


GUIDELINES

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Egyptian pediatric clinical practice guidelines for urinary tract infections in infants and children (evidence based)

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Abstract

Background: National evidence-based recommendations for diagnosis, treatment, imaging, and follow-up in urinary tract infection are crucial being a major health problem in pediatrics. Every region should follow international recommendations with respect to the disease local profile and available facilities for that area.

Methods: Based on AGREE II (the assessment tool of practice guidelines), Egyptian CGLs used *American Academy Pediatrics, *European Association Urology, European Society Pediatric Urology, and *Asian Association Urinary tract infections as its evidence-based references. Health questions were listed for evidence base answers adopted from selected CGLs after their permission. Key statements were approved by all members and further approved by the Egyptian Pediatric Guidelines Committee after local and international external peer reviewing.

Results: (1) Diagnosis recommendations: Urine culture with diagnostic colony counts is essential for diagnosis. Catheter samples are important for critical cases and non-toilet-trained cases *especially* when they show significant bacteriuria and pyuria. (2) Treatment plan included areas of debate as choice of antibiotic, oral versus intravenous, duration, antibiotic prophylaxis considering age, disease severity, recurrence, + risk factors, and imaging reports. (3) Imaging recommendations were tailored to suit our community. Renal bladder ultrasound is important for children with febrile UTI, due to the high prevalence of congenital anomalies of the kidney and urinary tract, paucity of prenatal ultrasound, and lack of medical documentation to reflect previously diagnosed UTI or US reports. We recommend renal isotopic scan and voiding cystography for serious presentation, high-risk factors, recurrence, and abnormal US. (4) Urological consultation is recommended: in urosepsis or obstruction, male infants < 6 months. Acute basal DMSA is recommended in congenital renal hypodysplasia. Six months post-infection, US and DMSA are recommended in severe pyelonephritis and vesico-ureteric reflux, where those with abnormal US or DMSA or both should have voiding cystography. (5) Follow-up recommendations include family orientation with hazards of noncompliance and monitoring at pregnancy.

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Conclusion: Diagnosis and treatment show strong recommendations. Imaging depends on patient assessment. Referral to a pediatric nephrologist and urologist in complicated cases is crucial. Follow-up after the age of 16 years in adult clinics is important.

Keywords: Evidence based, Guidelines, Urinary tract infections, Infants and children

Background

Most clinical guidelines for urinary tract infections (UTIs) come from Western countries, some from Asia, and almost none from Africa. The aim of these clinical guidelines is to have key statements that respect evidence-based international recommendations tailored to suit the community. These guidelines address the evaluation, diagnosis, and treatment of UTI in infancy and childhood. While the recommendations are suitable for the Egyptian community, international stakeholders can modify specific contents as needed, when system-level barriers hamper adoption of the best practice recommendations. The prevalence of symptomatic and asymptomatic bacteriuria in Egypt ranges between 22 and 14.6 and 11.4% [1–3]. The chief organisms were reported to be *Escherichia coli*, *Klebsiella*, *Proteus*, and *Pseudomonas* [4]. Vesico-ureteric reflux (VUR) is reported in 18–22% and renal scarring in 8–33% [4]. Congenital anomalies of the kidney and urinary tract (CAKUT) account for 44–33% of children with end-stage renal disease (2015/2017; Egyptian registry for ESRD) compared to 7% in the US 2005 registry [5]. Grading of risk factors associated with UTI has been reviewed by the Italian Society of Pediatric Nephrology (PN) [6]. The diagnosis of UTI depends on clinical features confirmed with significant bacteriuria. The plan of radiologic imaging should consider the safety, sensitivity, and limitations of different modalities. Therapy depends on the severity of the clinical features.

Methods

A Pediatric Nephrology Work Group (PNWG) was constituted with members from all universities. None of the participants had competing interests or potential

conflicts. During 2017–2018, the work group reviewed the pediatric literature specifically guidelines to select those suitable to our community. Updates were based on evidences generated over the past decades and adapted from the Asian Association Urinary tract infection/ Sexually transmitted diseases (AAUS), European Society Pediatric Urology (ESPU), European Association Urology (EAU), and American Academy Pediatrics (AAP) to cover diagnosis, treatment, imaging, and follow-up. Based on AGREE II [7], guidelines from AAP, AAUS, and EAU/ESPU were selected as references for adoption or adaptation [8–10]. AGREE II (2017) is the new international tool for the evaluation and assessment of practice guidelines (Table 1). It is valid and reliable, comprises 23 items organized into 6 quality domains for scoring with the final overall rating report [7]. Clinical questions (Table 2) were put in PICOH format (Patient population, Intervention, Professionals, Outcomes, Healthcare settings/content) (Table 3) [11, 12], searching for evidence-based answers. Evidences were reviewed by a clinical epidemiologist to revise its reference and quality (which guideline? evidence level rating? adopted or adapted?). Recommendations were formulated and peer reviewed followed by a re-review by the working group [11]. The guidelines were adopted in 2018, with a proposed update in 2021.

Evidence levels and recommendation grades

Evidence-based practice uses the best current evidence in making decision about the care of the patient when grading recommendations. Levels of evidences called hierarchy of evidence are assigned to studies based on the methodological quality of their designs, validity,

Table 1 Agree II

AAP 2012	Total	Final score	Asian 2015	Total	Final score	European 2014	Total	Final score
Domain 1	139	79.90%	Domain 1	97	91.11111111	Domain 1	32	72.22222222
Domain 2	121	67.40%	Domain 2	93	86.66666667	Domain 2	30	66.66666667
Domain 3	341	72%	Domain 3	242	84.16666667	Domain 3	81	67.70833333
Domain 4	127	71.50%	Domain 4	94	87.77777778	Domain 4	31	69.44444444
Domain 5	161	67.20%	Domain 5	110	75	Domain 5	36	58.33333333
Domain 6	84	70.80%	Domain 6	62	86.66666667	Domain 6	21	70.83333333
Total domain	973	71.50%	Total domain	698	84.49275362	Total domain	231	67.02898551
Overall agreement	46	79.20%	Overall agreement	29	80	Overall agreement	10	66.66666667

Table 2 Health questions**Health questions used to develop this adapted CPGL**

These questions concern children 1 month to 16 years with UTI, attending the primary health care service units treated by general pediatricians or general physicians and those managed in specialized Pediatric Nephrology units. They aim to identify those with risk factors, recurrent or complicated presentations, improve child's symptoms, prevent complications, and shorten the duration of hospital admission.

