Upadates in Management of Urinary Tract Infection in Febrile Infants/Children <24 Mo of Age
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Rationale:
- UTI/pyelonephritis is the most common bacterial infection found in infants with fever without a source (FWS)
- Febrile UTI is associated with upper tract involvement (“pyelonephritis”) in >70% of infants and young children, therefore the terms are often used interchangeably in this population
- UTI is usually an occult infection in young children, and must be considered in any young child presenting with fever without specific localizing signs and symptoms
- Reasons to identify and treat febrile UTI in young infants include:
  - To identify and treat the cause of the fever, preventing morbidity/other serious infections (sepsis/meningitis)
  - To prevent patients with structural abnormalities of the urinary tract from suffering recurrent infections, which may lead to renal scarring or end stage renal disease (ESRD)
- In 2011, the AAP revised its 1999 Clinical Practice Guideline for initial febrile UTI, with some significant changes in the recommendations for diagnosis and management
- This review refers to febrile infants/children <24 mo of age, without source for fever unless otherwise noted, with a first UTI, and no known anatomic or neurologic abnormalities associated with recurrent UTI.

This review will address the following questions:
1. Which infants/children should be tested for UTI (who is at risk?)
2. How should urine be obtained for testing for UTI?
3. How should UTI be diagnosed?
4. How should UTI be treated?
5. What imaging and follow up are recommended for a child with a first UTI?

Question 1: Which infants/children should be tested for UTI? (who is at risk?)

Background:
- Decisions to test and treat for UTI must take into account both the prior probability of UTI (estimated risk/clinical suspicion) and physician’s level of concern (e.g.: how much will a missed UTI hurt this patient?)
- See Table 1 in appendix
- UTI should be considered in ALL infants < 24 mo of age with FWS, but other risk factors should be considered to decide if testing is warranted, as well as what to do with the results
- The 2011 AAP guideline recommends that urine be collected in infants who are ill enough to be treated with antibiotics immediately, and in those who are “not low-risk”
  - They seem to define “not low risk” as >1-2% risk of UTI

Evidence:
A. Age/Gender/Circumcision
1. Febrile infants <3 mo, regardless of gender or circumcision status, are high risk and high concern
   a. Infants <4 wks: ~15% overall (Lin, Bressan, Bilovsky)
   b. 1-3 months: ~10% prevalence overall
      1. Uncircumcised boys at highest risk (up to 19%, ~2% in circ boys, Newman et al)
      2. In infants <3 mo of age, febrile UTI may be accompanied by bacteremia in 10-15%
2. Infants 3-24mo
   a. Girls: Risk of UTI hovers around 5-10% between 3 and 24 months of age
      1. Ethnicity: white girls > risk of UTI than African American girls
   b. Boys: circumcision remains the most important risk factor for boys under 1 (Singh-Grewal, 2005, Shaikh, 2007)
      1. Circumcised boys: Overall prevalence of UTI is low: < 0.2%
      2. Uncirc boys: rate of UTI 5-20 times higher than in circumcised boys, but falls rapidly after 6 mo
      3. Ethnic differences: ↓ risk in Latino boys, even when adjusted for circumcision
      4. Risk of UTI very low after 12 mo of age, circumcised or not
B. Other historical factors:
1. Duration of fever - Probability of UTI (and of upper tract involvement) increases with duration of fever.
   a. Eg: Newman et al found that duration of fever >24 hours increased odds of UTI by 80% in infants <3 mo
   b. Bacteriuria may resolve spontaneously, so increased concern if fever ≥2 days duration
2. Lack of source for fever - UTI is more likely if there is no other source for fever on history/PE
a. Multiple studies suggest that the risk of UTI goes down by at least 50% if a viral source (clinical or microbiological) is present
b. However, risk of UTI remains ~5% in the highest risk infants (eg:<3 mo) even when a viral infection is found as cause of fever (Levine, Titus)

3. **Combination of findings more helpful than one finding alone:**
   a. Shaikh (2007) reported that fever >39 for >48 h and no source for fever increased odds of UTI by 4
   b. Gorelick et al (2007) validated a prediction rule for girls with FWS including 5 risk factors (white race, age <12 mo, temperature >39, fever >2 days, no fever source). If all 5 negative: <1% risk of UTI

