Consensus Guidelines for Management of Pediatric Urinary Tract Infection (UTI): Northern California Pediatric Hospital Medicine Consortium

Executive summary

Objectives

1. To define the clinical circumstances under which testing for UTI is indicated and reduce unnecessary testing for UTI.
2. To ensure the method of testing for UTI is appropriate based on age and probability of UTI.
3. To elucidate the appropriate laboratory studies and imaging for children with UTI and reduce the use of high-radiation studies.
4. To recommend appropriate empiric antibiotic therapy in children with suspected or confirmed UTI.
5. To define admission criteria for children with UTI.
6. To suggest appropriate subspecialty consultation in non-typical clinical circumstances.

Recommendations

How to Test

- Choice of collection method should take into account the prior probability of UTI, the age of the child, parental preference, and the implications of a false positive or false negative result. *The UCSF PHM consortium strongly recommends that bag specimens not be sent for culture, but in the circumstance of parental refusal or inability to obtain a catheter specimen, this method should be documented and stringent interpretation criteria should be applied when the culture result returns.*
- When to Send a Culture
    - Urine cultures should be sent for **all children <6 months suspected of UTI** *regardless of UA results*
    - Urine cultures should be sent for **all children < 12 year old with urinary symptoms and a positive UA** (+LE and/or +nitrites)

Labs

- Blood culture and LP may be indicated based on age and clinical appearance of patient. Other labs are not routinely recommended.

Imaging

- RBUS (ultrasound of kidneys and bladder) is indicated for first time febrile UTI in patients <6 mo. Other imaging not routinely recommended.

Treatment

- Empiric antibiotic guidelines and recommendations on duration of therapy can be found here: http://idmp.ucsf.edu/pediatric-guidelines-urinary-tract-infections-community-onset

Methods

This guideline was developed through local consensus based on published evidence and expert opinion as part of the UCSF Northern California Pediatric Hospital Medicine Consortium.

Metrics Plan

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Northern California Pediatric Hospital Medicine Consortium. Originated 06/2016. Last modified 04/2018.
Approved by UCSF IDMP/Antimicrobial Subcommittee: 4/2018, Med Subcommittee 6/2018

Approved by UCSF Pharmacy and Therapeutics Committee: 8/2018

UCSF Benioff Children's Hospitals

Consensus Guidelines for Management of Pediatric Urinary Tract Infection (UTI), Age < 12 years: Northern California Pediatric Hospital Medicine Consortium

Introduction

Criteria for Use of Guideline:

- Inclusion/Exclusion Criteria: This guideline is designed for use in all children under age 12 years of age with suspicion for or known community-acquired UTI, with the exception of those children who have kidney transplants, indwelling catheters or urinary tract instrumentation, or are immunocompromised.

Children in Whom There May be Concern for UTI

- Fever without a source in select infants
  - Infants < 3 months of age: Fever (T≥38) without source
  - Infants/Toddlers ≥ 3 months of age: Fever of ≥39 for > 24 hrs without a source in uncircumcised boys and girls < 2 years of age
- Historical risk factors (to be considered along with clinical risk symptoms)
  - Known history of vesicoureteral reflux or other urogenital malformations
  - Previous UTI's (UTI history should be carefully confirmed)
  - Recent bladder catheterization

Common Uropathogens (include in empiric coverage):

- Enteric Gram negatives (i.e. *E.coli, Klebsiella* spp*., Proteus* spp.)

Less common uropathogens (NOT routinely included in empiric coverage):

- Enteric Gram negative rods with potential antibiotic resistance
  - ESBL-producing organisms (e.g. fraction of *E. coli, Klebsiella* spp.)
  - Organisms with potential ampC-production (e.g. *Enterobacter* spp*, Citrobacter* spp)
- *Pseudomonas aeruginosa*: increased concern in patients with hospital-acquired UTI, indwelling catheters, significant prior antibiotic exposure
- *Enterococcus* spp*
- *Candida* spp*

*These organisms are more likely to represent colonization or contamination when isolated from urine cultures. Correlate with clinical picture, consider confirmatory culture.

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Definitions:
UTI: A combination of clinical symptoms, pyuria, and positive urine culture with >50,000 CFU/ml of a single uropathogenic organism on an appropriately collected urine culture.