1	What are the risk factors of UTI that should be searched for?
2	When the suspicion of UTI would be aroused?
3	When to ask for urine analysis? What tests to ask for?
4	When would the physicians ask for a urine culture? What is the best technique to get the urine sample for culture?
5	When to start empirical antibiotics and which to be used? Oral or parenteral? Duration?
6	What is the duration of antibiotic therapy proved by culture?
7	When the suspicion of resistance to the therapy would be aroused?
8	When to recommend prophylactic antibiotic?
9	When further blood investigations would be requested, such as kidney function, acute phase reactants and complete blood count?
10	When would the general practitioner refer patients to specialized PN care services and pediatric nephrology units?
11	When to refer to the urologist?
12	When would the physicians request abdominal ultrasound? When and what further imaging might be needed?
13	Follow-up recommendations and suggested documentation.

and applicability to patient care, thus given the grade or strength of recommendation (Fig. 1). The highest levels are designed to be unbiased with less risk of errors and fit to guide practice decisions. Strong evidence includes clinical practice guidelines using systematic reviews with meta-analysis, systematic reviews alone, randomized controlled trials, and non-randomized control studies. The weakest level of evidence includes authorities' opinion or expert committee report. The following Table 4 represents an example for evidence level and recommendation grading as an example used by the Spanish Argon Institute of Sciences.

Results

Key statements (diagnosis, treatment, imaging, follow-up) Diagnosis recommendations

The diagnosis of UTI The diagnosis of UTI is difficult in neonates and infancy where fever without a focus may be the chief presentation. Clinical features alone may not be sufficient to diagnose UTI. Confirmatory laboratory tests are required (LE1a, GR: A; EAU/ESPU) (LE: 1, GR: A; AAUS).

Clinical features of lower UTI as well as upper in relation to age are shown in Table 5 [13].

Features suggestive of UTI or predicting kidney damage (risk factors) include recurrent fever of unknown focus, previously suggested or confirmed UTI, poor urine flow or abnormal voiding pattern, constipation or bladder bowel dysfunction BBD, abnormal fetal ultrasonography, family history of renal disease, abnormal back and spine, abnormal external genitalia, e.g. phimosis or fused labia (EL2) (AAP), females (EL3) (AAP), uncircumcised boys (EL3) (AAP), formula feeding (EL2), and hygiene [6, 13–17].

When to ask for urine tests? Infants and children with features suggestive of UTI, fever ($\geq 38^{\circ}\text{C}$) without localization or with an alternative site of infection who remain unwell and refractory to treatment (EL3) (AAP 2011, AAP 2019) [10, 18].

What urine tests are needed? Urine analysis (dipsticks for nitrites and leukocyte esterase and microscopy for pus cells and bacteria). Urine culture should be done in all cases.

When to ask for a urine culture? Age <3 years, recurrent UTI, positive result for either nitrites or leukocyte esterase or both, clinical symptoms do not fit with dipstick, suspecting pyelonephritis APN, no response to antibiotic treatment after 48 h, and those who are seriously ill [19].

Table 3 PIPOH model

Modified ADAPTE Tool 6 Health Questions (PIPOH) Checklist	
PATIENT POPULATION (P)	
Gender: Male <input type="checkbox"/> Female <input type="checkbox"/> both genders <input type="checkbox"/>	
Age group: Child <input type="checkbox"/> Adult <input type="checkbox"/> Elderly <input type="checkbox"/> Specific age: ___ 1 month to 16 years (Years)	
Disease/condition: ___ first attack and recurrent attacks _____	
Comorbidity: No <input type="checkbox"/> Yes <input type="checkbox"/>	
If yes, Specify: _____	
INTERVENTION (I)	
Diagnosis <input type="checkbox"/> Specify: _____ (e.g. clinical, laboratory, radiological/ imaging, ... etc. or All)	
Treatment <input type="checkbox"/> Specify: _____ (e.g. medical, pharmacological, , physiotherapeutic, urologist if abnormal resultsetc. or All)	
Prevention <input type="checkbox"/> Management (All) <input type="checkbox"/>	
PROFESSIONALS (P)	
Physicians <input type="checkbox"/> Clinical Specialty: ___ primary health care physician, nephrologist, urologist, and radiologist. _____	
Nurses <input type="checkbox"/> Specify: _____	
Pharmacists <input type="checkbox"/> Specify: _____	
Allied Health Professionals <input type="checkbox"/> Specify: _____ (e.g. technicians, therapists, ... etc.)	
OUTCOME(S) (O)	
Primary (specific) outcomes: ___ diagnosis and treatment of children with UTI _____	
Secondary (general) outcomes: Specify: ___ identification of highly risk patients, prevention of complications and shorten the duration of hospital stay. Prevent recurrence of UTI. _____	
Others: reduce incidence of late complication such as CKD, HTN and pregnancy related complications _____	
HEALTHCARE SETTINGS/ CONTEXT (H)	
Type: Primary <input type="checkbox"/> Secondary <input type="checkbox"/> Tertiary <input type="checkbox"/>	
Healthcare Sector:	
Governmental : MoH <input type="checkbox"/> University <input type="checkbox"/> Military <input type="checkbox"/> Health Insurance Organization <input type="checkbox"/>	
Other: Specify: _____	
Non-Governmental: NGO <input type="checkbox"/>	
Other: Specify: _____	
Hospital <input type="checkbox"/> Specify: ___ governmental and non-governmental _____	
Specify Department: _____ pediatric _____	
Outpatient Clinic <input type="checkbox"/> Specify: ___ governmental and non-governmental _____	
Other: <input type="checkbox"/> Specify: _____	

How to collect the urine sample? Pre-toilet-trained children who are seriously ill, with or without suspected UTI, require urgent antibiotic therapy. We recommend urine to be collected by either bladder catheter or suprapubic aspirate (SPA) (EL3, GR: A; AAUS); since SPA is a painful procedure, we prefer catheterization. When UTI is less suggested and the clinical features are not serious to indicate immediate therapy with antibiotics, urine may be collected by a urine bag; positive or equivocal results are confirmed with a catheter sample. The Quick Wee voiding stimulation method is also suggested as an option [18–20]. For toilet-trained children, a clean-catch mid-stream morning sample is recommended (Fig. 2).

