

UTI in Children, Investigations Dilemma

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- **Untreated UTI can lead to renal scarring**

- **Over diagnosis can lead to misuse of antibiotics and unnecessary imaging**





- 5Y Old girl
- Dysuria
- No fever
- 1st attack
- Doctor ask for
- Urine analysis + culture and sensitivity
- US
- VCUG
- Spiral CT
- CBC, CRP BLOOD CULTURE



- 1 y old boy
 - 4th attack of fever rigors and hospital admission
 - hypertensive
 - underweight
- Doctor ask for
- CBC, CRP
 - described antibiotics



Points to Be Covered

- **Background**
- **Definitions**
- **Classification**
- **Investigations**

PAEDIATRIC UROLOGY, European Association of Urology 2020

**Arab Republic of Egypt National Pediatric Clinical Guidelines Committee NPCGC Pediatric Nephrology National Guidelines Work Group
EVIDENCE-BASED CLINICAL PRACTICE GUIDELINES (CGLs)**

-Urine Sampling

- Urine Testing

- Imaging

Points to Be Covered

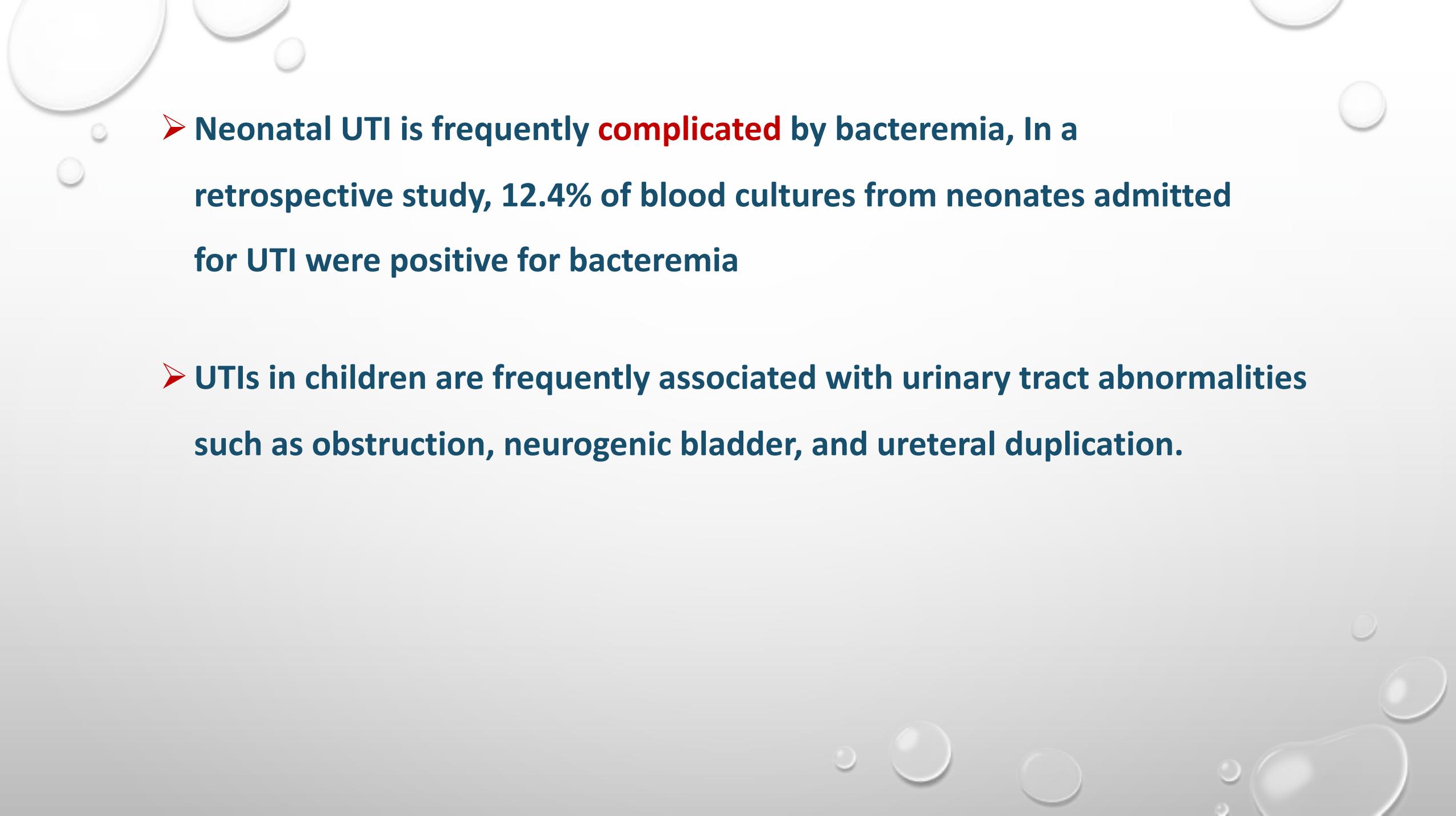
- **Background**
- **Definitions**
- **Classification**
- **Investigations**

