Summary of ESPID Guideline for Complicated Urinary Tract Infections in Children

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Based on:

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This summary should be read in conjunction with the full guideline in The *Pediatric Infectious Disease Journal* available here.

Definitions

- UTI (upper / pyelonephritis) is defined by
  - clinical characteristics (child with fever and suspected infection), and
  - inflammation of the urinary tract (urine analysis with pyuria), and
  - significant bacteriuria in culture.
- **Complicated UTI (cUTI) is defined by children with UTI who have an increased likelihood/risk of failing conventional management.**
- Risk categorized by:
  - localized risk: significant anatomical or functional urological abnormality, multiple recurrent UTI
  - generalized risk: neonates, non-urological underlying condition (renal and non-renal)
  - severe clinical presentations: sepsis, severe renal parenchymal disease.

Table 1: The five subgroups of cUTI defined in this guideline

	Subgroup	Reason for inclusion
1	Known significant anatomical or functional urological abnormality (including post instrumentation)*	High risk for complications (nephronia, abscess), high risk of recurrences or unusual pathogens especially when receiving prophylaxis
2	Multiple recurrent UTI**	High risk of unusual pathogens or undiagnosed urological disorder
3	Severe clinical presentation***	Toxic presentation, impaired renal function, not improved after 48 hours, extensive tissue involvement
4	Non-urological underlying conditions	Immunocompromised, renal transplant, diabetes, high risk for severe presentation, extensive tissue involvement (nephronia, abscess, emphysematous pyelonephritis) and unusual pathogens
5	Neonates	Immature immune system, high risk of bacteremia, high risk of unusual pathogens

* Not: grade I-II; non-dilating vesicoureteral reflux (VUR) or mild antenatal hydronephrosis
** Not: asymptomatic bacteriuria
*** Not: fever alone

Investigations and diagnosis

Initial investigations

- Patient history including
    - urological malformations and surgical/instrumentation history,
    - other medical history,
    - UTI recurrence and urosepsis.
- Urine collection via
    - clean catch,
    - catheterization or
    - suprapubic aspiration.
    - **indwelling catheter or urine bag is <u>not</u> adequate**.
- Urine analysis, culture and susceptibility testing in all children regardless of age and complicating features (**table 2**).
- Additional blood investigations for cUTI may include inflammatory markers, blood culture, urea, creatinine, and electrolytes (**table 2**).
- An acute ultrasound scan is helpful in some clinical situations (table 2).

Progress assessment

- Keep reassessing. If progress is not as expected at 48 hours, consider complications of infection and/or differential diagnosis, and investigate accordingly, rather than simply changing antibiotics.
- Repeat urine testing is only needed if there is inadequate response to treatment.

Table 2: Summary of diagnostic and other initial investigations in children with cUTI

Diagnostic investigations for children with suspected UTI	
Urinalysis	Required for all children with suspected UTI False POSITIVE: post-surgery/instrumentation, inflammatory condition, e.g. Kawasaki disease False NEGATIVE: neonates, pathogens with low inflammatory response, e.g. *Enterococcus* spp
Urine culture	Gold standard for UTI diagnosis False POSITIVE: contamination, children with functional urinary tract conditions False NEGATIVE: prior antibiotics, some severe parenchymal disease (nephronia, abscess)

Additional investigations for children with suspected/confirmed cUTI									
	Initial investigations					Further imaging to consider**			
Subgroup	Renal function tests	Acute phase reactants	Full sepsis work-up	Blood culture	Acute renal US***	CT	MRI/ MRU	DMSA scan	MCUG***
1 Known significant urological abnormality*	✓	✓			✓			✓	✓
2 Multiple recurrent UTI	✓							✓	✓
3 Severe clinical presentation	✓	✓		✓	✓	✓	✓	✓	✓
4 Non-urological underlying conditions		✓	✓		✓			✓	✓
5 Neonates	✓	✓	✓	✓	✓				

US – ultrasound, MCUG – micturating cystourethrogram, CSF – cerebrospinal fluid, MRI –magnetic resonance imaging, MRU – magnetic resonance urography