How to interpret results of the urine analysis? The nitrite test is not a sensitive marker because

Pseudomonas and most gram-positive bacteria do not produce nitrites. The test may also be negative with frequent voiding. Overall, the test has a sensitivity of 79% and a specificity of 87%. Results of leukocyte esterase are not reliable. The test has a sensitivity of 50% and a specificity of 98%. Dipstick test, with positive either LE or nitrites (sensitivity 88%, specificity 79%) or both (sensitivity 45%, specificity 98%), is helpful for the diagnosis [13]. Leukocyturia and bacteriuria: Patients with febrile UTI show leukocytes in urine with a low count. Low count bacteriuria with multiple pathogens and no leukocyturia suggest contamination. Bacteriuria without pyuria in asymptomatic patients is interpreted as asymptomatic bacteriuria [18, 21]. Urine samples should be refrigerated to avoid the overgrowth of organisms. Urine culture is the gold standard to diagnose UTI. The cutoff

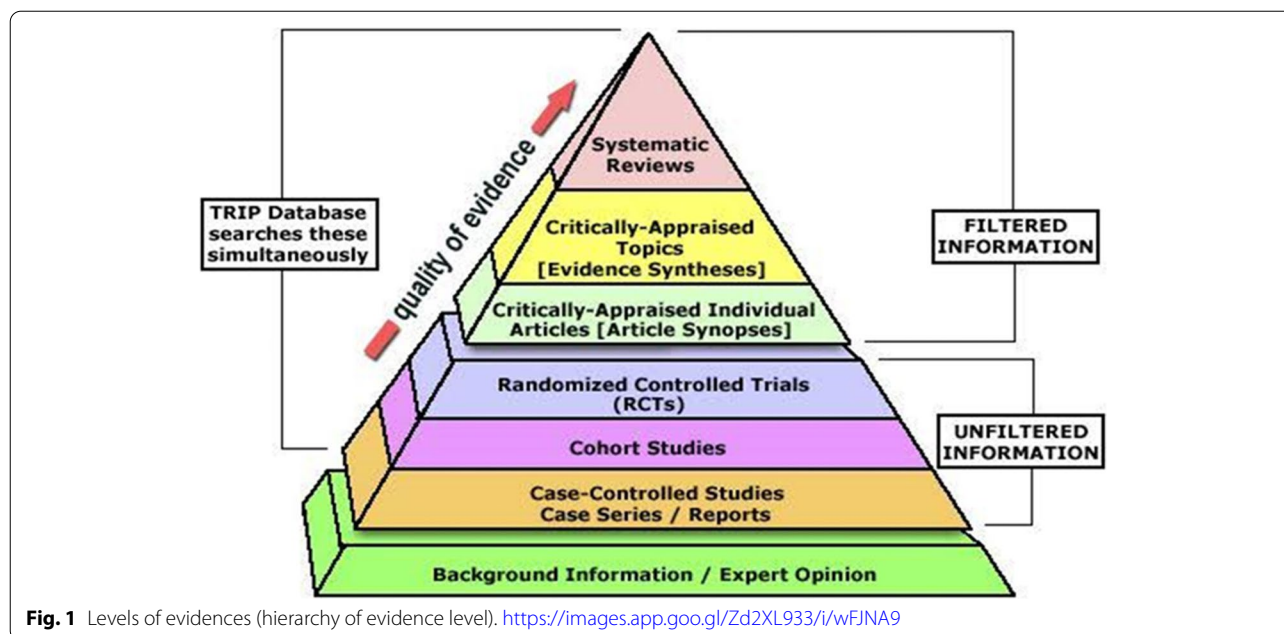


Fig. 1 Levels of evidences (hierarchy of evidence level). <https://images.app.goo.gl/Zd2XL933/i/wFJNA9>

