pediatric urinary tract infections and constipation

community pediatric symposium, September 13, 2019

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background

• Range of presentation
  o Uncomplicated cystitis → severe febrile infections (→ renal scarring, CKD)

• >1.1 million office visits yearly

• Estimated inpatient cost of > $180 million\textsuperscript{1,2}
• Affects 2.4-3% of children annually
  o 1st year of life: boys > girls
    • 10x higher risk in uncircumcised vs circumcised boys
  o After age 1: girls > boys
    • Overall childhood risk of UTI: boys 2%, girls 8%

• Delayed testing (33%) or missed diagnosis (50%) in febrile UTI common in practice\(^3\)
  o Cystitis – typically no long term sequelae
  o Upper tract infections – potential for permanent renal scarring \(\rightarrow\) HTN, impaired renal function
  o Febrile patient without obvious source: evaluate for UTI
evaluation - history

• Risk Factors leading to pediatric UTIs
  o Gender (<1 year = male; >1 year = female)
  o Caucasian race (>Hispanic, African American)
  o Uncircumcised status (first 6-12 months)
  o Fecal and Perineal Bacterial Colonization
  o Anatomic abnormalities
    • Hydronephrosis, UPJ or UVJ obstruction, VUR, infection stones, infected non-functioning renal segments, fistulae (vesicointestinal, urethrorectal, vesicovaginal)
  o Sexual activity
  o Bladder and Bowel Dysfunction (BBD)
  o Neurogenic Bladder
  o Iatrogenic Factors
    • **Indwelling Catheters** - judicious use and prompt removal
  o Immunocompromised state
evaluation - history

• Older children/adolescents able to describe symptoms
• Must have high index of suspicion in kids <2-3 years old
• Consider:
  - Patient age and gender
  - First or recurring infection
  - Febrile (>100.4°F) or afebrile UTIs
  - Any known GU tract abnormalities (from pre- or postnatal RBUS, etc.)
  - Prior surgeries
  - Family history of UTI
  - Sexual history in adolescents
  - Drinking (what, how much) and voiding habits
  - Bowel habits (esp constipation, infrequent BMs)
  - Associated nausea/emesis
  - Urinary urgency, frequency or dysuria
  - Poor appetite or failure to thrive
  - Lethargy
  - Hematuria
evaluation – physical exam

• To include:
  • Palpation of abdomen, suprapubic region, costovertebral angles
  • Focused exam of external genitalia
    o Lesions
    o Discharge
    o Foreign bodies
    o Tenderness
    o Labial adhesions (girls)
    o Phimosis (boys)
    o Meatal stenosis (boys)
diagnosis

• Do not delay testing for UTI in febrile children without apparent source of infection$^5$
  o Association between delay in treatment of febrile UTI and permanent renal scarring

• Obtain urine specimen BEFORE administering any antibiotics$^4,6,7$
  o Urinalysis and culture

• Urinalysis suggestive of infection:
  o Positive leukocyte esterase or nitrite
  o Leukocytes or bacteria seen on microscopy

• Confirm findings with urine culture
diagnosis – obtaining the sample

- Clean Catch specimen
- Bagged urine specimen
- Catheterization
- Suprapubic Aspiration (SPA)
diagnosis – obtaining the sample

• Clean Catch specimen
  o Sufficient in toilet trained children to evaluate for possible UTI
  o Wash hands – soap and water
  o Clean genitals with towlette (one swipe, front to back in females)
  o Collect mid-stream sample
  o Do not touch inside of container or lid
  o >100,000 cfu/mL of single uropathogen confirms diagnosis of UTI
  o <50,000 cfu/mL, or multiple organisms suggest contamination

• Bagged urine specimen
• Catheterization
• Suprapubic Aspiration (SPA)
diagnosis – obtaining the sample

- Clean Catch specimen
- Bagged urine specimen
  - Children not yet toilet trained
  - Convenient
  - High risk of contamination by perineal flora
  - In general, only helpful if negative
  - If urinalysis suggests UTI, second sample should be collected through catheterization or suprapubic aspiration
- Catheterization
- Suprapubic Aspiration (SPA)
diagnosis – obtaining the sample

