

# Urinary Tract Dilation in the Fetus and Neonate

Katherine Vincent, DNP, NNP,\* Heidi J. Murphy, MD, MSCR,\* and Katherine E. Twombly, MD†

\*Division of Neonatology, Department of Pediatrics, Medical University of South Carolina, Charleston, SC

†Division of Pediatric Nephrology, Department of Pediatrics, Medical University of South Carolina, Charleston, SC

## PRACTICE GAPS

Recently, a multidisciplinary consensus developed terminology and a classification system to grade perinatal urinary tract dilation (UTD). This also included a proposed evaluation and management schema of UTD to provide unifying descriptions. Although the efficacy of prenatal intervention remains unproven, postnatal evaluation of UTD is necessary to detect renal and urinary tract pathology that may require close evaluation or surgical intervention. The prognosis of UTD ranges from spontaneous resolution to end-stage renal disease.

## OBJECTIVES *After completing this article, readers should be able to:*

1. Correctly diagnose and quantify urinary tract dilation (UTD) antenatally or postnatally using the current standard of assessment, the UTD classification system.
2. Recognize different imaging modalities and their appropriate uses for diagnosing congenital anomalies of the urinary tract.
3. Summarize the pathophysiology of common congenital anomalies of the urinary tract that cause UTD.
4. Apply the UTD classification system management schema to dictate frequency and timing of renal ultrasound follow-up in the clinical setting.

## ABSTRACT

Urinary tract dilation (UTD), previously known as hydronephrosis, is the most common congenital condition identified on prenatal ultrasonography. UTD can be physiologic and resolve spontaneously or can be caused by various congenital anomalies of the urinary tract, which can lead to renal failure if not treated properly. In 2014, a multidisciplinary consensus group established UTD definitions, a classification system, and a standardized scheme for perinatal evaluation. Various imaging modalities are available to help diagnose the cause of UTD in fetuses and neonates and to help identify those patients who may benefit from fetal or early postnatal intervention. In this article, we will review the diagnosis and quantification of antenatal and postnatal UTD based on the UTD classification system, outline the imaging studies available to both evaluate

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## ABBREVIATIONS

APDRP	anterior-posterior diameter of renal pelvis
CAKUT	congenital anomalies of the kidney and urinary tract
DRS	diuretic renal scintigraphy
ICC	intraclass correlation coefficient
MRU	magnetic resonance urography
PUV	posterior urethral valve
RUS	renal ultrasonography
SFU	Society for Fetal Urology
UPJ	ureteropelvic junction
UTD	urinary tract dilation
UTI	urinary tract infection
UVJ	ureterovesical junction
VCUG	voiding cystourethrography
VUR	vesicoureteral reflux

UTD and determine its cause, briefly review the most common causes of UTD in the fetus and neonate, outline management strategies for UTD including the role for fetal intervention and prophylactic antibiotics, and report on the outcome and prognosis in patients with UTD.

## INTRODUCTION

Urinary tract dilation (UTD), previously referred to as hydronephrosis, is the most common congenital condition identified on prenatal ultrasonography and affects 1% to 4.5% of all pregnancies. (1)(2)(3) UTD can be physiologic or pathologic. Physiologic UTD accounts for 64% to 94% of prenatally diagnosed UTD and is of little long-term clinical consequence or significance as it typically resolves by 2 years of age. (1)(3) Pathologic UTD is often associated with congenital anomalies of the kidney and urinary tract (CAKUT) and occurs at the level of the kidney, ureters, bladder, or urethra. (4) Most prenatally diagnosed UTD cases are of the physiologic type and resolve spontaneously; however, pathologic UTD can be life-threatening and may require fetal intervention (rarely) or early postnatal intervention. (5)

Historically, no standard method or classification system has been used across subspecialties to define and grade UTD in the fetus and newborn. A significant lack of uniformity in defining and grading UTD existed, with multiple grading systems available. (6)(7)(8)(9)(10) Because of this lack of uniformity, sparse data exist to consistently correlate severity of prenatal UTD with postnatal pathology or outcomes. Clinical practices also vary considerably in the management of UTD.

As a result of this wide diversity in terminology and practice, representatives from 8 societies (the American College of Radiology, American Institute of Ultrasound in Medicine, American Society of Pediatric Nephrology, Society for Fetal Urology [SFU], Society for Maternal-Fetal Medicine, Society for Pediatric Urology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound) met in 2014 to form a multidisciplinary consensus panel. (11) Goals of the consensus panel were to propose: 1) unifying descriptions of UTD for prenatal and postnatal evaluation and quantification, and 2) a standardized scheme for perinatal UTD evaluation. The consensus panel yielded what is now known as the “UTD classification (or grading) system.”

The aim of this review is to outline the diagnosis and quantification of antenatal and postnatal UTD using the UTD classification system; summarize the imaging studies available to evaluate UTD and determine its cause; briefly review the most common causes of UTD in the fetus and neonate; outline management strategies for

UTD, including review of the role for fetal intervention and prophylactic antibiotics; and report on the outcome and prognosis in patients with UTD.

## UTD: DIAGNOSIS AND DEFINITION

Prenatal ultrasonography is routinely performed in the United States, and the components of this ultrasonography, including anatomic survey with targeted kidney and bladder evaluations, are guided by the clinical management guidelines of the American College of Obstetricians and Gynecologists. (12) To diagnose and quantify UTD, anterior-posterior diameter of renal pelvis (APDRP) measurements are obtained using transverse ultrasound images of the anterior-posterior plane of the kidney (Fig 1). The APDRP is determined by measuring the maximal diameter of the intrarenal pelvis. Other parameters assessed with ultrasonography, as recommended by the multidisciplinary consensus panel and comprising the UTD classification system, include calyceal dilation (present or absent centrally [ie, the major calyces] or peripherally [ie, the minor calyces]), parenchymal thickness, parenchymal appearance, ureter anatomy, and bladder anatomy. (11) Prenatally, the presence of oligohydramnios is also evaluated. Dilation of the ureter or posterior urethra is considered abnormal as is increased bladder wall thickness or the presence of a ureterocele. Transient visualization of the ureter postnatally, however, can be normal.

