Human and Social Dimensions That Arose with the Early Cases of Fetal Surgery to Correct Myelomeningocele

by

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ABSTRACT

This thesis reviews the initial cases of fetal surgery to correct myelomeningocele, a severe form of spina bifida, and discusses the human and social dimensions of the procedure. Myelomeningocele is a fetal anomaly that forms from improper closure of the spinal cord and the tissues that surround it. Physicians perform fetal surgery on a developing fetus, while it is in the womb, to mitigate its impacts. Fetal surgery to correct this condition was first performed experimentally in the mid-1990 and as of 2020, it is commonly performed. The initial cases illuminated important human and social dimensions of the technique, including physical risks, psychological dimensions, physician bias, and religious convictions, which affect decision-making concerning this fetal surgery. Enduring questions remain in 2020. The driving question for this thesis is: given those human and social dimensions that surround fetal surgery to correct myelomeningocele, whether and when is the surgery justified? This thesis shows that more research is needed to answer or clarify this question.

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INTRODUCTION

In the 1980's, research surrounding fetal surgery as an innovation suggested that fetuses that present with a common deformity of spina bifida may benefit from prenatal correction through the use of fetal surgery. (Simpson, 1999). Fetal surgery is a procedure that surgeons perform on a developing fetus while it is in the womb, to correct a fetal anomaly. One of those anomalies includes spina bifida, which results from improper development and closure of the spine and spinal cord. Physicians at Vanderbilt University in Nashville, Tennessee, were some of the first to attempt fetal surgery to correct spina bifida in the early 1990's. During those initial experiments, researchers used sheep as research subjects to study the most minimally invasive type of fetal surgery, endoscopy. After those initial experiments, fetal surgery to correct spina bifida began to evolve. Researchers began performing the endoscopic procedure on sheep in the mid 1990's and then advanced to using hysterotomy techniques—a large incision such as those used in cesarian sections—on human women to perform surgery on their fetuses in the late 1990's, due to the limitations that accompany the endoscopic technique.

In some cases, the innovative fetal surgeries did correct the anomalies, but they also raised several practical, safety, ethical, legal, and policy questions. This thesis will examine the phenomenon and then look at some of the human and social dimensions that arose in the 1990's and still exist as of 2020.

CHAPTER 1

BACKGROUND AND CONTEXT

This thesis is split into three sections: general background on fetal surgery to correct myelomeningocele, a review of the first few cases of surgeons performing this type of intervention, and an account of some of the human and social dimensions that arose. In the initial background section, I explain the fetus as a developing organism and how it can develop myelomeningocele through both genetic and environmental factors. I then describe how spina bifida is a neural tube defect, meaning that it affects the brain, spinal cord, and surrounding tissues, and lay out the different types of spina bifida. In the next part of the background section, I explore how the severity of the anomaly is correlated with its location and size but indicate that it is often a non-lethal anomaly. I then outline the process of fetal surgery and detail the process of opening the pregnant woman's abdomen and uterus to operate on the fetus.

Myelomeningocele is a fetal anomaly that begins to emerge while the fetus is in the womb. A human fetus is an unborn, developing organism that has attained its basic structure and is aged anywhere from eight-weeks after conception until birth (Merriam-Webster). During development, fetal anomalies can occur. An unexpected condition or change to a fetus during pregnancy is often termed as a fetal anomaly (Mercy, 2020). There are two general types of fetal anomalies, structural and functional. Structural anomalies affect a developing fetus's body parts, including the lungs, heart, limbs, and facial features. Functional anomalies affect how the systems and body parts work. Some of those systems include the brain and nervous systems. Spina bifida is a functional anomaly because it affects the spinal cord function. Anomalies put not only the fetus at risk but often the pregnant woman as well, since they have a significant contribution to fetal and maternal morbidity, and mortality (Harrison, 1996).

Fetal anomalies can occur in three different ways: genetically, meaning that they are inherited; environmentally, which are usually due to exposures of the pregnant woman; and abnormalities of unknown or undetermined origin (Milunsky and Milunsky, 2015). Spina bifida is caused by both genetic or environmental factors, according to the National Institutes of Health, a government agency responsible for biomedical research (NIH, 2017). Worldwide, an estimated 7.9 million infants are born with a major congenital malformation per year, according to Aubrey and Jeff Milunsky, geneticists and authors of the book *Genetic Disorders and the Fetus*. In 2010, in the United States, chromosomal anomalies, deformations, and congenital malformations or deformities led to the largest rate of infant death, at 20.8 percent or 5,107 infant deaths out of 24,586 infants born within the year, compared to any other category of causation (Milunsky and Milunsky, 2015). Spina bifida is the most common neural tube defect according to the National Organization for Rare Disorders, a non-profit that provides support for individuals with rare disorders (NORD Staff, 2019). A neural tube defect is a defect that affects the brain, spinal cord, or spine (MedlinePlus, 2019). Around 1,500 to 2,000 infants, out of about four million births, are born with spina bifida per year in the United States (NORD Staff, 2019).

Spina bifida is a fetal anomaly that begins to form during the first few weeks of pregnancy, and it occurs when the spinal cord of a fetus and the tissues that surround it fail to develop properly. Spina bifida is classified as a neural tube defect, meaning it involves the spinal cord, brain, and the tissues that surround them. Spina bifida can also affect the bones of the spine. Normally during the development of the fetus, the right and left sides of the fetus' backbone will join to cover the spine (Medlineplus, 2020). For a fetus that has myelomeningocele, the backbone and spinal canal do not full close before birth. When the tissues and bones do not fully close, the fetus has an incomplete spinal cord. Often a fetus with myelomeningocele will have a sac filled with part of its neural tube that will protrude from its back. According to the Mayo Clinic, an academic medical center, the neural tube begins to form early in gestation, and it closes twenty-eight days post-conception (Mayo Clinic, 2019). The CDC states that spina bifida starts to develop during the first few weeks of pregnancy (CDC, 2020). There are four types of spina bifida, ranging in severity (NIH, 2017).

The severity of the anomaly is influenced by factors like the location, type, and size of the defect. According to the NIH, all of the spinal nerves that are located beneath the malformation are affected, so the higher the malformation is on the back, the greater the amount of damage to nerves and muscle function in the fetus (NIH, 2017). There are four different types of spina bifida: closed neural tube defects, occulta, meningocele, and myelomeningocele. Closed neural tube defects, or closed NTD's, are the first type of spina bifida. Closed NTD's are a group of spinal defects where the fat, bones, or membranes do not grow properly within the spinal column. The anomaly is normally covered by a layer of skin on the fetus' back. Closed NTD's are rare and often times cause few to no symptoms, according to the NIH (NIH, 2017). The second type, occulta, is the most common type of spina bifida, estimating that it occurs in 10 to 20 percent of the general population, with many not knowing that they have it (NIH, 2017) (Cleveland Clinic). Occulta is a piece of skin that covers an opening on the vertebrae. It is also the least severe out of the four different types, and rarely causes symptoms or impairments according to the NIH. The third type, meningocele, occurs when the spinal cord does not close properly that results in an abnormal sac pushing out of the fetus' back. The sac can be filled with fluid, spinal nerves and tissues, and meninges. Meninges are membranes that line and enclose the brain and spinal cord. The last type of spina bifida is myelomeningocele that occurs when the bones of the spinal column do not properly close and results in parts of the neural tube that protrude through an opening on the fetus' back. Usually, myelomeningocele is the only type of spina bifida that surgeons perform fetal surgery on because it is the most severe (NIH, 2017). The signs and symptoms of the types of spina bifida can vary, but in many cases, the anomaly is not life-threatening. The health issues that accompany spina bifida are often unique to the person depending on the location, size, and severity of the defect (NIH, 2017).

Many health issues may result from spina bifida, with some presenting more commonly than others. A few of the common health issues include problems with mobility and physical activity, incontinence, neurological problems, and back problems like pain and scoliosis, according to the Center for Disease Control and Prevention, a government agency responsible for promoting and protecting health. Scoliosis is a condition where the spine has a sideways curvature that often appears as an S-shape. Even though numerous possible health issues may accompany spina bifida, it is often not detrimental to the quality of life, according to Mark R. Foster, who is a doctor that specializes in treatments involving the spine and musculoskeletal system (Foster, 2019).