Pyelonephritis: A UTI with bacterial infection of the kidneys. Involvement of the kidneys in this guideline does NOT automatically constitute a complicated or atypical UTI. This is different from terminology commonly used in adult medicine and reflects the commonality of upper urinary tract involvement in otherwise healthy young children with UTI.

Atypical pathogens: Infection with organism other than *E. coli, Proteus* spp, or *Klebsiella* spp

Evaluation

H&P – important information to obtain:

- HPI:
    - Fever (without another reason/source)
    - Urinary symptoms (dysuria, frequency, urgency, withholding, incontinence, hematuria)
    - Urine odor (parental history)
    - Pain (abdominal, flank, back)
    - PO tolerance/hydration status
    - Stooling history (particularly constipation/withholding)
- PMHx:
    - Elevated blood pressure
    - Poor growth
    - Previous UTI (UTI history should be carefully confirmed to ensure that prior UTIs were not actually contamination/asymptomatic bacteriuria)
    - Vesicoureteral reflux (particularly high-grade)
    - Antenatally diagnosed renal abnormality
    - History of urine withholding
    - Circumcision status
    - History of frequent or recent bladder catheterization
    - History of chronic (or recent) constipation
    - Diaper / toilet training status

PE:

- Growth (height and weight), development
- Blood pressure
- External GU exam: Evidence of vulvovaginitis or balanitis/posthitis, circumcision status
- Abdominal or flank tenderness
- Evidence of urinary tract obstruction
- Periorbital or extremity edema

Urine Evaluation: Who and How to Test (See Appendix II and III for flow chart).

Collection Method

- Choice of collection method should take into account the prior probability of UTI, the age of the child, parental preference, and the implications of a false positive or false negative result.

- In general:
    - Infants < 6 months of age should have urine collected by catheter
    - **For children >6 months of age who are toilet trained or can urinate into a cup (e.g. induced urination[4], opportunistic collection),** obtain urine via clean catch for UA and culture.
        - Parental supervision of pre-test cleansing and mid-stream clean-catch should be done to reduce contamination in children <6 years of age or older if developmentally appropriate.
    - For children >**6 months of age in whom clean catch is UNABLE to be obtained**, send bag or catheter specimen for UA. In children >1 year, if unable to obtain clean catch, bag preferred to catheter specimen for UA. If UA positive, send catheter specimen for culture.

- There is a role for shared decision making with parents in determining how to test for UTI. Some parents may prefer to test earlier at the time of initial presentation, even if fever has been less than 24-48 hours, to prevent a return visit, whereas others may want to limit intervention. Similarly, some parents may prefer a definitive result with catheter urine specimen for UA and urine culture, whereas some parents may refuse or strongly object to catheterization for any specimen.
    - *The UCSF PHM consortium strongly recommends that bag specimen NOT be sent for culture, but in the circumstance of parental refusal or inability to obtain a catheterized specimen, this method should be documented and stringent interpretation criteria should be applied when the culture result returns.*
- A negative **urinalysis (UA)** from a bag specimen has a similar negative predictive value to catheter specimen in average risk patients.
- Always document method of collection (catheter, bag, clean catch).
- A clean catch can be obtained in multiple ways, but generally refers to a midstream urine from a cleansed perineum into a sterile container.
- While this guideline does not apply to patients with known immunocompromised including neutropenia, it is important to avoid catheterizing patients who are known or suspected to be severely neutropenic.

1. Children with KNOWN RISK FACTORS for UTI (including but not limited to *multiple previous UTIs, known GU anomaly, high-grade VUR, recent catheterization, frequent or recent GU instrumentation*) – see Flowdiagram "Appendix 1"

- Presenting with:
    - Nonspecific symptoms (including but not limited to: fever without a source, abdominal pain, vomiting without diarrhea)

      OR

    - Focal signs/symptoms of UTI (including but not limited to: dysuria +/- fever, flank pain, suprapubic tenderness/pain

      - **Infants < 6 months of age**: Send catheter specimen for UA and urine culture.
      - **Infants >6 months of age:** Send bag, clean catch, or catheter specimen for UA. In children >1 year, if unable to obtain clean catch, bag preferred to catheter specimen for UA. If UA positive, send clean catch if able, otherwise send catheter specimen for culture.

