with death as the result of muscle failure.[36] The use of postnatal cellular therapy of MDs has been dismal due to the immunological reaction to allogenic donor cells and to dystrophin itself.[37] The use of myogenic stem cells has the ability to overcome all the problems with postnatal cellular therapy. The early gestational period is the only time in development or life that large numbers of stem cells migrate to seed tissue compartments. The relative size of the fetus would allow for large scale transplantation of doses of stems that would not be possible in the postnatal period. Further, the exciting new developments of manipulating fetal tolerance to allow donor-specific or protein specific transplantation make therapies for MD a new reality.[38] The normal myogenic stem cells would migrate to the muscles and thereby prevent the progressive degeneration of the muscles seen in classic MD.

Neural tube defects (NTD) occur in roughly 1/1000 pregnancies and are related to folic acid deficiency, often as a result of the genetic defect in handling of folic acid in the tetrahydrofolate reductase pathway. The CDC noted in a 1992 study that supplementation of women without risk factors for NTDs with a multivitamin with 400 micrograms of folic acid at least one month prior to conception and continuing through the first trimester decreased the NTD rate by 50%.[39] A more recent article by Evans, et al., 2004, notes at least a 30+% decrease in NTDs in the general population of women in the United States without risk factors for NTDs with folic acid fortification of food stuffs.[40] With a previously affected infant or first degree relative with an NTD (sibling/parent) patients need 4 mg/day preconceptually for at least a month prior to pregnancy and continuing through the first trimester.[41] This therapy results in a greater than 70% reduction in the recurrence of NTDs in this at-risk patient population.[41] Diagnosis of an NTD is most often made by an elevated screening maternal serum alphafetoprotein (MSAFP.) Neural tube defects may be seen on obstetrical ultrasound with the classic signs: "Lemon sign" with collapse of cerebral hemispheres to appear lemon-like, a dilated posterior fossa with Chiari II malformation, and/or an open neural defect in the spine

The recommendation used to be made to abort these babies. Now, however, there is an exciting new in utero surgery for these babies' defects. There is a National Institute of Child Health and Human Development (NIHCD) study for surgery for NTDs. It is the Management of Myelomeningocele Study or "MOMS" study.

The study involves 200 total women with 100 pregnancies randomized into either of two groups: in utero surgery or routine obstetrical follow up. Three centers are participating: Children's Hospital of Philadelphia, PA;

University of California, San Francisco, CA; and Vanderbilt University Medical Center, Nashville, TN. The inclusion criteria are:

Highest lesion T1 through S1
Hindbrain herniation (Chiari II malformation) by MRI
Maternal age 18 or older
Gestational age 19 0/7 to 25 5/7 weeks for randomization

The major exclusion criteria are:

Non-resident of US
Multifetal pregnancy
Obesity with BMI > 35
Abnormal karyotype or other anomalies
Current or planned cerclage, incompetent or short cervix documented preterm labor, placenta previa or abruption
History of spontaneous preterm birth < 37 weeks
Maternal HIV/AIDS, Hepatitis B or C
Uterine anomaly or contradiction to surgery or anesthesia
Unable to travel or make follow-up at 12 and 30 months

Information for enrollment into the study is found at:

www.spinabifidamoms.com
1-866-275-6667 (or 1-866-ASK-MOMS)

Teratomas (sacral/pharyngeal) are the most common tumor of fetus and neonate.[42] The incidence is 1/40,000 births and malignant invasion is rare.[42] These tumors are thought to arise from the primitive knot (Hensen's node) or caudal cell mass that has escaped normal inductive influences.[43]

Unfortunately, fetal mortality is due to high-output shunting with heart failure and hydrops with placentomegaly. These tumors may also produce the "mirror syndrome" with maternal findings that mimic severe preeclampsia with elevated blood pressure, abnormal laboratory, and significant maternal edema.[44]