-Urine Sampling

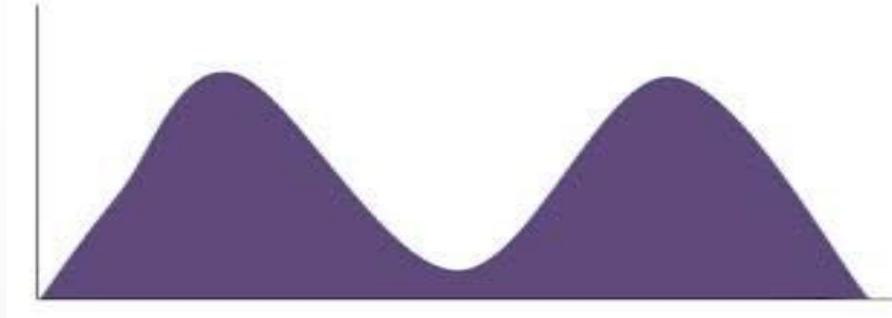
- Urine Testing



- ◆ UTIs most common serious bacterial infection in childhood.
- ◆ UTI occurs in 1.6% of boys and 7.8% of girls.
- ◆ 1st 3 months of life: more common in boys (3.7% vs 2.0%).
- ◆ Febrile UTIs in children, with or without VUR renal scarring
HPT and CKD.

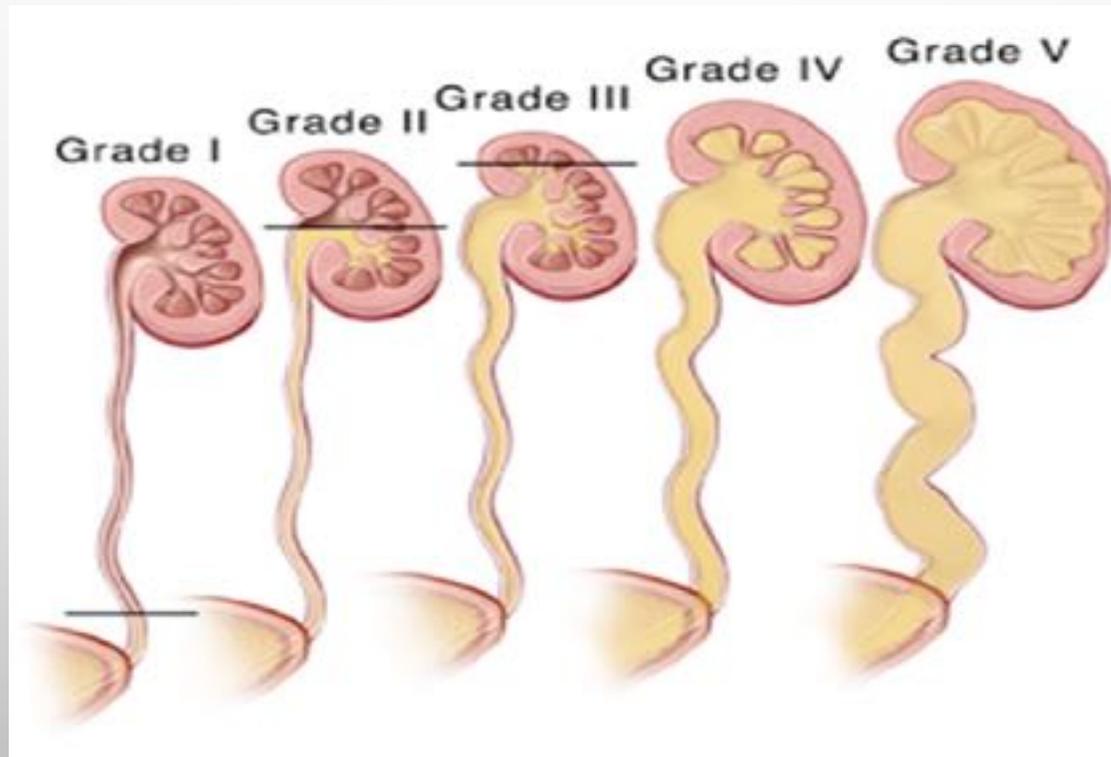
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- Neonatal UTI is frequently **complicated** by bacteremia, In a retrospective study, 12.4% of blood cultures from neonates admitted for UTI were positive for bacteremia
 - UTIs in children are frequently associated with urinary tract abnormalities such as obstruction, neurogenic bladder, and ureteral duplication.

- The peak age of UTI is bimodal, one peak **in infancy** and the other peak usually at the time of **toilet training** for many children.



- *E. coli* causes most UTIs in all pediatric age groups; the remaining causes are usually gram-negative enterobacteria (eg, *Klebsiella*, *P. mirabilis*, *P. aeruginosa*); frequently implicated gram-positive organisms are enterococci and coagulase-negative staphylococci (eg, *S. saprophyticus*).

- For children with **high-grade** vesicoureteral reflux (VUR), antibiotic prophylaxis is given **until surgical correction is done**; with lesser grades of VUR, the benefit of prophylactic antibiotics is unclear and close monitoring for recurrent UTI may be an acceptable management strategy for individual children.