Historically, the terminology used by pediatric specialists to describe dilation of the kidney and urinary tract varied considerably. For example, different clinicians used the terms “pyelectasis,” “pelviectasis,” and “hydronephrosis” interchangeably to describe dilation of the renal pelvis. (13) Though these terms may have been used interchangeably, different clinicians used these terms to imply various, differing findings; one clinician may have used hydronephrosis to denote mild UTD, whereas another clinician may have used the same term to indicate significant dilation of the renal pelvis and calyces. (11) These differences in terminology created confusion among physicians and potentially affected patient care. At the aforementioned 2014 multidisciplinary consensus panel conference, recommendations were made for consistent use of the term “urinary tract dilation (UTD)”, and the panel recommended avoiding nonspecific terms including



**Figure 1.** Measurement of the anterior-posterior renal pelvic diameter (APRPD) with ultrasonography. This renal ultrasound image was obtained in a 1-month-old male infant born at 28 weeks' gestation. To assess for urinary tract dilation, the APRPD is measured in a transverse view using the maximum diameter and found to be 0.399 cm which is within normal limits.

hydronephrosis, pyelectasis, pelviectasis, uronephrosis, urinary tract fullness, urinary tract prominence, and pelvic fullness. (11)

Both prenatal and postnatal UTD classification criteria were developed from existing grading systems, with the chief among them being the 2010 SFU classification system and APDRP measurements (Fig 2A and Fig 3B). (11)(14) The SFU grading system is a qualitative assessment of hydronephrosis based on the degree of dilation in the renal pelvis and ureter and the degree of cortical thinning. The APDRP system is a quantitative assessment of the degree of renal pelvis dilation determined by measuring the greatest diameter of the renal pelvis on ultrasonography in the transverse plane. Classification of UTD, both prenatally and postnatally, is based on the presence of the most concerning features on ultrasonography.

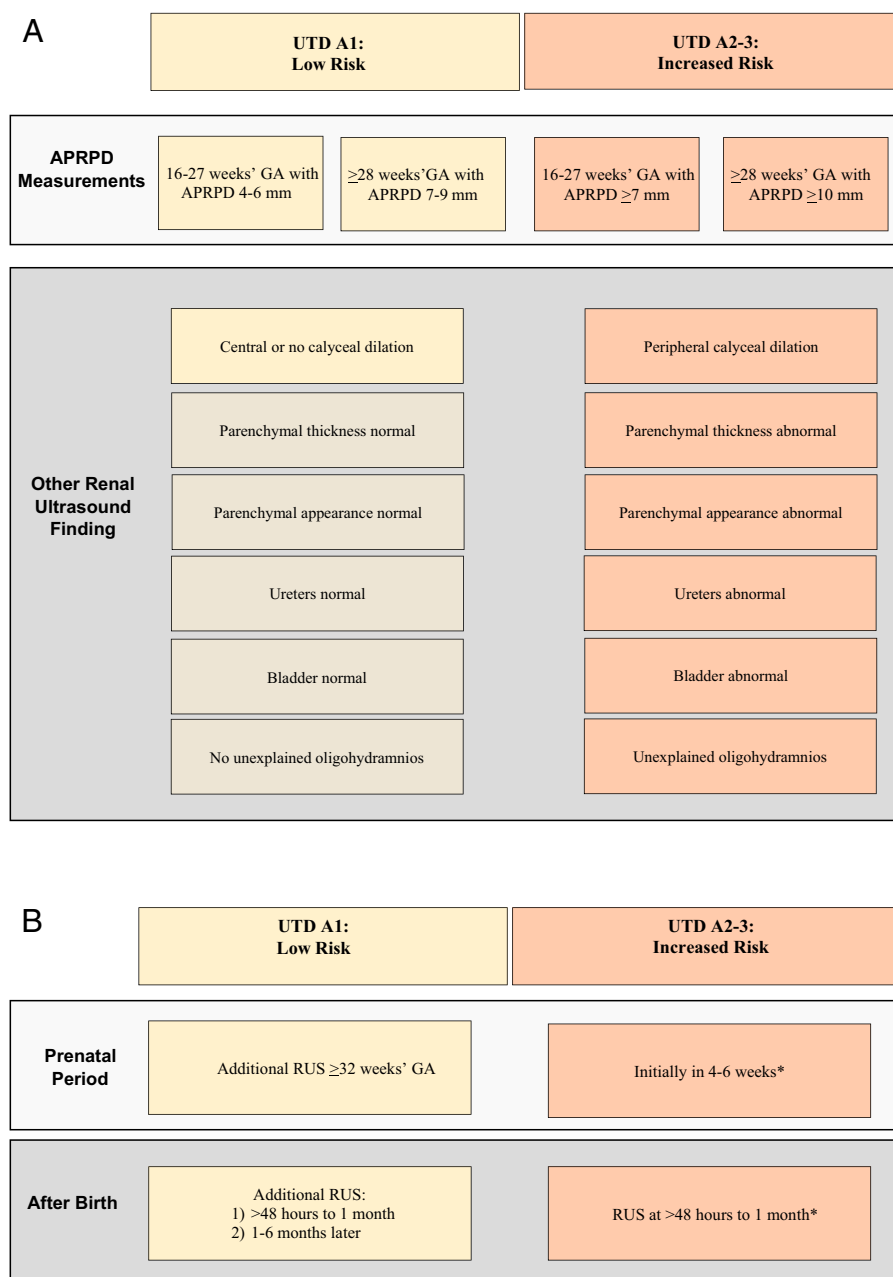
Prenatally, UTD is categorized using the letter A (for antenatal) and numbers 1 to 3, with each increasing number denoting more significant UTD and increasing risk for postnatal pathology (Fig 2A). UTD A1 is considered low risk whereas UTD A2 and A3 suggest increased risk of significant postnatal pathology and CAKUT (based on studies assessing correlation of APDRP measurements and postnatal pathology). (15)(16)(17)(18)(19) Specific APDRP thresholds based on gestational age are available to define and quantify UTD prenatally. (11) The APDRP should measure less than 4 mm at 16 to 27 weeks of gestation, less than 7 mm at more than 28 weeks of gestation, and less than 10 mm at 48 hours after birth. Due to the

difficulty in distinguishing central and peripheral calyceal dilation on prenatal ultrasonography, the UTD grading system includes a combination of A2 and A3 with the creation of only 2 categories, low-risk UTD (A1) and high-risk UTD (A2–3).

