Hydronephrosis in the Fetus and Neonate: Causes, Management, and Outcome
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Hydronephrosis is one of the most commonly identified prenatal anomalies, and the severity may vary from mild to severe, depending on the underlying cause, many of which stem from disruptions in the formation of the renal collecting system. Permanent renal damage may occur if the condition progresses before birth, and in some cases, oligohydramnios may result in lung hypoplasia, a potentially fatal condition. Many cases resolve spontaneously before birth, but for those that do not, the additional prenatal evaluation can identify cases sufficiently severe to require fetal intervention to preserve renal function. The benefits of these interventions are not completely clear and must be balanced against the significant risks of the procedures and their sequelae as well as the questions that remain about long-term efficacy. For other cases, a process of further evaluation before and after birth is warranted, and factors such as cause, severity, and whether the condition is uni- or bilateral are used to formulate decisions about additional assessment and potential intervention. The long-term outcome of the common causes of hydronephrosis and the impact of each of these factors and medical and surgical intervention on this outcome are reviewed.

Objectives After completing this article, readers should be able to:

1. Delineate the major causes of hydronephrosis in the fetus and neonate and how severity is graded.

2. Describe the indications for and potential benefits of fetal intervention.

3. Describe postnatal evaluation, follow-up evaluation, and long-term outcome of hydronephrosis.

Introduction

Before the advent of routine fetal ultrasonography during pregnancy, hydronephrosis was discovered only when symptoms manifested in the newborn period or pain or urinary tract infections were investigated in older infants and children. Often, by the time of diagnosis, significant and permanent renal damage already had occurred. In the present era, hydronephrosis is one of the most commonly diagnosed findings on prenatal examinations, with estimates of incidence ranging between 1% and 5% (1) of all pregnancies or between 40,000 and 160,000 new patients in the United States each year. The many underlying causes as well as the wide spectrum of outcomes have resulted in a significant debate about the proper evaluation and management of prenatally identified hydronephrosis. Evaluation may include discomfort and radiation exposure, and definitive treatment involves surgical correction with variable efficacy and attendant risks, making it desirable to limit unnecessary intervention whenever possible. At the same time, severe cases may result in irreversible prenatal renal damage, and less severe conditions that persist and evolve after birth also can lead to permanent renal scarring and permanent damage during childhood. (2) For some fetal conditions, the associated oligohydramnios can result in lung hypoplasia, if it is present in midgestation. Evaluation and management of each case must balance these opposing factors by avoiding overevaluation of benign conditions while ensuring appropriate care of the more significant ones.
Causes
Hydronephrosis may be caused by obstruction due to either urologic or nonurologic factors. The most common of these are outlined in Table 1. Of the cases identified prenatally, 48% have no specific cause and resolve before birth, and another 15% are due to physiologic changes in which no specific anatomic anomaly can be discerned. Anatomic anomalies can occur at any level of the urinary tract and may affect one or both sides, but they commonly occur where embryonic structures divide, including ureteropelvic or vesicoureteral obstructions (accounting for about 11% of cases), vesicoureteral reflux (9% of cases), or obstruction at the urethrovescular junction (posterior urethral valves [PUV], about 1% of cases identified prenatally). Readers may wish to refer to the ultrasonographic images of hydronephrosis provided in the article by Kennedy (Neonatal. 2002;3:e214–e219), which illustrate these sites of obstruction.

The embryologic development of the kidney itself is well understood and is diagrammed in the accompanying article in this issue on congenital renal abnormalities. Development begins from the intermediate mesoderm, first as the primitive pronephros, which has no known function. This rudimentary kidney develops around the third week of gestation and subsequently regresses. It is followed by another transient kidney, the mesonephros, a remnant of which remains as the Wolffian or mesonephric duct, which gives rise to portions of the epididymis and ductus deferens in males. An outpouching of this duct forms the ureteric bud, which reciprocally interacts with the mesenchyme of the definitive metanephros or future kidney, when this structure first appears during the fifth week of gestation. As a result of this interaction, the mesenchymal cells differentiate to form nephrons and renal interstitium, while the ureteric bud develops into the collecting system.

The detailed embryology of the collecting system and how obstruction to urine flow can develop is not well understood at present. Final canalization of the ureter is achieved only at the end of embryogenesis, maturation of this structure continues after birth, and connections between the bladder and posterior urethra are not completed until late in gestation. Many questions remain about the development of the collecting system and what alternate means of urine flow must exist for the fetus. Possibly, the urachus is the route for draining urine in early gestation, and it is likely that other not yet identified transient mechanisms exist at different times. The existence of these alternate routes may explain why bladder dilation and hydronephrosis due to urethral anomalies, such as PUV, sometimes becomes apparent only late in gestation, even though the obstruction in the urethra or vesicourethral junction was present much longer.