These tumors may be diagnosed as early as 14 weeks by obstetrical ultrasound.[45] They are seen as a distal caudal or intra-abdominal mass. Teratomas may look cystic, solid, or mixed in appearance on ultrasound. The differential diagnosis of this mass on ultrasound includes renal tumors, ovarian tumors, or myelomeningocele.[46] Obstetrical Doppler flow ultrasound will assist in documenting effects of shunting in the baby.[42] There will be evidence of high flow in the lesion as well as high

outflow rates in the fetal heart. There may even be elevated fetal umbilical cord and middle cerebral artery Dopplers. Careful antepartum monitoring is necessary and there may need to be in utero intervention if heart failure develops. The newest technique for therapy involves ablation of feeder vessels with a radiofrequency ablation probe through a laparoscopic in utero method.[47] The small numbers so far (5 cases) appear to demonstrate that this new technique is superior to surgical resection.[47]

The twin-twin transfusion syndrome (TTTS Syndrome) is most commonly a problem with monochorionic (shared placenta) twins with an incidence 10-20% of monochorionic twins.[48] The syndrome is defined in the twins as: a growth discordance of 50%+, a marked difference in amniotic fluid (polyhydramnios and anhydramnios with a "stuck twin"), and divergent fetal hematocrits at birth (anemic "donor twin" and polycythemic "recipient twin").[48] The major etiology for TTTS is thought to be shunting with vascular anastamoses between the twins with a "pump-donor" twin and a "recipient" twin.[48] The smaller donor twin often has severe oligohydramnios to anhydramnios with growth restriction while the recipient twin has polyhydramnios and hydrops from volume overload. The obstetrical ultrasound findings include:

> Monochorionic twins
> 50% discordance
> Severe oligohydramnios donor ("stuck twin")
> Polyhydramnios in recipient
> Unequal placental sharing
> Arteriovenous communication by Doppler

Favorable prognosticators (after Callen, *Ultrasonography in Obstetrics & Gynecology*, 4th edition, 2000, pg 776)[49]:

> Late-onset growth differences
> Late-onset polyhydramnios
> No hydrops
> No placentomegaly
> No cardiac failure

Unfavorable prognosticators (after Callen, *Ultrasonography in Obstetrics & Gynecology*, 4th edition, 2000, pg 776)[49]:

> Early-onset growth differences (<20-22 weeks)
> Early-onset polyhydramnios
> Hydrops

Placentomegaly
Fetal cardiac failure

The workup of the TTTS Syndrome include: chromosomes for both twins, detailed anatomic surveys (including fetal echocardiography) for associated anomalies, and detection of vascular anastamoses.
    Therapies may include:

        Serial amnio-reductions
        Creation of window between membranes
        Aggressive oral protein supplementation ("protein shakes") therapy for severe hypoproteinemia
        Fetoscopic laser ablation of communicating anastomosis:
            Dr. Julian De Lia of Milwaukee reports 153 total cases.
            Latest 67 cases from De Lia show:
                Mean gestational age 21 weeks (range 18-24.5 weeks)
                55/67 (82%) one survivor and 94/134 babies surviving
                37 with surviving twins/18 one twin survivor/12 none
                4/93 (4.3%) with significant handicap with mean follow up of 60 months (range 48-84 months)[50]

For further information contact:

        TTTS Foundation:
        National Office
        Longbeach Parkway
        Bay Village, Ohio 44140
        Voice: 440-899-TTTS
        Fax: 440-899-1184
        Website: www.tttsfoundation.org

Centers for referral include:

        Dr. Julian De Lia, M.D. (creator of laser therapy)
        St Joseph Regional Medical Center
        5000 West Chambers Street
        Milwaukee, WI 53210-1688
        Phone: 414-447-3535
        Fax: 414-874-4506