2. Children WITHOUT known risk factors for UTI (see flowdiagram "Appendix 2")

a. All infants **<1 month of age with elevated, not otherwise explained, DIRECT (not indirect) bilirubin:** Catheterized UA and urine culture.

b. **Infants/children < 2 years of age (presenting with fever without a source):**

- **All infants < 3 months of** age with fever > 38 without apparent source (catheter collection for UA and urine culture)
    - UTI should also be CONSIDERED in infants < 3 months of age WITH an apparent viral source for fever, especially in uncircumcised boys and girls < 1 month of age
- **Girls and uncircumcised boys 3-6 months of age**, with fever >39 for > 24 hours (catheter collection for UA and urine culture)
- **Girls 6 months to 2 years of age, or uncircumcised boys 6-12 months of age**, with fever > 39 for > 24-48 hours
- Send bag, clean catch, or catheter specimen for UA. In children >1 year of age, if unable to obtain clean catch, bag preferred to catheter specimen for UA. If UA positive, send clean catch if able, otherwise send catheter specimen for culture.
- Could consider testing with < 24-48 hours of fever if other risk factors or historical findings are present (eg: dysuria, urine odor) in shared decision making with parents.

c. **Children > 2 years of age:**

- Presenting with **focal symptoms of UTI** (dysuria +/- fever, abdominal or back pain): Collect urine by bag or clean catch for UA. If UA positive, send clean catch if able, otherwise send catheter specimen for culture.
- Presenting with **fever without a source**: Consider UTI only in girls with fever > 39 for > 24-48hrs, AND particular concern for UTI (e.g. vague abdominal symptoms, developmental delay, parental concern, etc).

Collect urine by bag or clean catch for UA. If UA positive, send clean catch if able, otherwise send catheter specimen for culture.

Urinalysis (UA) Interpretation:

- Positive leukocyte esterase: very sensitive, but less specific for true infection (false positives are common)
    - Note: if no WBC on microscopy, more likely to be a false positive
- Positive nitrite: high specificity for UTI, but lower sensitivity
    - i.e. positive nitrite means likely UTI, but negative nitrite does not rule out UTI
    - Can also see positive nitrite in contaminated specimen if left at room temperature for too long
- Positive blood and protein: not specific for UTI
- Microscopy: >10 WBC/mm^3 is suggestive of UTI
- NOTE: UA should be interpreted in context of pretest probability (risk factors for UTI, urinary symptoms in child old enough to express them, etc)

Individual Risk Factors: Girls
White race Age < 12 mo Temperature ≥ 39°C Fever ≥ 2 d Absence of another source of infection

Probability of UTI	No. of Factors Present
≤1%	No more than 1
≤2%	No more than 2

Individual Risk Factors: Boys
Nonblack race Temperature ≥ 39°C Fever > 24 h Absence of another source of infection

Probability of UTI	No. of Factors Present	
	Uncircumcised	Circumcised
≤1%	a	No more than 2
≤2%	None	No more than 3

Figure 1: AAP 2011 Probability of UTI Among Febrile Infant Girls and Infant Boys According to Number of Findings Present. "a" Probability of UTI exceeds 1% even with no risk factors other than being uncircumcised.

When to send a culture:

- Urine cultures should be sent for **all children <6 months suspected of UTI** *regardless of UA results*
- Urine cultures should be sent for **all children < 12 year old with urinary symptoms and a positive UA** (+LE and/or +nitrites)

Urine Culture Interpretation

- **Results suggestive of true infection (not contamination or colonization):**

        - **+UA and >50,000 cfu/mL** of a *single uropathogen* from a catheter or clean catch specimen (2011 AAP UTI Guidelines)
        - Note: if bag specimen sent for culture because of parental refusal or inability to obtain catheter specimen, a higher threshold, such as >100,000 cfu/mL, should be used
- Presence of >1 organism or mixed urogenital flora are usually consistent with contamination. If there is strong clinical suspicion, repeat urine collection should be considered.

