Renal and Urologic Disorders

Adam Weinstein, MD
Assistant Professor Pediatric Nephrology
Children’s Hospital at Dartmouth Hitchcock
Disclosures

• I have no relevant financial relationships with the manufacturers(s) of any commercial products(s) and/or provider of commercial services discussed in this CME activity.

• I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.
Objectives

• Apply evaluation and management plans for young children with febrile UTI
• Consider the different causes of urinary tract dilation and congenital genitourinary malformations in children
• Monitor for and anticipate functional complications from febrile UTI, urinary tract dilation, and congenital genitourinary anomalies in children
Case Presentation

- 3 mo Caucasian girl presents with 3 days of fever. Today 103F, + mild URI symptoms, + non bloody/non bilious emesis x 2, no diarrhea. Eating less but normal urine output. No rashes
- PMHx noncontrib, older sister with sore throat
- Vitals Normal, Exam WNL
Febrile Urinary Tract Infection (UTI)

- Common and Important Illness in Pediatrics
  - Risk of Renal Scarring with resulting HTN and CKD
  - Difficult to distinguish cystitis from pyelonephritis in young children, so the presence of fever is often used to increase concern/suspicion for pyelonephritis
  - Many febrile UTIs may resolve on their own, but delays in treatment pose risk for complications including urosepsis, abscess formation, and renal scarring**
Febrile UTI

- Prevalence ~5% amongst all febrile infants 2-24 months
  - Female >2:1 Male
  - Slightly more common <12mos
  - Circumcision reduces risk but does not eliminate
  - Symptoms in older children**
    - Cystitis—dysuria, frequency, urgency, enuresis suprapubic pain
    - Pyelonephritis—the above plus fever, chills, nausea/vomiting, flank pain
  - Symptoms in infants/toddlers**—less specific
    - Fever, irritability, vomiting, decreased appetite, lethargy, hyperbilirubinemia, failure to thrive

- Consider UTI in all febrile children less than 24 months
Factors that increase risk for UTI

- **Girls**
  - White Race
  - Age < 12 months
  - Temp > 39°C
  - Fever 2 or more days
  - No other source

- **Boys**
  - Nonblack race
  - Temp > 39°C
  - Fever more than 24 hours
  - No other source

Adapted from UTI Clinical Practice Guideline, Pediatrics 2011
Probability of UTI

• Girls
  – <1% probability if 1 or fewer risks
  – <2% probability if 2 or fewer risks

• Boys—Circumcised
  – <1% probability if 2 or fewer risks
  – <2% probability if 3 or fewer risks

• Boys—Uncircumcised
  – >2% probability simply on the basis of fever

Adapted from UTI Clinical Practice Guideline, Pediatrics 2011
Significantly Increased Probability of UTI

- Definitely low threshold to evaluate if:
  - Prior history of febrile UTI
  - History of congenital GU anomaly**
Diagnosing UTI**

- **Urinalysis**
  - LE/nitrites/WBC—poor specificity
  - Combined highly sensitive—if negative, then unlikely UTI

- **Urine Culture**
  - Bag—Poor specificity, many false positives (PPV 15%).
    - If negative, then unlikely UTI
  - Catheterization >50,000 colony forming units (cfu) of a single urinary pathogen
Back to the Case

• Urinalysis obtained via Catheterization
  – + Leukocyte Esterase and + Nitrites
  – Microscopy with Many WBCs, 10-20 RBCs, +Bacteria
• Urine Culture obtained
• Diagnosis requires both urinalysis suggesting infection (pyuria, and/or bacteriuria) and at least 50K cfu of a urinary pathogen**
  – Most common urinary pathogen—E coli, large majority**
  – Other enteric organisms—gram neg rods, enterococcus**
Treatment of Febrile UTI in 2-24 month olds**

- Oral antibiotics are equally efficacious as IV antibiotics
- Cover the likely organisms empirically and can adjust antibiotics based on culture and sensitivity
  - Amoxicillin, Amoxicillin-clavulanate, Trimethoprim-Sulfamethoxazole, Cephalosporins
- Treatment for 7-14 days
  - 3 days works well for older children with uncomplicated cystitis but not sufficient for febrile UTI in infant-toddler
Follow-up Diagnostic Evaluation**

- Recurrence can occur
  - Treatment goal is for full resolution of symptoms
  - Prompt treatment of recurrences is necessary to avoid complications
  - Routine “repeat urine cultures” for tests of cure in asymptomatic children not recommended
- Ultrasound recommended after febrile UTI to identify anatomic abnormalities
  - in all children not yet toilet trained
  - in all boys
  - in toilet trained girls with recurrent UTIs (if not already done)
  - If applicable, more immediately to evaluate reasons for recurrence or poor/no response to antibiotics
Follow-up Diagnostic Evaluation**