Dr. Rubin Quintero, M.D.
Florida Institute for Fetal Diagnosis and Therapy
13601 Bruce B. Downs Blvd, Suite 160
Tampa, FL 33613
Phone: 888-338-2577
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Fetal arrhythmias include tachyarrthymias which are 8% of fetal rhythm disorders.[51] Tachyarrthymias are treated before 32-34 weeks, but if they occur after 32-34 weeks delivery is indicated. Before 32-34 weeks most physicians utilize maternal oral first line therapy of either first line: digoxin or flecainide; second line: oral therapy; Verapamil, procainamide, quinidine, and propanolol; or with intravenous therapy with infusion of adenosine via the umbilical cord to break tachycardia with possible loading therapy with digoxin after conversion to a sinus rhythm.[52] Bradyarrhthymias are seen in about 6% of fetal arrhythmia cases.[53] Bradyarrhthymias are common with structural defects (53%), have ventricular rates < 55 bpm , and require pacemakers post-delivery.[53] With bradyarrhthymias a check of maternal serum for possible Sjogren Syndrome A (SSA) or Sjogren Syndrome B (SSB) antibodies is indicated. The SSA or SSB antibodies attack the fetal conduction system in the heart, causing a heart block. If the SSA or SSB antibodies are present, maternal therapy with oral steroids might be indicated.

Hypoplastic left heart syndrome (HLHS) is usually the result of aortic/mitral dysplasia or aortic/mitral atresia. It is most often inherited as an autosomal recessive. The recurrence risk with one child is 4% and with two children is 25%. The ultrasound shows a small left ventricle with generally an absent or small mitral valve and/or aortic valve.   The prognosis may be poor with a very small left ventricle. Therapies include:

> Norwood in usually 3 stages to re-construct left ventricle
> Fontan to connect left atrium to tricuspid and right atrium to pulmonary artery

In utero therapy is the latest attempt to treat this disorder. It involves a videolaparoscopic procedure to place a catheter into the fetus to perform a fetal valvuloplasty to open the mitral or aortic valve. Once the mitral or aortic valve is opened, the blood flow will allow the left ventricle to grow normally and perhaps allow for either less complex or no surgical repair.[54] Balloon dilation of severe aortic stenosis in the fetus: potential for prevention of hypoplastic left heart syndrome: candidate selection,

technique, and results of successful intervention.[55] It is still too early to tell if this treatment will become the treatment of choice for HLHS.

Perinatal Hospice

Woven throughout this exciting science of in utero therapy resonates the concept that we have two patients. However, what therapy could be offered to those families with terminally ill babies? What could be done to provide care for terminally ill perinates? Many patients do not desire termination of pregnancy no matter what the anomalies or prognosis.[56] The proper response is to turn to *"The Perinatal Hospice"* which demonstrates ongoing care for the family and their baby, not abandonment. "Perinatal Hospice" is "Prenatal diagnosis of the terminally ill fetus in utero leading to perinatal hospice as part of the continuation of end of life care".[57]
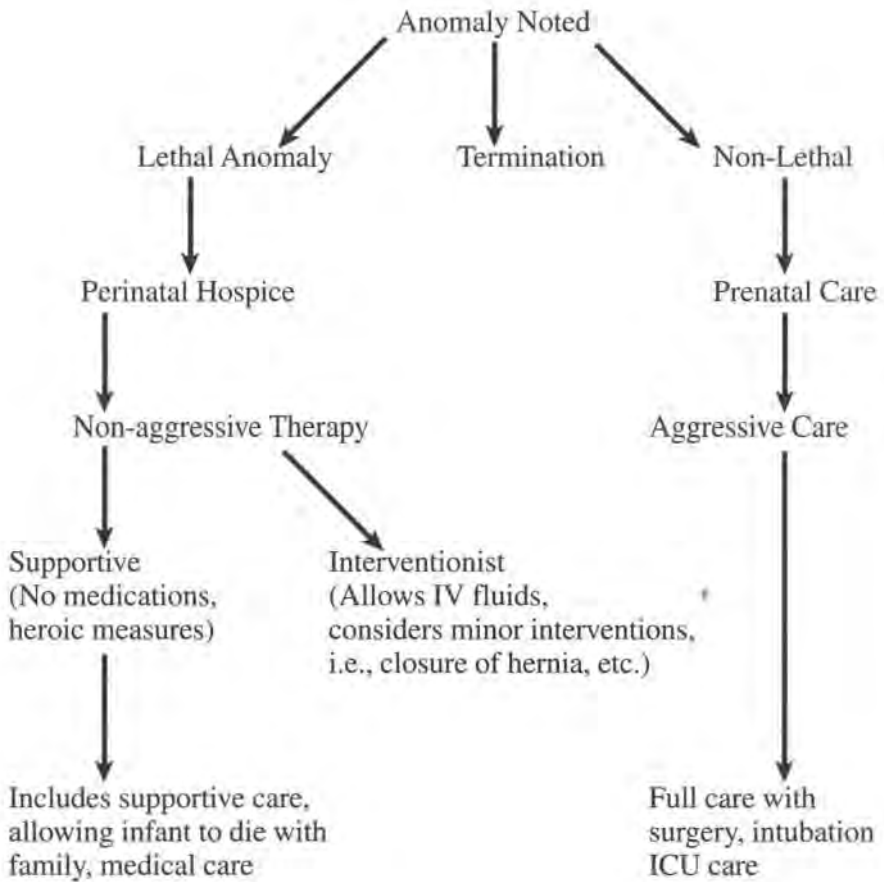
The "Perinatal Hospice" addresses the major concerns of patients and family which are: abandonment, fear, and pain for baby and mother. The "Perinatal Hospice" allows compassion, not abandonment, and enables physicians to fulfull our faith while utilizing our reason/science to expand our ability to care ethically for our patients.