• Clean Catch specimen
• Bagged urine specimen
• Catheterization
  o Children not yet toilet trained
  o More invasive
  o Significantly smaller risk of contamination
  o Diagnosis of UTI requires
    • Urinalysis suggestive of UTI, and
    • >50,000 cfu/mL of single uropathogen on culture

• Suprapubic Aspiration (SPA)
diagnosis – obtaining the sample

• Clean Catch specimen
• Bagged urine specimen
• Catheterization
• Suprapubic Aspiration (SPA)
  o Most invasive test
  o Lowest risk of contamination
  o Rarely needed
  o Diagnosis of UTI requires
    • Urinalysis suggestive of UTI, and
    • >50,000 cfu/mL of single uropathogen on culture
asymptomatic bacteriuria

• Asymptomatic child with
  o No pyuria
  o Significant growth (>100,000 cfu/mL) of single organism

• Common in children with neurogenic bladder, or performing CIC
• Occurs in 0.8% of preschool girls (even lower in boys)

• DO NOT TREAT WITH ANTIBIOTICS⁸
asymptomatic bacteriuria

• CDC Definition of UTI in patients with Neurogenic Bladder
  o Regardless of use of CIC or spontaneous void

• All 3 of the following
  o 100,000 cfu/mL of 1 or 2 organisms
  o 10 WBC/hpf on urine microscopy and/or leukocyte esterase ≥ 2+ on dipstick
  o At least 2 of the following symptoms
    • Fever >100.4°F
    • Gross hematuria (pink or red urine, not a spot of blood on catheter)
    • Abdominal, suprapubic or flank pain/tenderness
    • New/worsening incontinence
    • New/worsening urinary urgency, frequency or hesitancy
    • Pain with catheterization or urination
    • Malodorous/cloudy urine
asymptomatic bacteriuria

• Also, avoid treating symptoms in absence of positive urine culture
  o Urinary frequency
  o Urgency
  o Dysuria
  o Abdominal, suprapubic, genital pain

• Antibiotics inappropriate treatment of child with these or other vague urinary symptoms in absence of laboratory evidence of UTI
treatment

• Oral and parenteral antibiotics equally effective

• Empiric Antibiotics
  o Should be based on local antimicrobial sensitivity/resistance patterns (if available)\(^6,7\)
  o Adjust (as needed) according to culture sensitivities

• American Academy of Pediatrics (AAP) recommendations for empiric antibiotics:
  o Parenteral: third-generation cephalosporins, gentamicin, tobramycin, piperacillin
  o Oral: cephalosporins, sulfonamides, amoxicillin-clavulanate

• *Escherichia coli* = most common organism causing UTIs in pediatric patients
  o Any empiric antibiotics should cover this bacterium
treatment – antibiotic resistance

• Growing concern nationally
• Judicious and appropriate use of antibiotics

• Nationwide antibiotic resistance exhibited by *E. coli*\textsuperscript{9,10}

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Prevelance of <em>E. coli</em> resistance</th>
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</thead>
<tbody>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>21.3 – 24%</td>
</tr>
<tr>
<td>B-lactams</td>
<td>37.7%</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>45%</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
treatment - duration

• Uncomplicated cystitis:
  o 3-7 days of oral antibiotics
  o Post-treatment urine culture not needed if symptoms have resolved

• Pyelonephritis:
  o Outpatient vs Inpatient treatment
  o Inpatient treatment recommended for:
    • Toxic appearing patients
    • Children <2 months of age
    • Unable to tolerate PO medications
    • Patients in whom compliance may be an issue
  o 7-14 day course of oral antibiotics appropriate (after patient afebrile for 24-48 hours)^4,6,7
bladder and bowel dysfunction (BBD)

- Urinary and colorectal systems intimately related
- Patients should avoid holding urine or stool for prolonged periods of time
  - Urine stasis within the bladder can contribute to UTIs
    - Aim to empty bladder every few hours while awake
  - High concentration of bacteria on stool in rectal vault can contribute to UTIs
    - Children should have regular, soft bowel movements