- Voiding cystourethrogram (VCUG) is recommended for children (not yet toilet trained) if:
  - There is urinary tract dilation, scarring, or findings suggestive of vesicoureteral reflux or bladder outlet obstruction on Ultrasound
  - Recurrence of febrile UTI (even if normal ultrasound)
  - “Atypical” or “Complex” clinical circumstances
    - This last point is left somewhat open-ended and important to rely on clinical judgment and parental preferences, for example:
      - Clinical presentation with urosepsis vs outpatient presentation
      - Organisms other than E coli
      - Family history of congenital GU anomalies or reflux
Antibiotic Prophylaxis

- Conflicting data re: efficacy of antibiotic prophylaxis
- Some studies show benefit; many others show no benefit
- Pooling data together suggests no difference from placebo
  - Studies markedly heterogeneous
  - Many not controlled for antibiotic choice and/or dose or for underlying risks for UTI
  - There remains uncertainty with regards to this question on the febrile UTI population as a whole
Antibiotic Prophylaxis in VUR

- Multicenter prospective randomized placebo controlled trial (RIVUR) in 607 children 2-71 months old illustrates benefit of prophylaxis for children with VUR
  - Trimethoprim-Sulfamethoxazole for prophylaxis, consistent dosing
  - Reduced risk of recurrence febrile UTI by 50%
  - No effect on renal scarring/nephropathy
  - Increased incidence of organisms resistant to Trimethoprim-Sulfamethoxazole
Vesicoureteral Reflux (VUR)

- Graded 1 to 5
  - Grade 1 and 2 typically resolve spontaneously**
  - Grade 4 and 5 can resolve too, but are less likely to resolve**
- Treatment is Antibiotic Prophylaxis +/- Surgery
  - Effective at reducing recurrent febrile UTI
  - Neither have been demonstrated to prevent scarring or nephropathy outcomes
So why is VUR important?**

• Identifies a risk factor for recurrent febrile UTI
  – Treatment can be given to prevent UTI (surgical or medical)

• Diagnostic for individuals at risk for VUR Nephropathy
  – Treatment of the VUR itself may not modify the nephropathy
  – Diagnosis is helpful because applicable children can be monitored and treated for signs of progressing CKD like hypertension and proteinuria
Other Risks to Consider in Older Age Groups

• Postcoital Antibiotic Prophylaxis in female adolescents with recurrent UTI

• Dysfunctional voiding and Dysfunctional Elimination Syndrome
  – Clinical symptoms**— Dysuria, Frequency, Urgency, Enuresis, UTIs (more often cystitis)
  – Management—Bladder retraining, an empty bladder is a happy bladder
    • Scheduled Voids, Complete Emptying
    • Maintain dilute urine and avoid bladder irritants
    • Treat Constipation
Case Problem

• A 6 month old female infant has a fever of 39°C, irritability and decreased appetite. She has been previously well, no prior illness, no other symptoms.

• PE: essentially normal, vitals and activity are reassuring
  – Would you determine if this patient has a UTI? If so, how?
  – How would you treat this infant?
  – If this patient has a UTI, should her work-up include a Renal U/S or VCUG and if so, when?
  – If this patient had grade II reflux bilaterally, how would you treat her?
Take Home Points for Practice of Febrile UTIs in infants/toddlers

• Have low threshold to evaluate for UTI in patients with higher probability, in particular those with past UTI and/or urinary tract anomalies
• Diagnosis requires positive urinalysis and appropriately collected urine culture
• Diagnostic evaluation should include
  – renal ultrasound in all patients (with first febrile UTI)
  – VCUG in those with abnormal ultrasounds, a recurrent febrile UTI, or “atypical/complex” circumstances
Case

• 1 week old male presents w/progressive vomiting and abdominal distension
  – Minimal urine output, Breastfeeding 10 minutes every 4 hours, Baby progressively more tired; No medications, FHx no known medical conditions

• Exam
  – Afebrile, weight around birthweight
  – Distended abdomen dull to percussion, normal male external genitalia, circ’d
  – Otherwise normal, no other external abnormalities noted

• Labs—Creatinine 8.7!
Urinary Tract Dilation (Hydronephrosis)**

• Why look for Urinary Tract Dilation?
• Identify pathology prior to complications**
  – UTI
  – Nephro/uroolithiasis
  – Renal dysfunction, chronic kidney disease and kidney failure
Causes of Urinary Tract Dilation (UTD)**