Hospice uses a decision algorithm based on accurate prenatal diagnosis. (See Figure 1, page 205) Sophisticated obstetrical diagnostic ultrasound is utilized as well as amniocentesis for chromosomes and other related disorders. Only terminally ill fetuses with CONFIRMED diagnosis are included in hospice care. The staff involved in care include perinatal/ neonatal staffs, residents/MFM Fellows/students, ultrasonographers (RDMS), nursing services (L&D/antepartum/postpartum), social services, hospital chaplains/local pastors, and grief counseling.

As of December, 2004, Rockford Memorial Hospital (RMH) has provided care for 28 families meeting the criteria for participation in this "Perinatal Hospice" as part of the care in a community based perinatal referral center. A significant majority of these patients 21/28 (75%) have chosen the hospice alternative over early pregnancy termination. The seven pregnancy terminations consisted of fetuses with anencephaly (5 patients), trisomy 18, and triploidy. In the remaining patients, 5/21 (24%) had an intrauterine fetal demise and 16/21 (76%) delivered live born infants. All patients who experienced an intrauterine fetal demise had a vaginal delivery. Of the live born infants, there were 15 vaginal deliveries, four were preterm and eleven were at term. Obstetric indication or maternal request resulted in cesarean delivery for 1/21 (4%) at term. This cesarean section was performed for a child with acrania. The live born infants died within 20 minutes to 256 days after delivery. There were no maternal morbidities or mortalities. Hospice is safe for mother and of infinite value to the parents and family.

Figure 1

Sample Decision Algorithm

Anomaly Noted

Lethal Anomaly   Termination   Non-Lethal

Perinatal Hospice   Prenatal Care

Non-aggressive Therapy   Aggressive Care

Supportive   Interventionist
(No medications,   (Allows IV fluids,
heroic measures)   considers minor interventions,
                          i.e., closure of hernia, etc.)

Includes supportive care,   Full care with
allowing infant to die with   surgery, intubation
family, medical care   ICU care

In closing, let us consider the words of Thomas Sydenham (1624–1689) the "English Hippocrates."

> It becomes every person who purposes to give himself to the care of others, seriously to consider the four following things: First, that he must one day give an account to the Supreme Judge of all the lives entrusted to his care. Second, that all his skill and knowledge and energy, as they have been given him by God, so they should be exercized for His glory and the good of mankind, and not for mere gain or ambition. Third, and not more beautifully than truly, let him reflect that he has undertaken the care of no mean creature; for, in order that he may estimate the value, the greatness of the human race, the only begotten Son of God became himself a man, and thus enobled it with His divine dignity, and far more than this, died to redeem it. And fourth, that the doctor being himself a mortal being, should be diligent and tender in relieving his suffering patients, inasmuch as he himself must one day be a like sufferer.

SOLI DEO GLORIA (To God Alone be the Glory)!

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