Table 4 Level of evidence and grades of recommendation based on study design

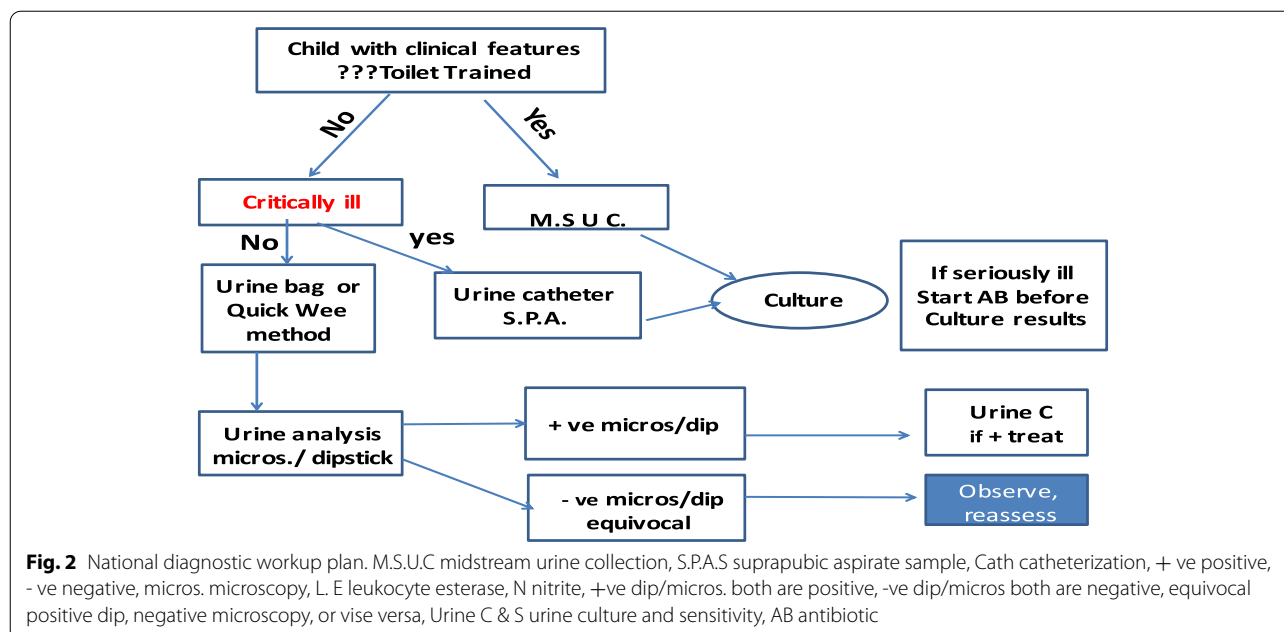
Level of evidence	
LE: I a	*Systematic review
LE: I b	*Level 1 studies masked comparison with a valid reference test, adequate spectrum of pt.
LE: II	Level II studies (have one of these *unrepresentative sample *inadequate comparison with the reference standard *unmasked comparison, case-control studies) *Systematic review of level II studies
LE: III	*Level III studies (have 2 or more described in level II studies) [12]
Grades of recommendations	
GR: A	*At least one meta-analysis, systematic review, or clinical trial rated 1++ , body of evidence of studies rated 1+ with the overall consistency of results
GR: B	*Body of evidence of studies rated 2++ applicable to the target, with the overall consistency of results or *Evidence extrapolated from studies rated 1++ and 1+
GR: C	*Body of evidence of studies rated 2+ applicable to the target, with the overall consistency of results *Evidence extrapolated from studies rated 2++
GR: D	*Evidence level 3 or 4 or extrapolated from studied 2+ *CGLs for UTI in children Argon Institute of Health Sciences (1+CS), 2011, SNS CGLs (1+CS) No 2009/01 [12].

Rating evidence level in Egyptian National CGLs was related to its reference guideline as adopted after their permission. AAP used L1, L2, and L3. AAUS used L1, L2, and L3 and GR: A, B, C, and D. EAU/ESPU used L1a, L1b, and L2 and GR: A, B, C, and D

Table 5 Clinical features in relation to age

Age group	Symptoms and signs
Infants and preverbal children	Fever, vomiting, lethargy, irritability, poor feeding, failure to thrive, abdominal pain, jaundice, hematuria, offensive urine, crying on passing urine
Verbal children	Dysuria, frequency, urgency, new-onset incontinence, abdominal or flank pain, suprapubic discomfort, vomiting, fever, hematuria, cloudy or offensive urine

level of bacterial count to diagnose infection depends on the method of urine collection. Urine culture is considered positive if the catheter sample has $\geq 50,000$ CFU/ml of micropathogen (EL 3) or clean-catch sample $\geq 100,000$ CFU (EL3) [18]. Other tests as blood leukocyte count, C-reactive protein, and erythrocyte sedimentation rate are not helpful to diagnose upper UTI. Procalcitonin is a satisfactory marker for renal parenchymal affection (LE3, GR: B; AAUS) [22].



The diagnostic workup is summarized in Fig. 2.

Treatment recommendations

When to start antibiotic therapy (AB)? We recommend to start empiric AB immediately after a urine sample is taken for culture in those with serious condition, recurrent presentation, with risk factors, or showing high clinical suspicion index of UTI (L2GR:A.AAUS). The reason behind that is to improve the clinical condition and prevent bacteremia and renal damage (L2GR:B.AAUS) [6, 22].

Which antibiotic to use? The choice of empiric AB depends on patient age, severity of clinical presentation, localization of UTI, expected pathogen, and resistance pattern in the community (L2GR: A, AAUS). Final AB to be adjusted after cultural results (L2GR: B; AAUS) [8, 22]. Common empiric parenteral AB are ceftriaxone, cefotaxime, ceftazidime, gentamycin, and tobramycin. Common empiric oral AB are amoxicillin clavulanate, trimethoprim sulfamethoxazole, cefixime, and cefpodoxime [9].

Which route? Initial therapy with oral or parenteral is equally efficacious for children >3 months with uncomplicated UTI. IV is indicated in young age, septicemia, vomiting or diarrhea, noncompliance, and complicated UTI (L2GRA, AAUS) [8, 22]. Treatment plan: For

infants and children with cystitis, we recommend oral AB for 3–5 days, e.g. cephalosporins 50–100mg/kg or TMP 5–6mg/kg, or TMP/sulfamethoxazole 56mg/kg, or amoxicillin/clavulanic 37.5–75mg/kg, or nitrofurantoin 3–5mg/kg. If the patient remains unwell, reassess and send urine for culture/sensitivity, in case another diagnosis has not been made. For patients with uncomplicated pyelonephritis, who are older than 6 months of age and who show normal US, we recommend to start oral empiric AB as cephalosporin and readjust after culture results (for 7–10 days total duration). If remains unwell, re-culture and refer to pediatric nephrologists. For complicated pyelonephritis, for all ages, we recommend parenteral ceftazidime and ampicillin or aminoglycoside and ampicillin for 7 days to be shifted to oral route when clinical condition allows (L1, B) (EAU/ESPU 2014) [9]. No sufficient data is available to compare 7- versus 14-day treatment course for APN. If gentamicin is prescribed, a single daily dose is recommended with monitoring renal function (L2) (AAP) [18, 23].

