### Urine Trouble: Pediatric UTIs in Primary Care

#### Primary Care Pediatrics Assembly Row, Somerville MA

Mass General Brigham

Mass General for Children

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## Learning objectives

- 1. Recognize the epidemiology, provenance and microbiology of urinary tract infections
- 2. Formulate a diagnostic plan based on assessment of symptoms and risk factors
- 3. Understand the general approach to therapeutic interventions and preventive methods

## General thoughts

- UTI are common bacterial infections in children
  - Around 10% of **neonates** with non-focal fevers have UTI
  - Prevalence of febrile UTI
    - Girls are generally more susceptible to boys
    - Highest prevalence is in the first 90 days of age (girls: 7.5%; circumcised boys: 2.4%; uncircumcised boys: 20.1%)
    - The prevalence of UTI decreases with increasing age
    - Overall, the prevalence of UTI in children younger than 19 years old is 7-8%
- UTIs can be divided in 3 categories:
  - Upper tract infection- Pyelonephritis
  - Lower tract infection- Cystitis
  - Asymptomatic bacteriuria

## General thoughts

- Localizing the infection <u>when possible</u> is helpful in formulating a therapeutic and management plan
  - It may be hard to differentiate cystitis from pyelonephritis in patients younger than 2 years old



#### Figure 1: Occurrence of UTIs according to age

(A) Occurrence of UTIs in girls. (B) Occurrence of UTIs in boys. UTI=urinary tract infection. Reproduced from Winberg and colleagues,<sup>2</sup> by permission of John Wiley and Sons.

## How is the infection acquired?

- Most common pathway: retrograde migration from the enteric flora
- Nosocomial seeding in hospitalized patients through instrumentation
- Hematogenous seeding during sepsis



Jian Ma, Linda Dairiki Shortliffe. Urinary tract infection in children: etiology and epidemiology. Urol Clin North Am. 2004 Aug;31(3):517-26

## Causative organisms

- E coli in ~ 90% of the cases
- Microbiology is different with age, immune status and risk factors (but E coli still predominates)
  - GBS in neonates and young infants
  - Pseudomonas aeruginosa in immunocompromised hosts, post-surgery, instrumentations, or anatomical defects
  - Proteus (urea-splitting organisms in kidney stones)
  - Viruses/ fungi in immunocompromised patients/ transplanted kidneys

#### Gram-negative rods

Citrobacter spp Escherichia coli Enterobacter spp Gardnerella vaginalis Klebsiella spp Morganella morganii Proteus spp Providencia stuartii Pseudomonas aeruginosa Serratia spp

*Gram-negative cocci* Neisseria gonorrhea

#### Gram-positive cocci

Staphylococcus aureus Staphylococcus epidermidis Staphylococcus saprophyticus Streptococcus group D Streptococcus faecalis Streptococcus bovis Streptococcus group B

#### Other pathogens

Candida albicans Chlamydia trachomatis Ureaplasma urealyticum



- A UTI diagnosis is based on evidence of infection on urine analysis (Pyuriapositive LE on dipstick or > 5 WBC/hpf on microscopy OR bacteriuria)
   AND
- Presence of a uro-pathogen in significant amounts

Roberts KB; Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. 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. **2011**;128(3):595–610

### Schematic for diagnosis of an infection of the urinary tract

Assess the likelihood of a urinary tract infection by evaluating the history, clinical examination and risk factors

## Diagnosis- assessment of risk

- <u>Before testing the urine</u>, assess the likelihood of UTI
  - History
    - In patients younger than 2 years old, a typical history may not be present
  - Clinical examination
    - In patients younger than 2 years old, typical symptoms may not be present
  - Factors conferring increased risk: Young age (<12 months), female sex (or uncircumcised young male infant), High grade fevers ( ≥39°C) lasting more than 2 days without focality or alternate source, history of UTI, urinary tract anatomical defects, Bladder- bowel dysfunction (such as constipation, incontinence, encopresis), clinical symptoms suggestive of UTI/pyelonephritis
  - May use online calculators