Severity
A uniform grading system of hydronephrosis severity is required to compare results between patients and different series, guide ongoing follow-up and management, and predict outcome. Specifically, monitoring severity can guide caregivers in determining which patients need additional prenatal evaluation or intervention and which need more extensive postnatal assessment by both ultrasonography and voiding cystourethrography (VCUG) to determine further care. Among the 50% of prenatally identified cases that do not resolve before birth, persistent uropathy may occur in 12% of mild, 45% of moderate, and 88% of severe hydronephrosis cases. (3) The most widely used grading system is that adopted by the Society for Fetal Urology (SFU) (Table 2). (4) Other grading systems often are employed in parallel with the SFU designations and rely primarily on measurement of the anteroposterior diameter of the pelvis in the transverse view. Dilation in excess of 10 mm in late gestation is considered significant hydronephrosis, (5) and additional measurement cutoffs have been identified at different gestational ages. Each of these sets of cutoff points has been developed in the hope of providing earlier and increased sensitivity and specificity in predicting later uropathy, but the highest positive predictive value comes from third trimester measurements, (6) with no patients who have measurements of less than 10 mm requiring

Table 1. Causes of Hydronephrosis

<table>
<thead>
<tr>
<th>No Identified Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urologic Anomalies</strong></td>
</tr>
</tbody>
</table>
| ● Ureteropelvic junction (UPJ) anomalies  
  – Anatomic anomalies  
  – Dysfunction of the UPJ |
| ● Ureterovesicular junction anomalies  
  – Vesicoureteral reflux  
  – Megaureter  
  – Ureterocele/ectopic ureter |
| ● Vesicourethral anomalies  
  – Posterior urethral valves  
  – Urethral atresia  
  – Urogenital sinus and cloacal anomalies |
| ● Miscellaneous disorders  
  – Collagen anomalies  
  – Prune–belly syndrome  
  – Tumors  
  – Neurologic impairment |
later surgery. (7) Many practitioners recommend considering further evaluation when the measurement exceeds 7 to 10 mm to ensure that none of the cases requiring intervention are missed. This measurement may prove to be conservative; a recent study found that among patients who had measurements less than 15 mm, the incidence of later urinary tract infection and need for surgery was very low. (8)

Of course, neither system of measurement completely assesses severity or is the only factor in determining management. Ultrasonographic examinations in late gestation also may help determine the morphology of the renal cortex, including the degree of parenchymal thinning, which provides additional data on which to base recommendations for further evaluation. Although bilateral disease occurs in fewer than one third of patients, it almost always is more severe than unilateral disease and uniformly requires further evaluation and possible intervention. It occurs most commonly among patients (males) who have lower tract or urethrovessicular junction obstructions, primarily due to posterior PUV. (9)

Prenatal Evaluation and Management
Most cases of hydronephrosis identified in the fetus require little additional evaluation before birth, other than repeat ultrasonography at appropriate intervals either to identify resolution or ensure that there is no disease progression. Serial evaluation of amniotic fluid volume also is undertaken as part of severity assessment. In some cases, however, the progression during fetal life may result in irreversible renal damage, and assessment and management must be aimed at preserving as much function as possible while weighing the risks to the developing baby. Several factors aid in formulating decisions, including the presence of oligohydramnios or evidence of abnormal renal function. (3) Once additional evaluation is indicated, a pediatric urologist should be involved directly in determining care.

Because the normal kidney can manufacture enough urine to ensure adequate amniotic fluid volume, unilateral disease almost never requires intervention. Indeed, even bilateral disease can be managed conservatively unless oligohydramnios develops. (10) Most of these cases occur in males, with obstruction due to PUV or urethral atresia, and the development of oligohydramnios before about 20 weeks’ gestation is highly associated with failure in lung growth, resulting in potentially fatal hypoplasia. There is, therefore, much interest in identifying cases of PUV, including identification of the so-called “keyhole sign” on ultrasonography, named for the shape of the dilated posterior urethra, an image of which can be found in the article by Kennedy (NeoReviews. 2002,3:e214–e219). The keyhole sign has been considered a specific sign for PUV, but it recently was found to be much less specific than bladder wall thickness and overall dilation. (11)

When the ultrasonographic evaluation reveals severe hydronephrosis, corrective or palliative intervention during fetal life may be considered. Evidence of abnormal renal function in the fetus may be helpful in determining the need for intervention, and normal values of the parameters of fetal urine are shown in Table 3. Limited evidence supports the utility of these measurements in predicting outcome, although the sensitivity and specificity of abnormal values in predicting poor outcome can be increased by obtaining serial measurements 48 to 72 hours apart. (12) Evidence of poor or deteriorating renal function in the presence of oligohydramnios may prompt consideration of fetal intervention. Before making the decision, it is important to rule out other major anomalies or chromosomal disorders and to ensure that the kidneys are otherwise normal, without evidence of dysplasia.