Similar to prenatal UTD, the postnatal (“P”) UTD classification system includes 3 categories each, assigned in part, by threshold APDRP measurements: low risk (P1, 10 to <15 mm APDRP), intermediate risk (P2,  $\geq 15$  mm APDRP), and high risk (P3,  $\geq 15$  mm APDRP) (Fig 3A). (11) Again, APDRP measurements correlate with risk of CAKUT or significant pathology. (20) If indicated, postnatal ultrasonography should be performed after 48 hours of age except in the case of suspected posterior urethral valves (PUVs) or low urine output, in which case, it should be performed immediately. If completed before 48 hours of age, renal ultrasonography (RUS) may yield a false-negative result due to underestimation of the degree of UTD when the infant is in an oliguric state and therefore should be repeated after 48 hours of age. (4)

Several studies have shown that the UTD classification risk score has interrater and intrarater reliability comparable to the SFU system. (21)(22) Back et al reported intraclass correlation coefficient (ICC) of APDRP measures of 0.99 ( $P < .001$ ) with high intrarater reliability of APDRP of each kidney (ICC  $> 0.95$ ;  $P < .001$ ) among a group of pediatric radiologists using the UTD grading system. (23) In an assessment of multidisciplinary intra- and interrater reliability of both the SFU and UTD classification systems, Rickard et al found that the overall interrater reliability was slightly higher for low-grade SFU than for UTD, but was poor for intermediate grades of UTD (ie, SFU grades II or III and UTD 2), regardless of classification system. (24)

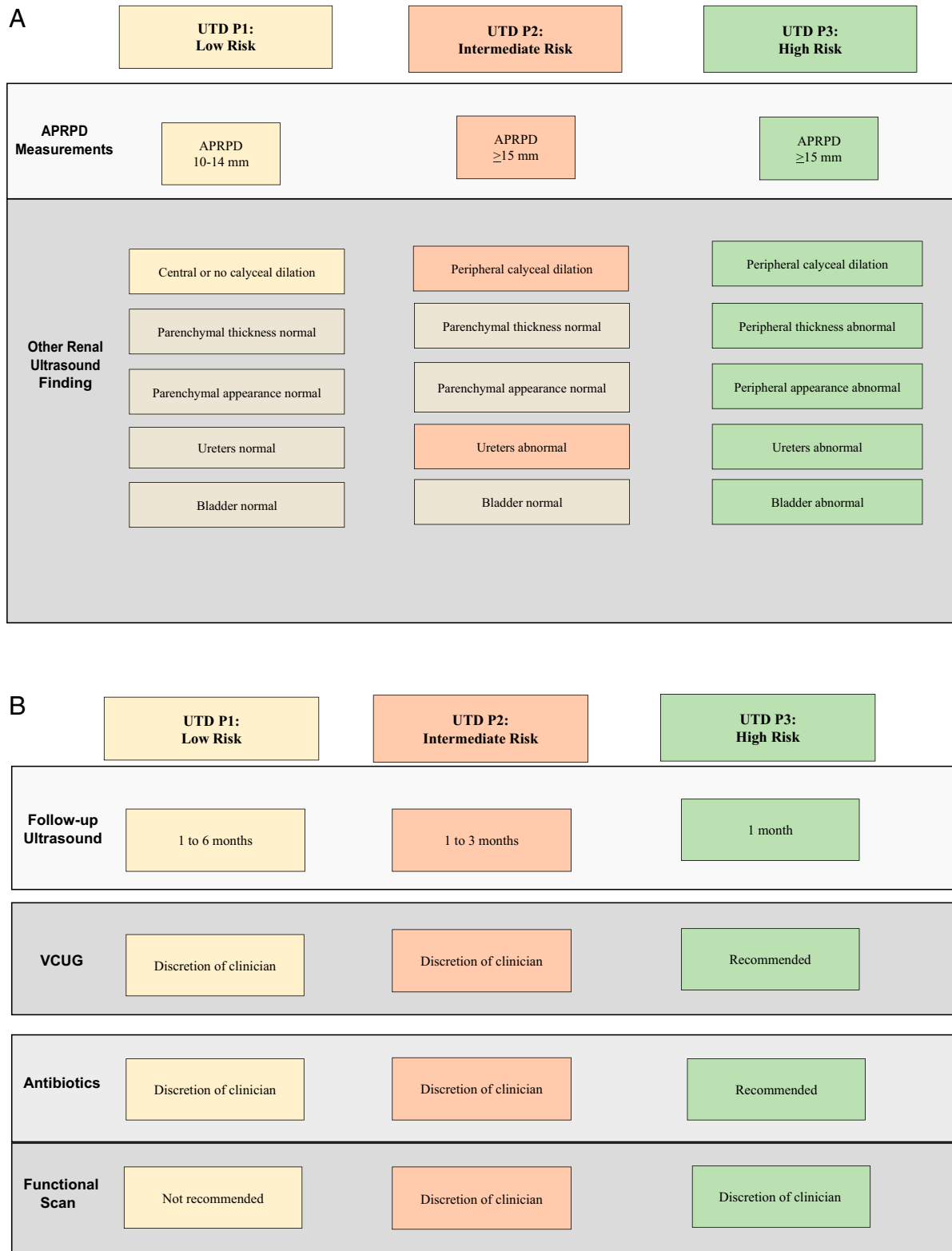
In the first assessment of the reliability and validity of the UTD classification system, Hodhod et al found that the UTD system reliably assessed UTD and independently predicted the need for surgical intervention. (25) Kaspar et al found that the UTD antenatal classification system (ie, UTD A system) applied retrospectively identified 90% of postnatally diagnosed CAKUT diagnoses (the remaining 10% were due to myelomeningoceles with vesicoureteral reflux [VUR] or UTD, which was not evident prenatally). (26) In this cohort, the sensitivity and specificity of the UTD antenatal classification system was 0.767 (95% confidence interval [CI], 0.577–0.901) and 0.836 (95% CI, 0.758–0.897), respectively. The system revealed important differences in severity of UTD with the UTD A2–3



**Figure 2.** Prenatal ultrasound findings, diagnostic criteria, and management scheme for prenatally diagnosed urinary tract dilation. A. Diagnostic criteria for UTD and prenatal renal ultrasound findings. B. Management scheme for prenatally diagnosed UTD. \*Certain pathologies such as posterior urethral valves or bilateral severe UTD may require sooner or immediate renal ultrasonography after birth. APRPD=anterior-posterior renal pelvis diameter, RUS=renal ultrasonography; UTD=urinary tract dilation. (Adapted from Nguyen et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation [UTD classification system]. *J Pediatr Urol.* 2014;10:982-989.)

category including more than 90% of the obstructive uropathies (no obstructive uropathies occurred in the UTD A normal category). The authors went on to conclude that this system may eventually be used to predict postnatal renal events and related UTD morbidity, but larger, prospective validation studies are needed. Braga and

colleagues similarly found that when comparing the predictive value of the SFU grading system and UTD classification system for future risk of surgical intervention or development of febrile urinary tract infections (UTIs), both systems “equally allowed for proper risk stratification and prediction of clinical outcomes.” (21)



**Figure 3.** Postnatal ultrasound findings, diagnostic criteria, and management scheme for urinary tract dilation. A. Diagnostic criteria for UTD and postnatal renal ultrasound findings. B. Management scheme for postnatally diagnosed UTD. APRPD=anterior-posterior renal pelvis diameter, UTD=urinary tract dilatation, VCUG=voiding cystourethrography. (Adapted from Nguyen et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation [UTD classification system]. *J Pediatr Urol.* 2014;10:982-989.)