* Including post-surgery/instrumentation
** Not necessarily to be done in the acute period
*** Not routinely necessary in children where urological abnormalities have recently been diagnosed

Management

Initial antibiotic route

- For most children with cUTI, trial oral antibiotics initially (**table 3**): if not severely unwell, for isolated urological abnormality (including post-surgery or urological implementation), isolated tachycardia and for most underlying conditions.
- Exceptions to consider IV: significant urological abnormality (VUR grades IV-V or obstruction), sepsis (tachycardia when afebrile, prolonged capillary refill time, hypotension and/or severe dehydration), renal nephronia/abscess, neonates and infants <2 months, post renal transplant, and immunocompromise with febrile neutropenia.

Empiric antibiotic choice

- Different cUTI subgroups have different uropathogen prevalence.
- Do an individualized risk assessment for resistant organisms based on underlying condition, prior antibiotic use, past culture results, local resistance patterns (e.g. ESBL prevalence) and hospitalization.
- Based on these, an empiric regimen can be chosen that covers likely pathogens and incorporates likelihood of resistance (**table 3**).
- Patients with recurrent infections may initially be treated based on past culture results.
- For children on antibiotic prophylaxis, a different antibiotic choice should be made for breakthrough infection.
- Targeted de-escalated monotherapy is recommended according to susceptibilities once available.

Antibiotic duration and IV-oral switch:

- For most children with cUTI, there insufficient evidence to support varying from current practice of a total of 10-14 days.
- When IV antibiotics are started (see above), recommended IV durations vary between ≤3 days and ≤7 days depending on the cUTI subgroup and presence of bacteremia, with early switch when the child is afebrile and clinically well (**table 3**).
- Longer total durations (up to 21 days) may be needed for renal abscesses or nephronia. Renal US after 14 days assesses progress for duration.
- For a frequently relapsing UTI with the same organism, rather than simply extending duration, investigate for an ongoing focal source of infection e.g. renal abscess, stone, urinary tract diverticulum.

Supportive management:

- Additional management depends on the cUTI subgroup and complicating features.
- This may involve anti-emetics, fluid resuscitation and management and occasionally intensive care support. There is no role for steroids. Surgically, temporary diversion may be needed for urinary obstruction, and percutaneous drainage considered for renal abscesses.

Table 3: Antibiotic treatment for subgroups with cUTI, including route, choice, and duration

Subgroup	Route	Empirical choice examples/classes*	Duration (days)
1 Known significant anatomical/functional urological abnormality**			
Obstruction or VUR grade IV-V	Initial IV then PO	Aminoglycoside OR broad-spectrum B-lactam	IV: Until afebrile/well Total: 10-14
VUR grade I-III, other	PO	Narrow-spectrum B-lactam	Total: 10
2 Multiple recurrent UTI†			
Known past resistance	PO, IV if no PO	Use previous susceptibility: e.g. aminoglycoside, fosfomycin	Total: 7-10
High risk*** of resistance	PO	TMP/SMX or quinolone	Total: 7-10
Low risk of resistance	PO	Narrow-spectrum B-lactam	Total: 7-10
3 Severe clinical presentation			
Sepsis (tachycardia when afebrile, low BP prolonged CRT, severe dehydration)	Initial IV then PO	Broad-spectrum B-lactam	IV: Until afebrile/well Total: 10-14
Extensive renal parenchymal disease (nephronia, abscess)	Initial IV then PO	Broad-spectrum B-lactam OR aminoglycoside	IV: Until afebrile/well Total: 14-21
4 Non-urological underlying conditions			
Other renal impairment	PO	Narrow-spectrum B-lactam or TMP/SMX	Total: 10
Non-renal: Immunocompromised	FN: IV then PO Otherwise: PO	IV: broad-spectrum or anti-pseudomonal B-lactam. PO: broad-spectrum B-lactam or TMP/SMX	IV: Until afebrile/well Total: 10
Non-renal: Other	PO	Narrow-spectrum B-lactam	Total: 7-10
5 Neonates and infants <2m			
With bacteremia	Initial IV then PO	Aminoglycoside ± narrow-spectrum B-lactam	IV: ≤7 Total: 10-14
No bacteremia	Well + >1m: PO Otherwise: Initial IV then PO	B-lactam (1st gen cephalosporin, amoxicillin-clavulanate) Aminoglycoside ± narrow-spectrum B-lactam	Total: 10-14 IV: ≤3 Total: 10-14