The decision to intervene is difficult because fetal intervention does not necessarily improve long-term outcome, and more than one third of patients have chronic renal failure, with another 22% having persistent renal insufficiency. The placement of draining vesicoamniotic shunts is risky. Shunt failure or displacement is common.

### Table 3. Normal Fetal Urine Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>&lt; 100 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>&lt; 90 mmol/L</td>
</tr>
<tr>
<td>Calcium</td>
<td>&lt; 2 mmol/L</td>
</tr>
<tr>
<td>Beta-2 microglobulin</td>
<td>&lt; 508 mmol/L</td>
</tr>
<tr>
<td>Osmolarity</td>
<td>&lt; 200 mmol/kg</td>
</tr>
<tr>
<td>Total protein</td>
<td>&lt; 0.2 g/L</td>
</tr>
</tbody>
</table>
and the procedures are associated with mortality or fetal loss rates as high as 43%, due to provoked preterm birth and infections. (13) On the other hand, such shunts can correct the early severe oligohydramnios, allowing for normal lung development and survival after birth, when conventional interventions may be performed.

Postnatal Evaluation

All babies who have a prenatal diagnosis of hydronephrosis should undergo at least a follow-up ultrasonographic examination after birth. This includes those who had transient pelvic dilation in the second trimester that resolved on ultrasonographic examinations before birth because as many as 29% of these patients have identifiable abnormalities on postnatal examinations and 12% have significant nephropathies. (6)(14) Similarly, patients who have mild hydronephrosis on fetal examinations may show worsening on postnatal evaluation, although the degree of dilation is stable or resolves after birth in most of these patients. (15) Consultation with a pediatric urologist should be requested, if it has not been done in the antenatal period.

Most practitioners wait a minimum of 7 to 10 days after birth to perform the first ultrasonographic examination. Such delay is advocated to ensure that the normal postbirth water losses will have occurred and that the infant’s hydration status will have normalized, reducing the likelihood of false-negative study results. Some investigators have found that early studies, performed at 48 hours after birth, while the baby is still hospitalized, may be adequate for initial evaluation. Although later studies ultimately may show some worsening of the hydronephrosis, cases of more severe disease always are evident on 48-hour ultrasonographic evaluations. (16) In addition, in none of the mild-to-moderate cases was the change between 48 hours and 7 to 10 days significant, nor did it change management. To ensure safety, almost all patients are given prophylactic antibiotics while awaiting ultrasonography, although little data support the value of this practice. The most common regimens are amoxicillin or a first-generation cephalosporin at a dose of 10 to 25 mg/kg per day.

The need for additional evaluation should be based on the findings of the postnatal ultrasonographic examination, which delineate obstructive processes that may require intervention. Beyond this, some practitioners advocate VCUG for all patients who have the antenatal diagnosis of hydronephrosis (17) to identify reflux that ultimately might result in renal injury. This practice captures all possible cases of reflux, but many practitioners note that reflux primarily occurs in patients who have more severe dilation or other abnormal ultrasonographic findings and that those who have minimal unilateral dilation on postnatal ultrasonography (diameter <15 mm) can be discharged without further evaluation. Others have found that the diagnosis of significant reflux is rare in patients who have mild degrees of unilateral dilation on prenatal examination and two normal ultrasonographic readings after birth (the initial one and a follow-up at 8 to 12 weeks), and they conclude that VCUG may not be indicated in these cases. (18) It is widely agreed that bilateral disease warrants VCUG and that significant disease also should be evaluated with nuclear renography to determine renal function.