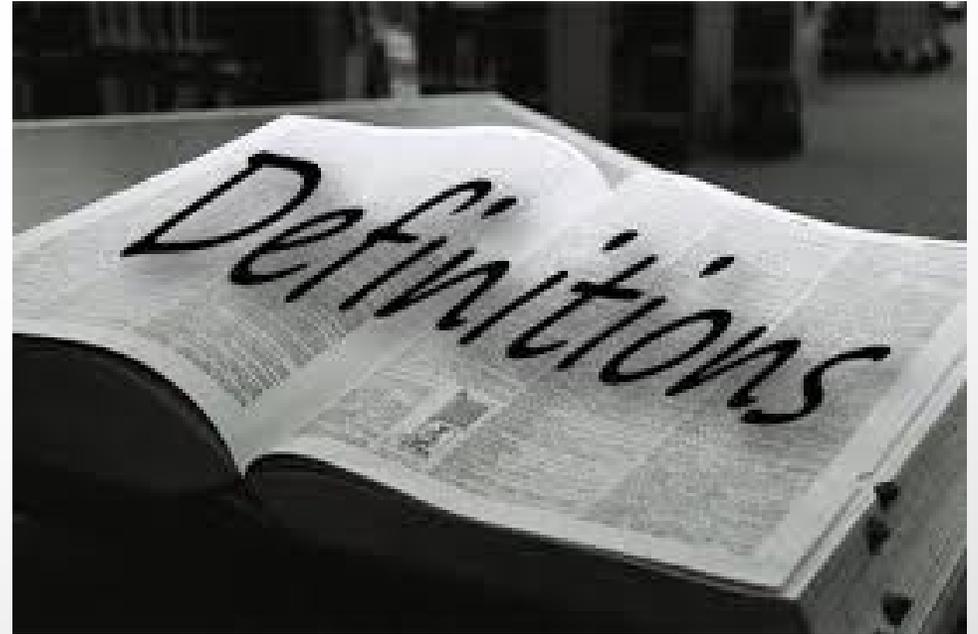


Presenting symptoms and signs in infants and children with UTI

Age group		Symptoms and signs		
		Most common	↔	Least common
Infants younger than 3 months		Fever Vomiting Lethargy Irritability	Poor feeding Failure to thrive	Abdominal pain Jaundice Haematuria Offensive urine
Infants and children, 3 months or older	Preverbal	Fever	Abdominal pain Loin tenderness Vomiting Poor feeding	Lethargy Irritability Haematuria Offensive urine Failure to thrive
	Verbal	Frequency Dysuria	Dysfunctional voiding Changes to continence Abdominal pain Loin tenderness	Fever Malaise Vomiting Haematuria Offensive urine Cloudy urine

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**Uncomplicated
UTI**

**Complicated
UTI**

Recurrent UTI

- ❖ Refers to the occurrence of infection in patients with an abnormal structural or functional urinary tract, or both, that involves the upper urinary tract and thus manifests as pyelonephritis.
- ❖ Is defined as the following: ≥ 2 episodes of UTI with acute pyelonephritis plus one episode of UTI with acute pyelonephritis plus one or more episodes of UTI with cystitis or lower UTI or three or more episodes of UTI with cystitis or lower UTI.
- ❖ Is defined as the invasion of a structurally and functionally normal urinary tract by a non-resident infectious organism.

Atypical UTIs

❖ Are defined as those that fail to respond after 48 hours of appropriate antibiotic treatment, have poor urine flow, abnormal kidney function, bladder or abdominal mass, infection by an organism other than e.Coli and onset of septicaemia.

Relapsing UTI

❖ Is defined as a renal mass caused by focal infection with liquefaction and may lead to the development of a renal abscess later on.

Acute lobar nephritis

❖ Is defined as a prompt recurrent infection with the same organism that occurs following treatment and implies there has been failure to eradicate the infection

Occult UTI

- * Fastidious and anaerobic bacteria may not be detected using standard culture.
- * Suspected when have leukocyte esterase positive and culture negative specimens.

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There are five widely used classification systems according to;

- 1) site**
- 2) episode**
- 3) severity**
- 4) symptoms**
- 5) complicating factors**

1- Classification according to site

- **Lower urinary tract (cystitis)**

is an inflammatory condition of the urinary bladder mucosa with general signs and symptoms including infection, dysuria, frequency, urgency, malodorous urine, enuresis, haematuria, and suprapubic pain.

- **Upper urinary tract (pyelonephritis)** is a diffuse pyogenic infection of the renal pelvis and parenchyma.

- The onset of pyelonephritis is generally abrupt.

- Clinical signs and symptoms include fever ($> 38^{\circ}\text{C}$), chills, costovertebral angle or flank pain, and tenderness.

2- Classification according to episode

The first UTI

may be a sign of anatomical anomalies that may predispose to complications of UTI and potential renal damage , Anatomical evaluation is recommended

Recurrent infection

can be divided into **unresolved** and **persistent** infection.

- In **unresolved infection**, initial therapy is inadequate for elimination of bacterial growth in the urinary tract

(inadequate therapy, inadequate antimicrobial urinary concentration [poor renal concentration/gastrointestinal malabsorption], and infection involving multiple organisms with differing antimicrobial susceptibilities).

- **Persistent infection** is caused by re-emergence of bacteria from a site within the urinary tract coming from a nidus for persistent infection that cannot be eradicated

(e.g. infected stones, non-functioning or poorly functioning kidneys/renal segments, ureteral stumps after nephrectomy, necrotic papillae, urachal cyst, urethral diverticulum, peri-urethral gland, vesicointestinal, rectourethral or vesicovaginal fistulas). (The PAEDIATRIC UROLOGY - LIMITED UPDATE MARCH 2020)

- same pathogen is identified in **recurrent infections**, but episodes of sterile urine may occur during and shortly following antimicrobial treatment.
- In **re-infection**, each episode can be caused by a variety of new infecting organisms, in contrast to **bacterial persistence** in which the same infecting organism is always isolated.
- However, the most common general pathogenic species is E. coli, which occurs in many different serotypes. Therefore, recurrent E. coli UTI does not equate to infection with the same organism

3- Classification according to severity

- **simple**

children may have only mild pyrexia; are able to take fluids and oral medication; are only slightly or not dehydrated; and have a good expected level of compliance.