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**Recommendations: Who to Test for UTI:**
1. Consider UTI in all infants and children 0-24 mo with fever without a source (FWS)
2. Using historical and clinical factors, estimate prior probability of UTI and concern for UTI (Tables 1,2)
3. **Test for UTI when probability >5% or concern is high**. This includes:
   - ALL infants < 4 weeks of age with T>38
   - ALL infants 1-3 mo with FWS (T>38)
   - And consider even in those with viral fever source, especially if other risk factors present
   - Selected infants 3-24 mo with FWS (T>39):
     - Girls: Test if fever ≥2 days, could watch/wait in those with fever duration <2 days
     - Uncircumcised boys < 6 mo of age and up to 12 mo if concern is high
     - Circumcised boys < 6 mo of age only if concern is high

*Using the AAP Guidelines recommendation to test infants with >2% risk of UTI would mean testing >50 infants to find one UTI. I think 5% is more reasonable, unless concern is very high, such as in neonates.

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**Question 2: How should urine be obtained for testing for a UTI?**

**Background:**
- Urine specimens are obtained for two reasons:
  - For screening urinalysis to increase/decrease prior probability of UTI, and help guide initial management
  - For urine culture, to confirm diagnosis of UTI, as well as identify causative organisms
- Four methods to obtain urine for testing in an infant or child <3 years of age:
  - Suprapubic aspiration (SPA): Rarely done currently; most accurate but also most invasive type of specimen
  - Bladder catheterization: Generally quick, accurate and clean, but may be traumatic
  - Urine bag:
    - Pros: Less invasive than cath, may also be less traumatic for child/parent
    - Cons: May take a long time, contamination may make results difficult to interpret (see below)
  - “Clean catch”: Be prepared for the unexpected clean catch while preparing to cath or bag a child!
- The 2011 AAP Guideline recommends a cath urine collection in infants ill enough to receive antibiotics
- Catheterization of all children at risk for UTI is invasive and not cost-effective

**Evidence:**

A. **Catheter specimen**:
   1. When done correctly, generally considered the best method for collecting a clean and sterile specimen
   2. Sens/spec of UA and cx comparable to SPA (using threshold for positive cx = 10,000 CFU/mL)

B. **Bag specimen**:
   1. **UA on bag specimen**:
      a. **Sensitivity** of bag UA at least as high as that of cath, but **specificity** of LE lower in bag (62-84% bag vs 91-94% cath: Schroeder 2005; McGillivray, 2005)
      b. This means that a negative bag UA more helpful than a positive one, and, as always, negative predictive value (NPV) is always best in patients with low prior probability of disease
         
         **Example:** For a patient with a low prior probability (~5%) of disease:
         - A positive UA of a bag specimen may increase prob to ~20%: *may not be enough to start empiric therapy, but may prompt you to send a clean specimen for culture.*
         - A negative UA, however, will lower your prior prob to <1%; *enough that culture is not needed*
         - Therefore, the utility of the bag UA depends on the prior probability (PP) of disease and what you will do with the results
   2. **Culture on bag specimen**:
a. Reported sensitivities and specificities vary widely depending on criteria used to define a "positive" culture (eg: >20,000 CFU/mL single org vs >100,000 CFU/mL single org) and collection technique (eg: quick collection from a clean perineum vs trip to cafeteria with bag on...)
b. Schroeder et al (2005) found that risk of ambiguous culture results from bag was 2.7 X that from cath, but absolute risk was small (7.4% vs 2.7% with cath).
   • Would need to do 21 caths to save one ambiguous culture.
c. As a rough guide:
   i. Best use of bag culture is for ruling OUT disease in low PP patient:
      ▪ A negative bag culture has good NPV when PP is low
      ▪ If bag grows 50-100,000 CFU/mL, repeat culture recommended to confirm
   ii. If using bag to rule IN disease: Using >100,000 single org as the threshold for a + culture (this threshold maximizes specificity at 85%)
      ▪ BUT at this threshold, sensitivity is also 85%, so 15% of pts with UTI have false negative!
      ▪ Using a lower + threshold further improves sensitivity, (but makes specificity/PPV very low)
d. Key point: utility depends on how the results modify the PP, and how you act on them...