Additional Laboratory Studies:

- Blood culture: recommended for febrile infants < 3 months of age or toxic-appearing child of any age per guidelines for fever without a source in infants
- LP: recommended for all febrile neonates (<28 days) or <3 months if ill-appearing
- Test of cure after treatment: NOT routinely recommended
- Metabolic panel/electrolytes/lactate: NOT routinely recommended
- CBC and CRP: NOT routinely recommended

Imaging:

- Renal (and Bladder) Ultrasound
    - Recommended **during acute illness if clinical course is severe**, and/or patient not responding to treatment as expected (e.g. within 48 hours of starting treatment) in order to diagnose complications (renal abscess, stone, etc)
        - Note: Renal ultrasound during acute infection can be misleading in diagnosis of urinary tract abnormalities: *E. coli* endotoxin can produce dilation, which might be confused with hydronephrosis or obstruction; and edema can cause changes in the size and shape of the kidneys, along with the echogenicity of renal parenchyma.
    - Recommended for all **infants <6 months of age with first time febrile UTI** (NICE guidelines, see Reference 3)
        - Timing depends on clinical situation: for infants who respond well to therapy, and who have good outpatient follow up, renal ultrasound can be deferred to after acute infection has resolved (4-6 weeks). Ability to obtain a quality study and ability for patient to follow up should be taken into account.
    - Recommended for recurrent UTI without another explanation in infants < 2 years of age
    - Consider renal ultrasound in child <2 years of age with complicated UTI or UTI with atypical pathogen
- VCUG

- **NOT routinely recommended after first febrile UTI**
    - Indicated if renal ultrasound shows severe hydronephrosis, bladder hypertrophy or other findings that would suggest either high grade VUR or obstructive uropathy
  - Consider in infants (< 2 years of age) with recurrent febrile UTI AND abnormal ultrasound
  - Note: The most common reason for recurrent UTI in children >1 year of age is voiding dysfunction: children in this age group should have an evaluation for voiding dysfunction (post-void residual, referral to urology, etc) before they have a VCUG.
- DMSA scan
  - NOT routinely recommended in the evaluation of UTI

Management

Who Should Receive Empiric Antibiotics?

*Note: A "positive UA" for the purposes of these guidelines is defined as positive leukocyte esterase or nitrite. As above, if microscopy is available, it should be used to guide decision-making. UA findings should also be interpreted in the context of method of collection.

- Empiric antibiotics should be given to:
  - Child <3 months of age with positive UA
  - Child 3 months – 1 year of age who is FEBRILE with a positive UA
  - Any child with a positive UA who is ILL/TOXIC-APPEARING
- In a child 3 months to 12 years of age who is AFEBRILE and WELL-APPEARING, it is reasonable to consider withholding empiric treatment if UA is mildly positive or equivocal (e.g.: LE only, low WBC count) while awaiting culture results. Conversely, if the history is very consistent with UTI and positive UA, start treatment empirically

Table 1: Empiric Treatment

Condition	First-Choice Therapy	Alternative Therapy	Comments
Urinary tract infection, community-onset, 2 months-12 years of age, outpatient therapy	**Patient without significant recent antibiotic exposure or known urinary tract abnormalities:** Cephalexin 25mg/kg/dose PO TID (max 500mg/dose) **If significant prior antibiotic exposure or urinary tract abnormalities:** Cefdinir 14mg/kg/dose PO daily (max 600mg/day)	**Beta lactam allergy:** Trimethoprim-sulfamethoxazole (Bactrim/Septra) 4mg/kg/dose trimethoprim PO BID (max 160mg trimethoprim/dose)	For infants < 2 months, refer to UCSF Pediatric Antimicrobial Stewardship Program Empiric Therapy Guidelines (at idmp.ucsf.edu) for "Fever Without a Source – Young Infant" for initial therapy then narrow based on organism and susceptibilities **Duration:** UTI without fever: 7 days UTI with fever in younger child: 10 days
Pyelonephritis, community-onset, inpatient therapy	**Inpatient:** Ceftriaxone 50mg/kg/dose IV q24h (max 1g/dose) **If candidate for PO therapy:** Cefdinir 14mg/kg/dose PO daily (max 600mg/day) **Narrowing of therapy is recommended based on urine culture isolate susceptibilities.	**Beta lactam allergy:** Ciprofloxacin 15mg/kg/dose IV/PO BID (max 400mg/dose IV, 500mg/dose PO) **These guidelines are based on UCSF BCH-SF Empiric Therapy Guidelines. Other reasonable options for empiric therapy may be preferred based on facility-specific guidelines, formulary, or local ID or pharmacist consultation. The 2011 AAP UTI guidelines list Gentamicin 7.5mg/kg/day divided q8 hours as a reasonable option, but practitioners should be aware of the nephrotoxicity of this option and the need to check levels.	ID consult recommended for complicated infection or concurrent bacteremia **Duration:** Beta lactams: 10-14 days Ciprofloxacin: 7 days