An outlook for an individual with spina bifida is largely influenced by the severity of the condition, but most children who have the condition can live happy and productive lives and survive well into adulthood, according to Foster (Foster, 2019). An unknown author from the *Post-Gazette*, a news media source in Pittsburgh, Pennsylvania, states that the average lifespan for a person with the condition is around thirty to forty years (Post-Gazette, 2008). Death may result from the condition, depending on the severity and the type, and according to Foster, most infants born with myelomeningocele die shortly after birth (Foster, 2019). The *Post-Gazette* author adds that renal failure is the most common cause of death for individuals with spina bifida (Post-Gazette, 2008). Renal failure occurs when your kidneys suddenly lose the ability to filer and excrete waste. If waste is not filtered and excreted from the body, waste may accumulate and create an imbalance in the body's chemical makeup (Mayo Clinic Staff, 2019). That chemical imbalance can be toxic to the body, leading to symptoms that can be fatal. With the considerable number of fetuses affected by anomalies like spina bifida, there have been many attempts to generate corrections for abnormalities.

With the development of certain technologies and innovations, including those that pertain to human genetics and imaging technologies, detection of some of the fetal anomalies that arise during pregnancy, including spina bifida, became more accessible in the mid-1950's. By the early 2000's, there was a rising urgency in medical care to gain more knowledge within the field of prevention and detection of fetal abnormalities because not much information was known, according to Milunsky and Milunsky, authors of *Genetic Disorders and the Fetus* (Milunsky and Milunsky, 2010). Different innovations, such as genetic testing, led to a gain in knowledge on detection of genetic anomalies. As stated in *Genetic Disorders and the Fetus*, genetic testing showed that 3,412 genes have been identified to cause phenotype-mutations and 7,000 uncommon genetic disorders are known. The ability to detect certain genetic anomalies sparked questions in research, one of them being whether the anomalies could be rectified before birth. After the introduction of those questions and ideas, experimental treatments and procedures were later attempted in order to correct anomalies before birth. (Milunsky and Milunsky, 2015).

Knowledge about fetal anomalies has led to further advancements in detection and treatment. In the first and second trimester of a pregnancy, prenatal screening tests can detect many fetal abnormalities, including some environmental anomalies that genetic testing may not be able to detect. Blood and tissue sampling can test for genetic anomalies, and ultrasounds and other scans can detect structural anomalies. With these new technologies, procedures like fetal surgery have been created to correct malformations in utero.

According to the Children's Hospital of Philadelphia in Philadelphia, Pennsylvania, fetal surgery is favorable because it has been found that prenatal intervention has several benefits (The Children's Hospital of Philadelphia, 2019). The Children's Hospital of Philadelphia states "More children in the prenatal surgery group were able to walk independently by the time they were school age, and they showed better gross and fine motor skills. They also demonstrated better control over their bladder and bowel movements; children who underwent prenatal surgery were almost six times as likely to go to the bathroom on their own than those operated on after birth" when they compared two groups of infants, with one previously undergoing fetal surgery and the other having undergone postnatal repair. They also state that fetuses who undergo fetal surgery are less likely to have additional surgeries after birth (The Children's Hospital of Philadelphia, 2020).

There are many types of fetal surgery, but the most common one used to correct spina bifida is open womb fetal surgery, or hysterotomy Open womb fetal surgery was established in the early 1960's in Auckland, New Zealand, and in the early 1980's, it began in the United States (O'Connor and O'Neil, 2011). This type of fetal surgery is performed between eighteen and thirty weeks of gestation (Sutton, 2008). Some types of fetal surgery, including hysterotomies, are more invasive than others (Sutton, 2008).

During the process of open womb fetal surgery or hysterotomy to correct spina bifida, the abdomen and uterus is opened by surgeons to gain access to the fetus and then the anomaly is surgically corrected while in utero. Generally, during the process of fetal surgery begins with anesthesia administered to the pregnant woman prior to the procedure to induce unconsciousness. They also have to do something to prevent the onset of labor, right? As of 2020, the fetus may also be given medications as needed for pain control and to avert movement (Saxena, 2009). Warmed fluids are pumped into the placenta to keep the amniotic fluid levels safe for the fetus and the pregnant woman. In order to repair the myelomeningocele in utero, the surgeon must operate on the fetus's back while it is still in the womb. After the repair is complete, any incisions that were made on the fetus and pregnant woman are closed through stitches, staples, or glue. The fetus then remains in the womb until the woman is ready to give birth. When prenatal surgery to correct myelomeningocele first became accessible, it was seen as a very exciting new technique, but it was also associated with many questions and risks. However, prenatal correction is not the only way to correct myelomeningocele.

Surgeons can perform postnatal surgery after birth and it only requires an operation on the newly born infant, in comparison to fetal surgery where both the pregnant woman and the fetus are operated on. When physicians correct myelomeningocele after birth, they use the same technique to repair the anomaly. The only difference between prenatal and postnatal repair that the surgeons do not have to operate on and open the pregnant woman for a postnatal repair. Before the first few cases of fetal surgery to correct myelomeningocele, surgeons used postnatal repair to correct the anomaly. To understand the issues involved and consider why fetal surgery is used at all, I will next introduce some key cases of clinical innovations that raised questions.

CHAPTER 2

CASES

In this next section, I evaluate some of the initial instances where surgeons perform fetal surgery to correct myelomeningocele, starting with some of the experiments performed at Vanderbilt University. In the early 1990's, physicians at Vanderbilt University in Nashville, Tennessee, were some of the first to attempt fetal surgery to correct myelomeningocele. Next, I discuss how, in 1993, physicians at Vanderbilt used two types of fetal surgery, an endoscopic technique and a hysterotomy technique, to practice surgeries on healthy fetal lamb models.

Next, I review how the Institutional Review Board at Vanderbilt halted experiments until 1998, due to the limited safety and efficacy demonstrated during initial experiments. In 1998, physicians at Vanderbilt reattempted fetal surgery to correct myelomeningocele. They used a hysterotomy technique, but this time they operated on human subjects. The 1998 attempt showed that myelomeningocele could be repaired prenatally using a hysterotomy technique, but the success of the repair and the safety of the procedure remained unclear. Physicians from a few other hospitals began performing the procedure after the experiments from Vanderbilt had been publicized and by 2003, fifty-six fetuses had been operated on. In 2003, the Management of Myelomeningocele Study (MOMS) began at Vanderbilt and two other institutions, with the goal of determining the safety of the procedure. In 2010, the study was stopped prematurely because they achieved their desired results, according to physicians, and as discussed further below.

1993 Physicians Perform Endoscopic Procedure on Pregnant Sheep

In 1993, Michael L. Copeland, Joseph P. Bruner, William O. Richards, Håkan W. Sundell, and Noel B. Tulipan, physicians from Vanderbilt University in Nashville, Tennessee, published an article titled "A Model for In Utero Endoscopic Treatment of Myelomeningocele," where they describe one of the first experimental attempts at fetal surgery to correct myelomeningocele, which they performed on fetal lambs. During the experiments, authors simulated the repair of myelomeningocele in utero using healthy fetal lambs. Authors state that they used healthy fetal lambs because lambs that already present with myelomeningocele would be difficult to find. There are several types of fetal surgery and the authors began experiments using an endoscopic technique. The endoscopic technique is a less-invasive type of fetal surgery that requires smaller incisions, compared to other types, such as hysterotomies, which fully expose the fetus (Bruner, 2003). Authors began with the endoscopic technique because it allows them to keep in utero conditions like the conditions that would exist if there was no incision made at all.

After a few initial procedures using the endoscopic technique, the authors switched to performing hysterotomies instead due to visibility and accessibility limitations with the endoscopic technique. All the lamb fetuses and pregnant sheep survived the procedures using both of the techniques. In "A Model for In Utero Endoscopic Treatment of Myelomeningocele," the authors find that even though prenatal correction of myelomeningocele using an endoscopic procedure is feasible, there are too many limitations and restrictions with this type of fetal surgery and suggest that definitive closure should be performed after birth, and that should be more research on the hysterotomy technique.

The authors of “A Model for In Utero Endoscopic Treatment of Myelomeningocele” collaborated on the article after they performed the study together at Vanderbilt University. The first author, Copeland, is a medical doctor who specializes in surgery of the brain and nervous system who was working at Vanderbilt at the time of the study (US News Doctors, 2020). The next author, Bruner, is a surgeon who specializes in obstetrics and gynecology, or OB/GYN, meaning that he specializes in surgical procedures that relate to female reproductive health (Bruner, 2003). Richards is also a surgeon who worked at Vanderbilt at the time and specializes in gastrointestinal health, or health of the stomach and intestines (Gastrointestinal SQUID Technology Laboratory, 2020). Another collaborator, Sundell, is a medical doctor who specializes in surgery that is performed on fetuses, neonates, and infants (Vanderbilt, 2010). The last author is Tulipan, and he is a medical doctor who also specializes in surgery of the brain and the nervous system (SOCKs, 2020).