When to hospitalize? Infants and children of any age with serious presentation or infants < 3 months with suspected UT or infants and children with a previous diagnosis of complicated or recurrent UTI (reflux, malformation, obstruction, renal scars) or those with atypical presentation as associated hypertension, proteinuria, anemia, and impaired renal functions should be hospitalized with immediate sepsis screen and urine culture and parenteral antibiotic (L1, B) EAU/ESPU [9],

(L2, GR: C; AAUS) [22]. Resistance to AB occurs with urologic anomalies, obstruction, resistant pathogen and in infants < 3months. Clinical examination of these cases shows fever, flank tenderness, and mass with leukocytosis, azotemia, and US report obstruction (L2GRB AAUS) [24–26].

When to recommend AB prophylaxis? The potential benefit of preventing recurrent UTI with AB prophylaxis should be weighed against the risk of AB resistance in future infections (L2GR: B AAUS) [22]. Therefore, it is considered in recurrent UTI with and without VUR. It is also indicated to prevent infection in grade (III–V) VUR (L1 b, GR: B) [23, 27]. Asymptomatic bacteriuria (no symptoms, significant bacteriuria, no pyuria) should not be treated with antibiotics (LE2, GR: B) EAU/ESPU, AAP [9, 18, 27].

When to refer to pediatric nephrologists? Infants < 3months age, serious presentation at any age, presence of RF, recurrent course, abnormal US, resistance to AB therapy, associated proteinuria, hypertension anemia, impaired kidney functions (consensus).

When should you ask for urologic consultation? Seriously ill suspecting urosepsis (LE1a, GR:A) (EAU/ESPU), obstruction (patient is oliguric with bladder or renal mass) (LE1b, GR:A) (EAU/ESPU), resistance to AB recommended by culture (LE2a, GR:B), abnormal US

suggesting obstruction, VUR, malformation (LE2a, GR:B EAU/ESPU) [9], voiding disorder, abnormal genitalia, sacral agenesis (L2, GR:B, AAUS) [22] for interference (nephrostomy, stent, diversion), and imaging plan (LE2a, GR:B) (EAU/ESPU) [9] (Fig. 6).

Imaging recommendations

Imaging studies are not routine investigations in every case with UTI. It is recommended by most clinical guidelines in recurrent, serious, resistant, positive high-risk factors (HRF) as < 6 months age boy, positive family history, and non-*E. coli*. They are either basal or follow-up [6, 18]. The aim of imaging is to localize the site of infection, look for anomalies or obstruction, VUR, and congenital or acquired renal scars (LE: 2, GR: B) (AAUS) [6, 10, 18, 22].

When and why to ultrasound? RBUS is the first recommended imaging tool. Most CGLs recommend US in UTI; when serious presentation, or high-risk patients, or recurrent UTI, or antibiotic resistant, or suspected obstruction [6, 9, 10]. AAUS recommends its routine use for any child with febrile UTI as soon as possible (L3, GR: C) (AAUS 2015) [22] and EAU/ESPU 2014 supports this if unavailable prenatal or pre-existing ultrasound (L2aGR: B) (EAU/ESPU) [9]. Tsai added to be followed 6 months later in children with severe acute pyelonephritis (APN) and those with vesico-ureteric reflux (VUR) (LE3, GR:

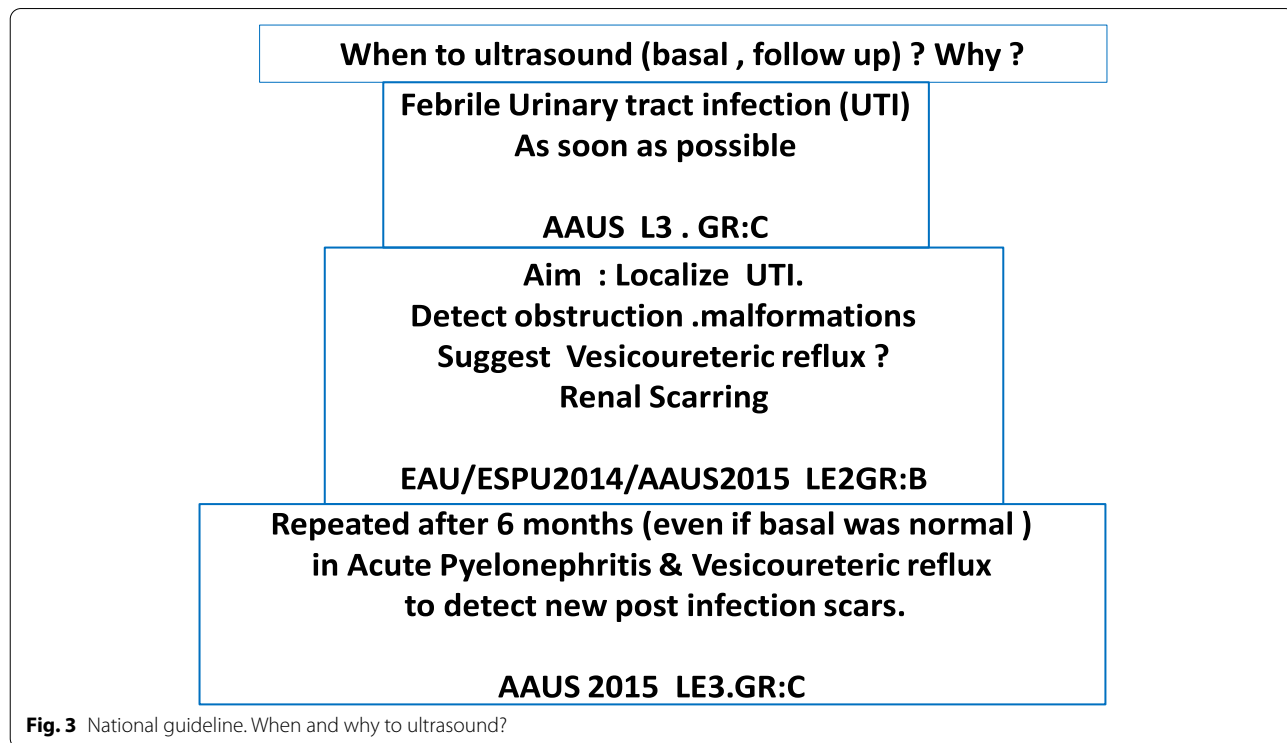


Fig. 3 National guideline. When and why to ultrasound?