Recommendations: How to Collect Urine
1. In high risk infants (<3 months of age, previous UTI) or a kid who looks sick enough to require IV antibiotics, obtain a catheter specimen (or SPA) and send for urinalysis AND culture
2. In low-moderate risk children, decide on preferred collection method with parent, (considering implications of + or negative UA) and send for UA
   - If the UA is negative, and PP is low, the specimen can probably be discarded, and no culture sent
   - If the UA is positive (see below for interpretation of UA)
      ▪ Send a sample for culture: catheter sample (preferred) or CLEAN bag sample
      - If you decide to send a bag sample for culture, develop a specific plan for interpreting the results, and consider the implications of false positives and negatives for the patient!
      ▪ Start empiric antibiotics, if indicated

Question 3: How should UTI be diagnosed?
Background:
   • Culture of a catheter or SPA sample of urine is the gold standard for diagnosis of UTI
     o Sensitivity and specificity of culture of cath specimen close to 100% when compared to SPA
   • Thresholds for a + culture vary from 10,000 to 100,000 CFU/mL of a single uropathogen
     o False positive urine cultures can occur due to
       ▪ Contamination of the urine (during collection)
       ▪ Asymptomatic bacteriuria (+ culture in the absence of symptoms)
     o Proposed thresholds for + cultures results attempt to minimize false positives, without missing UTI in infants with lower colony counts (eg: early UTI)
   • However, management decisions need to be made before culture results are final
   • Screening tests for UTI include dipstick urinalysis (UA), and UA with microscopy
     o A good screening test should impact management by reassuring us, or helping initiate treatment or workup
   • 2011 AAP Guideline recommends diagnosis of UTI based on + UA and > 50,000 CFU/mL of a single uropathogen on culture

Evidence:
1. Urine cultures
   a. Colony counts of 10-100,000 CFU/mL can occur with symptomatic UTI
   b. Asymptomatic bacteriuria may occur in ~1% of afebrile infants
   c. The 2011 AAP Guideline proposes 50,000 CFU/mL as threshold for positive culture
      i. However, some children with true UTI may have lower colony counts
2. Routine urinalysis (reagent dipstick test)
   a. Leukocyte esterase (LE) is the most sensitive single test (~90%); specificity is lower: (~70-80%)
      i. In general, the NPV of LE is very good, especially when patient has low/mod prior probability
      ii. False negative LE (negative LE with + culture) may occur due to lack of inflammatory response to UTI, but may also be due to asymptomatic bacteriuria
1. The 2011 AAP Guideline states that “the absence of pyuria in children with true UTI’s is rare” but there is no reference or quantification
   iii. **False positive LE** may occur from contamination of specimen by inflammation of perineum/prepuce
   b. **Nitrite** has much **higher specificity** (95-100%) but **lower sensitivity** (16-82%; best estimate ~50%) 
      i. This means that a+ nitrite is helpful, but a neg nitrite doesn’t R/O UTI.
   c. **Blood and protein** have low predictive value for UTI. **However, blood should add to concern for UTI**
3. **Microscopic examination:**
   a. Main advantage over dipstick is that it **quantifies inflammation** (# of WBC) and shows bacteria
      i. Probability of UTI increases with number of leukocytes
      ii. Presence of bacteria on micro of catheter specimen is highly predictive of + culture
   b. Micro is actually **less sensitive for LE than dipstick**, as test is usually reported positive for >5WBC
   c. Highly **dependent on technique** (ie: delay in examination, centrifugation)
4. A note on screening diagnostic tests and prior probability:
   a. Remember: **diagnostic tests modify prior probability** to make disease more/less likely in your patient
      i. **When prior prob is LOW** (eg: circ boys>6mo) the UA has good negative predictive value
         - Negative UA can be used to **RULE OUT UTI**
         - A UA + for LE alone is less helpful, but +nitrites is highly suggestive of UTI
      ii. **When prior prob is HIGH** (eg: infants < 3 mo, previous UTI)
         - Negative UA does not R/O UTI: confirmatory culture should be performed
         - Positive UA (LE or nitrites) should prompt empiric treatment