- **severe**

infection is related to the presence of fever of $> 39^{\circ}\text{C}$, the feeling of being ill, persistent vomiting, and moderate or severe dehydration.

4- Classification according to symptoms

- **Asymptomatic**

bacteriuria indicates attenuation of uropathogenic bacteria by the host, or colonisation of the bladder by non-virulent bacteria that are incapable of activating a symptomatic response (no leukocyturia, no symptoms).

Asymptomatic UTI includes leukocyturia but no other symptoms.

- **Symptomatic UTI,**

includes irritative voiding symptoms, suprapubic pain (cystitis), fever and malaise (pyelonephritis).

5- Classification according to complicating factors

- In **uncomplicated** UTI,

infection occurs in a patient with a morphologically and functionally normal upper and lower urinary tract, normal renal function and competent immune system.

This category includes mostly isolated or recurrent bacterial cystitis and is usually associated with a narrow spectrum of infecting pathogens that are easily eradicated by a short course of oral antimicrobial agents.

Patients can be managed on an outpatient basis, with an emphasis on documenting resolution of bacteriuria, followed by elective evaluation for potential anatomical or functional abnormalities of the urinary tract.

- All **neonates**, most patients with clinical evidence of **pyelonephritis**, and all **children** with known mechanical or functional obstructions of the urinary tract, are considered to have **complicated UTI**.

Mechanical obstruction is commonly due to the presence of posterior urethral valves, strictures or stones, independent of their location.

Functional obstruction often results from lower urinary tract dysfunction (LUTD) of either neurogenic or non-neurogenic origin and dilating vesicoureteral reflux (VUR).

- Patients with complicated UTI require hospitalization and parenteral antibiotics.

Prompt anatomical evaluation of the urinary tract is critical to exclude the presence of significant abnormalities .

If mechanical or functional abnormalities are present, adequate drainage of the infected urinary tract is necessary

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Especially in early infancy, it can be **challenging and depends on the mode of urine sampling**

Urine must be collected under defined **conditions and investigated as **soon** as possible to confirm or exclude UTI, especially in children with fever.**



In neonates, infants and non-toilet-trained children, there are four main methods with varying contamination rates and invasiveness to obtain urine

(1) Plastic bag attached to the cleaned genitalia:

This technique is most often used in daily practice. It is helpful when the culture results are negative. Also, if the dipstick is negative for both leukocyte esterase and nitrite, or microscopic analysis is negative for both pyuria and bacteriuria, UTI can be excluded without the need for confirmatory culture

However, if the genitalia are not cleaned and culture is delayed, a high incidence of false-positive results (85-99%) can be found

(2) Clean-catch urine collection:

The infant is placed in the lap of a caregiver or member of the nursing staff, who holds a sterile foil bowl underneath the infant's genitalia. The infant is offered oral fluids and urine collection is awaited

This is time consuming and requires proper instruction of the caregivers. There seems to be a good correlation between the results of urine culture obtained by this method and suprapubic aspiration (SPA), with a false-positive rate of 5% and false-negative rate of 12% ; however, the contamination rate is higher compared to SPA .

(3) Bladder catheterization:

In female infants and also in neonates, this technique may be an alternative to SPA, at a higher contamination rate ; In a prospective study using bladder catheterisation in febrile children aged < 36 months, contamination was defined by multiple pathogens, nonpathogens, or colony counts < 10,000 cfu/mL. True UTI was found in 10% of children and 14% of the cultures were contaminated.

Univariate analysis of potential predictors identified age less than six months, difficult catheterization, and uncircumcised boys. In children less than six months and uncircumcised boys a new, sterile catheter with each repeated attempt at catheterization may lead to less contamination ;otherwise SPA should be the method of choice.

(4) Suprapubic bladder aspiration:

This is the most sensitive method to obtain an uncontaminated urine sample in **young age group** , Using US to assess bladder filling, *Complications are rare and have been reported in only 0.22% of cases, ranging from transient haematuria to bowel perforation ; However, bladder puncture causes more pain than catheterisation in infants less than two months old.*

In older, **toilet-trained children** who can void, the use of **clean catch**, especially midstream urine, could be an acceptable technique for obtaining urine.

In infants, **a bag can only be used if the dipstick is negative**, otherwise the urine should be obtained through catheterisation or SPA.

Blood sampling is dependent on the clinical situation

Sensitivity and specificity of component of urinalysis, alone and in combination

Test	Sensitivity (Range), %	Specificity (Range), %
Leukocyte esterase test	83 (67-94)	78 (64-92)
Nitrite test	53 (15-82)	98 (90-100)
Leukocyte esterase or nitrite test positive	93 (90-100)	72 (58-91)
Microscopy, white blood cells	73 (32-100)	81 (45-98)
Microscopy, bacteria	81 (16-99)	83 (11-100)
Leucocyte esterase test, nitrite test or microscopy positive	99.8 (99-100)	70 (60-92)

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There are 3 methods that are commonly used for urinalysis:

(1) Dipsticks:

These are appealing because they provide rapid results, do not require microscopy, and are ready to use.

Leukocyte esterase (as a surrogate marker for pyuria) and nitrite (which is converted from dietary nitrates by most Gram-negative enteric bacteria in the urine) are the most frequent markers, and are usually **combined** in a dipstick test.

The conversion of dietary nitrates to nitrites by bacteria takes approximately four hours in the bladder

However, nitrite is not a very sensitive marker for infants, who empty their bladder frequently, and not all urinary pathogens reduce nitrate to nitrite.