C) (AAUS) (Figs. 3 and 4) [22]. The NICE group did not recommend it in the simple responsive first episode of febrile UTI if older than 6 months waiting for recurrence, and considered US essential only for complicated and recurrent cases of any age. The NICE group also avoided its use in the acute phase (except in atypical complicated cases) to avoid false-positive data [18, 28].

National CGLs recommend:

- Basal US imaging in UTI for any patient with febrile UTI and not only those with recurrent, resistant course or RE, once culture results are confirmative and not to wait for 6 weeks after (LE3, GR: C) (AAUS 2015) [9, 22, 28]. Our reasons rely on the high prevalence of congenital anomalies of the kidney and urinary tract (CAKUT) in our community (34–44% of ESRD), paucity of the antenatal US or patient documentation for previous UTI episodes or US reports, and family noncompliance for follow-up. US affords screening for malformations as well. Of note, in a cohort study of 107 Egyptian CAKUT patients (age range 2 weeks to 13 years), UTI was a predominant manifestation in 76% of patients, both obstructive and non-obstructive CAKUT patients, hence the paramount importance of imaging in pediatric UTI [29]. It is better to be as soon as possible to avoid family noncompliance with dropout for postponed imaging.
- We also recommend that whenever basal US suggests obstruction, congenital renal scarring, VUR, and also

when the patient is a male infant < 6months, infants of either sex, or with a serious presentation at any age or with abnormal genitalia, urological consultation must be done. These patients may need urgent interference (ureteric diversion, stents) or further imaging as mercaptoacetyltriglycine diuretic renogram (MAG3), voiding cystourethrography (VCUG), dimercaptosuccinic acid scan, and acute DMSA (ADMSA) [9, 28] (Fig. 6).

- These CGLs also recommend, for those with acute pyelonephritis (APN), or those with VUR, to repeat ultrasound (follow-up US) 6months after an acute episode of UTI to report for new scars (LE2, GR:C) (AAUS) [9, 22] (Figs. 3 and 4). European CGLs confirmed the US role in all forms of UTI for making further imaging plans as DMSA and VCUG as being more sensitive in the diagnosis of VUR or renal scars (LE2a EAU/ESPU) [9]. US follow-up in recurrent cases is essential to follow renal growth as well [4] (Figs. 3 and 4).

When and how to extend imaging behind US (Reno gram/VCUG) (Figs. 3, 4, and 5) Because of the limited sensitivity of US in the diagnosis of VUR and renal scarring, Egyptian CGLs 2018, AAUS 2015, and EAU 2014 recommended to extend imaging behind US to DMSA and VCUG for severe acute pyelonephritis, vesico-ureteric reflux, abnormal basal or 6months post-infection follow-up US, recurrent UTI, and presence of risk factors (RFs) (L3GR:C, L2GR:B AAUS15) [22] (Figs. 4 and 5). NICE 16 recommends to extend the imaging plan behind RBUS only for atypical, recurrent, young age below 3 years,