The article was split into five untitled sections. In the first section, the authors state that they obtained four healthy pregnant sheep for the procedures and they describe why they performed the procedures on healthy fetal lambs. In the next section, the authors describe how they made three small incisions through the pregnant sheep’s abdomen and then submitted endoscopes through the holes in order to operate on the fetal lamb. In the third section, the authors state that they practiced performing a skin graft on the healthy fetal lambs in order to replicate the procedure that would be performed when correcting myelomeningocele. In the next section, the authors state that the endoscopic technique resulted in limitations and so they performed an additional procedure on the lambs using a hysterotomy technique. In the last section, the authors describe how correction of myelomeningocele prenatally using an endoscopic technique is possible but it is accompanied with restrictions, and at the time of publication, the authors believed that the hysterotomy technique might be feasible but it needed to be experimented with more before it was performed on humans.

In the initial section, the authors state that they chose four healthy pregnant sheep to perform the procedures on. During the study, the authors timed pregnancies in four different mixed-breed female sheep. The fetal lambs that were part of the study were healthy and did not have any anomalies. According to the authors, fetal lambs that already presented with myelomeningocele would be difficult to find. The lambs were used as animal models to test the feasibility of endoscopic fetal surgery to correct myelomeningocele.

In the second section, the authors state the initial steps of the endoscopic procedure which include administering amnesia and making an incision through the abdomen of the pregnant sheep. The authors state that they waited until the sheep were approximately ninety-days gestation before they performed the surgery. To begin the procedure, the authors administered anesthesia to the pregnant sheep in order to put them to sleep. They state that they made an incision on the midline of the abdomen of the sheep, passing through the layers of the abdominal wall to expose the uterus. The anatomy of the stomach of a female consists of a layer of skin, followed by an abdominal wall, and then a uterus that lies underneath. The fetus is located within the uterus of a pregnant female. During the endoscopic procedure, there is not a large incision through the uterus. The only large incision passes through the abdomen of the pregnant sheep, which is different compared to other techniques. During other techniques, like a hysterotomy, a direct incision is made through the uterus to fully expose the fetus. After they make the initial incision, they move the sheep fetus into a position with its back facing up, in order for the authors to operate on its back.

The authors continue in the second section and state that they initially chose to use an endoscopic technique during fetal surgery because it is a less-invasive technique when compared to other types of fetal surgery, and they describe how they used probes to perform the surgery. They add that the endoscopic technique would allow them to preserve in utero conditions more effectively when compared to the other techniques. After an incision is made through the abdomen and the fetal lamb is secured, the researchers made three small holes in a triangular shape through the uterus of the pregnant sheep and used surgical tools to generate a port for probes to enter. A port is a small, metal or plastic, hollow disc that is inserted beneath the skin. Ports can be used during surgery for various reasons but in this case, ports were used to separate the skin of the hole that was made through the sheep's uterus. The plastic or metal port creates a covered pathway through the uterus of the female, and through this pathway, they can insert different probes through the uterus to reach the fetus. The holes where the ports were inserted, were made through cautery incisions. During the cautery incisions, the physicians make a one-centimeter long incision and use an extremely hot rod to burn the blood vessels and tissues within the incision, to lessen the amount of blood lost. Two ports were placed horizontally above the lower portion of the sheep fetus' back and the other port was located above the higher midline portion of the back. Endoscopes, or flexible tubes with a camera, and/or light, and/or surgical tool located at the end of it, were placed through the ports. The image from the endoscope was displayed on a monitor so the physicians could see the fetus. and the placement of the endoscopes, without fully exposing the fetus (CHOP, 2020).

In the next section, the authors explain how they performed a skin graft to simulate surgical coverage of an opening that would be caused from myelomeningocele. A skin graft is a piece of skin that has been removed from one part of a body and transplanted to another. During their research, the authors had no way of generating myelomeningocele in the sheep fetuses, so their main goal of the experiment was to perform a successful skin graft procedure on the sheep fetuses through fetal surgery, to determine the efficacy of the procedure. According to the authors, to correct myelomeningocele in utero, a skin graft would have to be performed to cover the part of the spinal cord that failed to develop or close properly. During initial experiments, the authors obtained a piece of skin from an unspecified location on either the pregnant sheep, or the fetal lamb, that they would later use as a skin graft on their sheep fetus.'

The authors continue in the third section to explain how physicians remove a piece of skin from the sheep fetus' back, or they remove a piece of skin from the pregnant sheep, and they described how they practiced grafting that area. In order to generate standard conditions for a skin graft, the authors removed a piece of skin from the midsection or side of the fetus' back using endoscopic scissors or forceps, an instrument that can be used to move or spread tissues. After the layer of skin was removed, it was either grafted with the same removed skin from the fetus or the graft obtained from the pregnant sheep. Once they successfully put a graft in place with an adhesive, they then remove the endoscopes and ports, and if any amniotic fluid was lost it was replaced with saline. Amniotic fluid surrounds the fetus in the amniotic sac, and it has many functions, including the transfer of water and nutrients from pregnant woman to fetus. Substituting lost amniotic fluid will ensure that the fluid levels inside the amniotic sac does not drop too low, according to the authors (Haynes, 1995). After the procedure, the authors observed the recovery of the sheep, and after their recovery, half of the sheep, including the pregnant female and the developing fetus, were killed through euthanasia.

In the fourth section, the authors state that they then performed an additional skin graft procedure using a hysterotomy technique on two of the recovered fetuses. During the hysterotomy technique, the authors made a large incision through not only the abdominal wall but the uterus as well, fully exposing the fetal lamb. For that technique, they did not use endoscopes but instead performed the surgery directly through the large opening made by the incisions. The authors state that during the hysterotomy procedure, they removed a portion of a muscle on the sheep fetus' back and they also removed portion of the meninges that surrounded a section of the spinal cord. The meninges are membranes that encase the brain and spinal cord, and they act as a supportive and protective layer. They did not explain the reason for the removal of the muscle and meninges. After the removal, the remaining sheep were euthanized. Although they carried out additional experiments using this technique, the authors state that hysterotomies have been previously associated with uterine irritability and notable fetal morbidity and that additional research needs to follow using the hysterotomy technique. The authors state that their main interest was to investigate the feasibility of endoscopic techniques to prevent those risks, but they do not state their reason for performing additional hysterotomy procedures on the two sheep.

In the last section, the authors state the endoscopic procedure comes with several limitations and suggest definitive closure postnatally, until more research has been done using the hysterotomy technique. Three weeks later the sheep were euthanized, and the authors dissected them to determine if the procedure was successful. They state that scar-less or near scar-less healing was noted in all the fetal sheep. They add that not all the grafts adhered correctly, which could be due to the placement of the graft and type of glue that was used. There was no fetal or maternal morbidity associated with the procedure, according to the authors. They add that although early experiments made the endoscopic procedure seem feasible, the limitations to the endoscopic technique caused it to be an unrealistic goal. The limited view of the graft site through the endoscopes made precision difficult, according to the authors. Due to low visibility through the endoscope while inside the womb, it was likely that fragile fetal tissue could be accidentally torn by the surgical tools that were attached to the endoscopes.

As previously discussed, an open wound may result from the myelomeningocele anomaly and amniotic fluid may get into that wound while the fetus is in the amniotic sac. According to the authors, studies performed on fetal rabbits and pigs suggest that components of amniotic fluid may inflict injury to an open wound and may inhibit the healing of a wound (Haynes, 1995). They add that the goal of the skin graft through the endoscopic procedure was to create a patch to block the exposure of the wound from myelomeningocele to amniotic fluid (Larson et al., 2010).

In 2013, surgeons from the Kyungpook National University School of Medicine in Daegu, Korea, published a study with nearly opposite findings. They found that stem cells, or cells with the potential to develop into different types of cells that aid in repair, from amniotic fluid shortened wound healing periods (Dug Yang et al., 2013) (Medline Plus, 2020). These findings suggest amniotic fluid may aid wound healing.

At the time of the experiment, definitive closure through a hysterotomy while in utero would be too complicated to perform on humans and would be associated with a higher risk of maternal morbidity, according to the authors. They suggest that definitive closure to correct myelomeningocele should be performed after birth. The authors stated that more research on the hysterotomy technique needed to be performed before it could be performed on human participants (Copeland et al., 1993). Through the next few years, the authors from Vanderbilt continued to research the technique and in 1998, that research moved from animal to human models.