**Recommendations: Making the Diagnosis of UTI**
1. Diagnostic testing for UTI should consider infant’s **prior probability of UTI and the risk to the patient of false negative and/or false positive results**
   - Send a catheter specimen for UA and culture in any sick or high risk infant, as the accurate diagnosis of UTI is essential in these infants
2. **Ideal use of the UA is to impact immediate management decisions**
   - The diagnosis of UTI can be **ruled out in lower risk infants** with a negative UA (catheter or bag)
   - **Treatment for UTI can be initiated based on + UA results** (but confirm with culture)
   - Add micro on + UA if quantifying WBC will help you decide to start treatment
3. **Interpreting positive UA results:**
   - **LE alone:**
     - Send a **confirmatory culture**
     - **Start empiric treatment** if: prior probability is high or pt is high risk, or if micro shows high # WBC’s or + bacteria
     - OK to hold off on treatment and await culture results if suspicion is low and infant is well-appearing (eg: feeding well)
   - **+ LE and nitrite:**
     - **Start empiric treatment**, since specificity is high (false positives less likely)
     - A **confirmatory cx is still recommended** to confirm organism/sensitivities
4. **Interpreting negative UA results:**
   - If **prior probability is LOW**– probably OK to skip the culture (NPV is good!)
   - In infants with **high prior probability or risk of UTI**, send a confirmatory culture anyway (preferably a **catheter specimen**, as above)
5. **Diagnosis of UTI is confirmed by + UA and + cath culture with > 50,000 CFU/mL of a uropathogen**
   - If a bag specimen is sent for culture, use threshold of > 100,000 CFU/mL
   - If clinical suspicion/risk is high, consider treating for UTI if
     - UA is + and cath culture grows > 10,000CFU/mL single organism
     - UA is negative and cath culture grows > 50,000 CFU/mL single organism

Question 4: How should we treat a UTI?
**Background:**
- Failure to identify and treat a UTI could theoretically result in undesirable consequences such as urosepsis, abscess or other serious infections
- Recurrent UTI in combination with urinary tract abnormalities could cause renal damage
- Choices for treatment include **PO or IV antibiotics, outpatient vs inpatient therapy, short vs long course**

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Evidence:

A. Risk of urosepsis with UTI:
   1. Risk of bacteremia with febrile UTI as high as 15% in 1-3 month age group (Newman et al) but virtually none > 6mo.
   2. However, complication rates, in infants treated for pyelonephritis, are low
      a. Spontaneous resolution may occur in up to 90%; septic shock and death are rarely seen
B. Prevention of renal scarring:
   1. Although associations are reported between recurrent UTIs in the presence of UT abnormalities and renal scarring, causality and efficacy of treatment have not been established (see below)
C. Mode of treatment:
   1. IV vs PO: IV antibiotics were previously the standard of care for young children with pyelonephritis
      a. In 1999, a large RCT found oral outpatient therapy (cefixime) as effective as IV therapy in febrile infants and children > 2 months of age with UTI (Hoberman et al, 1999)
      b. In this study, the first dose of antibiotics was administered in clinic, either IV/IM or PO
      c. Subsequent studies have supported these results (2007 Cochrane review, Montini, 2007) even in infants <2 months, although numbers in this age group were limited.
   2. Choice of agent: Local susceptibility patterns should dictate initial antibiotic choice:
      a. PO: Keflex covers 90% of E. coli in the S.F. area, amox and trim/sulfa have more resistance
      b. IV: Ceftriaxone +/- gentamicin has good renal penetration and broad coverage for E. coli and other likely organisms
      i. Parenteral therapy is highly effective in cases of failed PO treatment, and bacteremia.
D. Duration of treatment:
   1. A 2002 meta-analysis (Keren et al) concluded that abx courses from 7-14 days resulted in fewer treatment failures and recurrences than courses < 7 days for febrile UTI. No advantage to >14 days.
   2. 2007 Cochrane review (Hodson, 2007) supported these findings, with 10 days generally recommended.

Recommendations: Treatment of UTI

1. Prompt treatment of UTI’s is recommended in infants and children, especially in those at high risk for or with documented urinary tract abnormalities
2. Outpatient PO therapy recommended well-appearing children > 2 months of age
   ➢ Cephalexin (Keflex) a good first-line choice for local sensitivities in the S.F. area
   ➢ In very young/high risk infants, give first dose of antibiotics IM/IV and consider a follow-up visit in 24-48 hours to document response to therapy and tolerance of PO antibiotics
   ➢ 7-14 days of therapy recommended (10 is a good compromise)
3. Admit for IV antibiotics if
   ➢ Toxic-appearing
   ➢ Unable to tolerate PO’s
   ➢ Younger than 2 month of age (until blood cultures negative/urine sensitivities known, pt afebrile)
   ➢ Still febrile after 48 hours of effective PO antibiotics (based on sensitivities)
   ➢ Suspected poor compliance with meds/follow up
4. Follow up:
   ➢ Document clinical response within 48 hours in all patients
   ➢ If still febrile in 48 hours, modify antibiotics based on culture results, or consider admission for IV antibiotics

Question 5: What imaging and follow up are recommended for a child with a first UTI?