## University of Pittsburgh online calculator

<b>UTTICALC</b> Version For children 2 to 23 months of age.	Calculation Results	
Probability of UTI based on clinical charact	eristics	Please note: The pretest probability of UTI for your patient is relatively <b>LOW</b> (i.e., less than 2%). Many clinicians would not obtain a urine sample in such a patient
Enter child's clinical characteristics below (all fields are req	uired)	endri 2 /0/. Many cancelans would not obtain a enne sample in such a patient.
Age < 12 months	Ves No	
Maximum temperature ≥ 39 °C (i.e., 102.2°F)	○ Yes ○ No	Calculation Results
History of UTI*	○ Yes ○ No	The predicted probability of UTI for your patient is between 2% and 5%. Please refer
Female or uncircumcised male	Yes No	to your patient's predicted probability and consider testing based on individual
Other fever source**	◯ Yes ◯ No	level, a cutoff of ≥2% detects ~95% of UTIs, and cutoffs of ≥3% and ≥4% detect ~90% of UTIs.
Duration of fever ≥ 48 hrs	○ Yes ○ No	
Probability of UTI		Calculation Results
Calculate		The predicted probability of UTI for your patient is ≥ 5%. Strongly consider obtaining urine sample to test for UTI.
*Parent reported or documented history of UTI **Other fever source can include (but is not limited to): acute otitis media, upper respiratory tract infection (i.e., any cough or congestion	), gastroenteritis, pneumonia, meningitis, bronchiolitis, and viral syndrome.	
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https://uticalc.pitt.edu/ Last accessed 11/24/2024

### Schematic for diagnosis of an infection of the urinary tract

Assess the likelihood of a urinary tract infection by evaluating the history, clinical examination and risk factors

If your evaluation is concerning, send urine for testing

Send urine for analysis microscopy and culture

• If pre-test evaluation suggests low likelihood of UTI, you should consider not testing the urine.

## Diagnosis- urinalysis and microscopy

- Urinalysis findings of pyuria and a positive nitrite test are diagnostic aids which may be helpful in making a provisional diagnosis.
- Ensure the submitted sample is fresh (<1 hour at room temperature or up to 4 hours when refrigerated)
  - Nitrite Converted from nitrate by GNR UTI; Typically needs >4 hours in bladder to do so
    - Poorly sensitive ~50% (Not all UTI are GN and issues in diapered)
    - Highly specific (>95%- Rare false positives)
  - Leucocyte esterase (LE)- surrogate marker for pyuria
    - Sensitivity and specificity is around 80%
  - Pyuria (> 5 WBC/hpf in centrifuged sample)
    - Sensitivity and specificity is also around 80%
  - Bacteriuria
    - By definition, asymptomatic bacteriuria has no pyuria

## Diagnosis- urinalysis and microscopy

- The two-step process (6 months- 24 months of age)
  - Reasonable alternative in non-toxic children without risk factors
  - Significantly decreases rates of catheterization without missing UTIs

Lavelle JM et al. Two-Step Process for ED UTI Screening in Febrile Young Children: Reducing Catheterization Rates. Pediatrics. 2016 Jul; 138(1):e20153023

## University of Pittsburgh online calculator

	UTIC	alc Version 3.0	Calculation Results	×
For children 2 to 23 months of age.			The predicted probability of UTI for your patient is ≥ 5%. Stro urine sample to test for UTI.	ngly consider obtaining
Probability of UTI based on cli	nical characteristics	Probability of UTI based on clinica	al & laboratory characteristics	
Enter child's clinical characteristics belo	w (all fields are required)	Only enter available test results; leave fields bla	ank for test results that are not available.	
Age < 12 months	● Yes ○ No	Nitrite	🔿 Yes 🔷 No	
Maximum temperature ≥ 39 °C (i.e., 102.2°F)	• Yes O No	Leukocyte esterase	•	
History of UTI*	• Yes O No	WBC/mm <sup>3</sup>		
Female or uncircumcised male	• Yes No	(If not available, leave blank. Do not substitute WBC/hpf)		
Other fever source**	● Yes ○ No	Bacteria on Gram stain (If not done leave blank; do not substitute	🔿 Yes 🔷 No	
Duration of fever ≥ 48 hrs	Yes O No	bacteria on urinalysis) Clear stain selection		
Probability of UTI	20.43%	Probability of UTI		
Calculate	lear	Calculate	Clear	
*Parent reported or documented **Other fever source can include (but is not limited to): acute otitis med congestion), gastroenteritis, pneumonia, meningitis	l history of UTI lia, upper respiratory tract infection (i.e., any cougl , bronchiolitis, and viral syndrome.	nor		