Source: Benioff Children's Hospital – San Francisco Antimicrobial Stewardship Program: 2016 Empiric Antimicrobial Therapy Guidelines, at idmp.ucsf.edu

- ***Note: Consider follow up after 48-72 hours to assess response to treatment***

Admission Criteria:

- Clinically ill-appearing/toxic-appearance
- Severe dehydration/inability to tolerate PO liquids, requiring IV fluids
- Neonates (age <28 days of age) with fever
- Infants age 29-60 days of age with fever & positive UA
    - In most cases these patients should be admitted
    - In the case of a child who is very well-appearing and well-hydrated with good guaranteed follow up within 24 hours and reliable caregivers and no other high risk lab abnormalities, it is not unreasonable to discharge following a dose of IV/IM antibiotics with a prescription for oral antibiotics
    - All patients in this age group should have a blood culture prior to discharge.

- Urine culture positive for multi-drug resistant organism, without any good options for oral treatment
    - ID consult strongly recommended before admission in these patients: can help decide if admission is necessary as there may be oral antibiotic treatment options that are not apparent
- Unable to tolerate oral medications
    - If this is the only criteria for admission but the child is otherwise hydrating orally, consider other oral or IM options (e.g. flavoring medication, increased teaching, etc)
- Poor follow up
- Failure to respond to outpatient therapy
    - Most patients will become afebrile and show clinical improvement after 48-72 hours of adequate antibiotic therapy
- Positive blood culture
    - In many cases, routine UTI management may be appropriate, but not in all cases. Consult ID if there is clinical uncertainty.

Refractory UTI:

If patient remains febrile after 48-72 hours and/or is clinically worsening, consider suppurative complications as well as resistant or unusual organisms. Consider obtaining renal ultrasound.

If patient is stable, review culture results and consult ID prior to broadening antibiotics.

Treatment Duration:

- See Table 1 for full specific recommendations, but in general:
- Febrile Community-acquired UTI: 10 days
- Community-acquired UTI without fever: 7 days

Subspecialty Consultation:

- Pediatric Infectious Disease:
    - Consider for severe infection or concurrent bacteremia
        - Note: at BCH-SF, ID consultation is standard for all patients with positive blood cultures.
    - Consider if no response to treatment within 48 hours or fever >48-72 hours after starting treatment
    - If unusual organism or resistance pattern
    - If patient is severely immunosuppressed/immunocompromised or has other risk factors not covered in this guideline.
- Consider urology consultation for:
    - Urinary tract obstruction
    - Patient with known history of urologic abnormalities or recent instrumentation
    - Abnormal imaging
    - Recurrent UTI evaluation (voiding dysfunction, constipation, etc)

Discharge Criteria:

- Clinically improving with improving fever curve
- Adequate PO liquid intake and tolerating oral antibiotic
- Appropriate follow-up available

References

1. AAP Clinical Practice Guideline. Urinary Tract Infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. 2011. *Pediatrics*. 128,3: 595-610.

2. Marmor A. Evidence-based review of diagnosis and management of urinary tract infection in febrile infants/children <24 months of age. *UCSF Wiki.* March 2012.

3. National Institute for Health and Clinical Excellence. Urinary tract infection in children: NICE guideline. June 2010. https://www.nice.org.uk/guidance/cg54

4. The QuickWee trial: protocol for a randomised controlled trial of gentle suprapubic cutaneous stimulation to hasten non-invasive **urine collection** from **infants**.Kaufman J, Fitzpatrick P, Tosif S, Hopper SM, Bryant PA, Donath SM, Babl FE. BMJ Open. 2016 Aug 10;6(8):e011357. doi: 10.1136/bmjopen-2016-011357.