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient (no pathology)</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Vesicoureteral Reflux</td>
<td>10-40%</td>
</tr>
<tr>
<td>Ureteropelvic Junction Obstruction</td>
<td>10-30%</td>
</tr>
<tr>
<td>Ureterovesical Junction Obstruction</td>
<td>5-15%</td>
</tr>
<tr>
<td>Posterior Urethral Valves</td>
<td>1-5%</td>
</tr>
<tr>
<td>Other</td>
<td>Less common</td>
</tr>
</tbody>
</table>

Adapted from Multidisc. Consensus Classification of UTD, J Ped Urol, 2014
Prenatal Diagnosis

• Most UTD is diagnosed prenatally
• With many transient/benign etiologies uncovered:
  – important to come up with approaches that evaluate those who have increased risk for problems**
  – but not extensively over-evaluate those with low or no risk**
Postnatal Imaging

• Infants < 48 hours old have lower hydration/make less urine—this impacts the interpretation of the UTD

• Delay Imaging beyond 48 hours **Unless**
  – Oligohydramnios or other concerns for kidney function
  – Prenatal concern for bladder outlet obstruction
  – Bilateral Severe/Increased Risk Dilation
  – Follow-up Concerns
Postnatal Imaging

- 15-45% of children with prenatal UTD and an initial normal postnatal US can later develop worsening.
- In one study, 5% of children who ultimately required surgery for UTD had a normal 1 week ultrasound but abnormal 1 month ultrasound.
- Recommendation is for a second Ultrasound one to six months later**
Impacts on long-term renal function**

- Children born with fewer nephrons (e.g. from congenital anomalies) are at risk for progressive loss of function
- At first, function may be normal or relatively normal
  - Then, growth and its associated metabolic demands may outpace the ability of the kidney(s) to grow and compensate
  - When this process begins, serum creatinine is maintained as normal (through compensation—increased filtration pressures of remaining glomeruli)
- Proteinuria, hypertension generally early signs
  - Diagnostic for this problem, sometimes called “hyperfiltration”
  - They are also treatment targets that impact functional outcomes
Management Algorithm

• So given excellent prognosis in many, but interventions needed in some, who should be monitored and how?

• Postnatal Ultrasound Normal**
  – Repeat ultrasound in 1-6 months, if still normal, then confirmed as “transient” etiology
Management Algorithm

• Postnatal Ultrasound—Low Risk UTD (Mild)**
  – Repeat ultrasound in 1-6 months, if normal, then repeat again in 6-12 months, if still normal then confirmed “transient” etiology
  – If still present, then may need further evaluation
    • Anatomic evaluation
    • Functional evaluation
  – If no clinical sequelae and ultrasound is normal apart from low risk UTD (e.g. renal sizes are normal), further eval apart from ultrasound monitoring can be at discretion of provider/family
Diagnostic Evaluation**

• Anatomic Evaluation
  – Retroperitoneal (Renal/Bladder) Ultrasound
  – Voiding Cystourethrogram (VCUG)
  – Diuretic Functional Renal Scan (MAG3 Renal Scan)

• Functional Evaluation
  – Blood Pressure
  – Urinalysis (in particular for proteinuria)
  – Serum Lytes, BUN, Creatinine
  – Serial Retroperitoneal Ultrasound assessing growth
Management Algorithm

• Postnatal Ultrasound—Intermediate Risk UTD (Moderate)**
  – Non urgent referral (urology/nephrology) for diagnostic evaluation
Management Algorithm

• Postnatal Ultrasound—High Risk UTD (Severe)**
  – Timely referral (both urology and nephrology) for anatomic and functional diagnostic evaluation
  – Same day evaluation for
    • Oligohydramnios or other concerns for kidney function
    • Prenatal concern for bladder outlet obstruction
    • Bilateral Severe/Increased Risk Dilation
Worsening Urinary Tract Dilation

• Typically, any worsening urinary tract dilation suggests a pathologic cause (rather than a transient cause)
• An indication for further evaluation or repeat evaluation
Back to Case

• VCUG diagnosed posterior urethral valves
• Ablated and patient had subsequent polyuria (post-obstructive diuresis) and gradual correction of creatinine
• 5 years later, no Urinary Tract infections, normal blood pressure, normal urine protein
• Good growth and development, serum Creatinine remains 0.2 to 0.3 mg/dL
Bladder Outlet Obstruction