## EVALUATION OF PRENATAL AND POSTNATAL UTD: IMAGING STUDIES

The initial clinical challenge among infants with UTD is to discriminate those who will likely have significant urologic abnormality and therefore benefit from early detection and intervention, from those infants who have transient, physiologic UTD and would unnecessarily be exposed to radiation or invasive procedures if advanced imaging is pursued. (1)(22) The ultimate goal in UTD evaluation is to detect anomalies and then intervene as necessary to preserve renal function and prevent complications such as febrile UTIs, flank pain, renal calculi, hypertension, and renal failure. (1)(4) RUS, voiding cystourethrography (VCUG), diuretic renal scintigraphy (DRS), and magnetic resonance urography (MRU) are imaging modalities commonly used in postnatal evaluation of UTD.

### Renal Ultrasonography

RUS is the least invasive imaging modality to evaluate UTD and is the initial step in diagnosing CAKUT (ie, pathologic UTD). To avoid underestimating UTD due to oliguria in the newborn period, the first postnatal RUS should be delayed until 48 hours after birth, if possible, and ideally obtained between 5 and 30 days of age, except when an infant is suspected to have PUVs, low urine output, or complex renal abnormalities, in which case imaging should be performed immediately after birth. (4)(27) An RUS should evaluate the entire urinary tract including the renal parenchyma, ureters, and urinary bladder. (22) RUS requires no radiation exposure, and serial RUS can determine if UTD is worsening or resolving as well as help determine when and if intervention is needed. (22)

### Voiding Cystourethrography

When a UTD is present, VCUG is helpful to evaluate for other lower urinary tract disorders such as VUR, renal duplication anomalies, PUVs, and megaureters. (1)(4) During VCUG, a Foley catheter is placed in the bladder, and a radiopaque contrast agent is instilled. (3) Although VCUG is a more invasive study than RUS and risks radiation exposure, it is absolutely necessary in the evaluation of some disorders, and it is indicated as soon as possible after birth in neonates with suspected PUVs. (4) VCUG is also recommended for severe UTD, but its use is more controversial for mild to moderate UTD. (4)

### Diuretic Renal Scintigraphy

DRS is used to evaluate upper urinary tract obstruction in infants with UTD and is usually performed no sooner

than 6 weeks of age to allow renal blood flow maturation. (4) DRS is also an invasive study that involves placement of a Foley catheter, intravenous hydration, administration of a diuretic, and a small dose of Tc-mercaptoacetyltriglycine. (22) DRS measures both renal function and renal drainage, but it is inferior to RUS or MRU for evaluating anatomic anomalies. (4)(22) The diagnostic accuracy of DRS is highly variable, and therefore, it should only be ordered in consultation with a pediatric urologist or nephrologist. This is because results can be false positive in infants with large collecting systems that do not allow the appropriate time to fill before diuretic administration. (4)(22)

### Magnetic Resonance Urography

MRU uses gadolinium contrast to provide both T1- and T2-weighted magnetic resonance images of the kidney. (1)(22) It measures both glomerular filtration rate and renal transit time and provides detailed anatomic information. (1) It is being used more often in the evaluation of severe UTD, because it is a better predictor of some forms of CAKUT than RUS, VCUG, and DRS. (1)(22) However, its use is limited by lack of availability at some centers, cost, and need for sedation. (1)(22) This test should also only be ordered in consultation with a pediatric urologist or nephrologist as less expensive and less invasive tests might be more appropriate.

## CAUSES OF UTD

When a neonate is diagnosed with UTD, it is important to differentiate between physiologic UTD and CAKUT. (5) Most frequently, UTD in the neonate is caused by incomplete obstruction of the urinary tract (ie, physiologic UTD) or VUR. (28) Other CAKUTs account for 20% to 30% of all prenatally diagnosed congenital anomalies and are the most common causes of chronic kidney disease in children. (29)(30) Physiologic UTD and the most common CAKUTs will be briefly discussed here, including ureteropelvic junction (UPJ) obstruction, ureterovesical junction (UVJ) obstruction (also known as “obstructed megaureter”), VUR, ureterocele, PUVs, and prune belly syndrome (Table). (31) A comprehensive review of CAKUT is available and recommended for more detailed information. (32)

### Physiologic UTD

Physiologic UTD is typically transient and may be caused by narrowing of the ureter, which leads to urinary flow obstruction. It usually resolves as the fetus matures or by



**Table.** Causes of Pathologic Urinary Tract Dilation

Causes	Diagnoses
Renal malformation	Vesicoureteral reflux
	Ureterocele
	Posterior urethral valves
Atretic, narrow, or aperistaltic ureteral segment	Ureteropelvic junction obstruction
	Ureterovesical junction obstruction
Others	Prune belly syndrome

Adapted from Jain S, Chen F. Developmental pathology of congenital kidney and urinary tract anomalies. *Clin Kidney J.* 2019;12(3):382-399. doi: 10.1093/ckj/sfy112.

2 years of age. (3) Physiologic UTD is clinically insignificant and accounts for most cases of mild, prenatally diagnosed UTD. Studies show that the degree of UTD correlates with an increased risk of significant pathology, therefore, lower degrees of UTD are more likely to reflect physiologic UTD than higher degrees of UTD. (19)

### UPJ Obstruction

UPJ obstruction is an obstruction that occurs at the site of ureter insertion into the renal pelvis. The obstruction may result from incomplete recanalization of the proximal ureter, abnormal ureteral musculature development, abnormal peristalsis, polyps, or external compression by an accessory vessel. UPJ obstruction is the most common cause of prenatal UTD, accounting for up to 41% of UTD cases. (3)(29) It is often unilateral (most frequently occurring on the left) and occurs more commonly in male patients. UPJ obstruction may happen in isolation, may be associated with other congenital anomalies (ie, VUR), or may be related to an underlying genetic syndrome. Signs and symptoms of delayed presentations (if UTD is not detected on prenatal ultrasonography or if ultrasonography is not performed) include flank pain, nausea, emesis, and UTIs. (29)(31) Diagnosis of UPJ obstruction may be suspected based on RUS findings of UTD and negative VCUG results but is confirmed via DRS.