Background:

- Febrile UTI may be the presenting sign of a urinary tract (UT) abnormality such as posterior urethral valves or vesicoureteral reflux (VUR)
  - Posterior urethral valves (PUV) is a rare congenital anomaly of the male urethra, and is most frequently diagnosed prenatally
    ▪ It carries a high risk of progression to ESRD (15-20%), regardless of frequency of UTI’s or age at surgical repair
    ▪ PUV is typically also associated with voiding dysfunction and elevated creatinine

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• VUR is a functional retrograde flow of urine during voiding, most typically caused by a developmental abnormality at the vesico-ureteral junction.
  ▪ Previously thought to cause recurrent UTI and thus lead directly to renal scarring or ESRD, this relationship has been drawn into question in recent years (see below)
  ▪ Grades of VUR: based on degree of urinary reflux into ureter/kidney
    • Grade I (lower ureter only) through V (into renal pelvis, with dilation)
• Imaging would only be cost-effective if the following were true:
  1. Clinically significant UT abnormalities are prevalent in children with first-time UTI’s
  2. These abnormalities lead to recurrent UTI’s/renal damage
  3. Treating these abnormalities leads to better outcomes
    ▪ Management of VUR (surgical correction) could help us to prevent renal damage ONLY IF
      • There is a causal relationship between VUR, recurrent UTI, renal scarring and ESRD and
      • Treatment of VUR is successful at preventing both VUR and those consequences
    ▪ Prophylactic antibiotics have been previously recommended to prevent UTI in kids with VUR
• Comparison of imaging strategies:
  1. Ultrasound
    a. Advantages:
      ▪ Relatively inexpensive and non-invasive.
      ▪ Can identify significant UT obstruction (such as PUV) as well as anatomic abnormalities of the kidneys (hydronephrosis, acute inflammation or dystrophy), ureters (dilatation, duplication, ureteroceles) and bladder (hyptertrophy, vesicoceles)
      ▪ Good sensitivity for high grades of reflux (IV-V) and negative predictive value is generally good (~85%) (Hoberman, Mahant)
      ▪ Best specificity if performed after resolution of infection
    b. Disadvantages:
      ▪ Overall, poor sensitivity for VUR (sens 30-62%; spec 75-85%)
    c. Abnormal results: warrant further investigation or at least follow up
    d. Negative results: best negative predictive value in patients with low prior prob
  2. VCUG
    b. Disadvantages: Expensive and invasive, involves radiation (0.1-0.9mSv)
    c. May be performed 3-4 days after patient begins responding to therapy
    d. Nuclear version (RNC) = ↓ radiation dose, but lower resolution, and requires IV access
  3. DMSA Scan
    a. Technetium-99m Dimercaptosuccinic acid given IV -> differential uptake into proximal tubular cells can be seen on imaging 2-3 hrs later
    b. Advantages: Best study for diagnosing renal scars. Radiation to bones and ovaries minimal
    c. Disadvantages: IV administration needed; impact on management questionable (eg: by the time scarring is present, unlikely to impact management, and may not predict future course)

Evidence:

A. Risk factors for clinically significant UT abnormalities/obstruction:
  1. History: Abnormal urine stream, reduced growth, oligohydramnios, elevated blood pressure or high serum creatinine (all associated with severe congenital UT obstruction, like PUV)
  2. Clinical: Young age, ill appearance, recurrence of UTIs or severe course/poor response to treatment
  3. Lack of prenatal ultrasound: A normal prenatal ultrasound after 30 weeks gestation reduces the chance of finding a significant abnormality after the 1st UTI to less than 1% (Hoberman, 2003)

B. Rates of high-grade VUR in first-time UTI
  1. Prevalence of any grade VUR among children with first UTI is 30-50%, depending on population
  2. However, 96-98% of VUR in children with 1st UTI is ≤Grade III (Hoberman, 2003)
     a. 76 VCUG’s would need to be done to identify one child with VUR ≥ grade IV (Newman, 2006)

C. Relationship between VUR, UTI, renal scarring and ESRD
  1. Renal scars more common in children with high grade VUR
     a. Pennesi (2008) found that among kids with first time UTI and VUR ≥ grade 2, 38% had renal scars, while baseline rates of scarring in children with first time pyelo is 5%-10%
     b. High grades of VUR (≥3) are associated with increased relative risk of scarring compared to no VUR and risk of renal damage increases with increasing grades of VUR (Blumenthal, 2005)
  2. However, relationship between UTI, VUR and NEW scarring remains unclear
a. UTI recurrence rates similar between children with/without VUR (Garin, 2006; Pennesi, 2008)
b. Scarring does not usually progress with UTI recurrence (scars may represent pre-natal insults)
c. Scarring from recurrent UTI in the absence of VUR has been reported (Blumenthal, 2005)
d. Renal scars in males more likely to be congenital, those in females more likely acquired