- BBD seen in children without any neurologic disorder, but suffer from infrequent voiding, constipation, and/or bladder overactivity
- Well-recognized association between bladder dysfunction and UTI
- PCPs can evaluate for BBD and initiate initial measures to address this problem\(^\text{12}\)
  - Conservative treatment
    - Voiding behavior modification (timed voids, double voids, spread-leg voids in females)
    - Treat constipation if present
  - Directed therapy
    - Typically based on results of uroflow study, post-void residual; may require formal urodynamic study

- Treatment of constipation has been shown to decrease UTI recurrence\(^\text{11}\)
  - 234 patients in Iowa with chronic constipation and daytime incontinence (29%), nighttime incontinence (34%) or UTIs (11%)
  - After at least 1 year of follow up, no recurrence of UTIs (and significant improvement in incontinence (89% and 63%)
constipation - the why…

• 3-5% of pediatric visits
• 25% of pediatric GI referrals
• Constipation-related ED visits 2006-11

  Visits increased 42% (all ages)
  Highest rate: infants (<1 year old)
  Mean cost per visit increased to $2300
  Total national cost more than doubled to >$1.6 billion (2014 $)
  In Anthem top 5 potentially avoidable ED (PAED) visit reasons

van den Berg et al., Am J Gastroenterol 101:2401, 2006
Sommers et al., Am J Gastroenterol 110:572, 2015
constipation - collaboration

- Dayton Children’s Health Partners (DCHP)
- Dayton Children’s Division of Gastroenterology & Nutrition
  - Co-management program for constipation
  - Help educate & support primary care pediatricians to manage & treat functional constipation in the primary care setting
guiding principles for co-management

1. Safe, effective, & timely patient-centered care
2. Effective communication between primary & specialty care
   - assuring safe & coordinated transitions of patient care
   - foster and sustain a professional relationship between and among healthcare providers
3. Network promoting access:
   - to the right care
   - at the right time
   - in the right place
   - at the lowest cost
What is functional constipation?

1. 2 or fewer defecations in the toilet per week in a child of a developmental age of at least 4 years
2. At least 1 episode of fecal incontinence per week
3. History of retentive posturing or excessive volitional stool retention
4. History of painful or hard bowel movements
5. Presence of a large fecal mass in the rectum
6. History of large diameter stools that can obstruct the toilet

After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.
Patient presents with constipation
- History
- Physical exam with perianal inspection, consider digital rectal exam

Red flags?

Disimpaction Protocol
- yes
- Disimpaction effective?
  - yes
  - Repeat Disimpaction Protocol
  - no
  - Maintenance Therapy
    - yes
    - Effective?
      - yes
      - If patient is doing well, continue maintenance for at least 6 months
      - no
      - Consider laboratory studies
        - Contact pediatric gastroenterologist for phone consultation
    - no
      - if no response to therapy

- no
- Impaction or encopresis (soiling) present?
  - yes
  - Phone consultation with pediatric gastroenterologist
  - no
red flags

**history**

- Constipation in the first month of life
- Delayed passage of meconium (>48 hours)
- Family history of Hirschsprung disease or celiac disease
- Ribbon stools
- Blood in stools in the absence of anal fissures
- Failure to thrive, poor feeding
- Fever
- Bilious vomiting

**physical exam**

- Abnormal thyroid gland
- Severe abdominal distension
- Abnormal perianal inspection
- Decreased lower extremity strength/tone/reflexes
- Tuft of hair on spine or sacral dimple
- Extreme fear during anal inspection
- Evidence of bowel obstruction
## Disimpaction Protocols

