Patient Information Sheet
Lower Urinary Tract Obstruction (LUTO)

You have recently learned that your baby has a lower urinary tract obstruction (LUTO). 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 lower urinary tract obstruction?

Lower urinary tract obstruction (LUTO), also known as a bladder outlet obstruction, is a condition that is caused by abnormal development of the urinary system. The urinary system in our body is generally made up of two kidneys that filter the blood and remove waste products as urine. Urine is moved from the kidneys into the bladder via tubes called the ureters, and the urine is held in the bladder until the baby urinates. The urine then leaves the bladder and the body via a tube called the urethra. LUTO happens when there is a blockage or an obstruction in the urethra that does not allow all of the urine to leave the bladder. This causes the urine to back up into the bladder, ureters, and the kidneys. The back-up of the fluid causes the bladder to get very large and the back-up of fluid in the kidneys may damage them and preventing them from working.

Sometimes the blockage at the urethra is small and some urine still leaves the bladder. Other times the blockage may be severe, and no urine leaves the bladder. The most common cause of obstruction in boys is called posterior urethral valve (PUV), which is an abnormal flap of tissue in the urethra that blocks the bladder. In girls, the most common cause of blockage is underdevelopment of the urethra, known as urethral atresia. The information that follows will mainly discuss LUTO caused by PUV.

How many babies are found with LUTO?

It is not known exactly how many babies are born with LUTO but it is thought to happen in approximately 1 in 5,000 to 1 in 20,000 pregnancies. Approximately 1 in 4,000 to 1 in 7,500 boys have PUV specifically.

What causes LUTO?

In majority of babies with LUTO, the exact cause is not known. For these babies, LUTO is thought to be a "multifactorial" condition, meaning that multiple factors (including genetics and the environment) influence the development of the kidneys and the bladder. For some babies LUTO is the only problem seen on ultrasound (isolated). However, some babies with LUTO may have additional problems, like a heart defect.

Some babies with LUTO 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 LUTO.

There have also been reports of families with multiple family members having LUTO or other kidney problems, suggesting that some cases are "hereditary", or passed down in the family.

What problems could be associated with LUTO for my baby and how are they treated?

Starting at about 14 to 18 weeks of pregnancy the baby's kidneys start producing the urine that makes up most of the amniotic fluid around the baby. The amniotic fluid helps cushion the baby inside your belly and allows the baby to move. Amniotic fluid is also swallowed by the baby which helps the baby's lungs grow and develop.

Typically babies that have a mild blockage have normal amniotic fluid and may not have many serious problems. They may have a higher chance of having urinary tract infections (UTIs) or bladder dysfunction. For babies with mild blockage the doctors may recommend a kidney (renal) ultrasound shortly after the baby is born and may recommend performing a test called a voiding cystourethrogram (VCUG), a special X-ray that looks at the kidneys making urine. For some babies a surgery to open the blockage and to correct the urethra may need to be performed.

Babies with severe obstruction typically have more serious problems. These babies usually have either low amniotic fluid (oligohydramnios) or no amniotic fluid (anhydramnios) surrounding them in your belly. Since amniotic fluid is needed for the baby's lungs to grow, low or no amniotic fluid causes underdeveloped lungs. This is usually not compatible with life outside the womb and up to 8 out of 10 babies with LUTO pass away either before or shortly after birth. For babies that do survive their kidneys are often damaged to the point where they do not work. When the kidneys do not work they are not able to filter and clean the blood so these babies may need to get peritoneal dialysis followed by a kidney transplant. In peritoneal dialysis a tube, also known as a catheter, is place inside the baby's belly (peritoneal cavity). A cleansing fluid which helps absorb waste from the blood is circulated through the tube and thrown away once it leaves the body. Kidney transplant usually does not happen until baby is at least 2 years old.

In general, there is no treatment that can help produce amniotic fluid or help with lung growth if the kidneys are not working. In most severe cases of LUTO where the kidneys are still working a procedure known as vesicoamniotic shunting may be offered. In this procedure a tube is inserted into the baby's belly to help drain the urine from the bladder into the amniotic sac. This may prevent fluid from backing up into the kidneys and damaging them and may also help to increase the amniotic fluid level, helping the lungs grow. This is something that can only be done in pregnancies with male babies where PUV is suspected. For other cases of LUTO there may be some investigational therapies to increase amniotic fluid to help the lungs grow. However, the lungs are still likely to be underdeveloped and most of these babies, even if they survive, still require dialysis and renal transplant after birth. These procedures are only performed in a limited number of centers by specialists experienced at treating babies with LUTO before birth. Some parents may choose to end a pregnancy that has been diagnosed with bilateral MCDK.

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

Depending on your current gestational age, a number of additional tests may be offered to you. If LUTO is found during a routine ultrasound, a more detailed ultrasound will usually be performed to look more carefully at the baby's body parts. In some cases a fetal echocardiogram (an ultrasound of the baby's heart) and/or a fetal MRI 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:

<u>Diagnostic Tests</u>

Depending on your gestational age and the amount of amniotic fluid around the baby, two diagnostic testing options may be available including chorionic villus sampling (CVS) or amniocentesis. These are diagnostic tests in which a small sample of placenta or amniotic fluid is obtained to examine the baby's chromosomes. Because these procedures are considered invasive procedures, there is a risk, likely less than 1%, for complications that can lead to miscarriage.

If you choose to pursue a CVS or amniocentesis, 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.

<u>Screening Tests</u>

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. In cases of LUTO where the baby passes away an autopsy may also be recommended. 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 birth defect, 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 these 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 these chromosome or genetic conditions before delivery. Other people feel that they want more information as soon as possible. After gathering all of the information you need about LUTO and available testing, you should make the decision that is right for you and your family.

What is the chance for this to happen again?

Parents of a baby with LUTO are often worried about the chance for it to happen in another pregnancy. If the LUTO is isolated and not part of a genetic condition and there is no other family history, the chance for LUTO to happen again is <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 LUTO. 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 also find it useful to have a consultation with a maternal-fetal medicine physician (physician that specializes in high-risk obstetrical care), a nephrologist (kidney doctor), a urologist (urinary tract doctor), and/or neonatologist (NICU doctor) prior to delivery. You may also find it useful to have a consultation with a palliative care doctor to make a delivery or birth plan you and your family are comfortable with. 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. We encourage you to talk to your genetic counselor or healthcare provider to learn more about what might be helpful for you.