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Assess the likelihood of a urinary tract infection by evaluating the history, clinical examination and risk factors

• If pre-test evaluation suggests low likelihood of UTI, you should consider not testing the urine.

If your evaluation is concerning, send urine for testing

Send urine for analysis microscopy and culture

Start empiric therapy if UTI is suspected

- Ensure the appropriate specimen is sent
- Consider using the two-step process
- If the biochemical and microscopic analysis of the urine is not concerning, consider withholding antibiotics waiting for culture

## University of Pittsburgh online calculator

	Calculation Results		
	The posttest probability of UTI for your <b>equal to 5%</b> ). Many clinicians would tre while awaiting	patient is relatively HIGH (i.e., <b>greater than or</b> at such a patient with antibiotics empirically urine culture results.	
Probability of UTI based on clir	ic	Close   on clinic	cal & laboratory characteristics
Enter child's clinical characteristics below	(all fields are required)	Only enter available test results; leave fields	blank for test results that are not available.
Age < 12 months	• Yes No	Nitrite	• Yes 🔷 No
Maximum temperature ≥ 39 °C (i.e., 102.2°F)	🔿 Yes 💿 No	Leukocyte esterase	3+
History of UTI*	🔿 Yes 💿 No	WBC/mm <sup>3</sup> (If not available, leave blank. Do not substitute	10
Female or uncircumcised male	• Yes No	WBC/hpf)	
Other fever source**	• Yes No	Bacteria on Gram stain (If not done leave blank; do not substitute	Yes No
Duration of fever ≥ 48 hrs	Yes No	Clear stain selection	
Probability of UTI	4.35%	Probability of UTI	75.85%
Calculate	ar	Calculate	Clear
*Parent reported or documented **Other fever source can include (but is not limited to): acute otitis media congestion), gastroenteritis, pneumonia, meningitis, l	history of UTI a, upper respiratory tract infection (i.e., any cough o pronchiolitis, and viral syndrome.	r	
https://uticalc.pitt.odu/			

Last accessed 11/24/2024

# Therapy

 It is helpful to delineate site of infection as this will impact type of antibiotic and duration of therapy

Characteristic	APN	Uncomplicated Cystitis
Age distribution	More common in younger children	Typically in children aged $>\!\!2$ y
Fever <sup>130</sup>	>38°C	Afebrile or low-grade fever $\leq$ 38°C
Recent viral illness <sup>131</sup>	NA	Viral cystitis
Systemic symptoms	Common	Uncommon
Local symptoms	Flank pain and/or tenderness	Dysuria, urgency, frequency, urinary incontinence, suprapubic pain, and/or hematuria
Causative agent	Bacterial ( <i>E coli</i> is the commonest)	Bacterial ( <i>E coli</i> is the commonest), viral, fungal, and chemical
Urinary findings		
Gross hematuria	Uncommon	May have fresh blood and clots <sup>101,102</sup>
Urine culture for bacteria	Positive	Negative results in viral, fungal, and chemical cystitis
RBUS	Normal or may reveal edema and hyperemia of kidney	Normal or may reveal thickened urinary bladder wall, debris in the bladder
Renal complication	Renal scarring	None

NA, not applicable.