1998 Physicians Perform Hysterotomy Technique on Human Fetuses

In 1998 Joseph P. Bruner and Noel B. Tulipan published "Myelomeningocele Repair in Utero: A Report of Three Cases," in the *Journal of Pediatric Neurosurgery*. In their article, they review an experiment they performed at Vanderbilt University, which is one of the first instances where experimental fetal surgery to correct myelomeningocele was performed on a human fetus. The experiment participants consisted of three pregnant women whose fetuses were diagnosed with myelomeningocele through ultrasound imaging. During the experiment, Bruner and Tulipan performed fetal surgery using a hysterotomy technique to correct myelomeningocele on the three pregnant women and their fetuses, to test the feasibility of the procedure. In the article, the authors state that the surgeries were successful for all three of the pregnant women and their fetuses, and that they recovered without complications, making it one of the first times that fetal surgery to correct myelomeningocele was successfully performed on a human fetus.

The two authors of “Myelomeningocele Repair in Utero: A Report of Three Cases,” Joseph P. Bruner and Noel B. Tulipan, were two of the surgeons who performed and authored the previous study that was discussed, “A Model for In Utero Endoscopic Treatment of Myelomeningocele.”

In “Myelomeningocele Repair in Utero: A Report of Three Cases,” the authors separate the article into four different sections. In the first section titled “Background,” the authors describe how they believe that previous research provides evidence that intrauterine environments may cause the myelomeningocele to worsen. In the next section, “Methods,” the authors state that they performed a hysterotomy on three pregnant women whose fetuses had been diagnosed with myelomeningocele. In the third section titled “Results,” the authors state that all three of the fetuses recovered without incidence. In the last section titled “Conclusions,” the authors state that even though there are limited participants that took part in the study, it provides evidence that fetal surgery to correct myelomeningocele is feasible.

In the first section titled “Background,” Bruner and Tulipan state that evidence accumulated throughout the ten years prior to publication led them to believe that intrauterine environments may cause myelomeningocele to worsen while it is exposed in the womb. Research prior to the experiment that was performed on fetal pigs and rabbits, suggests that amniotic fluid may cause trauma to myelomeningocele and might prevent an open wound from healing. As previously discussed, in most cases of myelomeningocele, the spinal cord protrudes from the back of the fetus and the tissues surrounding the spinal cord fail to close properly, resulting in an open wound. Bruner and Tulipan suggest that closure of the tissues surrounding the deformity may encourage healing of those tissues and improve neurologic outcome of the affected fetus.

In the next section, "Methods," Bruner and Tulipan state that the participants had to have been previously diagnosed with fetal myelomeningocele and add that fetal surgery was performed at twenty-eight weeks of gestation. The three pregnant research subjects elected to take part in the experiment, but how the participants found out about the experiment is not stated. The authors address the fact that the subject group was relatively small and suggest a larger study for future research. The requirements for entry into the study includes diagnosis of myelomeningocele in the fetuses through ultrasound imaging. According to the authors, around twenty-eight weeks of gestation, the three participants underwent fetal surgery. According to MedlinePlus, an online index of medical related materials, a standard pregnancy lasts between thirty-eight to forty-two weeks, so the procedure was performed during the third trimester of the pregnancy.

In the "Methods" section, the authors state that they performed a hysterotomy on the pregnant women to obtain access to the fetus. To begin the experiment, Bruner and Tulipan made a large incision through the abdomen and then through the uterus of the pregnant women. They then operated on the fetus to close the myelomeningocele anomaly on the fetus' back. After the operation, they closed both the pregnant woman and the fetus' wounds using staples and glue.

In the next section titled "Results," Bruner and Tulipan state that the three patients experienced some minor preterm contractions after surgery but that those subsided and all three recovered without incidence. According to the authors, the females experienced contractions directly after surgery but that they subsided five days after surgery. After the contractions subsided; the pregnant women were released. Between thirty-three weeks and thirty-six weeks gestation, the pregnant women returned to the university to have a c-section (Mayo Clinic, 2020). The authors state that all three of the fetuses showed neurological function that was expected with the given anomaly when they returned for evaluation. They add that one of the infants had to have an additional surgery after birth which was related to the anomaly. They state that all of the pregnant women and fetuses recovered after the surgery.

In the last section, "Conclusions," the authors state that the study included a limited number of participants but that the results from the study show that fetal surgery to correct myelomeningocele is possible through a hysterotomy technique. They state that low morbidity occurred with their experiments. They also state that the study included a low number of participants and suggest that additional studies with more participants is needed to determine how beneficial the surgery is. (Bruner and Tulipan, 1998)

After the hysterotomy technique on a human fetus in 1998, experimental surgery continued, and several other institutions started to research the technique. By 2003, fifty-six pregnant women and fetuses had been operated on using the hysterectomy technique.

2003 Management of Myelomeningocele Study

In 2003, researchers from seven institutions collaborated on the Management of Myelomeningocele Study, abbreviated as (MOMS), to compare two different techniques that are used to repair myelomeningocele, prenatal fetal surgery, and postnatal surgery. Several experiment reviews appeared based on the study, but the primary one discussed throughout this thesis is, “A Randomized Trial of Prenatal Versus Postnatal Repair of Myelomeningocele.” Many investigators collaborated on the study, including some of the surgeons who took part in early experiments from Vanderbilt University. According to the authors, prior to the 2003 experiment, more than 200 fetuses had surgical procedures performed in utero to repair myelomeningocele. They state that previous procedures that experimented with fetal surgery to correct myelomeningocele did not use control groups, which they believe was needed when studying the efficacy of a new surgical technique. Investigators add that prior experiments only studied the efficacy of fetal surgery to repair myelomeningocele and did not study the safety of it. Investigators performed the MOMS trial in 2003 to study the safety of fetal surgery to repair myelomeningocele for human fetuses but they ended the study earlier than expected in 2010 because they believed that they had obtained the desired results (NIH, 2020).

Investigators from several different institutions collaborated on the MOMS trial, but three major ones that took part in it. Those three include the University of California at San Francisco (UCSF) in San Francisco, California, the Children’s Hospital of Philadelphia (CHOP) in Philadelphia, Pennsylvania, and Vanderbilt University Medical Center in Nashville, Tennessee. Vanderbilt University collaborators include Joseph P. Bruner and Noel B. Tullipan, both of which took part in some of the initial procedures performed in 1993. Other sponsors and collaborators include the George Washington

University Biostatistics Center in Bethesda, Maryland, the Eunice Kennedy Shriver National Institute of Child Health and Human Development in Waltham, Massachusetts, the University of Pittsburgh in Pittsburgh, Pennsylvania, the University of Houston in Houston, Texas, and The University of Texas Health Science Center, Houston in Houston, Texas (NIH, 2020) (Pollesche, 2017). Even though many organizations and institutions contributed to the study, experimentation on human subjects was only performed at UCSF, CHOP, and Vanderbilt. Universities and hospitals in the United States were asked to not perform fetal surgery to repair myelomeningocele while the trial was ongoing.

In “A Randomized Trial of Prenatal Versus Postnatal Repair of Myelomeningocele,” the authors split the article into four main sections. In the initial section titled “Background,” the authors state that myelomeningocele is the most common and most severe type of spina bifida and add that it may be improved through prenatal repair. The second section titled “Methods” is where the authors state that they used a control group and an experimental group in the study and with women enrolled in the study randomly assigned to one of them. The next section, “Results,” is where the authors discuss the primary outcomes, which were improved ability to move from the infants from prenatal surgery but an increased risk to preterm delivery and a higher chance of the incision site rupturing during the premature delivery. In the last section titled “Conclusions,” the authors state that improved motor function and decreased need for shunting resulted from prenatal surgery but that it resulted in increased maternal and fetal risks, when compared to postnatal surgery.

In the initial “Background” section, the authors state that myelomeningocele is a common anomaly that often results in several other anomalies, making it the most severe type of spina bifida. They add that previous research suggests that the anomalies from myelomeningocele may worsen throughout the course of the pregnancy. According to the authors, prior research suggests that prenatal repair may improve the quality of life for the fetus, when compared to postnatal repair. They state that although previous studies have suggested that prenatal surgery may be successfully performed, the safety of the procedure is still in question. The goal of the MOMS trial is to test the safety of prenatal surgery to correct myelomeningocele.