The test is helpful when the result is positive, because it is highly specific (i.e. there are few false-positive results)

(2) Microscopy:

This is the standard method of assessing pyuria after centrifugation of the urine with a threshold of five white blood cells (WBCs) per high-power field (25 WBC/ μ L) [In uncentrifuged urine, > 10 WBC/ μ L has been demonstrated to be sensitive for UTI and this could perform well in clinical situations However, this is rarely done in an outpatient setting.

Criteria for UTI in children (adapted from the EAU Guidelines on Urological Infections)

Urine specimen from suprapubic bladder puncture	Urine specimen from bladder catheterisation	Urine specimen from midstream void
Any number of cfu/mL (at least 10 identical colonies)	$> 10^3 - 10^5$ cfu/mL	$> 10^4$ cfu/mL with symptoms $> 10^5$ cfu/mL without symptoms

Voided samples Bag collection Midstream catch	$\geq 10^8$
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3) Flow imaging analysis technology:

This is being used increasingly to classify particles in uncentrifuged urine specimens .

The numbers of WBCs, squamous epithelial cells and red cells correlate well with those found by manual methods

Urine culture

- After **negative** results for dipstick, microscopic or automated urinalysis, urine culture is generally not necessary, especially if there is an alternative source of fever.
- If the dipstick result is positive, confirmation by urine culture is strongly recommended.
- In severe UTI, $> 10^5$ cfu/mL can be expected.
- However, the count can vary and be related to the method of specimen collection, diuresis, and time and temperature of storage until cultivation occurs
- The classical definition of $> 10^5$ cfu/mL of voided urine is still used to define a significant UTI
- The American Academy of Pediatric Guidelines on Urinary Tract Infection suggest that the diagnosis should be based on the presence of both pyuria and at least 10^5 cfu/mL.
- Mixed cultures are indicative of contamination.
- Pyuria without bacteriuria (sterile pyuria) may be due to incomplete antibiotic treatment, urolithiasis, or foreign bodies in the urinary tract, and infections caused by *Mycobacterium tuberculosis* or *Chlamydia trachomatis*

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IMAGING STUDIES

❖ US

❖ VCUG

❖ RENAL SCINTIGRAPHY

➤ DMSA

➤ DTPA

➤ MAG3

❖ OTHERS E.G. CT, MRI, VIDEO URODYNAMICS

Ultrasound

- Renal and bladder US within 24 hours is advised in **infants with febrile** UTI to exclude obstruction of the upper and lower urinary tract.
- Post-void residual (PVR) urine should be measured in toilet-trained children to exclude voiding abnormalities as a cause of UTI.
- Elevated PVR urine volume predicts recurrence of UTIs in toilet-trained children

Radionuclide scanning

- Changes in dimercaptosuccinic acid (DMSA) clearance during acute UTI indicate pyelonephritis or parenchymal damage, correlated well with the presence of dilating reflux and the risk of further pyelonephritis episodes, breakthrough infections and future renal scarring. In the acute phase of a febrile UTI (up to
- four to six weeks),
- DMSA-scan can demonstrate pyelonephritis by perfusion defects. detected after three to six months
- These findings are different in neonates.
- After the first symptomatic, community-acquired UTI, the majority of renal units with VUR grade III or higher had normal early DMSA scanning

Voiding cystourethrography

- The gold standard to exclude or confirm VUR is VCUG.
- ***Due to the risk of renal scarring, VCUG is recommended after the first episode of febrile UTI in boys and girls depending on sex, age and clinical presentation***
- Performance of early VCUG in patients with proven sterile urine does not cause any significant morbidity
- Another option is doing **DMSA first**, followed by VCUG if there is renal cortical uptake deficiency after UTI
- **Bladder and bowel dysfunction (BBD)** are risk factors for which each child with UTI should be screened upon presentation.
- Normalisation of micturition disorders or bladder over-activity is important to lower the rate of UTI recurrence.
- If there are signs of BBD at infection-free intervals, further diagnosis and effective treatment are strongly recommended
- Treatment of constipation leads to a decrease in UTI recurrence
- Therefore, exclusion of BBD is strongly recommended in any child with febrile and/or recurrent UTI, and it
- should be treated if there is evidence of BBD

Renal & Bladder U/S

- Pros: noninvasive, no radiation
- Cons: cannot reliably demonstrate inflammation, renal scarring; no info on renal function

VCUG

- Pros: affects treatment decisions that theoretically reduce risk of renal scarring
- Cons: radiation, expense, discomfort

Recommended imaging schedule for infants younger than 6 months

Test	Responds well to treatment within 48 hours	Atypical UTI ^a	Recurrent UTI ^a
Ultrasound during the acute infection	No	Yes ^c	Yes
Ultrasound within 6 weeks	Yes ^b	No	No
DMSA 4–6 months following the acute infection	No	Yes	Yes
MCUG	No	Yes	Yes