<table>
<thead>
<tr>
<th>Time of Day</th>
<th>Age 1-2 Years (15 to 22 pounds)</th>
<th>Age 2-4 Years (22 to 44 pounds)</th>
<th>Age 5-10 Years (45 to 88 pounds)</th>
<th>Older than 10 Years (Over 88 pounds)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morning</strong></td>
<td>Take ½ chocolate senna laxative square</td>
<td>Take 1 chocolate senna laxative square</td>
<td>Take 1 + ½ chocolate senna laxative squares</td>
<td>Take 2 chocolate senna laxative squares</td>
</tr>
<tr>
<td><strong>Throughout the Day</strong></td>
<td>Mix 2.5 capfuls of PEG3350 powder in 16 ounces of fluid Drink it all over 4-8 hours</td>
<td>Mix 4 capfuls of PEG3350 powder in 20 ounces of fluid Drink it all over 4-8 hours</td>
<td>Mix 7 capfuls of PEG3350 powder in 32 ounces of fluid Drink it all over 4-8 hours</td>
<td>Mix 14 capfuls of PEG3350 powder in 64 ounces of fluid Drink it all over 4-8 hours</td>
</tr>
<tr>
<td><strong>Evening</strong></td>
<td>Take ½ more chocolate senna laxative square</td>
<td>Take 1 more chocolate senna laxative square</td>
<td>Take 1 + ½ more chocolate senna laxative squares</td>
<td>Take 2 more chocolate senna laxative squares</td>
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*Keep on clear liquids the day of clean-out!*
tips for disimpaction

1. For school-aged children, start bowel clean-out on Friday after school.

2. Finish PEG 3350 (MiraLAX) within 4-8 hours or as quickly as possible.

3. If unsatisfactory results, repeat up to 3 days. Parents should call their provider if still not clear.

4. Make sure the child is on a clear liquid diet for the duration of the clean-out, otherwise the clean-out will take too long.
maintenance

therapy
1. Balanced diet
2. Fluids
3. Behavioral modification including daily toilet sitting
4. Daily maintenance laxative therapy at an appropriate dose

medications

*Osmotic laxatives*: TO BE GIVEN EVERY DAY

- PEG 3350/ MiraLAX ← Squishes

*Stimulant laxatives*: add if needed for infrequent stools

- Chocolate laxative squares/ Senna ← Pushes
tips for maintenance therapy

1. Daily dose of osmotic laxatives should be adjusted so that the patient is having daily bowel movements that are approximately oatmeal consistency.

2. If stopping stimulant laxatives that have been given consistently, the dose needs to be slowly weaned off to prevent re-impaction.

3. If not improving despite following clean-out and maintenance recommendations, consider referral to pediatric GI.
what to tell families

1. Written home instructions.
2. Sit on the toilet 2-3 times daily, 5-10 minutes each time.
3. Footstool or other object so that they have a solid base to push.
4. Positive reinforcement, not punishment.
5. Explain encopresis to the parent and child.
what to tell families

6. Trial of stopping milk for 2-4 weeks might be considered.
7. Explain the importance of a balanced diet and fluids.
8. Set a follow-up appointment within several weeks.
9. Encourage follow-up phone calls to remain on track.
10. Do not stop medications without contacting your child’s provider.
when to refer for pediatric GI evaluation

1. “Red flags” present in history or physical exam

2. Patient not responding to disimpaction or recommended daily dose of laxative

3. Consider labs if not improving:
   - CBC, BMP, thyroid studies, tissue transglutaminase IgA, total IgA level, lead level (if at risk)

4. If referring, send:
   - All growth curves, Lab & radiology results, radiology images on CD (if not obtained at Dayton Children’s)
case study 1
4 yo female with 2 week history of daytime vomiting

- ROS revealed + urinary frequency + daytime urinary incontinence, and alternating liquid and hard stools
- KUB revealed large stool burden
- No constipation “red flag” symptoms
- Exam unrevealing, normal neuro exam

Diagnosed with constipation and impaction
case study 1: initial PCP visit

- Parents educated on diagnosis, disimpaction, and maintenance

- Handouts provided and reviewed during office visit

- Asked to follow-up in 2-4 weeks

- Phone nurses called family within the week of first office visit
  - Parents reported success with patient’s clean-out – transparent stools
  - Given reminder for follow-up
  - Encouraged to continue PEG3350 maintenance

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age 2-4 years (22 to 44 pounds)
case study 1: follow-up visit/ maintenance