In the “Methods” section, the authors describe the inclusion criteria, which includes the fetus having myelomeningocele in a specific location, evidence of hindbrain herniation in the fetus, and the pregnant women being between certain ages. The researchers state that before the study was performed, review boards approved the study at each institution where it was performed. The researchers state that the inclusion criteria was specific. To be enrolled in the study, the women must have been pregnant with a fetus that had been diagnosed with myelomeningocele. The myelomeningocele must have been located between the bottom of the neck and top of the tailbone of the fetus. To be enrolled, the women must have also been at least eighteen years old, and the fetus must have evidence of hindbrain herniation.

Hindbrain herniation is a deformity where parts of the brain move downwards toward a hole at the bottom of the skull, called the foramen magnum. The foramen magnum is the hole that the spinal cord goes through to connect to the brain. Hindbrain herniation may occur for several different reasons, and one of them includes a pressure difference that results from spina bifida. When spina bifida results in a pouch that protrudes from the lower back, it may cause a pressure difference in the cerebrospinal fluid, which then may cause hindbrain herniation in the brain (Williams, 1981).

The authors state in the “Methods” section that, along with hindbrain herniation as an inclusion factor, there were also several exclusion factors. Some of those include additional fetal anomalies separate from myelomeningocele, the pregnant woman having a high body mass index, and if she has previously had a preterm birth. According to the authors, all of those factors could negatively impact the surgery or the study as a whole. They state that a high body mass index or an additional anomaly may make the surgery more dangerous. They add that if a woman has already had a preterm birth, then she may be more likely to have another one, which could negatively impact the study because then researchers would not be able to tell if a preterm birth was the result of the surgery or if it was because of other factors.

The authors continue in the “Methods” section to state that the participants were evaluated before the study, given written consent, and then randomly placed in the experimental or control group. They state that women interested in the study contacted a coordinating center. If the women passed basic eligibility, then they would be directed by the coordinating center to one of the three clinical centers. There they would be evaluated for further eligibility criteria at the clinical center and if they qualify, would be given a written consent form. The information given on the form is not detailed in the article. The authors then state that the participants were randomly assigned to the control group receiving postnatal surgery, or the experimental group receiving prenatal surgery with a one to one ratio.

In the same section, the authors describe how they performed a hysterotomy on the experimental group and postnatally closed the myelomeningocele for participants in the control group. In the experimental group, the researchers performed a hysterotomy once the women had reached twenty-six weeks gestation, using the same technique as earlier described. According to the authors, they made a large incision through the abdomen and uterus of the pregnant woman and then they operated on the myelomeningocele on the fetus' back. They state that women in the experimental group stayed close to their assigned clinical center until they reached thirty-seven weeks gestation. At thirty-seven weeks, the women who had fetal surgery returned to the hospital to have a c-section. The women who were part of the control group also returned to the clinical center at thirty-seven weeks for a c-section, except their fetuses were operated on directly after birth. Once the anomalies had been surgically addressed, the infants and the pregnant women were required to return to the clinical center when the infants hit twelve and thirty months of age. When they returned, researchers performed both neurological and physical exams in the experimental groups and control groups in order to compare the outcomes from both.

In the next section titled "Results," the authors note that participants who received prenatal surgery had a higher risk of experiencing preterm labor, and/or maternal and fetal morbidity. On 7 December 2010, the data and safety monitoring committee for the study met and concluded that the study should be stopped early due to efficacy seen in fetal surgery. At the time the study ended, 183 pregnant women had taken part. According to the authors, there were no maternal deaths. Maternal morbidity pregnancy complications were more common in the experimental group who received prenatal surgery. They also state that fetuses that underwent prenatal surgery were on average delivered around thirty-four weeks gestation with 13 percent of that group experiencing premature births. Fetuses that underwent postnatal surgery on average were born at thirty-seven weeks, with no premature births in that group. Two of the fetuses died in each group while in the womb, before any operations took place.

They continue in the “Results” section to state the primary outcomes from both prenatal and postnatal surgeries. The first was infant death and the need for additional surgeries after the repair performed during the study. It is not clear why they combined infant death and the need for additional surgeries as one primary outcome. They do not state exact numbers for either group. The only information given about those primary outcomes was a percentage, where the authors grouped infant death and the need for additional surgeries together. 68 percent of infants from the experimental group and 98 percent of infants from the control group either died or required additional surgeries related to their myelomeningocele anomaly. At the twelve month and thirty-month evaluations, the experimental group who received fetal surgery, had more control over their body movements. It was also found that infants that underwent prenatal surgery had better motor function when compared to the postnatal group, but both groups had similar cognitive abilities.

In the “Discussion” section the authors state that several variables improved from fetal surgery when compared to postnatal surgery, but prenatal surgery was associated with higher risks of preterm labor and maternal and fetal morbidity. Some of the variables that improved include body movement and brain function, infant death, and the need for additional surgeries after the initial procedure. They add that, although prenatal surgery is seen to improve those factors, the surgery is also associated with increased maternal and fetal morbidity and prematurity. They also report that prenatal surgery was associated with a higher rate of preterm births when compared to postnatal repair. Lastly, they state that the benefits of prenatal surgery must be balanced with the risk of prematurity and both fetal and maternal morbidity (Adzick et al., 2011).

From the above description of the early cases of fetal surgery to correct myelomeningocele, we can see that clinical researchers had brought a potentially exciting new innovation to the treatment of the most severe case of spina bifida. Not all the procedures were successes, however. The procedures exposed both the pregnant woman and the fetus to considerable risk. Several issues arose in regard to the practical, ethical, legal, and safety of fetal surgery to correct myelomeningocele. For example, is it ethical to perform fetal surgery on both the pregnant woman and the fetus when the pregnant woman receives no direct benefit from the procedure? I review some of the most enduring questions next.

CHAPTER 3

HUMAN AND SOCIAL DIMENSIONS

In this section, I review enduring human and social dimensions of fetal surgery to correct myelomeningocele. This section examines four main dimensions. In the first section, titled "Physical Risks," I discuss the risks imposed during the first few initial cases at Vanderbilt and review the physical risks to both the pregnant woman and the fetus from fetal surgery to correct myelomeningocele. I also review the physical outcomes from the surgery for the fetus/infant and the practicality of the procedure. In the next section, "Psychological Dimensions," I discuss how a pregnant woman's psychology may cause her to subject herself to a surgery that she might not otherwise consider because of the idea of hope. Is it possible that the idea of the fetus becoming her future child, may drive her to proceed forward with the surgery without fully considering her other options? The third section titled "Physician Bias" is where I describe a study that shows that physicians may have a bias towards fetal surgery in comparison to postnatal repair because of the allure of interesting technical work. Is it possible that the physicians are enticed by the advanced techniques of the procedure and, if so, would that bias make them recommend fetal surgery to correct myelomeningocele over other techniques? In the last section, "Religious Convictions," I discuss how religion may influence a woman's decision once she finds out that her fetus presents with an anomaly.

Physical Risks

In some of the first cases at Vanderbilt, performed by Bruner and Tulipan, practical and ethical questions arose even though those fetal surgeries seemed to offer a few benefits to the infants, such as better motor skills than infants who underwent postnatal repair. Key among these issues were the surgical risks to the pregnant woman, limited visibility during the procedure, and outcomes for the fetus that were poorer than the outcomes that were reported. On this last point: during an interview with Wall Street Journal reporter Ron Winslown in 1999, Bruner and Tulipan report results that suggest early surgeries had far poorer outcomes for the fetuses than their articles stated. In the interview, Bruner states that the results of the first few surgeries on sheep were an "unmitigated disaster," due to the lack of accessibility, or the ability to access the fetus for surgical manipulation using endoscopic techniques. Winslow also states that, out of the four human fetuses that they performed some of the first procedures on, two later died and the other two were born prematurely. In the published reports on those procedures, the surgeons never state this sort of outcome (Ron Winslow, 1999).

There are several different physical risks borne by the pregnant woman during fetal surgery to correct myelomeningocele, including possible risk during the procedure and after completion. One of the issues associated with fetal surgery is that the procedure subjects two lives to an invasive surgery, the pregnant woman's and the fetus's. The pregnant woman has no direct benefit from fetal surgery according to Joshua Copel and his colleagues, authors of *Obstetric Imaging: Fetal Diagnosis and Care* (Copel et al., 2018). The pregnant woman must undergo the invasive procedure in order for the fetus to be operated on prenatally, and there are surgical risks that she is subjected to during that process. Some of the risks that the pregnant woman is subjected to include: anesthesia complications like nausea or vomiting, bleeding complications such as a hemorrhage or blood clots, injury to the body such as accidental incisions, paralysis, breathing problems, complications during the healing process such as infection or scarring, and many more (CHOP, 2020).