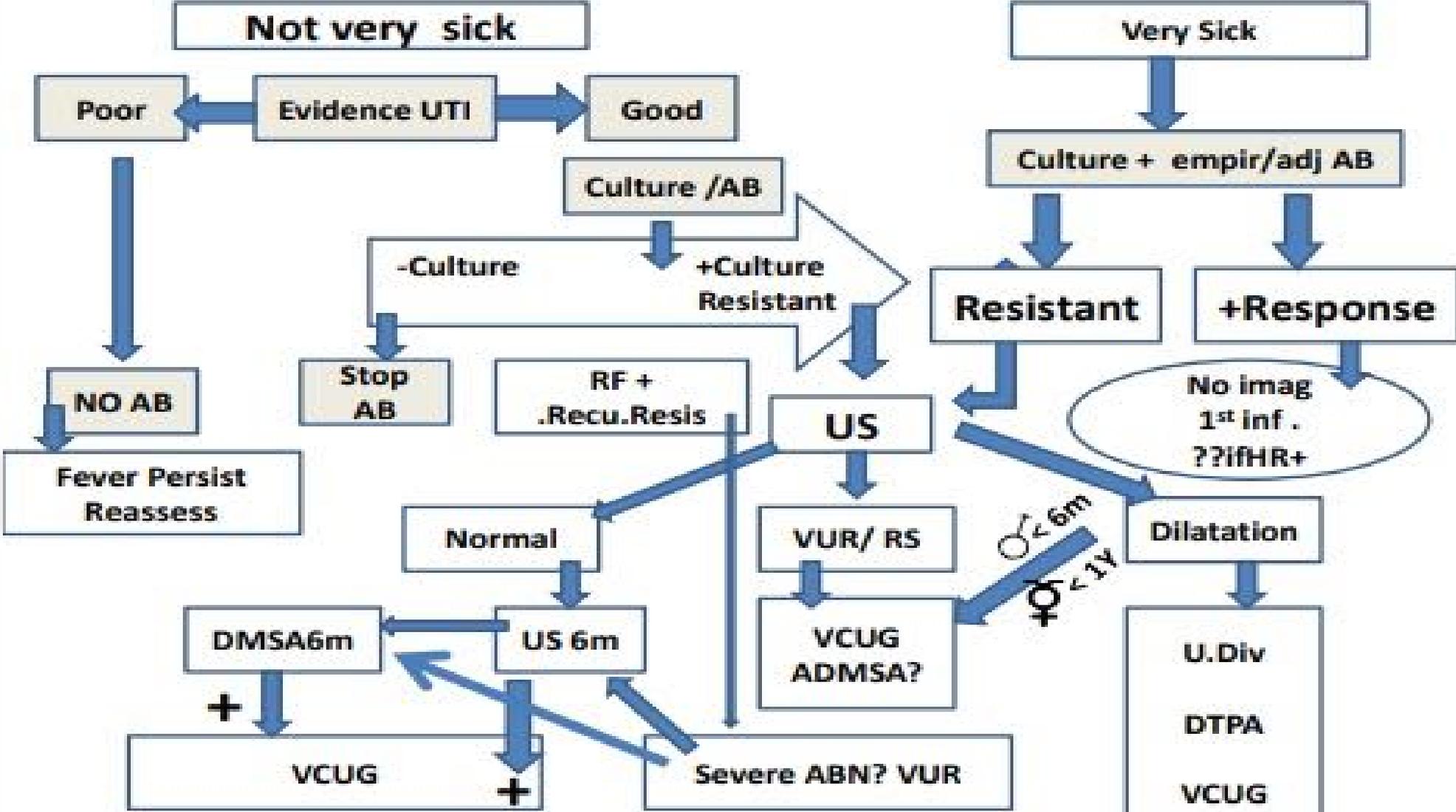
Recommended imaging schedule for infants and children 6 months or older but younger than 3 years

Test	Responds well to treatment within 48 hours	Atypical UTI ^a	Recurrent UTI ^a
Ultrasound during the acute infection	No	Yes ^c	No
Ultrasound within 6 weeks	No	No	Yes
DMSA 4–6 months following the acute infection	No	Yes	Yes
MCUG	No	No ^b	No ^b