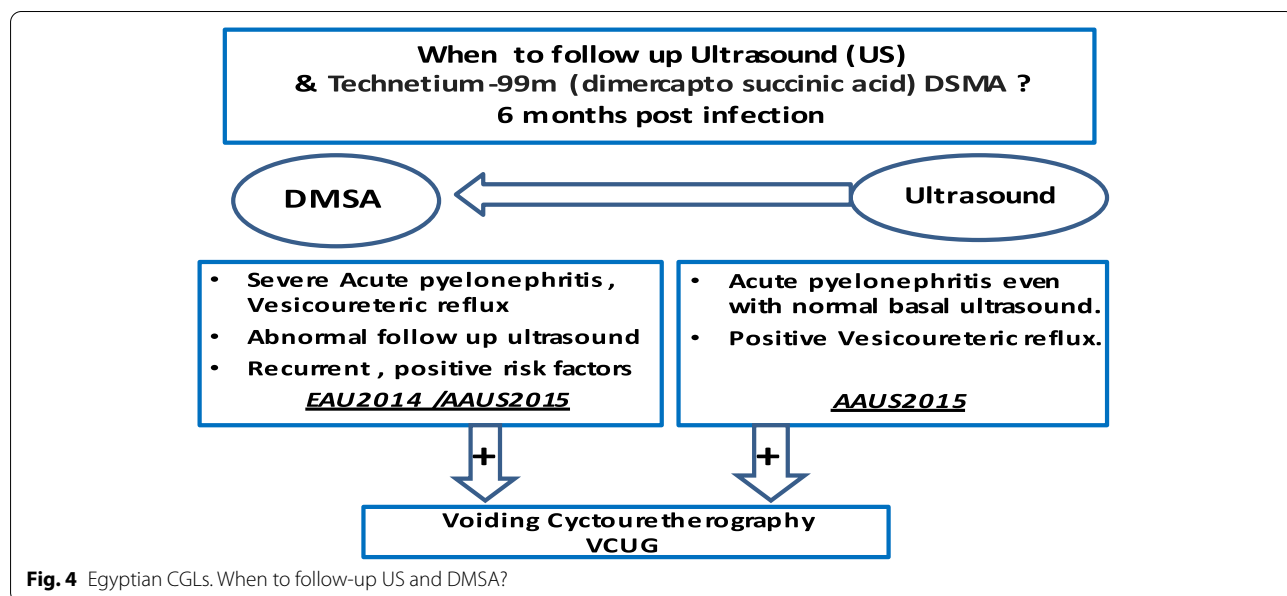
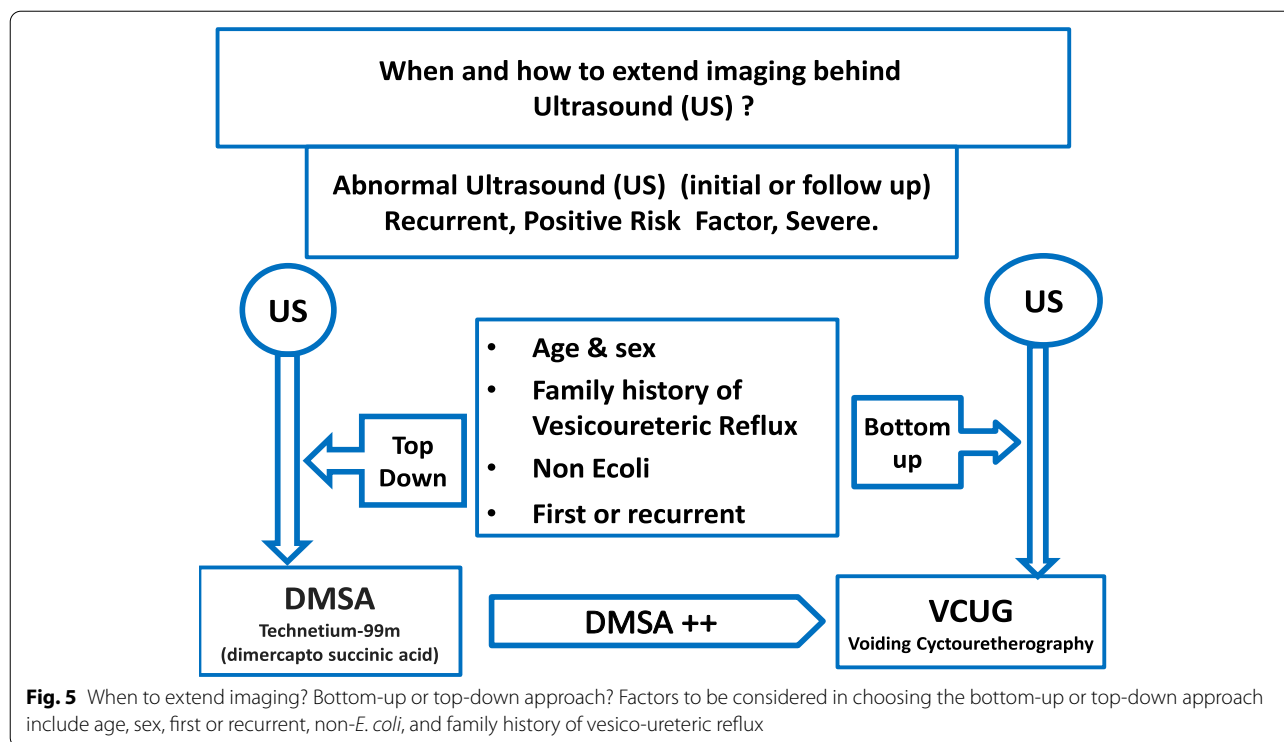


Fig. 4 Egyptian CGLs. When to follow-up US and DMSA?



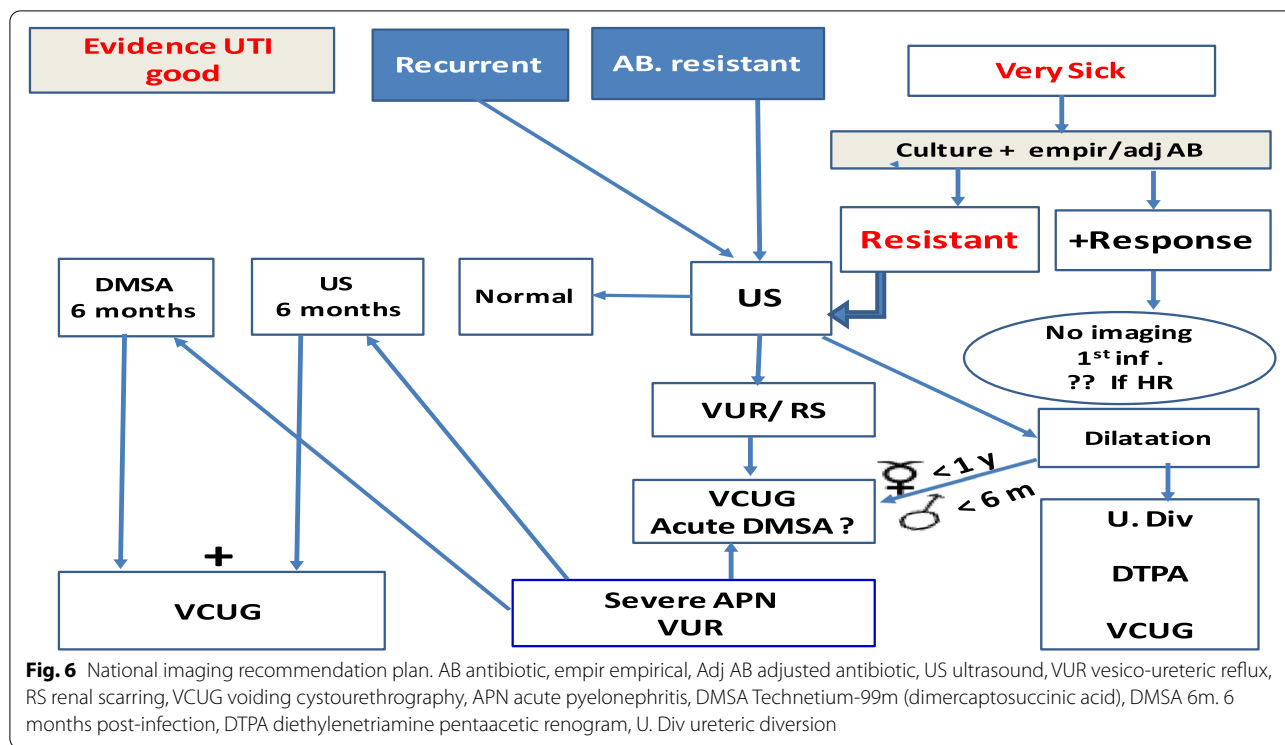
positive family history of VUR, and abnormal RBUS. Extended imaging will avoid missing VUR and RS [30].