3. Progression to ESRD is rare (~5/million), and may not be related to VUR or UTI
a. 5-12% of pts with ESRD have “reflux nephropathy” as a cause, BUT
b. Salo (2011) found that < 1% of >1000 patients with ESRD had childhood UTI’s as a cause, and all of those patients had structural abnormalities of the kidney
c. Depending on your causative assumptions about UTI, VUR and ESRD, authors have estimated the risk of ESRD after a single episode of pyelo between 1/10,000 (Craig) and 1/1 million (Blumenthal)
d. Aggressive treatment of VUR in last 30 years has not decreased rates of ESRD from “reflux nephropathy”, despite effectively curing VUR (Craig, 2000)

D. Efficacy of surgical management of VUR
1. Surgical management usually highly successful at curing VUR
   a. Re-implantation of ureter into bladder, or injection into bladder wall to improve VUJ function
2. However, there is no evidence to support the efficacy of surgical management of VUR in preventing either recurrence of infection or renal scarring.
   a. Craig et al (2000) found no change in rates of ESRD due to reflux nephropathy in the last 40 years, despite new treatment practices.
   b. A 2004 Cochrane review on the topic concluded: “it is uncertain whether the identification and treatment of children with VUR confers clinically important benefit”.

3. Medical vs surgical management:
   a. Cochrane review (Wheeler, 2004) found that rates of recurrent UTI and scarring were similar between those receiving medical alone (antibiotics) vs medical+surgical management.
   b. Further controlled trials are needed (eg; surgical management vs placebo/no treatment)

E. Prophylactic antibiotics
1. Multiple recent studies have shown that antibiotics fail to prevent recurrent UTI, reduce VUR or prevent scarring, and may increase bacterial resistance in subsequent UTI’s
2. Examples:
   a. Garin (2006): RCT of 236 children with 1st time UTI, both with and without VUR (grades I-III only) randomized to receive antibiotic prophylaxis or close follow up.
      - No significant difference between the two groups in recurrence of pyelo (~5%), or of UTI (~20%), rates of scarring (~5%) or resolution of VUR.
      - For children with VUR, recurrent pyelo significantly more likely in those on antibiotics (and more resistant organisms)
      - The majority of cases of recurrent pyelo occurred in those with grade III reflux
   b. Pennesi (2008): RCT of 100 children < 30 mo with grades II-IV reflux after first UTI, randomized to receive antibiotics or not for 2 years
      - Rates of UTI recurrence (36 vs 30%), persistent VUR (62 vs 80%) and renal scarring (40 vs 36%) were similar in abx vs control groups
   c. Conway (2007) described factors associated with UTI recurrence in a cohort of 611 kids < 6 years
      - Antibiotics did NOT reduce risk of UTI recurrence, but were associated with increased rates of resistant organisms
   d. Montini (2008): RCT of 338 kids with 1st UTI, +/- reflux, randomized to abx vs placebo for 1 year
      - No sig difference between abx vs placebo groups (with or without reflux) in recurrent UTI
   e. RIVUR trial: multicenter RCT of prophylactic antibiotics vs placebo in >600 kids with 1st UTI and grade I-IV reflux – currently underway

F. Impact of selective imaging strategies
1. Pennesi, 2012: Retrospective review of 406 kids with 1st UTI; selective imaging (all got US, those with abnormal US or recurrent UTI got VCUG and DMSA); mean F/U of 4 years
   a. 7.4% had abnormal US (60% < 6mo of age), 13.3 % of these had scarring and VUR of IV
   b. 4.4% had another UTI – 11% of these had scarring and VUR of IV
   c. 29% of those with VCUG had VUR (86% were in those with abnormal US)
   d. Overall, renal scar in 6 kids (1.5%): ALL had grade IV VUR, and 4/6 were < 6 mo
   e. Conclusion; reduced imaging still revealed useful diagnoses
2. Schroeder, 2011: Retrospective review comparing selective imaging strategy to routine US/VCUG
a. Results: 130+ patients in each group
b. With selective imaging, no change in UTI recurrence, or detection of grades 4 and 5 VUR
c. Significant decrease in imaging, use of abx, and detection of grades 1-3 VUR
d. Conclusion: selective imaging reduces resource use without compromising care