These recommendations have been combined into a management algorithm: (19)

1. All patients who have a prenatal diagnosis should undergo ultrasonographic examination in postnatal week 1.
   a. Those who have minimal dilation (<15 mm) are discharged.
   b. Those who have bilateral disease should undergo VCUG and renography. Severe cases should be considered for surgical intervention according to the criteria in Table 4; milder disease is followed with observation.
   c. Those who have unilateral disease are considered for surgery if the dilation is severe; the others are followed with repeat ultrasonography after 8 to 12 weeks of observation.
2. If follow-up ultrasonography documents improvement, the patient can be discharged. If there is persistent hydronephrosis of Grade 2 or higher, renography is performed and surgery or continued observation is considered according to the criteria in Table 4.

Management

The fundamental management paradigm is to prevent renal injury and chronic failure from obstruction and reflux, avoiding unnecessary invasive monitoring or surgery while still ensuring sufficient monitoring to identify those patients in whom surgery is required. High-grade obstruction still requires surgical intervention, but the biggest change in recent management has been the shift from immediate surgery for repair of all obstruction to a practice of serial imaging for less severe cases and intervention according to the criteria outlined in Table 4. (20) As a result, only about 25% of patients who have unilateral disease eventually require surgery, and the use of a 15-mm cutoff identifies patients who have an ultimate need for surgery in most cases. (21) The more
Table 4. Criteria for Surgery or Observation (20)

Consider Surgery:
- Anteroposterior diameter >30 mm
- Anteroposterior diameter >20 mm with calyceal dilation
- Renal function <30%
- Worsening renal function
- Worsening hydronephrosis
- Symptoms

Continued Observation:
- Prophylactic antibiotics
- Renal ultrasonography every 2 to 12 months, as indicated
- Repeat renography if ultrasonography documents worsening or symptoms develop
- Discharge if improved, surgery if indicated

For patients who have bilateral disease, postnatal evaluation soon after birth is necessary to identify PUV, so a catheter can be placed for temporary drainage and comfort while preparing for valve ablation or vescicostomy. These more definitive procedures are critical in preventing further injury to the bladder and alteration in bladder dynamics and are very effective in promoting healing and reducing later bladder dysfunction. (23) This may prevent the high incidence of bladder dysfunction (40%), uremia (32%), and moderate renal failure (21%) found in adult males treated with older methodologies for PUV when treatment was delayed until several months of age or later. (24)

Hydronephrosis from other causes usually is followed with observation and periodic monitoring, with surgical intervention indicated for worsening hydronephrosis or deterioration of renal function, as outlined in Table 4. (25)(26) Most cases of megaureter do well with continued observation, with 30% requiring surgery. (24) Intervention for ureteroceles, ectopic ureter, or renal duplication is indicated if VCUG shows significant reflux. Multicystic dysplastic kidney does not itself require intervention, but VCUG and renography often are employed to differentiate this condition from severe ureteropelvic junction obstruction and to evaluate the contralateral normal kidney. (27)

Conclusion
Hydronephrosis is a common condition in the fetus and newborn that has a wide range of causes and severity. Most cases resolve without therapy and can be managed conservatively, especially if the initial severity grades are mild. For more severe cases, close monitoring for progression, associated alterations in renal function or reflux, and the occurrence of symptoms can be used effectively to identify those patients in need of surgical intervention. Although many affected patients have some degree of permanent renal impairment, this approach appears to minimize risks while avoiding unnecessary procedures and interventions.

References
specific is it for the diagnosis of posterior urethral valves? Ultrasound Obstet Gynecol. 2009;34:419–423
5. Hydronephrosis is one of the most commonly diagnosed findings on fetal ultrasonography, with an estimated incidence of 1% to 5% of all pregnancies. Of the following, most cases of fetal hydronephrosis are the result of:

A. Collagen disorder.
B. No identifiable cause.
C. Ureteropelvic junction obstruction.
D. Urogenital sinus anomaly.
E. Vesicoureteral reflex.

6. Monitoring the severity of fetal hydronephrosis can guide caregivers in determining the need for additional prenatal evaluations or intervention. Of the following, the third trimester ultrasonographic assessment that has the highest positive predictive value for the development of fetal nephropathy is:

A. Amniotic fluid volume.
B. Anteroposterior diameter of renal pelvis.
C. Degree of calyceal distension.
D. Morphology of renal cortex.
E. Urinary bladder wall thickness.

7. All infants who have a prenatal diagnosis of hydronephrosis should have at least a follow-up ultrasonographic examination after birth. The precise timing for this postnatal evaluation remains unconfirmed. Of the following, the recommended age for postnatal ultrasonographic evaluation of infants who have prenatal diagnoses of hydronephrosis is:

A. At birth.
B. 1 week of age.
C. 1 month of age.
D. 1 year of age.
E. 6 months of age.