

## ***Clinical Significance and Genetic Counseling for Common Ultrasound Findings***

### **Patient Information Sheet Tracheoesophageal Fistula with Esophageal Atresia**

You have recently learned that your baby has a tracheoesophageal fistula with an esophageal atresia. We expect that you may have questions about what this could mean for your developing baby. Hopefully, this information will address some of your concerns; however, we encourage you to speak to your genetic counselor or healthcare provider for more information. It is important to remember that anyone can have a baby with a birth defect. Birth defects occur in 2-5% of all births and are rarely caused by something that the parents did or did not do before or during pregnancy. Currently, there are no tests available to detect all health problems.

#### ***What is TEF/EA?***

Tracheoesophageal fistula (TEF) is an abnormal development of the trachea (breathing tube or “windpipe”) that connects the nose and the mouth to the lungs. Esophageal atresia (EA) is an abnormal development of the esophagus (the swallowing tube or “food pipe”) that connects the mouth to the stomach. Typically the trachea and the esophagus run side by side through the neck and chest, and are not connected to each other. Very early in the baby’s development the trachea and esophagus start as a single tube that splits into two separate tubes. TEF happens when the trachea and esophagus do not split properly and there is a connection between them. EA happens when there is a blockage of the esophagus or part of the esophagus is missing.

Babies can have either a TEF or an EA, but most babies have both a TEF with an EA, referred to as TEF/EA. TEF/EA may be suspected on ultrasound if no stomach bubble is seen in the baby and there is extra fluid around the baby (polyhydramnios). A chest X-ray after the baby is born is needed to confirm TEF/EA. There are several different types of TEF/EA and the type may not be determined until the baby is born.

#### ***How many babies are found with TEF/EA?***

An average of 1 in 3,500 (0.03%) babies are born with a TEF/EA.

#### ***What causes TEF/EA?***

In majority of babies with TEF/EA, the exact cause is not known. For these babies, TEF/EA is thought to be a “multifactorial” condition, meaning that multiple factors (including genetics and the environment) influence the development of the esophagus and trachea. For some babies TEF/EA is the only birth defect (isolated). However, 30 to 70% of babies with TEF/EA may have additional birth defects, such as a heart problem.

Some babies with TEF/EA may have a chromosome problem or a genetic syndrome. In order to understand a possible chromosomal cause or genetic syndrome cause, it is helpful to know a little about chromosomes. Chromosomes are packages of genetic information that carry the instructions (genes) necessary for our growth and development. Typically, there are 23 pairs of chromosomes in each cell of our bodies. One copy of each pair is from our mother and one copy of each is from our father. The first 22 pairs of chromosomes are the same in males and females. The last pair is known as the sex chromosomes and they determine our gender. Females typically have two X chromosomes and males usually have one X and one Y. It is important to have the correct amount of genetic material to have typical development. Sometimes there is an imbalance of genetic material that may cause birth defects. The imbalance may be caused by an extra or missing whole chromosome or sometimes only by extra or missing pieces of chromosomes. Some genetic conditions are caused by changes in one or more genes in our genetic make-up that result in a particular set of characteristics or features (also called a syndrome). A genetic imbalance or genetic syndrome can produce birth defects and physical changes such as TEF/EA.

Occasionally babies with TEF/EA may have a clustering or combination of specific birth defects but no genetic cause. Most common of these is called VACTERL association. Each letter of VACTERL stands for a type of abnormality: vertebral, anus, cardiac, TEF/EA, renal, and limb. Rarely, certain medications, maternal illnesses, or other exposures during early pregnancy may cause TEF/EA.

#### ***What problems could be associated with TEF/EA for my baby and how are they treated?***

Because babies with an EA have a blockage in the esophagus, the baby will not be able to swallow saliva or food after birth, which would cause vomiting and coughing. Because the breathing and swallowing tubes are connected, baby may breathe food or other

things into the lungs which may cause breathing problems and lung infections. How severe this is may depend on the type of TEF/EA baby has.

Most babies with TEF/EA will have one or more surgeries after birth. In most cases surgery happens within a few days after delivery, but is not emergent. Most babies with isolated TEF/EA survive and do really well after the surgery, but some may have complications such as breathing problems and may require a special breathing (endotracheal) tube, may have reflux, or may require a feeding (gastrostomy) tube. Intelligence is typically within normal limits. Babies that have TEF/EA with other birth defects and/or chromosome problems may not do as well before or after surgery and may have more complicated health or developmental problems. Some parents may choose to end a pregnancy that has been diagnosed with TEF/EA.

During pregnancy polyhydramnios can cause the uterus to be larger than normal and may lead to preterm labor or the water to break. Because of this the doctors may recommend a procedure called an amnioreduction to remove the excess fluid around the baby. This fluid is removed by inserting a thin needle through the belly and into the amniotic sac and pulling out the extra fluid. Babies who are born prematurely may have more complications than those born at term.

