Transposition of the Great Arteries (TGA) [1]

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Transposition of the great arteries or TGA is a potentially fatal congenital heart malformation where the pulmonary artery and the aorta are switched. The switch means that the aorta, which normally carries oxygenated blood, carries deoxygenated blood. There are two types of the malformation, d-TGA where no oxygen reaches the body and l-TGA where some oxygenated blood circulates. In the US, the Centers for Disease Control estimate that about 1,901 infants are born each year with TGA, or about one for every 2,000 births. Throughout history, physicians classified TGA as a condition that causes blue babies and hypothesized it was a fatal condition. With the development of corrective surgeries, studies on the causes of TGA, and improved prenatal diagnosis [2] have allowed for the survival rate for those with TGA to approach almost one hundred percent.

The heart is has a systemic circuit and a pulmonary circuit, each comprised of two chambers, an atrium on top and a ventricle beneath that. The systemic circuit is located on the left side of the heart, and pumps blood oxygenated in the lungs out from the heart to the rest of the body through the aorta. The pulmonary circuit is located on the right side of the heart, and takes the deoxygenated blood returning to the lungs for oxidation through the pulmonary artery.

Many fetuses with TGA survive to full-term but die soon after birth when the ductus arteriosus closes. The ductus arteriosus is a hole between the pulmonary artery and the aorta in the fetus [3], which allows for blood to mix in utero. The ductus arteriosus closes at birth so that oxygenated and deoxygenated blood no longer mix, because the lungs inflate to oxygenate blood.

After the ductus arteriosus closes, the survival of an infant can depend greatly on the type of TGA they have. The d-TGA form is more severe because the arteries connect to the wrong sides of the heart, leading to cyanosis. Instead of blood leaving the pulmonary system and going to the aorta, the blood immediately returns to the lungs. Blood from the body is left circling the systemic circuit with no oxygen. Infants with d-TGA risk organ failure due to their organs not receiving the oxygenated blood and nutrients they need to function, making it the more severe form of TGA. In l-TGA, the organs get oxygenated blood because the right and left ventricles are also switched, which means that deoxygenated blood still gets to the lungs. That form of TGA has fewer side effects because the body receives oxygenated blood and the lungs get deoxygenated blood. Typically that type of TGA does not require surgical correction.

Matthew Baillie described the anatomical structure of TGA in 1793 while at St George’s Hospital in London, England. Baillie described an affected infant while still alive and later reported findings of the infant’s autopsy in his book The Morbid Anatomy of some of the Most Important Parts of the Human Body. Baillie described the living child as having unusually bright coloration, with colder than normal skin, and reported that the infant breathed normally. After the autopsy, Baillie described the anatomy of TGA and found that the aorta and pulmonary artery arose from the wrong ventricles. He concluded that the coloration of the skin was caused by the flowing of blood in two distinct circuits, never mixing except through the limited amount that flowed through the mostly closed ductus arteriosus, which was so small that he was only able to fit a crow quill through. Baillie’s clinical description of TGA allowed other physicians to begin characterizing the condition.

After Baillie described the anatomy, John Richard Farre, a physician in London, England, named the defect a transposition of the aorta and pulmonary artery in his 1814 book Pathological Researches on Malformations of the Human Heart. Farre mentioned not only the term transposition, but also listed symptoms of several cases, including the first one Baillie had mentioned. He described the blue coloration of those affected with cyanotic heart malformations, including but not limited to TGA. Farre called those infants blue babies. That grouping of blue babies included TGA and tetralogy of fallot, a similar heart defect where the aorta is misplaced, a condition that slows blood flow to the lungs. Farre also noted that the infants born with that condition had irregular respiration, poor nutrition, neurological side effects such as seizures, loss of consciousness, paralysis, and intermittent quickening of the heart’s pace. However, few surgical corrections existed for those with TGA until the early-1900s, when surgical corrections began.

In 1939 Robert Gross and John Hubbard, who worked as physicians in Boston, Massachusetts, performed the first correction of a congenital heart condition where the ductus arteriosus fails to close after birth. They performed surgery on a seven-and-a-half-year-old girl and permanently closed her ductus arteriosus with a silk tie, which allowed Gross and Hubbard to cut off the ductus arteriosus. Gross and Hubbard published their results in 1939 article titled “Surgical Ligation of a Patent Ductus Arteriosus.” Helen Taussig cited that corrective surgery, as inspiration for her first steps toward exploring surgical correction for blue babies at Johns Hopkins University [4], in Baltimore, Maryland, in 1944. Taussig along with Alfred Blalock, a surgeon, and his assistant
with insulin-dependent diabetes. Abu-Sulaiman stated that the results demonstrated a need for prenatal screening in this risk for congenital heart defects in the diabetic population, with a one percent incidence of TGA in the pregnant women studied at the King Khalid University Hospital in Riyadh, Saudi Arabia, involved 100 births with diabetic mothers and showed an increased another possibility for increased risk of TGA is maternal influence such as diabetes. A study done throughout 2000 and 2001 at another possibility for increased risk of TGA is maternal influence such as diabetes. A study done throughout 2000 and 2001 at the Hospital for Sick Children [8], other teratogens were explored during this time frame as well, including retinoic acid, which was explored as early as 1961.

Exposure to retinoic acid is one of the most well understood risk factors in the development of TGA. Since 1961, scientists observed that a high dose of vitamin A correlated to an increase in TGA. Harold Karter and Josef Warkanny performed experiments on mice treated with retinoic acid, which displayed TGA at an eighty to ninety percent rate. More current research includes the 1995 and 1997 research by Hiroshi Yasui, in Tokyo, Japan, on retinoic acid in mice. Yasui and his team built on the research of Karter and Warkanny, and examined how retinoic acid impacted embryological development.

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Advanced maternal age is another maternal risk factor that puts the fetus [3] at risk for developmental issues such as TGA. Assia Miller, a medical doctor, with her partners, published an article in the American Journal of Medical Genetics that showed a link between advanced maternal age and the incidence of TGA through a study of five counties in Atlanta, Georgia. The study observed 5,289 infants, as well as fetuses’ from 1968 to 2005, who had an isolated congenital heart defect. Miller observed that the adjusted prevalence ratio for mothers who had infants or fetuses with TGA increased with maternal age. Pregnant women who were over thirty-five years old were at a higher risk than younger pregnant women.

Damien Bonnet and his team in Paris, France recommend diagnosing TGA on fetuses versus after delivery. They studied the benefits of diagnosing before and after birth, and found that diagnosing before delivery was better overall than diagnosing after delivery. Bonnet and his team found those diagnosed before delivery were admitted to the ICU unit between 1.4 to 2.9 hours, while those diagnosed after delivery weren’t admitted until forty-six to one hundred hours after delivery. They also found an increased risk for complications including multi-organ failure, neurological distress, and acidic blood that can lead to shock or death in infants diagnosed after birth.

**Sources**

16. Kalter, Harold and Josef Warkany “Experimental Production of Congenital Malformations in Strains of Inbred Mice by
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Subject

Topic
Disorders [43]

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Arizona State University. School of Life Sciences. Center for Biology and Society. Embryo Project Encyclopedia.

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Articles [44]

Last Modified
Wednesday, July 4, 2018 - 04:40

DC Date Accessed