## "Fetal Surgery" (1996), by Michael R. Harrison

In 1996, Michael R. Harrison published "Fetal Surgery" in the American Journal of Obstetrics and Gynecology. In the article, Harrison describes the importance of fetal surgery and the techniques used to correct defects in fetuses. As a fetus develops in the uterus, it can develop abnormalities that may become debilitating or fatal. Harrison discusses cases that show how physicians can use fetal surgery to repair such abnormalities, including obstructions in the heart or urinary tract, or organs or muscles whose malformations impair function. Harrison states where knowledge is lacking within the field or where surgery would be inappropriate, such as in the modification of a cleft lip, which can be fixed after birth and as such does not merit the risks of surgery. In the article, Harrison provides a summary of what information existed about fetal surgeries in 1996, which helped physicians explore fetal surgery and make further advancements.

Fetal surgery is surgery performed on a fetus before it is born. During development, the fetus can develop abnormally in ways that can cause health problems or death, either before or after birth. In his article, Harrison notes how the diagnosis of these abnormalities had relatively recently, in the 1980s and 1990s, become possible through improvements in imaging technology, such as ultrasound, which uses high-frequency sound waves to produce images of structures within the body, and therefore lets physicians look at the developing fetus without having to operate on the pregnant person. Harrison also discusses that researchers developed techniques to perform fetal surgery on other animals, such as monkeys or lambs, which demonstrated the viability of fetal surgery and helped develop the procedure. As a practicing surgeon at the Fetal Treatment Center at the University of California, San Francisco, or UCSF, in San Francisco, California, Harrison was one of the leading experts in practicing fetal surgery, which was still very new at the time of publication. Throughout the article, Harrison uses the term "malformation" to refer to fetal abnormalities, a medical term which refers to structural defects, or problems in the shape or function of parts of the body, which occur during fetal development.

Harrison is the founding director of the Fetal Treatment Center at UCSF. He received his MD from Harvard Medical School in Cambridge, Massachusetts, in 1969, after which he completed his surgery training at Massachusetts General Hospital in Boston, Massachusetts, and a pediatric surgery fellowship at the Children's Hospital of Los Angeles in Los Angeles, California. His professional specialty is in fetal surgery, in which he has helped develop new techniques such as in utero stem cell transplantation to treat immunodeficiencies. As of 2021, he is Professor Emeritus of Surgery and Pediatrics and the Director Emeritus of the Fetal Treatment Center at UCSF.

Harrison divides "Fetal Surgery" into five sections. In an unnamed first section, he states that, although most fetal malformations are best treated after birth, medical advances have saved many fetuses which required treatment in utero, or in the uterus. In the second section, Management of Mother and Fetus, Harrison describes the process of fetal surgery. Harrison includes images of the fetus during fetal surgery and diagrams showing the process of fetal surgery. In the third section, The Risks and Benefits, Harrison weighs the risks and benefits of fetal surgery for the fetus and person carrying the fetus, particularly the risk of death of the fetus if left untreated compared to medical risks to the pregnant person from surgery. In the fourth section, Fetal Problems Amenable to Surgical Correction Before Birth, Harrison discusses the birth defects that can be corrected through fetal surgery and the techniques used to do so. In the last section of the article, The Past and Future of Fetal Intervention, Harrison discusses the small number of the abnormalities that physicians can correct in utero, as well as areas of fetal surgery that future physicians can advance with new technology and knowledge.

The first section is a single paragraph in which Harrison states that, although most fetal malformations can be treated after birth, there are some that require treatment before birth, and advances in fetal surgery since the 1980s have helped many fetuses. In the second section of the article, Management of Mother and Fetus, Harrison discusses the ways physicians perform fetal surgery and conduct post-surgical care for the fetus and the pregnant person. Researchers first tested techniques used for fetal surgery on other animals, like monkeys and lambs. After they demonstrated those techniques were successful, Harrison and other physicians began to perform fetal surgery on humans.

According to Harrison, the fetal surgery process starts with detection of a malformation, often through ultrasound. If a physician decides that they can correct the malformation through fetal surgery, a surgeon will perform the procedure. The operation starts with a breach in the uterus, usually made with an incision on the pregnant person's abdomen. The surgeon will inject the fetus with narcotics and muscle relaxers in order to reduce pain and movement. A warm saline solution surrounds the fetus during the procedure to prevent a lack of amniotic fluid, some of which will be lost when the uterus is opened. Physicians monitor the fetus using various techniques, depending on the deformity. After surgery, the surgeon closes the uterine incision using absorbable sutures. Medical caretakers monitor both the fetus and pregnant person until they can be discharged from the hospital and conduct outpatient monitoring and fetal sonograms at least once a week until birth.