***What further testing may be offered and what will it tell me?***

Depending on how far along you are in pregnancy, a number of additional tests may be offered to you. If the TEF/EA is found during a routine ultrasound, a more detailed ultrasound will usually be performed to look carefully at the baby's body and check for signs and symptoms of TEF/EA. In some cases fetal MRI and fetal echocardiogram (a specialized ultrasound looking at the baby's heart) may also be recommended. You may be referred to a high risk maternal-fetal-medicine (MFM) doctor or a fetal center, which is a high risk center where various specialists may gather to review the health problems identified in your baby, as well as the potential causes and prognosis.

You may also be offered different types of genetic tests. There are two types of prenatal tests, diagnostic and screening:

Diagnostic Tests

Depending on how far along you are in pregnancy an amniocentesis procedure may be offered. The amniocentesis is a diagnostic test in which a small sample of amniotic fluid is obtained to examine the baby's chromosomes. This fluid is obtained by inserting a thin needle through your belly and into the amniotic sac. Because the procedure is considered an invasive procedure, there is a risk, likely less than 1%, for complications that can lead to miscarriage.

If you choose to pursue an amniocentesis, or if you have an amnioreduction performed, you may be offered an additional test called a chromosome microarray (CMA). It is used to identify small missing or extra pieces of the baby's chromosomes that may be associated with genetic conditions. CMA cannot detect all genetic conditions and may detect variations in the chromosomes that have uncertain clinical significance. Parental blood samples may help to clarify the meaning of a variation, but effects of these changes may not be known until after the baby is born. CMA may also detect information such as non-paternity and close relationships between parents. In addition to CMA, you may also be offered testing for specific genetic syndromes to look for changes in one or more genes.

Screening Tests

There are multiple screening tests to determine the chances for a baby to have a chromosome condition. These screening tests cannot diagnose or rule out the presence of a chromosome condition but may be used to help you decide whether or not you would like to pursue a diagnostic test.

Cell-free DNA (cfDNA), also referred to as Non-Invasive Prenatal Testing (NIPT) or Non-Invasive Prenatal Screening (NIPS), is a screening test for certain chromosome conditions. During pregnancy, some of your baby's placenta's chromosome material is in your blood, along with your own chromosome material. Cell-free DNA screen is a blood test that measures the amount of chromosome material in your blood to determine if your baby could have an extra chromosome. This test screens for Down syndrome, trisomy 18, trisomy 13 and may also screen for some less severe conditions that are caused by different numbers of the X or Y chromosome. Cell-free DNA screen may also screen for several conditions caused by small missing pieces of chromosomes. While cell-free DNA screen is a good screen, it is not a diagnostic test, like the amniocentesis. The detection rate for these chromosome conditions is typically between 90-99%. Other screening blood tests (often called a triple, quad, penta, or first trimester screen) may also be offered.

The risks, benefits, and limitations of screening and diagnostic testing options should be discussed with you by your genetic counselor or other health care provider. Follow-up counseling and referrals for support can be made if a chromosome condition is detected prenatally. As with all situations in which prenatal testing is discussed, it is your decision whether or not this test is done.

It is important to remember that prenatal screening and testing cannot detect or rule out all genetic conditions. After the baby is born, if additional birth defects or developmental delays are noted, an examination by a pediatric geneticist may be recommended. The geneticist may recommend that a small amount of blood be taken from the baby to evaluate for a chromosome or genetic problem. This examination and possible additional tests are important, since an accurate diagnosis will provide you with the best information regarding the prognosis for your baby, the cause of the TEF/EA, the risks to future children and that of other family members, as well as to determine appropriate tests to be offered to you in future pregnancies.

The decision to have one or more of the tests or to do no additional testing is a difficult and personal one. There is no one right decision. Some people will decide to have no further testing because they do not feel they need to know if their baby will have any of the genetic and chromosome conditions before delivery. Other people feel that they want more information as soon as possible. After gathering all of the information you need about TEF/EA and available testing, you should make the decision that is right for you and your family.

***What is the risk for this to happen again?***

Parents of a baby with TEF/EA are often worried about the risk for it to happen in another pregnancy. If the TEF/EA is isolated and not part of a genetic condition and there is no other family history, the chance to have another baby with a TEF/EA is approximately 1%.

***What do I do now?***

This information is only intended as an introduction to some of the terms and tests that you have already heard or will be hearing about from your genetic counselor and healthcare provider. We hope that this information sheet will be helpful as you begin to understand more about TEF/EA. We understand that any time something of concern is found through prenatal screening and testing, parents are going to be worried. Please don't hesitate to contact your genetic counselor with any questions or concerns you have. We are here to help you and your baby.

You may find it useful to have a consultation with a maternal-fetal medicine physician (physician that specializes in high-risk obstetrical care) and a pediatric surgeon to discuss the specifics about the TEF/EA and management for your pregnancy. You may also find it useful to have a consultation and an evaluation performed at a fetal center experienced at taking care of babies with TEF/EA. Your doctor may recommend delivery at a tertiary care center, a hospital equipped to take care of babies with TEF/EA. However, depending on your specific case and what hospital you are seen at, your health care provider may recommend additional consultations and tests that are not discussed here. Support groups, either online or in person, can provide comfort for families facing this diagnosis. One-on-one therapy or family therapy may also be useful, both during and after the pregnancy.