### UVJ Obstruction (Obstructed Megaureter)

UVJ obstruction, or obstructed megaureter, are terms used to describe distention of the ureter, which results in impaired urinary flow and accounts for 5% to 10% of prenatally diagnosed UTD. (29)(33) It is also more common in male patients. UVJ obstruction can be congenital, related to maldevelopment of the distal ureter or the presence of a ureterocele, or acquired, and is classified into 3 categories—refluxing, obstructed, or nonrefluxing and nonobstructive. (34) Diagnosis of UVJ obstruction is made via DRS with negative findings on VCUG.

### Vesicoureteral Reflux

Approximately 7% to 35% of patients with prenatally diagnosed UTD are postnatally diagnosed with VUR, making it the third most common urologic diagnosis that presents with prenatal UTD. (1) VUR is caused by a defective junction between the ureter and the bladder, which results in retrograde flow of urine from the bladder to the ureter and upper urinary tract during bladder contraction. Ectopic ureter insertion into the bladder wall is hypothesized to be the underlying cause in most primary VUR cases, resulting in shortening of the intravesicular ureter. This type of VUR may have a genetic component with an increased incidence noted among first-degree relatives. (3) Secondary VUR results from bladder outlet obstruction and is typically bilateral. VUR is also more common in male patients. (33) Seventeen percent of children have VUR, and it is present in 30% of children who have UTIs. (29) VUR is diagnosed via VCUG and is graded from I to V, with grade I indicating lowest severity and grade V indicating highest severity. Each kidney may have differing grades of VUR. Notably, there is a poor correlation with degree of UTD on prenatal or postnatal ultrasonography and the risk of developing VUR. (11)(22)

### Obstructing Ureterocele

A ureterocele is a cystic dilation of the distal ureter that causes obstruction of urine flow and subsequently UTD and is more common in girls. (29) Rarely, it can prolapse through the urethra in females. (29) Infants often present with a severe, febrile UTI. (35) VUR is present in 50% of obstructing ureteroceles. (35)

### Posterior Urethral Valves

PUVs occur typically in boys due to a congenital membrane that forms in the urethra, resulting in complete or partial obstruction of the posterior urethra and an inability of the fetus and/or neonate to empty the bladder. A few case reports of PUVs in girls have been published. (31)(33)

Failure of mesonephric duct regression may also contribute. PUVs are the most common cause of lower urinary tract obstruction, affecting 1 in 5,000 to 8,000 live male births. (3) This bladder obstruction typically leads to a thickened, dilated and trabeculated bladder, bilateral hydroureter, dilated posterior urethra with a keyhole sign, UTD, and often oligohydramnios. (29) Postnatally, newborns may have palpable, distended bladders with poor urinary stream along with renal and pulmonary insufficiency. If severe, oligohydramnios can result in pulmonary hypoplasia and Potter syndrome, a congenital disorder characterized by physical changes such as characteristic facies with epicanthal folds, low-set ears, flattened noses, recessed chin, pulmonary hypoplasia, and lower extremity skeletal deformities; severe oligohydramnios and Potter syndrome predict adverse postnatal outcomes such as chronic renal failure and death. (1) PUVs are diagnosed via VCUG and frequently are associated with VUR. Severe bladder obstruction from PUVs can lead to renal dysplasia and cause progressive renal failure. (29)

### Prune Belly Syndrome

Prune belly syndrome (also known as Eagle Barrett syndrome) is a rare defect that consists of a triad of anomalies—UTD, abdominal wall muscular deficiency, and cryptorchidism, however, the severity of these findings is variable. (29) Infants with prune belly syndrome can also have other gastrointestinal, cardiovascular, pulmonary, and musculoskeletal associations. A genetic component is suspected in some cases, as 2 potential causative genes have been identified. Infants with prune belly syndrome are almost always male. (36)(37) UTD is due to smooth muscle being replaced by collagen and fibrous tissue, causing elongated, tortuous ureters and an enlarged, distorted bladder with poor contractility, which may be accompanied by megaureters and renal dysplasia. (36) The UTD can cause VUR, incomplete bladder emptying, and recurrent UTIs.

### UTD MANAGEMENT

Management of UTD is driven by underlying diagnosis, and management of each CAKUT is beyond the scope of this review. More detailed information regarding management of specific CAKUT diagnoses can be found elsewhere. (32) Here, management of the UTD itself will be reviewed. The UTD classification system proposed by the consensus panel in 2014 includes proposed management schemes depending on the type and degree of UTD (Fig 2B and Fig 3B). (11)

In the case of antenatal UTD (Fig 2B), for those with UTD A1 (ie, low-risk group) diagnosed before 32 weeks of gestation, additional prenatal ultrasonography should be performed when the affected fetus is at a gestational age greater than or equal to 32 weeks. If the previously detected UTD is resolved and the fetus has normal renal parenchyma, bladder, and ureters, no further follow-up is necessary. If UTD A1 persists or if it has progressed to UTD A2–3, 2 additional RUS evaluations are recommended after birth—one beyond 48 hours but before 1 month of age and a second scan 1 to 6 months later, as clinically indicated. For those with UTD A2–3 (ie, increased risk group) prenatal ultrasonography should be performed 4 to 6 weeks after diagnosis (sooner if PUVs or severe UTD is suspected). Depending on the findings of this repeat RUS, subsequent RUS evaluations with interval assessments of UTD should be performed, but the timing of these should be at the discretion of the clinician. In the presence of UTD A2–3, prenatal consultation with pediatric urology and/or pediatric nephrology is recommended, particularly if surgical intervention is anticipated or if there is significant renal dysfunction after birth. After birth, postnatal RUS should be performed immediately if PUVs are suspected or after 48 hours but before age 1 month if PUVs are not suspected. (11)

In the case of postnatal UTD noted on an RUS performed at the appropriate time (Fig 3B), for those with UTD P1 (ie, low-risk group), follow-up RUS is recommended in 1 to 6 months. For those with UTD P2 (ie, intermediate risk group), follow-up RUS is recommended in 1 to 3 months. Further assessment with VCUG and prescription of prophylactic antibiotics should remain at the discretion of the clinician, depending on the underlying diagnosis for those with UTD P1 or P2 because the optimal management strategy still is significantly controversial. A functional scan is typically not recommended for those with UTD P1 but is at the discretion of the clinician for those with UTD P2. For those with UTD P3 (ie, high risk group), follow-up RUS at 1 month, VCUG, and prophylactic antibiotics are all recommended. The decision to obtain a functional scan is at the discretion of the clinician and made in conjunction with either a pediatric urologist or nephrologist and again depends on the underlying diagnosis. (11)

Notably, the consensus panel reports that this UTD classification system is not intended to become a definitive, final classification system but rather should be used to encourage consistent terminology, aid in intraprovider communication around perinatal UTD, and serve as a



starting point for observation and study. Validation and modification of these classification categories and management schemes is necessary and ongoing.