## Therapy- General guide

- Empiric therapy should be guided by local resistance patterns to uro-pathogens → Keep an updated antibiogram handy from your local microbiology lab.
- Broader spectrum therapies (third generation cephalosporins; Amox/Clav) for empiric therapy in upper tract infections, febrile UTIs and/or recurrent infections.
- Nitrofurantoin, TMP/SMX or first generation cephalosporins in cystitis and afebrile infections
- Tailor therapy according to subsequent sensitivities
- Most infections can be treated all <u>orally</u>- start therapy as soon as possible before bacterial confirmation if UTI is suspected
- Duration of therapy:
  - 10 days for APN and upper tract disease
  - 3-5 days are sufficient for cystitis

#### <u>Notes</u>

- Amoxicillin should not used for UTIs
- Cephalexin covers most E coli isolates and can be used in upper tract infections once sensitivities are available
- All cephalosporins do not cover Enterococci

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Evaluate the results of the culture

- Ensure the appropriate specimen is sent
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- If the biochemical and microscopic analysis of the urine is not concerning, consider withholding antibiotics waiting for culture

## Diagnosis- culture



Appropriate collection method	Quantitative parameter (colony forming units/mL)
Suprapubic bladder aspiration	10 <sup>3</sup> ( <b>1000</b> )
Bladder catheterization	10 <sup>4</sup> (10 000- <b>50 000</b> )
Mid-stream urine	10 <sup>5</sup> (50 000- <b>100 000</b> )





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Evaluate the results of the culture

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- Ensure the appropriate specimen is sent
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- Stop antibiotics if culture is negative/ not suggestive of infection
- Adjust antibiotics if needed

## Therapy- Additional thoughts

- USE YOUR CLINICAL JUDGEMENT
- Be skeptical if:
  - Presence of squamous epithelial cells on urinalysis
  - Cultures were obtained from a bag specimen (or other non-sterile techniques)
  - Cultures were obtained after antibiotic therapy
  - There is bacterial growth but no concomitant inflammatory response (Asymptomatic bacteriuria)
  - Polymicrobial growth and/or growth of non-uropathogens in culture

## To image or not to image

- <u>RBUS</u>- no radiation
  - All febrile infants (2-24 months old) should undergo an US examination
  - RBUS can be falsely abnormal in acute infection (hydronephrosis, tissue edema, etc)
  - Unless clinically ill or not improving after 2-3 days of antibiotic therapy, RBUS should be performed sub-acutely

#### • VCUG (Voiding cystourethrography)-

- VCUG should not be routinely performed after the first UTI
  - Less than one-third of children with their first UTI have VUR; and of these, fewer than 10% have grade 4 to 5 VUR
- VCUG should only be performed if RBUS is abnormal or if there is recurrence of febrile UTI
- <u>DMSA</u>- Gold standard to assess renal injury
  - Rarely changes acute clinical management
  - Could be considered in children with recurrent febrile UTIs or those with renal parenchymal abnormalities on RBUS
  - Should be delayed 4-6 months after the acute infection

## Renal scarring

- APN-induced scarring is the result of the presence of proinflammatory factors, recruitment of neutrophils and resultant fibrosis. ? Genetic role
- Factors of risk associated with renal scarring:
  - Delay in initiating antibiotic therapy (>72 hours of fevers)
  - Recurrent UTIs (prevalence of scarring increases from 3% after the first UTI to 30% after 4 infections)
  - Non-E coli UTI
  - Vesico-urethral reflux (namely grades 4 and 5)

## Preventive therapies

- Prevention and treatment of constipation
- Avoidance of urine withholding behavior in toilet-trained children
- Daily cleaning in uncircumcised males. Circumcision may be needed with phimosis or recurrent UTIs.
- Antimicrobial prophylaxis:
  - Some studies suggest that prophylaxis decreases the risk of recurrent UTIs especially in patients with high grade VUR and BBD
  - No study to date have demonstrated a preventive benefit of renal scarring with antibiotic prophylaxis
  - The 2011 AAP practice guidelines (reaffirmed in 2016) do not recommend prophylactic antimicrobials following the first febrile UTI in children 2 to 24 months
  - A selective approach to antibiotic prophylaxis may be best. Antibiotic prophylaxis should be considered in patients with young age, recurrent UTIs, presence of BBD, anatomical abnormalities, and high-grade reflux.

## References

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### Discussion