Published Children's Hospital Guidelines / Pathways

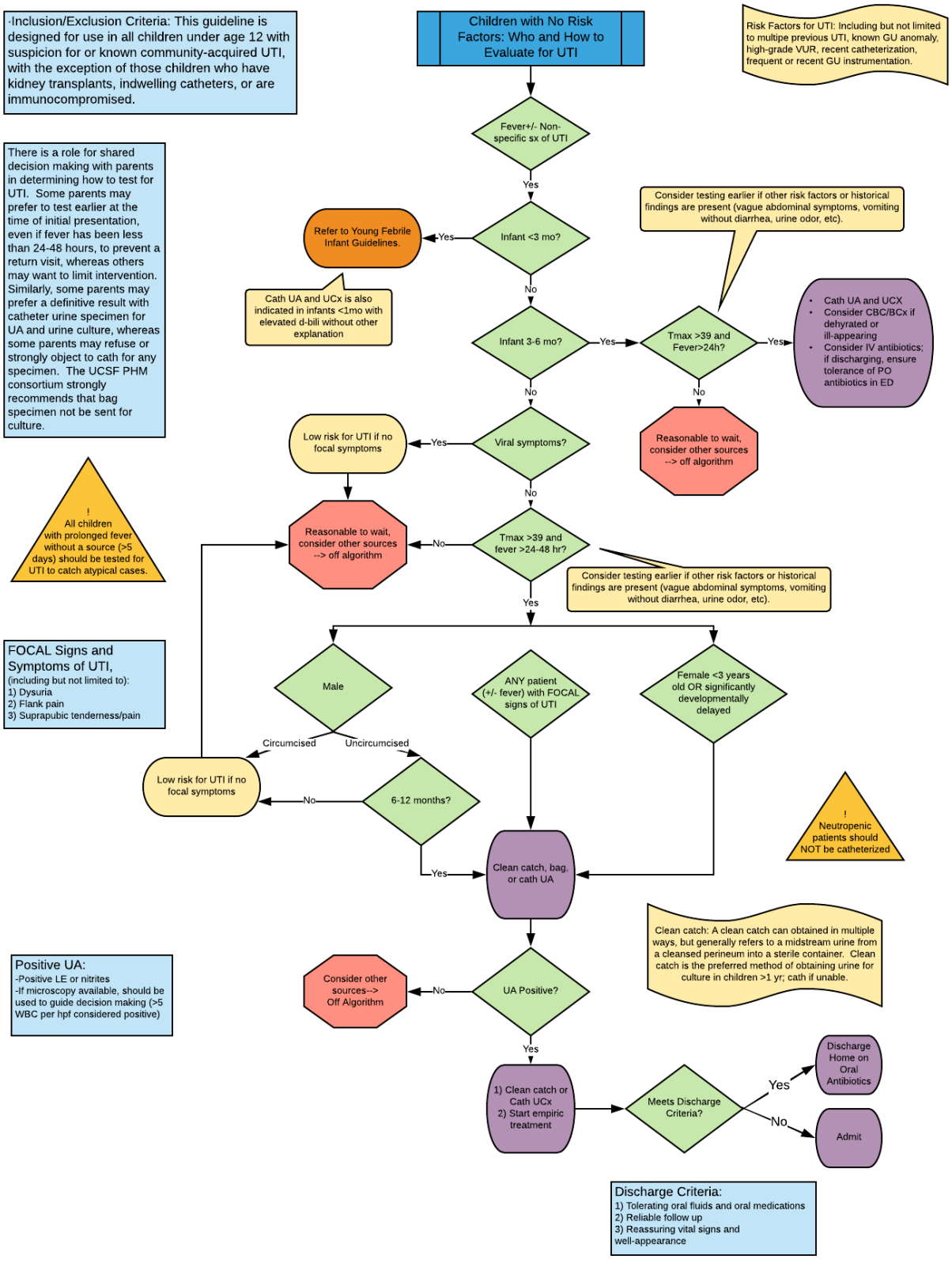
Children's Hospital of Philadelphia (CHOP)

Cincinnati Children's

Seattle Children's

UCSF BCH San Francisco, Pediatric Antimicrobial Stewardship Program BCH Community Acquired UTI Empiric Antibiotic Therapy Guildelines. http://idmp.ucsf.edu/pediatric-guidelines-urinary-tract-infections-community-onset

APPENDIX I: Who and How to Test for UTI: Children Without Known Risk Factors



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APPENDIX II: Who and How to Test for UTI: Children With Known Risk Factors