- Posterior Urethral Valves (males) most common**
- Less common causes: Urethral Stenosis or Atresia
- High pressure system in utero may result in oligohydramnios, hydronephrosis and b/l renal dysplasia
- If severe, may develop Potter’s syndrome**:  
  - in utero oligo-uric Renal failure, Pulmonary hypoplasia, limb deformities
  - (aside— any cause of in utero oligo-uric renal failure, also including Autosomal Recessive Polycystic Kidney Disease or b/l renal agenesis, can result in Potter’s syndrome)
Bladder Outlet Obstruction/Posterior Urethral Valves**

• Many children develop renal tubular dysfunction
  – Renal tubular acidosis, renal salt wasting, or urinary concentrating impairment (nephrogenic diabetes insipidus)
  – High pressure system causes impaired renal tubular development and functions—abnormalities in salt, water, acid regulation

• Even with normal kidney function, many children have a dysfunctional high pressure trabeculated bladder
  – may need medical therapy and/or catheterization to void

• Treatment of Posterior Urethral Valves is surgical ablation of valves but afterwards requires supportive management of renal dysplasia and dysfunctional bladder
Bladder Dysfunction

- Prune Belly (Eagle Barrett) Syndrome**—one example
  - Weak abdominal wall musculature
  - Undescended testes
  - Ureter, Bladder, and Urethral abnormalities
    - Abnormal mesenchymal development—weak or deficient peristalsis & muscular development
    - Megaureter, low pressure poorly emptying bladder
    - Hydronephrosis, recurrent infections ➔ varying renal dysplasia ➔ kidney failure
    - Males, No confirmed genetic basis
Case

• 1 week old female
• Prenatal imaging, noted cystic mass in location of L kidney; R kidney appears structurally normal
• Born fullterm, healthy, voided spontaneously. Making stool regularly, feeding appropriately, and maintaining hydration. Family history—an aunt born with solitary kidney
• On exam, active vigorous baby, L sided abdominal mass, Otherwise normal exam
Congenital Urinary Tract Malformations**

- Ectopic Kidney
  - Pelvic Kidney, Horseshoe Kidney, Duplications
- Dysplasia
  - Aplasia, Hypoplasia, Dysplasia, Multicystic Dysplastic Kidney
- Urinary Tract Dilation (Hydronephrosis)
  - Ureteral Obstruction
  - Vesicoureteral Reflux
  - Bladder Dysfunction
  - Bladder Outlet Obstruction
Multicystic Dysplastic Kidney (MCDK)

• An extreme form of dysplasia
  – This kidney is non-functional
• By strict definition a non-reniform collection of cysts
  – Appears as a collection of grapes
  – No identifiable “renal” tissue
Multicystic Dysplastic Kidney (MCDK)**

- Most cases are now identified on prenatal ultrasonography
  - Formerly detected as a neonatal abdominal mass
  - Most often unilateral and generally asymptomatic
    - If on left and presses against stomach → Gastroesophageal Reflux
  - ? Increased incidence of Hypertension and ? Increased incidence of UTI
    - Only if contralateral kidney and/or lower urinary tract also abnormal
      (which is the minority of cases, but a significant minority—20-40%)
  - Previous concern for increased risk for renal malignancy not supported by more recent longitudinal data
Management of MCDK and other forms of ectopia/dysplasia**

• Assess contralateral ("healthy") kidney
  – If normal, patient with excellent long-term prognosis
  – If abnormal may need support to prevent or delay chronic renal insufficiency (hypertension, proteinuria)

• Assess lower urinary tract
  – Ultrasound
    • if indicated VCUG, Functional Renal/GU Scans
  – If abnormal, higher risk for urinary tract infections, renal scarring, and poorer prognosis
Take Home Points for Practice

• Urinary Tract Dilation is often mild and transient, but may also cause risk for urosepsis, renal failure, and other complications
• Conservative monitoring (including serial ultrasounds and low threshold to evaluate for UTI) can be done in primary care for those with low risk (mild) findings; higher risk findings on imaging warrant referral and more in depth genitourinary imaging and functional evaluation
• Suggested change of Practice: How to screen for early CKD
  – Functional complications to consider in practice include UTI, hypertension, proteinuria; in severe cases, renal insufficiency and/or renal tubular dysfunction such as renal tubular acidosis, salt wasting, and urinary concentrating impairment
Suggested Reading

• Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months Pediatrics. DOI: 10.1542/peds.2011-1330

• The RIVUR Trial Investigators. Antimicrobial Prophylaxis for Children with Vesicoureteral Reflux. NEJM, 2014. DOI: 10.1056/NEJMoa1401811