When a specific underlying UTD pathology is identified, treatments should be directed to the underlying diagnosis. Historically, management of UPJ obstruction was surgical, but now only approximately one-half of patients require surgery; because of the potential for spontaneous resolution over time in some cases, a shift has occurred to increased observation only with RUS and DRS. (1)(29) Percutaneous nephrostomy drain placement is a temporizing measure for relief of obstruction in some patients. If surgery is required, as is the case in 20% to 25% of children with UPJ obstruction, pyeloplasty is performed in open fashion, laparoscopically, or robotically with the goal of maximizing long-term renal function. (3)(5)(14)(29) Surgery is still controversial in UPJ obstruction, and long-term studies are needed to determine what percentage of neonates managed with observation become symptomatic in adulthood. Prophylactic antibiotics may be recommended by some clinicians in the case of high-grade UTD with UPJ obstruction (see “UTI Prophylaxis” section). When UVJ obstruction is detected, urinary stasis, recurrent UTIs, and loss of renal function can all occur, in which case, prophylactic antibiotics may be considered, and surgery, if indicated. (3)(34) Surgical options include endoscopic repair or an open reconstruction. (29) However, up to 70% to 80% of megaureters resolve spontaneously. (3)(29)

Management of VUR depends on the severity of VUR along with the presence or absence of associated renal parenchymal disease. Similar to physiologic UTD, lower grades of VUR often resolve spontaneously as the intravesicular ureter elongates with growth. (29) Treatment of VUR may include prophylactic antibiotics, but this also remains controversial except in the case of high-grade VUR after a febrile UTI. (1)(3)(29) Severe VUR can lead to hypertension, glomerulosclerosis, proteinuria, renal scarring, and loss of renal function if both kidneys are involved (ie, chronic kidney disease due to so-called reflux nephropathy). (3)(28) Surgical intervention includes either endoscopic injection of collagen to provide a ball-valve effect to prevent urinary reflux or ureteral reimplantation. (31)

Ureterocele may require surgical intervention, which can be endoscopy or open reconstruction and depends on whether the ureterocele is ectopic or intravesical and whether VUR is present. (35) Prognosis after surgery in these patients is good. (29)

When PUVs are diagnosed, prenatal intervention is controversial and not readily accessible in many centers (see “Fetal Intervention” section); laser valve ablation of the congenital membrane or vesicoamniotic shunt placement are options. (38)(39) Postnatally, infants suspected to have PUVs need a Foley catheter and immediate RUS and VCUG. Surgical treatment is endoscopic valve ablation or a vesicostomy if the urethra is too small for ablation or if the obstruction persists. (29) Treatment of prune belly syndrome requires optimizing urinary tract drainage, which may require vesicostomy or reconstructive surgery. (29)(36) Renal insufficiency must be managed and can require dialysis or renal transplantation later in childhood. Many clinicians may prescribe prophylactic antibiotics. Male children will also have a bilateral orchiopexy before 1 year of age and some will require reconstruction of the abdominal wall. (29)

## FETAL INTERVENTION

Prenatal investigative interventions of UTD are only offered at specific, highly specialized centers, and remain controversial due to high complication rates for the pregnant woman and fetus as well as variable results and insufficient data to show long-term benefits. (22) To date, fetal interventions for UTD are indicated primarily for cases of PUVs with significant oligohydramnios but preserved renal function as seen on serial fetal urine samples; urethral atresia, a rare congenital anomaly causing lower urinary tract obstruction, is an alternate indication. (22) In the case of PUVs, before prenatal intervention, some centers require evaluation of urine electrolytes, with a minimum of 3 fetal urine samples obtained with fetal bladder aspirations at 48- to 72-hour intervals, with 2 abnormal urinary markers indicating borderline prognosis and 3 abnormal markers indicating poor prognosis. (1)(5) If an infant or fetus has good urine parameters such as appropriate urinary sodium, calcium, osmolality,  $\beta_2$ -microglobulin, and total protein levels, vesicoamniotic shunt or prenatal fetoscopic valve ablation can be considered. (1)(29)

Surgical intervention can be offered in the setting of severe oligohydramnios with bladder distention and bilateral hydronephrosis if other serious anomalies have been ruled out with ultrasonography, the fetal karyotype is normal, the fetus is a singleton, and the fetus has good or borderline urinary markers. (5)(29) The goal of fetal intervention should be prevention of pulmonary hypoplasia by correcting oligohydramnios due to pulmonary hypoplasia as a main cause of mortality in fetal lower urinary tract obstructions. (5) Fetal surgical interventions may be successful in relieving lower urinary tract obstruction but

often occur too late in gestation to reverse or rescue the severe respiratory and renal consequences. Typical antenatal surgical options include vesicocentesis, vesicoamniotic shunting, fetal cystoscopy, and valve ablation. The most common fetal intervention is the vesicoamniotic shunt with the goal of relieving the obstruction and correcting oligohydramnios by diverting urine into the amniotic space via a catheter. The catheter is placed into the fetal bladder under ultrasound guidance, with the proximal ends remaining in the amniotic space. (1) Vesicoamniotic shunt placement is a high-risk procedure, with up to a 48% rate of complications such as shunt migration, bladder fistula, bowel herniation, urinary ascites, preterm labor, and chorioamnionitis. (1)(3) This procedure also has a high fetal mortality rate of up to 43%. (1) Fetal cystoscopy is another procedure with similar complications as a vesicoamniotic shunt but allows for bladder cycling and direct visualization of the cause for lower urinary tract obstruction. (22)