After fetal surgery is performed, the pregnant woman must have a c-section for her current pregnancy, which means two surgeries within a short period of time (Cardinal Glennon Children's Hospital, 2020). She must have a cesarean section because, if she were to have a vaginal birth, the pressure from the neonate as it is traveling down the birth canal may cause her incision to re-open (Anna Smajdor, 2010). When the pregnant woman goes to give birth, surgeons re-open her incision site, and they deliver the fetus through that incision. (Anna Smajdor, 2010). In some cases, it may be possible for later pregnancies to be delivered vaginally, but a cesarean section is recommended due to the risk of the incision rupturing (C.S. Mott Children's Hospital, 2020).

The fetus may also be subject to certain physical risks, including infection, bleeding, preterm birth, and even stillbirth (CHOP, 2020). Even though the fetus is at risk for severe complications, the ethical concerns about this risk are lower. The fetus has the potential to directly benefit from the procedure, through correction of its anomaly, while the pregnant woman receives no direct physical benefit to herself.

Even though fetal surgery to correct myelomeningocele may benefit some, only a small number of fetuses that present with myelomeningocele will be candidates for the prenatal surgery due to the physical size and location of their anomaly. In a trial published in 2011 titled "A Randomized Trial of Prenatal versus Postnatal Repair of Myelomeningocele," Scott Adzick and colleagues examined the differences between pre and postnatal correction, and noted that prenatal correction through fetal surgery may be beneficial, but only for carefully selected fetuses. The anomaly must be a specific size and in a certain location for a fetus to be a viable candidate for the surgery (Adzick et al., 2011). Nichelle Whitehead, a doctor who specializes in obstetrics and gynecology, states that she wishes that the percent of fetuses who might benefit from fetal surgery could be higher (De La Bastide, 2017).

Another issue raised is that myelomeningocele is not always life-threatening and that it only becomes life-threatening if other conditions arise. The anomaly only becomes life-threatening if the fetus develops hydrocephalus. Hydrocephalus is a buildup of cerebrospinal fluid in the brain, which can be life-threatening (Children's Hospital at Vanderbilt, 2020). Anna Smajdor, a research ethicist states, "The risks imposed on women whose fetuses undergo surgery are thought to be justified only if the life of the fetus is in danger." (Anna Smajdor, 2010). She also states that other anomalies that are not life-threatening should have a correction performed after birth. In some, but not all cases of myelomeningocele, a fetus may be susceptible to hydrocephalus which may cause the anomaly to become life threatening. If a fetus does contract hydrocephalus, it is generally not treated until after birth.

In a study performed by Giorgio Carrabba and colleagues in 2019, prenatal fetal surgery to correct myelomeningocele was performed on five pregnant women and after the surgery was performed and the five infants were born, three of them contracted hydrocephalus. Wouldn't this mean that one of the main benefits of prenatal surgery, which is the correction of an anomaly prenatally in order to prevent it from worsening, isn't actually a benefit to this type of procedure at all because the anomaly can still become life-threatening even after said correction? Scott Adzick, a medical doctor who works at the Center for Fetal Diagnosis and treatment, states that at least 80 percent of fetuses with myelomeningocele contract hydrocephalus. He also states that 46 percent of spina bifida patients that have shunts put in, have complications with them within the first year (Adzick, 2009). There are some indications that prenatal surgery may improve hydrocephalus outcomes for the fetus but as of 2009, it was still an unproven benefit says Adzick. According to the Children's Hospital of Philadelphia, some of the main benefits of prenatal surgery to correct myelomeningocele are that those infants are less likely to need a shunt to correct hydrocephalus and their quality of life will be improved, but as we have read that may not always be the case. If improvement for hydrocephalus outcomes through fetal surgery is an unproven benefit for the fetus, and the main life-altering symptom may not be improved, then is it worth subjecting the pregnant woman to the procedure if the surgery can be performed after birth?

Another physical issue with the surgery is that some of the main life-altering symptoms of the condition are not improved through fetal surgery. Nichelle Whitehead states that bladder incontinence, a main symptom of spina bifida, is not improved from prenatal surgery, when compared to postnatal correction. (De La Bastide, 2017).

After researching the initial cases where fetal surgery was performed to correct myelomeningocele, several additional hypothetical questions arose in reference to the physical outcome for the fetus. One of those is: if the anomaly would require additional surgeries postnatally for the myelomeningocele to be fully repaired, why wouldn't surgeons just perform one procedure after birth to repair both the hydrocephalus and the myelomeningocele? Many fetuses and infants that undergo correction of myelomeningocele of any kind must have additional surgeries on the affected area, even if they had a prenatal correction performed (Adzick et al., 2011). Potential benefits from fetal surgery include scar-less healing and a safer operation space in comparison to an operation room where there are more bacteria present. If additional surgeries must be performed after birth, and the area where scar-less healing took place must be re-opened, wouldn't that likely cause scarring and undo the benefit of scar-less healing?

Psychological Dimensions

An important dimension of decision making in respect to fetal surgery to correct myelomeningocele is the psychology of the pregnant woman and the complex relationship between her and her fetus. Mark Bilton, a clinical ethics consultant, discusses the relationship in an article titled, "Parental Hope Confronting Scientific Uncertainty: A Test of Ethics in Maternal-Fetal Surgery for Spina Bifida." The article is an analysis of interviews conducted with pregnant women who participated in the MOMS study at Vanderbilt University. Bilton states that if a pregnant woman plans to carry-out her pregnancy and has the intent to become a mother, an extraordinarily complex relationship develops between her and her future child. He states that a pregnant woman will subject herself to nearly anything to protect her future child. That idea of protection, and her instincts to nurture, may cause a woman to subject herself to a situation that she ordinarily would not. It may cause her to be somewhat blinded to the risks of the procedure that she is subjecting herself to. After hearing the potential benefits to prenatal correction through something like fetal surgery, the idea of hope may cause that to be the only path she sees, and she may cancel out the idea of any other intervention (Bilton, 2005).

Physician Bias

Another ethical question is whether physicians have any preference towards prenatal versus postnatal surgery because they are enticed by the engagement with the technique rather than the outcomes for the woman or fetus. According to the Children's Hospital of Philadelphia, "Fetal spina bifida surgery is one of the most exciting developments in the history of treatment for birth defects" and it is known that physicians like to treat. Due to things like hope, and the complex relationship between the pregnant woman and fetus, I believe that it is especially important that physicians be clear about the appeals of the procedure to themselves, as well as to the patients, when discussing possible interventions with pregnant women whose fetuses have been diagnosed with myelomeningocele. The physician's role is to suggest the best possible intervention for each circumstance (Lockwood, 2004). Joe Leigh Simpson, a doctor who specializes in obstetrics and gynecology, states in an article titled "Fetal Surgery for Myelomeningocele Promise, Progress, and Problems" that it is known that physicians like to treat. He also states that the idea of performing a complex procedure like fetal surgery, may be enticing to physicians. (Simpson, 1999) Is it possible for that enticement to cause the physicians to overestimate the benefits of prenatal surgery?

A study titled "Physician Views Regarding the Benefits and Burdens of Prenatal Surgery for Myelomeningocele," published in 2017, sent a group of 1200 practicing physicians a questionnaire to collect their attitudes on the different interventions to repair myelomeningocele. The questionnaire listed different scenarios and questions, and from those, physicians were asked which intervention they would suggest, fetal surgery or postnatal intervention. One of the questions asked physicians if they felt that fetal surgery placed an unacceptable burden on pregnant women and their families. 68 percent of the physicians did not believe that fetal surgery placed an unacceptable burden on them. 65 percent of the physicians believed that denying fetal surgery as an intervention is unfair to the future child. Also, 94 percent of the physicians would suggest fetal surgery over postnatal correction for any circumstance. From the scenarios given, the researchers determined that physicians may have professional and personal bias towards prenatal surgery to correct myelomeningocele (Antiel et al., 2017).