Academic Society Guidelines/Recommendations:
1. British National Institute for Health and Clinical Excellence (NICE) – August, 2007 (Figure 1)
   - Recommends selective imaging, based on age and atypical/recurrent infections
     i. Renal ultrasound: ALL infants < 6 mo, and those 6-24 mo with atypical or recurrent UTI
     ii. VCUG: Infants < 6 mo of age with atypical or recurrent UTI
     iii. DMSA scan: ALL infants with atypical or recurrent UTI
   - Recommends against antibiotic prophylaxis
2. 2011 AAP Clinical Practice Guideline – September, 2011
   - Revised the previous 1999 AAP recommendation for VCUG for all children < 2 with first UTI
   - Recommendations
     i. Renal ultrasound (US): for ALL infants with 1st febrile UTI (acutely if complicated UTI)
     ii. VCUG
        ▪ Indicated for: infants with obstructive uropathy or high-grade VUR on US
          (hydronephrosis, scarring), or “atypical or complex” circumstances
        ▪ Recommended after the 2nd UTI
     iii. Follow up: prompt medical attention for febrile illnesses

Marmor Recommendations: Imaging and Follow Up After First Febrile UTI
1. Choice of imaging strategy should consider
   - Prior probability of UT abnormality, ability to change management, consequences of false positive/negative results, and parental/physician preference
2. Renal Ultrasound
   - During acute infection in: infants of any age with poor response to treatment
   - Within 6 weeks of infection in:
     ▪ Infants < 3 mo of age with 1st uncomplicated UTI (only if no 3rd trimester prenatal UTI)
     ▪ Infants <24 months with recurrent or atypical UTI (unusual organism or clinical course)
   - Responding to ultrasound results:
     ▪ If normal, or VUR grade ≤ III: Continue to promptly diagnose and treat UTI’s
     ▪ If signs of anatomic abnormality or obstruction: obtain VCUG, consult urology, increase surveillance for UTI’s
     ▪ If VUR grade ≥ IV (eg: hydronephrosis): consult urology, increase surveillance for UTI’s, consider VCUG
3. VCUG
   - Will only change management if infant is a candidate for surgical repair of obstruction or VUR
     (eg: recurrent pyelo, decreased renal function, high concern for damage to kidneys)
   - VCUG recommended in:
     ▪ Any infant with ultrasound showing urinary tract obstruction
     ▪ Infants with or VUR grade IV or V AND recurrent UTI in whom surgical correction is being considered
4. DMSA scan
   - Used for documentation only, as most scarring is prenatal, and non-progressive
   - Consider:
     ▪ If renal scarring is suspected and knowing the extent of existing scars may help guide management (eg: h/o severe/recurrent UTI, severe obstruction/hydronephrosis, abnormal creatinine)
5. Other strategies to consider if imaging is not desired/refused
   - Close follow-up, aimed at early diagnosis and treatment of UTI recurrences
6. Additional follow up after 1st UTI
   - Prophylactic antibiotics are NOT recommended for prevention of recurrent UTI, even in children with known reflux (grades I-III)
     ▪ Limited data in children with high-grade reflux (grades IV and V)
Could be considered in consultation with urology along with close surveillance for UTI

Prompt evaluation for future febrile illnesses is recommended

REFERENCES:

34. Newman TB. Much pain, little gain from voiding cystourethromgrams after urinary tract infection. Pediatrics 2006; 118: 2251
37. NICE Recommendations : http://www.nice7y68u.org.uk/nicemedia/pdf/CG54quickrefguide.pdf
42. Shaikh N et al. Does this child have a urinary tract infection? JAMA Dec 2007;298:2895-2904
# APPENDIX