A recent systematic review and meta-analysis of antenatal interventions for congenital fetal lower urinary tract obstruction found that overall estimated survival was higher in the vesicoamniotic shunt group (64/112 fetuses [57.1%]) compared to the control group (52/134 [38.8%]; odds ratio [OR], 2.54; 95% CI, 1.14–5.67). (40) Postnatal renal function, evaluated between 6 months and 2 years of age in survivors, was also better in the vesicoamniotic shunt group compared to the control group (OR, 2.09; 95% CI, 0.74–5.9). When evaluating the long-term results in 45 infants who underwent fetal cystoscopy, perinatal survival and normal renal function at 6 months were both higher in the intervention group compared to the control group (OR, 2.63; 95% CI, 1.07–6.47 and OR, 1.75; 95% CI, 1.05–2.92, respectively). (40)

## UTI PROPHYLAXIS

Another area of controversy in relation to UTD is the postnatal use of antibiotic prophylaxis to prevent UTIs, particularly in those with UTD and VUR. Recurrent UTIs in children can cause renal scarring and nephron loss. (11) In neonates, risk factors for UTIs include female sex, boys who are uncircumcised, and higher-grade UTD. (1)(22)

Unfortunately, there are inconsistencies in the literature regarding the effectiveness of antibiotic prophylaxis in preventing UTIs, especially with low-grade UTD. (41)(42)(43)(44)(45)(46)(47)(48)(49)(50) A 2013 systematic review showed that in patients with low-grade UTD, UTI rates were similar regardless of whether antibiotic prophylaxis was used, however, children with high-grade UTD

who do not receive antibiotic prophylaxis have a higher UTI risk than those who receive antibiotic prophylaxis (28.9% vs 14.6%). (41) In a 2015 meta-analysis, antibiotic prophylaxis reduced the risk of recurrent febrile or symptomatic UTI (pooled OR, 0.63; 95% CI, 0.42–0.96) among children with VUR. (48) However, notably, if UTI did occur, the risk of an antibiotic-resistant organism was increased (pooled OR, 8.75; 95% CI, 3.52–21.73). (48) In a 2019 updated Cochrane review in children with primary VUR, antibiotic prophylaxis made little or no difference to the risk of repeat symptomatic UTIs (relative risk [RR], 0.77; 95% CI, 0.54–1.09) and febrile UTIs (RR, 0.83; 95% CI, 0.56–1.21) at 1 and 2 years of age and had little or, most importantly, no difference to risk of new or progressive renal damage (RR, 0.73; 95% CI, 0.33–1.61) at 1 to 3 years of age. (50) Importantly, the evidence for these results was of low quality, and again, prophylactic antibiotics increased the likelihood of bacterial drug resistance (RR, 2.97; 95% CI, 1.54–5.74). (50)

An American Urological Association clinical guideline on the management of infants less than 1 year of age with VUR recommends antibiotic prophylaxis for 1) children younger than 1 year who have VUR and a history of febrile UTI, and 2) children younger than 1 year with VUR grades III–V. They suggest antibiotic prophylaxis may be an option in children younger than 1 year with VUR grades I–II. (51)

Currently, the UTD classification system resulting from the 2014 consensus panel recommends antibiotic prophylaxis for UTD P3 (high-risk group) but leaves it to the discretion of the clinician for both UTD P1 (low-risk group) and UTD P2 (intermediate-risk group). (11) In neonates, amoxicillin is typically prescribed for prophylaxis with orally available cephalosporins as a potential alternative. (52) The decision to provide antibiotic prophylaxis is complex and should include multidisciplinary discussion with the family and consideration of risk of antibiotic resistance, anticipated compliance with antibiotic regimen, and expense. (53)

## ROLE OF NOVEL BIOMARKERS

Fetal and postnatal biomarkers are a new tool being used to aid in diagnosis, management, and prognostication of UTD and CAKUT. Currently available diagnostic tools detect functional changes of the fetal kidney but are unable to accurately assess the potential for postnatal deficits. (54)(55)(56)(57) Biomarkers may aid in detection and quantification of fetal UTD and uropathy as well as

prenatal prognostication but how best to use these novel tools clinically is still being determined.

The following are several early biomarkers of progressive renal damage: serum and urinary  $\beta_2$ -microglobulin, urinary kidney injury molecule 1, urinary epidermal growth factor/monocyte chemotactic protein 1 ratio, and urinary neutrophil gelatinase-associated lipocalin. (4) Fetal serum  $\beta_2$ -microglobulin, a chain of the class I major histocompatibility antigens, is a surrogate marker of glomerular function and has high sensitivity and specificity for urinary tract malformation. (5)(54) Unlike other biomarkers, fetal serum  $\beta_2$ -microglobulin does not change with gestational age so it allows for longitudinal tracking of renal function; however, normative data are lacking, and studies to date have been in small numbers of patients with variable outcome measures being studied. (5)(54)

Fetal urinary biomarkers have also been investigated to assess fetal kidney function and predict postnatal outcomes. Obstruction of the fetal urinary tract alters key proteins, and urinary excretion of these key proteins may reflect severity of fetal renal injury. (54) Fetal urinary  $\beta_2$ -microglobulin is a surrogate marker of tubular function. (5) Fetal urinary  $\beta_2$ -microglobulin greater than 2 mg/L predicts a poor outcome. (5) A fetal urinalysis with urine sodium, chloride, osmolality, and calcium can provide useful information on fetal renal function. (5) Hypotonic fetal urine with sodium less than 90 mEq/L (90 mmol/L), chloride less than 80 mEq/L (80 mmol/L), and osmolality less than 180 mOsm/L (180 mmol/kg) in patients with bilateral UTD and no evidence of renal dysplasia is predictive of a good prognosis. (5)(29) Urinary calcium above 4.8 mg/dL (1.2 mmol/L) is predictive of a poor prognosis. (5) High-resolution magnetic resonance spectroscopy performed in the second and third trimester can measure amino acids, creatinine, and glucose in amniotic fluid and serve as biomarkers for renal maturation. (5) Creatinine increases in amniotic fluid with gestational age whereas glucose and amino acids decrease. (5) Further study is needed to determine which serum and urine analytes can be of highest clinical utility and used for prenatal prognostication accurately.