Religious Convictions

Another important dimension of decision making about prenatal fetal surgery is whether religion has any effect on the pregnant woman. Often, when a fetus presents with a life-threatening anomaly, an abortion will be given as an option for the pregnant woman. An abortion is a procedure to end a pregnancy (MedlinePlus, 2020). According to an investigative report written by the Agency for Healthcare Research and Quality, whose mission is to make healthcare safer, "conflict occurs when physicians advise terminating the pregnancy in cases of fetal disability, but pregnant women desire to continue the pregnancy despite a grim prenatal diagnosis. Religious beliefs and values often play into these decisions to continue the pregnancy and prompt the decision to undergo in utero procedures" (AHRQ, 2011). According to the British Pregnancy Advisory Service, a charity that provides abortions for women in Britain, many women opt for an abortion when a severe fetal anomaly is present (BPAS, 2020). Human Life International, a nonprofit organization that educates people to fight for pro-life policies, states "Abortion because of birth defects rejects the worth of the child as loved by God."

(HIL, 2020) Because of these beliefs, a woman may make a decision that is based on her faith.

As previously discussed, Mark Bilton interviewed pregnant women that underwent some of the first procedures to prenatally correct myelomeningocele at Vanderbilt University and the results showed that some pregnant women may allow their faith to guide their decision when considering prenatal surgery. Bilton reported that many of the pregnant women said that they were undergoing the prenatal surgery in order to follow a religious belief and stated that "their experience interpreted as somehow indicating an intuitive sense of following a path laid out by God right up to the point of coming to Vanderbilt and undergoing the surgery" (Mark Bilton, 2020). Is it possible that the women may subject themselves to an invasive surgery that has no direct benefit to them because, unwilling to consider abortion, they see prenatal surgery as preferable to carrying the fetus to term without attempting to address the medical issues.

CONCLUSION

My driving question for this thesis has been, given the enduring physical risks, psychological dimensions, physician bias, and religious convictions that surround fetal surgery to correct myelomeningocele, whether and when is this surgery justified? As we have learned, fetal surgery to correct myelomeningocele started as an experimental procedure and as of 2020, is now performed frequently in many different hospitals across the nation. Two hospitals have specifically reported that they have each performed over 300 of these surgeries (Vanderbilt, CHOP, 2020). We have seen that there are many different human and social dimensions surrounding the surgery that remain active as of 2020. Some of those include: many physical risks, such as infection, to both the pregnant woman and the fetus, while the pregnant woman receives no direct benefit from the surgery; psychological dimensions, such as the complex relationship between a pregnant woman and her fetus; possible physician bias that favors prenatal surgery over postnatal repair; and religious convictions that may influence a pregnant woman's decision.

The human and social dimensions I have discussed are just some those present with this technique, but they are among the most enduring, as of 2020. After researching fetal surgery to correct myelomeningocele, it is still unclear as to whether or when it may be surgically or psychologically justified to perform this type of procedure. Many human and social dimensions that effect the surgery and the parties involved. How these dimensions are weighed when fetal surgery to correct myelomeningocele is being considered is unclear. As of 2020, there is no scale for weighing these dimensions and no clear concept of how to create one. More research needs to be performed to determine how these dimensions should be considered, or weighed, before fetal surgery is performed.

Also unknown is how these human and social dimensions work together. For some people, certain factors may influence their decision more than others. Take, for example, a religious, pregnant woman whose fetus has hydrocephalus. Even though her fetus has a life-threatening condition, the woman may be unwilling to consider abortion, due to religious convictions, and thus see fetal surgery is her only option. How would these dimensions affect each other and how would one go about weighing the effect of them? Would it even be possible?

There are still many questions that need to be answered, or at least clarified, before fetal surgery to correct myelomeningocele should no longer considered experimental. The procedure may seem enticing at first glance, but, with the complex human and social dimensions of the surgery, is the procedure really as beneficial as it seems? After researching fetal surgery to correct myelomeningocele, it is still unclear as to whether or when it may be surgically or psychologically justified to perform this type of procedure, which is why more research needs to be performed.

REFERENCES

Agency for Healthcare Research and Quality. (2020). “Agency for Healthcare Research and Quality (AHRQ).” Accessed October 20, 2020. https://www.ahrq.gov/.

American Medical Association. (2016). AMA principles of medical ethics. Retrieved October, 23, 2019, from https://www.ama-assn.org/delivering-care/ama-principles-medical-ethics

Bijma, Hilmar H., Agnes Van Der Heide, and Hajo I. J. Wildschut. (2008). "Decision-Making after Ultrasound Diagnosis of Fetal Abnormality." Reproductive Health Matters 16.31 82-89. Web. https://link.springer.com/article/10.1007/s11296-007-0070-0 (Links to an external site.)

British Pregnancy Advisory Service. (2015). “Termination of Pregnancy for Fetal Anomaly,” https://www.bpas.org/get-involved/campaigns/briefings/fetal-anomaly/.

Bruner, Joseph P. (2003). “Maternal-Fetal Surgery.” Clinics in Perinatology 30, no. 3 (September 2003): xiii–xvi. https://doi.org/10.1016/s0095-5108(03)00088-5.

C.S. Mott Children’s Hospital. (2020). “Fetal Interventions and Procedures | CS Mott

Children’s Hospital | Michigan Medicine.” Accessed October 20, 2020. https://www.mottchildren.org/conditions-treatments/peds-fetal-medicine/fetal-interventions-and-procedures.

Cardinal Glennon Children’s Hospital. (2019). “Fetal Surgery.” Cardinal Glennon

Children’s Hospital. https://www.ssmhealth.com/cardinal-glennon/fetal-care-institute/advanced-procedures/fetal-surgery

Casper, M. (1998). The making of the unborn patient: a social anatomy of fetal surgery. Rutgers University Press.

Children’s Hospital of Philadelphia. (2019). “About Fetal Surgery for Spina Bifida (Myelomeningocele).” Children’s Hospital of Philadelphia. https://www.chop.edu/treatments/fetal-surgery-spina-bifida/about

Cleveland Clinic. (2020). “Spina Bifida: Types, Tests, Treatment & Prevention.” Accessed October 20, 2020. https://my.clevelandclinic.org/health/diseases/8719-spina-bifida.

Copeland, M. L., J. P. Bruner, W. O. Richards, H. W. Sundell, and N. B. Tulipan. (1993). “A Model for in Utero Endoscopic Treatment of Myelomeningocele.” Neurosurgery 33, no. 3 (September 1993): 542–44; discussion 545. https://doi.org/10.1227/00006123-199309000-00043.

De La Bastide, Danielle. (2017). “Groundbreaking Surgery Performed on Fetus While the Mother’s Uterus Is Outside Her Body,” Interesting Engineering. November 1, 2017. https://interestingengineering.com/groundbreaking-surgery-performed-on-fetus-while-the-mothers-uterus-is-outside-her-body.

Eom, Hye Mi, Young Nam Kim, Byung Hee Choi, Eun Jeong Jeong, Jung Mi Byun, Dae Hoon Jeong, Moon Su Sung, Kyung Bok Lee, Ki Tae Kim, and Hye Kyoung Yoon. (2016). “Chorioamniotic Membrane Separation Caused by the Seromucinous Collection from a Placental Chorioangioma.” Obstetrics & Gynecology Science 59, no. 3: 233. https://doi.org/10.5468/ogs.2016.59.3.233.

European Tissue Repair Society 3, no. 4 (December 1995): 467–72. https://doi.org/10.1046/j.1524-475X.1995.30411.x.

Foster, Mark R., (2019). “Spina Bifida.” E Medicine Health. https://www.emedicinehealth.com/spina_bifida/article_em.htm#what_is_spina_bifida

Girorgi, Anna., Reviewed by Gonzalez, Andrew. (2018). “Laparoscopy: Purpose, Preparation, Procedure, and Recovery.” Accessed June 10, 2020. https://www.healthline.com/health/laparoscopy.

Grady, Allison. (2005) “The Importance of Standard of Care and Documentation.” AMA Journal of Ethics;7(11):756-758. Web. https://journalofethics.ama-assn.org/article/importance-standard-care-and-documentation/2005-11

Grady, Denise. (2017). “To Mend a Birth Defect, Surgeons Operate on the Patient Within the Patient - The New York Times.” Accessed June 10, 2020. https://www.nytimes.com/2017/10/23/health/fetal-surgery-spina-bifida.html.