<table>
<thead>
<tr>
<th></th>
<th>Most concerning</th>
<th>Somewhat concerning</th>
<th>Somewhat reassuring</th>
<th>Most reassuring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>&lt; 6 mo</td>
<td>6-12 mo</td>
<td>12-18 mo</td>
<td>&gt;18 mo</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td>White</td>
<td>Black</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex/ circumcision</strong></td>
<td>Uncirc male &lt;3 mo</td>
<td>Female or uncirc male 3-6 mo</td>
<td>Circ male &gt; 6 mo or uncirc male &gt; 1 year</td>
<td>Circ male &gt; 1 year</td>
</tr>
<tr>
<td><strong>Temperature</strong></td>
<td>T&gt;40 (LR =2.5*)</td>
<td>T 39-40 (LR=1.4*)</td>
<td>T &lt;39 (LR=0.7*)</td>
<td>T&lt;38.5</td>
</tr>
<tr>
<td><strong>Appearance</strong></td>
<td>Ill (toxic)</td>
<td>Sick, but alert and consolable</td>
<td>Well appearing</td>
<td>Smiling, happy</td>
</tr>
<tr>
<td><strong>Duration of illness</strong></td>
<td>&gt;3 days</td>
<td>2-3 days</td>
<td>&lt; 2 days</td>
<td>&lt;1 day</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>No other source for fever + additional symptoms (dysuria, frequency, urine odor, vomiting)</td>
<td>No other source, but no concerning symptoms (LR= 1.5*)</td>
<td>Possible other source for fever, or common virus like RSV (LR=0.7*)</td>
<td>Clear other source for fever (LR= 0.3*)</td>
</tr>
<tr>
<td><strong>Past history</strong></td>
<td>Previous UTI, known urinary tract abnormalities, recent instrumentation</td>
<td></td>
<td>No previous UTI or known UT abnormalities</td>
<td></td>
</tr>
</tbody>
</table>

*To use likelihood ratio to calculate posterior probability:
1. Convert prior probability to prior odds (Odds = Probability/1-Probability)
2. Multiply prior odds by LR to get posterior odds
3. Convert posterior odds to posterior probability (Probability = Odds/1+Odds)
# Figure 1: National Institute for Health and Clinical Excellence (NICE) Recommendations:
August, 2007

## Children < 6 Months of Age

<table>
<thead>
<tr>
<th>Test</th>
<th>Responds well to treatment within 48 hours</th>
<th>Atypical UTI&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Recurrent UTI&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound during the acute infection</td>
<td>No</td>
<td>Yes&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Yes&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ultrasound within 6 weeks</td>
<td>Yes&lt;sup&gt;b&lt;/sup&gt;</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>DMSA 4–6 months following the acute infection</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>MCUG</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

<sup>a</sup>See box for definitions  
<sup>b</sup>If abnormal consider MCUG  
<sup>c</sup>In an infant or child with a non-E. coli-UTI, responding well to antibiotics and with no other features of atypical infection, the ultrasound can be requested on a non-urgent basis to take place within 6 weeks

## Children 6 Months to 3 Years of Age

<table>
<thead>
<tr>
<th>Test</th>
<th>Responds well to treatment within 48 hours</th>
<th>Atypical UTI&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Recurrent UTI&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound during the acute infection</td>
<td>No</td>
<td>Yes&lt;sup&gt;c&lt;/sup&gt;</td>
<td>No</td>
</tr>
<tr>
<td>Ultrasound within 6 weeks</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>DMSA 4–6 months following the acute infection</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>MCUG</td>
<td>No</td>
<td>No&lt;sup&gt;b&lt;/sup&gt;</td>
<td>No&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>See box for definitions  
<sup>b</sup>While MCUG should not be performed routinely it should be considered if the following features are present:  
- dilatation on ultrasound  
- poor urine flow  
- non-E. coli-infection  
- family history of VUR.  
<sup>c</sup>In an infant or child with a non-E. coli-UTI, responding well to antibiotics and with no other features of atypical infection, the ultrasound can be requested on a non-urgent basis to take place within 6 weeks

## Definitions

<table>
<thead>
<tr>
<th>Atypical UTI</th>
<th>Recurrent UTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seriously ill</td>
<td>≥2 episodes of UTI with systemic symptoms (pyelo)</td>
</tr>
<tr>
<td>Poor urine flow</td>
<td>≥3 episodes of UTI w/o systemic symptoms (cystitis)</td>
</tr>
<tr>
<td>Abdominal or bladder mass</td>
<td>1 episode of pyelo + ≥1 episode of cystitis</td>
</tr>
<tr>
<td>Raised creatinine</td>
<td></td>
</tr>
<tr>
<td>Positive blood culture</td>
<td></td>
</tr>
<tr>
<td>Failure to respond to treatment in 48 hrs</td>
<td></td>
</tr>
<tr>
<td>Infection with non-&lt;i&gt;E. coli&lt;/i&gt; organism</td>
<td></td>
</tr>
</tbody>
</table>