Follow-up visit

• Revealed resolution of vomiting and urinary symptoms

• Goal stools on the Bristol stool chart diary

• Maintenance instructions reviewed during office visit and on after visit instructions

• Encouraged to continue PEG3350 maintenance for at least 6 months and to follow-up in 6 months
imaging

• No always required; typically obtained in patients with febrile/recurrent UTIs
• AAP has issued evidence based guidelines re: appropriate imaging

• Order appropriately/judicisously
  o ALARA
  o Limit expense of care/diagnosis
  o Limit risks associated with invasive studies (i.e. catheterization, radiotracer injection)
imaging

- Renal and Bladder Ultrasound (RBUS)
- Voiding Cystourethrogram (VCUG)
- Dimercaptosuccinic Acid (DMSA) Renal Scan
imaging

• Renal and Bladder Ultrasound (RBUS)⁴,⁶,⁷
  o Safe and appropriate to obtain during active infection
  o Must obtain images of both kidneys and bladder
  o Should be obtained in ANY febrile infant with UTI
    • Especially in those without documentation of normal postnatal RBUS
  o Only imaging study after first febrile UTI in children 2-24 months
  o Should be obtained in children >2 years with recurrent UTI

• Voiding Cystourethrogram (VCUG)
• Dimercaptosuccinic Acid (DMSA) Renal Scan
imaging

• Renal and Bladder Ultrasound (RBUS)

• Voiding Cystourethrogram (VCUG)\textsuperscript{6,7}
  o Useful in identifying bladder emptying, vesicoureteral reflux (VUR) or urethral obstruction
  o Involves catheterization and retrograde instillation of contrast
  o Do not obtain until child is no longer symptomatic and afebrile for ≥24 hours
  o When to obtain?
    • Children <2 months with initial febrile UTI
    • Abnormal anatomy on RBUS (hydronephrosis, scarring, etc.)
    • Other atypical or complex situations
    • After second febrile UTI in children 2-24 months

• Dimercaptosuccinic Acid (DMSA) Renal Scan
imaging

- 7 y/o F, history of 3 febrile UTIs
- Right Grade 2 VUR
  - Prior VCUG: R Gr 4, L Gr 3 VUR
imaging

- 22 month F, h/o febrile UTIs
- Bilateral Grade 5 VUR
- Underwent bilateral reimplant because of recurrent infections despite abx ppx
imaging

• Renal and Bladder Ultrasound (RBUS)
• Voiding Cystourethrogram (VCUG)
• Dimercaptosuccinic Acid (DMSA) Renal Scan
  o Nuclear medicine study involving injection of radiotracer
  o Should not routinely be obtained after first febrile UTI
    • May be helpful in identifying renal scarring later on
  o Will demonstrate renal scarring and active pyelonephritis
    • Cannot distinguish between the two
    • If evaluating for scarring, do not obtain until 4-6 months after acute pyelonephritis
imaging

• DMSA scan from patient 1
• Asymmetric renal function, L>R
• Scarring of right upper pole
• Stable from prior exams
• Currently being observed off antibiotics
antibiotic prophylaxis

• No universally applicable answer

• Most commonly used in children with VUR
  o Controversial
  o Children <1 year with VUR
  o Children >1 year with high grade (dilating) VUR

• In all patients with VUR, prophylaxis reduces risk of UTI recurrence, but does not alter rate/development of renal scarring\textsuperscript{13}

• Swedish study showed decreased in both UTI recurrence and new renal scarring
  o Females age 1-2 years
  o High grade VUR
surgical management of vur

• Many options available
  o Endoscopic, laparoscopic, open surgical techniques

• Higher resolution rates with open technique (98.1%) compared to endoscopic therapy (83%)

• When to consider?
  o Higher grades of VUR
  o Breakthrough/recurrent febrile UTIs while on prophylaxis
  o Presence of renal scarring
when to refer

• Consider referral in the following situations:
  o VUR (especially high grade)
  o Abnormal RBUS results
  o Congenital GU tract abnormalities
  o Recurrent or severe UTIs
  o Febrile UTI in an infant
  o Urinary urgency, frequency or enuresis in absence of infection