Table 6.15 Recommended imaging schedule for children 3 years or older

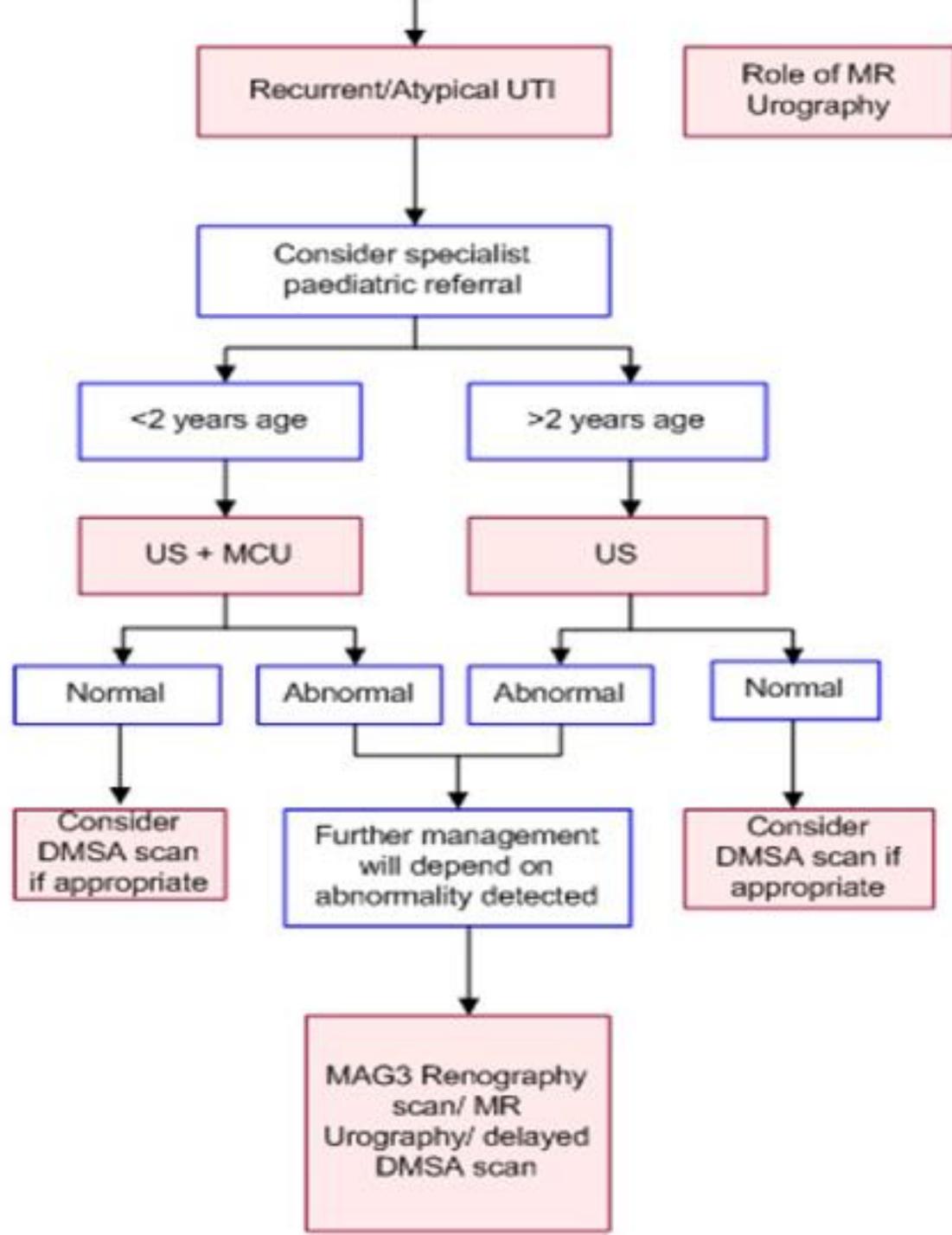
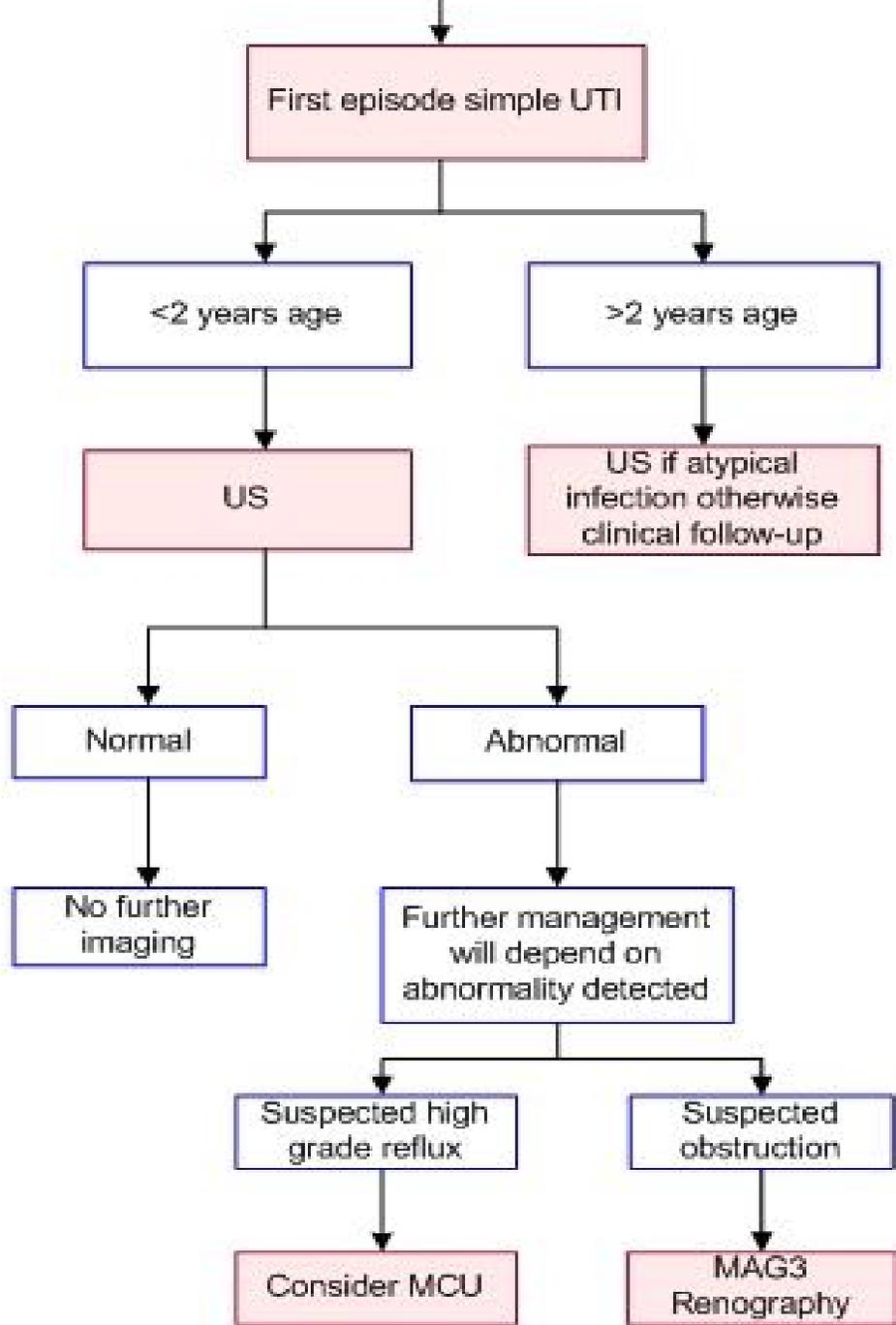
Test	Responds well to treatment within 48 hours	Atypical UTP ^a	Recurrent UTP ^a
Ultrasound during the acute infection	No	Yes ^{b,c}	No
Ultrasound within 6 weeks	No	No	Yes ^b
DMSA 4–6 months following the acute infection	No	No	Yes
MCUG	No	No	No