## OUTCOMES AND PROGNOSIS

UTD prognosis depends on many factors, including underlying etiology, and ranges from spontaneous resolution to progressive end-stage renal disease. Although it can take years for disease evolution or resolution, there are many predictors of postnatal outcomes. (58) Some prenatal predictors seen on ultrasonography include the grade and severity of UTD, the presence or absence of bilateral UTD, abnormal renal parenchyma, and oligohydramnios,

with the renal cortical appearance in the setting of oligohydramnios having the best predictive value for postnatal renal function. (1)(5)(30) Other predictors include prematurity, postnatal glomerular filtration rate less than 20 mL/min, and increased nadir creatinine concentration. (5) One study showed that postnatal bilateral anomalies and oligohydramnios were associated with impaired renal function and the need for surgical intervention. (30)

Globally, progressive worsening of antenatal UTD is associated with significant postnatal pathology. (11)(59) When lower urinary tract obstruction is detected, the presence of oligohydramnios or renal cortical abnormalities and detection at a low gestational age are all independently associated with poor postnatal renal function. (11)(39) CAKUT is predicted based on the severity of renal pelvic dilation, ureteral dilation, parenchymal thinning, renal hyperechogenicity, and thickened bladder on initial postnatal ultrasonography in infants with antenatally detected UTD. (11)(20) Need for pyeloplasty is correlated with APDRP greater than 16 mm. (11)(18)

When a specific diagnosis is found in the setting of UTD, outcome and prognosis vary depending on that diagnosis. A comprehensive review is available. (60) Physiologic UTD typically resolves within the first 2 years of age. (3)(21) Prenatal resolution of UTD occurs in about 80% of cases in which APDRP was between 4 and 8 mm in the second trimester. (11) In patients with unilateral UTD, the contralateral kidney typically functions normally, and overall long-term renal function is good. However, the prevalence of anomalies of the contralateral kidney is increased in the presence of unilateral UTD including VUR that can lead to chronic kidney disease with proteinuria and hypertension. (29)(61) The prognosis for PUVs is poor, with 20% to 60% of patients progressing to end-stage renal disease by the second decade of life. (29)(61) Predictors of poor outcome in PUVs include prematurity, low birthweight, fetal bladder diameter greater than 15 mm in the third trimester, and initial creatinine concentration greater than 1.0 mg/dL (88.4  $\mu$ mol/L). (5)(29)(30) Significant associated renal dysplasia and UTIs are also poor prognostic signs. (62)(63)(64)(65)

## CONCLUSION

UTD is often physiologic and resolves spontaneously, but pathologic UTD must be followed closely before and after birth. Fetal intervention, postnatal surgical management of CAKUT, and antibiotic prophylaxis are controversial management strategies but indicated in some cases. The new UTD classification system and standardized scheme has helped unify terminology and guides clinicians in the diagnosis, quantification, and management of UTD.

## Summary

- Physiologic UTD is clinically insignificant and accounts for most UTD cases. (1)
- Pathologic UTD is caused by CAKUT, and prognosis can range from spontaneous resolution to end-stage renal failure if not appropriately treated. (28)
- The UTD classification system aims to improve communication among clinicians and standardize the grading system for UTD. (11)
- Several imaging modalities are available to diagnose the cause of UTD, but the clinical challenge is to identify infants who have pathologic UTD and will benefit from imaging and those infants who have physiologic UTD and would unnecessarily be exposed to radiation or invasive procedures. (1)(22)
- CAKUTs account for 20% to 30% of all prenatally diagnosed anomalies and are a major cause of UTD. (29)
- Fetal intervention for CAKUTs remains controversial but can be considered in specific cases, with vesicoamniotic shunt being the most common procedure used to reduce pulmonary hypoplasia and correct oligohydramnios. (1)(5)
- Antibiotic prophylaxis is likely unnecessary for low-grade UTD, but high-grade UTD has a much higher risk of UTIs when not treated with antibiotic prophylaxis, though antibiotic prophylaxis is associated with an increase in resistant organisms. (41)

## American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Understand indications for and methods of antenatal assessment of renal function.
- Recognize the clinical manifestations of anatomic abnormalities of the kidneys and urinary tract in infants.
- Know how to diagnose specific anatomic abnormalities of the kidneys and urinary tract in infants.

- Know the recommended supportive and corrective treatment of anatomic abnormalities of the kidneys and urinary tract in infants.
- Know how prenatal diagnosis of renal abnormalities affects postnatal management.

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1. The 2014 urinary tract dilation (UTD) classification system was the result of a consensus panel composed of representatives from radiology, ultrasonography, pediatric nephrology, and maternal-fetal medicine societies. To clarify differing terminologies, the main term recommended for denoting UTD was:
  - A. UTD.
  - B. Pylectasis.
  - C. Pelviectasis.
  - D. Hydronephrosis.
  - E. Uronephrosis.
2. Prenatal ultrasonography is performed during pregnancy at 20 weeks' gestation. The fetus is noted to have anterior-posterior renal pelvis diameter of 8 mm. Which of the following classifications for UTD is correct?
  - A. A1.
  - B. A2–3.
  - C. P1.
  - D. P2.
  - E. P3.
3. A neonate had prenatal ultrasonography that indicated UTD. Postnatal renal ultrasonography is planned. Which of the following statements concerning timing of ultrasonography is correct?
  - A. For asymptomatic patients, ultrasonography should be performed between 12 and 24 hours after birth.
  - B. To avoid underestimating UTD due to oliguria in the newborn period, unless there are clinical circumstances warranting earlier assessment, the first postnatal ultrasonography should be performed 48 hours after birth or later, ideally between 5 and 30 days of age.
  - C. Renal ultrasonography can be specific and focused on the renal collecting system, without a need for assessment of renal parenchyma, ureters, or bladder.
  - D. Voiding cystourethrography is the initial test of choice, before ultrasonography, for prenatal findings of urinary tract dilation.
  - E. If posterior urethral valves are suspected, ultrasonography will not be diagnostic and therefore, magnetic resonance imaging should be performed in the immediate neonatal period.
4. A neonate had prenatal ultrasound findings suspicious for UTD which is confirmed on postnatal ultrasonography at several days of age. Which of the following is the most likely cause of this finding?
  - A. Ureteropelvic junction obstruction.
  - B. Uterovesical junction obstruction, also known as obstructed megaureter.
  - C. Vesicoureteral reflux caused by multiple factors.
  - D. Posterior urethral valves.
  - E. Incomplete obstruction of the urinary tract, or physiologic UTD.

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5. A newborn male infant is noted to have findings of UTD on postnatal ultrasonography. He receives further evaluation and follow-up. One type of UTD is physiologic. Which of the following statements concerning physiologic UTD is correct?

- A. Most cases of physiologic UTD resolve by 2 months of age.
- B. Although it is called "physiologic," this condition leads to acute renal failure in more than 50% of affected patients.
- C. The degree of UTD has no relationship to the degree of pathology and outcomes.
- D. Physiologic UTD is typically transient and may be caused by narrowing of the ureter that leads to urinary flow obstruction.
- E. Physiologic UTD is an anatomic obstruction that occurs at the site of ureter insertion into the renal pelvis.