VUR = vesicoureteric reflux, CRT= capillary refill time, BP= blood pressure, FN=febrile neutropenia, B-lactam= beta-lactam antibiotic, TMP/SMX=trimethoprim/sulfamethoxazole, BBD=bowel-bladder-dysfunction, MDR=multi-drug-resistance

* Narrow spectrum B-lactam as per this guideline include amoxicillin/ampicillin, amoxicillin-clavulanate, 1./2.generation cephalosporin.
Broad-spectrum B-lactam as per this guideline include: 3./4.generation cephalosporin, piperacillin, piperacillin-tazobactam, carbapenems.

** Including post-surgery/instrumentation; if urological abnormality has led to recurrent UTIs, consider broad spectrum antibacterial empiric choice

*** *High risk of resistance* as per this guideline include recent (<3 months) treatment with broad spectrum antibacterial, underlying urologic abnormalities/CAKUT or functional abnormality/BBD, recent travel to areas with high antibacterial resistance, household member with known MDR Enterobacteriaceae

† If other cUTI group (e.g. urological abnormality or severe presentation) follow appropriate recommendations

Further management and follow-up

Antibiotic prophylaxis

- The benefit of continuous antibiotic prophylaxis (CAP) remains controversial and is reserved for cUTI subgroups (**table 4**).
- In neonates, amoxicillin is the drug of choice, while older children are recommended to use trimethoprim-sulfamethoxazole or nitrofurantoin.
- Duration of CAP should not exceed 3-6 months followed by critical reevaluation.

Further imaging

- Post acute infection, urinary tract US may help define urological abnormalities (**table 4**).
- US/CT/MRI can be useful to follow a renal abscess.
- MCUG and DMSA were done more extensively in the past but now are saved for specific instance where less invasive investigations do not give enough prognostic information, usually for children with severe urological abnormalities.

Referral

- Consult with a pediatric infectious diseases (PID) specialist in cases of resistant organisms and atypical progression.
- Where there is ongoing risk of renal damage that is unlikely to improve without surgical intervention, refer to a pediatric nephro/urology team. This is most common for children with significant urological abnormalities including high-grade VUR.

Table 4: Follow-up of cUTI subgroups (antibiotic prophylaxis, imaging, referral)

Subgroup	Continuous antibiotic prophylaxis	Imaging				Urology referral
		Ultrasound	MCUG/ DMSA	MRI/ CT	Other	
1 Known significant anatomical/ functional urological abnormality	• Spina bifida with high-grade VUR and/or CIC • High-grade VUR (III-IV) • Bladder/bowel dysfunction • Severe obstructive uropathy until surgical correction	Uroflowmetry for bladder/bowel dysfunction (as per local availability)				Persistence of high-grade VUR, evaluation of bladder function (urodynamics), intervention for bladder/bowel dysfunction
		✓ (acutely)	±		Uroflow-metry	
2 Multiple recurrent UTI***	• >3 UTI in 12 months	✓**	±		Cystoscopy	Consider evaluation of bladder function
3 Severe clinical presentation	Not routinely if first episode	✓ (acutely)	±	±		Persistence of high-grade VUR
4 Non-urological underlying conditions	Not routinely if first episode	✓ (acutely)	±	±		If cUTI interferes with underlying condition
5 Neonates and infants <2m	• High-grade VUR (III-IV) • Antenatal hydronephrosis (HN) • Ureteric dilatation and HN • HN and no circumcision	✓ (acutely)			Depends on pathology	High-grade VUR and complex anatomy

* Evidence only exists for antibiotic prophylaxis; recommendations for further imaging and referral are based on expert opinion and synthesis of other recommendations.
** If previous examinations are in the past (years)
*** UTI diagnosis based on adequate urine sampling method (see above). Do not include asymptomatic bacteriuria detection.