Fig 5 : National imaging recommendation plan



LET'S SUM IT UP

35
1/2
nouns
10%
18
10%
37
21
21
vowels
spelling
580
1/2
12





MCCQ'S

1- When you get urine culture for 2 successive times with the same organism

A- This is occult UTI

B- This is resistant UTI

C- This is atypical UTI

D- This is complicated UTI

2- Considerable sample in a septic neonate to diagnose UTI is

A- Urinary bag

B- Clean catch mid stream

C- Supra pubic aspirate

D- Blood culture

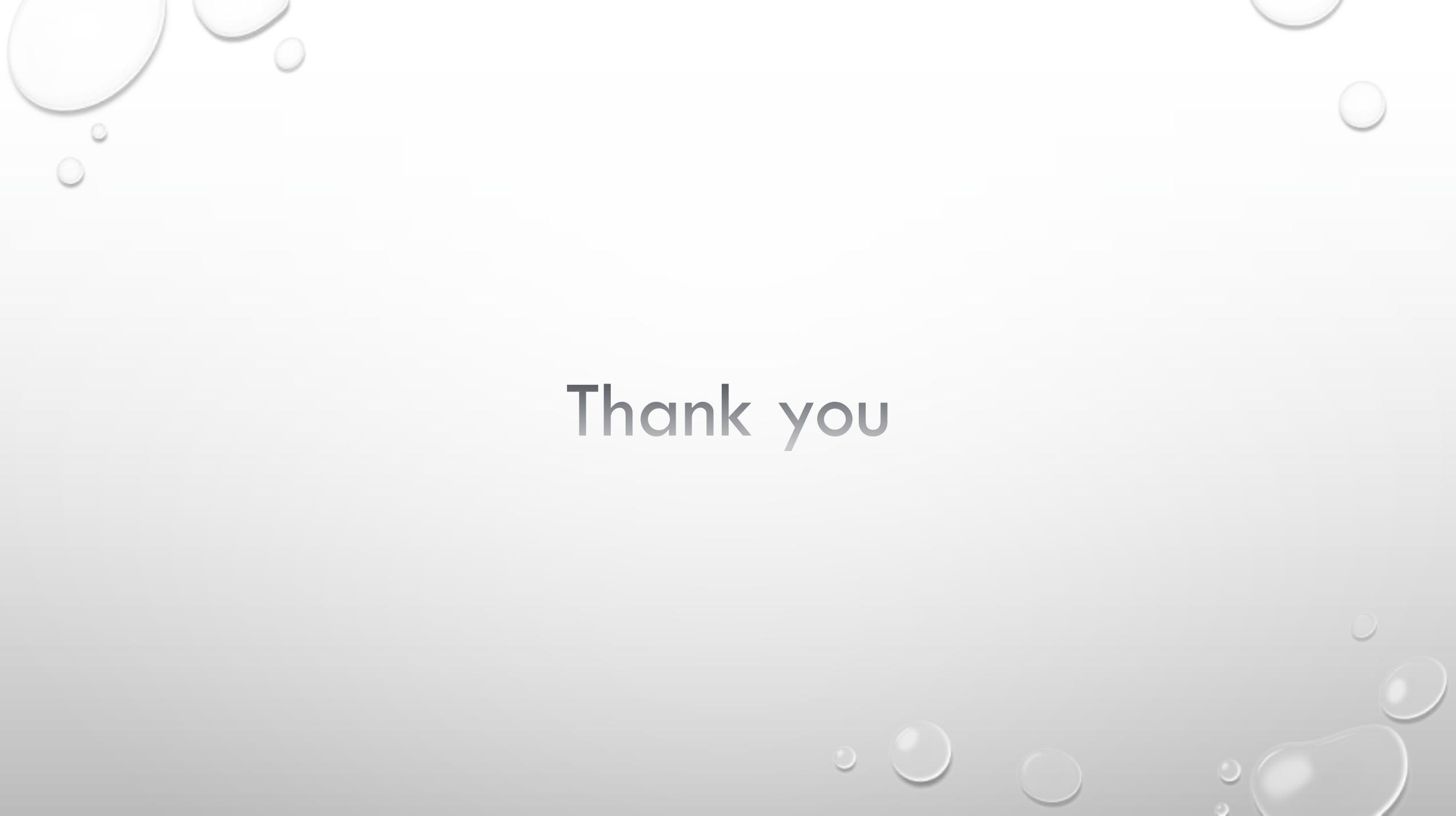
3- Which statement is false

A- US shouldnt be done in 1st attack of afebrile UTI age above 3years

B- VCUG is not recommended in cases of repeated UTI

C- In cases of severe VUR prophylactic antibiotics are recommended

D- Positive nitrite in urine analysis is a good positive test for UTI

The image features a light gray background with a subtle gradient. In the top-left and bottom-right corners, there are several realistic water droplets of various sizes, some overlapping. The droplets have highlights and shadows, giving them a three-dimensional appearance. The text "Thank you" is centered in the middle of the page.

Thank you