How to image (imaging plan)? Those with a critical presentation with suspected obstruction or male infant < 6months, infants of either sex, abnormal US (dilatation, hypodysplasia), need urological consultation for urgent interference (stent, diversion) and urgent imaging plan (MAC3 to diagnose obstruction, acute DMSA in renal hypodysplasia to detect scars, VCUG to diagnose PUV, VUR) as evident in our final imaging recommendation plan (Fig. 6).

DMSA is the gold standard for the diagnosis of acute pyelonephritis and renal scarring [31]. Acute DMSA during the acute phase of UTI is not recommended by most CGLs because of its high cost and radiation compared to its benefits [9]. It has selective indications, e.g. severe APN or congenital hypodysplasia (when reported by renal RBUS), or because of its diagnostic value in the acute phase that will suggest further imaging modality (L3, GR: C AAUS) [22, 28] (Fig. 6). Late DMSA is recommended 6 months after the acute phase to detect scars in those with severe APN, recurrent febrile UTI, high-grade VUR, abnormal renal US (basal or follow-up) (L3GRC AAUS 15) [22] [Fig. 4]. It could be done earlier than 6 months if recurrence occurs before the lapse of 6 months (LE3, GR: C) (AAUS) [22, 32, 33]. NICE 2016

recommends late DMSA (routine) for all atypical presentation (except > 3years of age) and recurrent at any age with febrile UTI with the exclusion of simple responsive first episode cases, to be only requested at recurrence [30].

VCUG is the gold standard imaging for the diagnosis and grading of VUR when compared to direct or indirect radionuclide scintigraphy or voiding ultrasonography [10, 18, 22, 30]. It is recommended for diagnosis and grading of VUR. Either a top-down (US/DMSA/± VCUG) or bottom-up approach (US/VCUG ± DMSA) is used. The top-down approach is getting more commonly used in recurrent UTI, while in the first infection, VCUG is only indicated if either abnormal US or abnormal DMSA or both (LE2GR:B. AAUS) [22]. The bottom-up approach is recommended after the abnormal US suggestive of VUR at initial assessment for febrile UTI to be followed with DMSA, only for those diagnosed to show VUR (LE2GR: B, AAUS) [22]. The benefit of using the top-down approach is to reduce the number of VCUG performance. Multiple factors, as age, VUR grade, and first or recurrent UTI, determine which approach to use [9, 22] (Figs. 4 and 5). EAU CGLs recommend at initial evaluation the bottom-up with US/VCUG and listed top-down as an option (LE2a) [34].



The national imaging plan was adapted from AAUS and EAU/ESPU guidelines to suit our community (Fig. 6). Extended imaging recommendations as mentioned are limited to certain indications and not routine. Reasons for including them in these CGLs in detailed algorithms or flow charts are related to our local UTI profile in Egypt that show a high prevalence of anomalies (CAKUT with UTI 76% and with ESRD 33%), VUR (18.3 to 22% with grade 4 representing 60–66% and grades 1–3 representing 34–44%), and renal scarring 8–33% (polar scars 4–8%, total atrophy 11–18%). Nineteen to 38% out of 200 kidneys with UTI showed impaired renal growth [4]. However, with advancements in evidence-based medicine, many of the traditional links between UTI, VUR, and renal scarring have been changed. Other high-risk factors showed significance. Also, anti-reflux surgery was limited to high-grade and unsterile VUR, with restriction of antibiotic prophylaxis to recurrent UTI and VUR. Overall, our national imaging CGLs already presented respect scientific recommendations mostly accepted by others but tailored to our own cultural status.

Follow-up imaging and medical care recommendations

1. Those with a simple, responsive, first attack with no previous abnormal imaging are advised to come

back only on recurrence. Those with severe APN (with normal or abnormal US), or VUR, are advised to come back after 6 months for RBUS and DMSA. High-risk or recurrent UTI patients need repeated imaging in infancy and young age. All imaging reports should be documented and those with abnormal results should get patient/doctor appointment [29, 32].

2. Patients and their families should be oriented with details of treatment, local hygiene, and symptoms of recurrence; urine collection and storage for sampling; reasons for re-investigations (urine tests and/or imaging); and hazards of noncompliance. All patients' progress notes for UTI should be documented. Indicators of progress (blood pressure, kidney functions, proteinuria) are to be done every 6 months in bilateral and annually in unilateral lesions. Adolescent girls need monitoring at pregnancy. Transfer to adult service after the age of 16 years is crucial (consensus) [30].

Conclusion

Diagnosis and treatment show strong recommendations. Imaging plans depend on patient assessment. Referral to pediatric nephrologists and/or urologists is recommended in complicated cases. Follow-up after the age of 16 years in adult clinics is crucial.

Suggested areas for further research

- * Long-term cohort studies to establish links between UTI in infants and young children and reduced renal function and hypertension in adults
- * New noninvasive procedures for urine collection away from contamination?
- * Use of dynamic contrast RBUS for diagnosis of VUR
- * Molecular genetics for primary familial VUR and asymptomatic bacteriuria
- * Assessment of optimal treatment strategies (choice of AB, oral vs IV, duration, AB prophylaxis)
- * Imaging plans

Abbreviations

AAP: American Academy Pediatrics; AAU: Asian Association Urinary tract infections Sexually transmitted disease; AB: Antibiotics; APN: Acute pyelonephritis; CAKUT: Congenital anomalies of the kidney and urinary tract; EAU: European Association Urology; EPCGC: Egyptian Pediatric Clinical Guidelines Committee; ESRD: End-stage renal disease; ESPU: European Society Pediatric Urology; HRF: High-risk factors; PIPOH: Patient Intervention Professionals Outcome Healthcare settings; PNWG: Pediatric Nephrology Work Group; UTI: Urinary tract infection; RBUS: Renal bladder ultrasound.

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