In the third section of the article, The Risks and Benefits, Harrison discusses the dangers and the advantages of fetal surgery for both the gestational parent and the fetus. He also provides data on fifty cases of fetal surgery managed at UCSF. Harrison first discusses how surgeons must weigh the risks of the procedure against the benefits of repairing the malformation. The malformations or deformities can often be fatal or debilitating to the fetus, such as a congenital diaphragmatic hernia. The diaphragm muscle is a muscle that separates the abdomen from the chest, and in a congenital diaphragmatic hernia, the diaphragm fails to close during development of the fetus. The contents of the abdomen, like the stomach and liver, then move into the hole in the diaphragm. Congenital diaphragmatic hernias are often painful and can sometimes strangulate the tissues surrounding the diaphragm, causing those tissues to die. They can also become fatal if left untreated. In that case, the risks and benefits to the fetus are very clear. Harrison states that the risks and benefits of fetal surgery are harder to gauge for the pregnant person. The pregnant person must undergo pain and discomfort during the procedure, and may experience medical complications from their uterus being open or from anesthesia. Possible complications include infection and blood loss from opening the uterus and memory loss or breathing problems from anesthesia. Harrison goes on to state the safety of the pregnant person is more important than that of the fetus, and if the procedure may help the fetus but puts the pregnant person's life in danger, physicians will not perform it.

Harrison continues The Risks and Benefits to discuss how he and his colleagues at the Fetal Treatment Center at UCSF conducted fifty case studies on fetal surgery at UCSF in 1994 to understand how fetal surgeries affect the pregnant person. Harrison states that before that year, fetal surgery procedures were rare. However, he and his colleagues produced data on how well pregnant people survived those procedures. Harrison's team found no maternal deaths in their study, but they did record a rise in morbidity, or the amount of disease, in pregnant people who birthed the neonates preterm. Harrison indicates that one cause of that may be that the physicians performing fetal surgeries wanted to keep the fetuses in utero for as long as possible to further development. To do so, they gave pregnant people tocolytic medications, which suppress labor, to prevent preterm labor. Those medications have been known to cause pulmonary edema. Pulmonary edema, a condition where excess fluid builds up in the lungs and makes it difficult to breathe, developed in four of the fifty pregnant women included.

Harrison goes on to state that physicians who are going to deliver a neonate after a fetal surgery has been conducted must do so through caesarian section. A caesarian section is a surgical technique where surgeons open the pregnant person's abdomen and uterus to deliver a neonate, instead of letting the neonate emerge naturally through the vagina. Harrison explains that the incision made on the lower part of the uterus during fetal surgery usually does not heal well, and if the fetus passes through the lower part of the uterus during natural birth, the pressure may cause the incision to

## re-open.

In the following section, Fetal Programs Amenable to Surgical Correction Before Birth, Harrison discusses types of malformations that physicians may correct through fetal surgery. Harrison states that the malformations that justify fetal surgery are only those that affect organ development within the fetus, and that physicians should perform fetal surgery only if it will fix the problem. He states that there are therefore only a few malformations that physicians may fix through fetal surgery, but that medical advancement may increase the number of malformations that doctors can correct through fetal surgery. Harrison discusses many different malformations fetal surgery can repair, at the time of publication or in the future given adequate medical advances, such as hernias, organs with obstructions, or underdeveloped organs. For each condition he lists, Harrison describes the condition, impact on the fetus, the rationale for treatment through surgery, the result if not treated, and recommended treatment, all of which are summarized in Table II.

In the final section, The Past and Future of Fetal Intervention, Harrison discusses the importance of fetal surgery and the advancements that may persist, like treating other types of malformations and deformities with the basis of that knowledge. Harrison discusses how in the 1980s only a few fetal malformations were fixable due to lack of knowledge and experimentation. Harrison adds that physicians in the field still do not know how to prevent people from going into preterm labor, which can endanger the fetus. He also discusses the observation that fetuses will heal without a scar, which he states has encouraged more research on the superior healing ability of fetal tissues. Physicians must be cautious when performing fetal surgery, as they should only perform the procedure if it completely fixes the deformity and is the best option for both the fetus and the pregnant person.

In "Fetal Surgery" Harrison identifies common fetal malformations and the surgical interventions that can fix them. The information Harrison presents in the article has encouraged other researchers to study fetal surgery. As of October 2020, the article has been cited over 132 times, and the Fetal Treatment Center he helped found has continued to develop techniques to treat fetal malformations and improve treatment for fetuses in utero. Since the publication of Harrison's article, techniques to correct other malformations like spina bifida, a deformity in the spine that prevents the spinal cord from forming properly, have been identified.

## Sources

- 1. Harrison, Michael R. "Fetal Surgery." American Journal of Obstetrics and Gynecology 174 (1996): 1255–64. https://www.sciencedirect.com/science/article/pii/S0002937896706683 (Accessed October 21, 2020).
- 2. Maselli, Kathryn M., and Andrea Badillo. "Advances in Fetal Surgery." Annals of Translational Medicine 4 (2016): 394. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5107396/ (Accessed October 21, 2020).
- 3. Putnam, Luke R, Matthew T. Hartin, Kuojen Tsao, Francesco Morini, Bradley A. Yoder, Matías Luco, Pamela A. Lally, and Kevin P. Lally. "Congenital Diaphragmatic Hernia Defect Size and Infant Morbidity at Discharge." Pediatrics 138 (2016): 1–8. https://pediatrics.aappublications .org/content/138/5/e20162043.full (Accessed October 21, 2020).
- 4. UCSF Pediatric Surgery Lab. "Michael R. Harrison, M.D." UCSF Pediatric Surgery Lab. http s://pedsurglab.ucsf.edu/people/principal-investigators/michael-r-harrison,-md.aspx (Accessed October 21, 2020).