Harrison, Michael R. (1996). "Fetal Surgery." American Journal of Obstetrics and Gynecology 174.4: 1255-264. Web. https://www-sciencedirect-com.ezproxy1.lib.asu.edu/science/article/pii/S0002937896706683

Haynes, J. H., B. A. Mast, T. M. Krummel, I. K. Cohen, and R. F. Diegelmann. (1995). "Exposure to Amniotic Fluid Inhibits Closure of Open Wounds in the Fetal Rabbit." Wound Repair and Regeneration: Official Publication of the Wound Healing Society, https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1524-475X.1995.30411.x

Healthline. (2020). "Ultrasound: Purpose, Procedure, and Preparation." Accessed April 6, 2020. https://www.healthline.com/health/ultrasound.

Hirose, S. R., & Harrison, M. (2010). Fetal Therapy. In Ashcraft's Pediatric Surgery (pp. 125-132). Elsevier. https://www.sciencedirect.com/science/article/pii/B9781416061274000100

Jones, Rachel K., and Jenna Jerman. (2014). "Abortion Incidence and Service Availability in the United States, 2011." Perspectives on Sexual and Reproductive Health 46, no. 1 (March 2014): 3–14. https://doi.org/10.1363/46e0414.

Larson, Barrett J., Michael T. Longaker, and H. Peter Lorenz. (2010). "Scarless Fetal Wound Healing: A Basic Science Review." Plastic and Reconstructive Surgery 126, no. 4 (October 2010): 1172–80. https://doi.org/10.1097/PRS.0b013e3181eae781.

Lifebridge Health. (2020). "Prenatal Hydrocephalus," http://www.lifebridgehealth.org/BrainSpine/WhatisHydrocephalus.aspx#:~:text=In%20this%0condition%2C%20hydrocephalus%20is,brain%20to%20divert%20CSF%20fluid.

Lockwood, Alan H. (2004). "The Physician's Role in Society: Enhancing the Health of Individuals and the Public." AMA Journal of Ethics 6, no. 4 (April 1, 2004): 189–90. https://doi.org/10.1001/virtualmentor.2004.6.4.msoc2-0404.

Mayo Clinic Staff. (2019). "Acute Kidney Failure." The Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/kidney-failure/symptoms-causes/syc-20369048

Mayo Clinic. (2020). "C-Section - Mayo Clinic." Accessed June 10, 2020. https://www.mayoclinic.org/tests-procedures/c-section/about/pac-20393655.

Medline Plus. (2020). “Neural Tube Defects.” National Institutes of Health, U.S. National Library of Medicine. https://medlineplus.gov/neuraltubedefects.html

Medline Plus. (2020). “Stem Cells.” National Institutes of Health, U.S. National Library of Medicine. https://medlineplus.gov/stemcells.html

Merriam-Webster. “Fetus.” (2020). www.merriam-webster.com/dictionary/fetus

Milunsky, Aubrey and Milunsky, Jeff M. (2015). “Genetic Disorders and the Fetus,” Hoboken, NJ, USA: John Wiley & Sons. Web. https://ebookcentral-proquest-com.ezproxy1.lib.asu.edu/lib/asulib-ebooks/reader.action?docID=4187360&ppg=1

Moffett P, Moore G. (2011). “The standard of care: legal history and definitions: the bad and good news. West J Emerg Med. 2011;12(1):109–112. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3088386/

Monroe Carell Jr. Children’s Hospital at Vanderbilt. (2020). “What Is Myelomeningocele,” https://www.childrenshospitalvanderbilt.org/medical-conditions/myelomeningocele#:~:text=It%20may%20lead%20to%20weakness,of%20fluid%20in%20the%20brain.

Monroe Carell Jr. Children’s Hospital at Vanderbilt. (2020). “William F. Walsh, MD | Vanderbilt Children’s Nashville, TN.” Accessed October 20, 2020. https://www.childrenshospitalvanderbilt.org/doctors/walsh-william.

National Institutes of Health Staff. (2011). “Surgery Before Birth Improves Spina Bifida Outcomes.” National Institutes of Health: Department of Health and Human Services. https://www.nih.gov/news-events/nih-research-matters/surgery-birth-improves-spina-bifida-outcomes

National Institutes of Health Staff. (2017). “Spina Bifida.” National Institutes of Health: Department of Health and Human Services: National Center for Advancing Translational Services: Genetic and Rare Disease Information Center. https://rarediseases.info.nih.gov/diseases/7673/spina-bifida#diseaseCauseSection

National Organization for Rare Disorders Staff. (2019). “Rare Disease Database: Spina Bifida.” National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/spina-bifida/#affected-populations

O'Connor, Kathleen, O'Neil, Erica, "Fetal Surgery". *Embryo Project Encyclopedia* (2012-11-01). ISSN: 1940-5030 http://embryo.asu.edu/handle/10776/4201.

Philadelphia, The Children's Hospital of. (2014). "Fetal Surgery for Spina Bifida (Myelomeningocele)." Text. The Children's Hospital of Philadelphia, March 30, 2014. https://www.chop.edu/treatments/fetal-surgery-spina-bifida.
Philadelphia, The Children's Hospital of. (2020). "About Fetal Surgery for Spina Bifida (Myelomeningocele)." Text. The Children's Hospital of Philadelphia. Accessed June 10, 2020. https://www.chop.edu/treatments/fetal-surgery-spina-bifida/about.

Pollesche, Jessica. (2017). "Management of Myelomeningocele Study Clinical Trial (2003–2010) | The Embryo Project Encyclopedia." Accessed June 10, 2020. https://embryo.asu.edu/pages/management-myelomeningocele-study-clinical-trial-2003-2010.

Reporter, Vanderbilt University Medical Center's Weekly Newspaper. (2020). "Graduation 2010: Emeritus Faculty Honored for Years of Service (05/21/10)." Accessed June 10, 2020. https://www.mc.vanderbilt.edu/reporter/index.html?ID=8834.

Saxena, Kirti N. (2009). "Anaesthesia for fetal surgeries." Indian journal of Anesthesia vol. 53,5 :554-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2900087/

Sutton L. N. (2008). Fetal surgery for neural tube defects. Best practice & research. Clinical obstetrics & gynaecology, 22(1), 175–188. doi:10.1016/j.bpobgyn.2007.07.004 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2293328/

The Fetal Treatment Center, Benioff Children's Hospital. (2013) "Techniques of Fetal Intervention." UCSF. https://fetus.ucsf.edu/techniques-fetal-intervention

The Pittsburgh Post-Gazette. (2008). "Self-sufficient and Going Strong at 77, with Spina Bifida." The Pittsburgh Post-Gazette. https://www.post-gazette.com/news/health/2008/02/20/Self-sufficient-and-going-strong-at-77-with-spina-bifida/stories/200802200297

The University of Texas at Austin, Department of Government. (2020). "Profile for Patrick McDonald at UT Austin." Accessed May 7, 2020.https://liberalarts.utexas.edu/government/faculty/pjm438.

Tulipan, N., and J. P. Bruner. (1998). “Myelomeningocele Repair in Utero: A Report of Three Cases.” Pediatric Neurosurgery 28, no. 4 (April 1998): 177–80. https://doi.org/10.1159/000028645.

U.S. News, A World Report. (2020). “Dr. Michael L. Copeland, Neurosurgeon in Independence, MO | US News Doctors.” Accessed June 10, 2020. https://health.usnews.com/doctors/michael-copeland-246688.

Vanderbilt University Medical Center. (2020) “William O Richards | Gastrointestinal SQUID Technology Laboratory.” Accessed June 10, 2020. https://www.vumc.org/biomag/person/william-o-richards.

Vanderbilt University Medical Center. (2020). “Noel B. Tulipan, M.D. | Surgical Outcomes Center for Kids (SOCKs).” Accessed June 10, 2020. https://www.vumc.org/socks/person/noel-b-tulipan-md.

Washington University Orthopedics. (2020). “What Is Myelomeningocele? Causes, Diagnosis, Treatment.” Accessed April 6, 2020. https://www.ortho.wustl.edu/content/patient-care/6885/services/pediatric-and-adolescent-orthopedic-surgery/overview/pediatric-spine-patient-education-overview/myelomeningocele.aspx.

Williams, Bernard. (1981). “Chronic Herniation of the Hindbrain.” Annals of The Royal College of Surgeons of England 63, no. 1 (January 1981): 9–17.

Yang, J. D., Choi, D. S., Cho, Y. K., Kim, T. K., Lee, J. W., Choi, K. Y., Chung, H. Y., Cho, B. C., & Byun, J. S. (2013). Effect of amniotic fluid stem cells and amniotic fluid cells on the wound healing process in a white rat model. Archives of plastic surgery, 40(5), 496–504. https://doi.org/10.5999/aps.2013.40.5.496 45

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