Urinary Tract Infection in Children

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Outline

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Background

- One of the most common infections in children worldwide
- It may be difficult to recognize UTI in children because the presenting symptoms and signs are non-specific, particularly in infants and children younger than 3 years
- Collecting urine and interpreting results are not easy in this age group, so it may not always be possible to unequivocally confirm the diagnosis
- If not diagnosed and treated appropriately, it may lead to severe illness and long-term complications like renal scarring, proteinuria, hypertension and end stage renal disease
- The economic impact caused by UTI on society is significant

Definitions

- Asymptomatic bacteriuria
  - is absence of UTI signs or symptoms in a patient whose urine culture satisfies criteria for UTI
- Atypical urinary tract infection
- Recurrent Urinary tract infection

Definitions

Box 3 | Main characteristics of patients with atypical or recurrent urinary tract infection

Atypical (any of the following)

- Septicaemia or patient who looks seriously ill (see NICE guideline[2])
- Poor urine flow
- Abdominal or bladder mass
- Raised creatinine concentration
- Failure to respond to treatment with suitable antibiotics within 48 hours
- Infection with non-Escherichia coli organisms

Recurrent (any of the following)

- Two or more episodes of urinary tract infection with acute pyelonephritis or upper urinary tract infection
- One episode of urinary tract infection with acute pyelonephritis or upper urinary tract infection plus one or more episode of urinary tract infection with cystitis or lower urinary tract infection
- Three or more episodes of urinary tract infection with cystitis or lower urinary tract infection

Epidemiology

- At least 8% of girls and 2% of boys will have had a UTI by the age of 7 years
- The overall prevalence of UTI in children under 2 years of age with an undifferentiated febrile illness is approximately 5%
- Prevalence is higher among white than among black infants
- Uncircumcised boys in the first year of life have a >8-fold higher incidence than girls or circumcised boys
- White girls with fever >102.2°F (39.0°C), without another potential source of infection, have a 30% prevalence of UTI
- Girls have a 2- to 4-fold higher incidence of UTI than circumcised boys

Classification of UTI

- Non febrile or Lower UTI
  - Cystitis
  - Urethritis
- Febrile Upper UTI
  - Acute pyelonephritis

- Uncomplicated
- Complicated
  - Associated with:
    - Structural or functional abnormalities
    - Comorbidities
    - Recent instrumentation or surgery

Aetiology

- Primary Uropathogens – Independent capacity to cause UTI
  - *Escherichia coli* (85% of UTI)
  - *Klebsiella*
  - *Proteus*
  - *Enterobacter*
  - *Staphylococcus saprophyticus,* and
  - *Enterococcus.*

- Secondary Uropathogens- lower capacity to cause disease and colonizers of urothepithelium
  - *Pseudomonas*
  - *Serratia*
  - *Citrobacter*
  - *Staphylococcus aureus*
  - *Candida spp*

Table 1 – Characteristics of the most common uropathogens

Uropathogens		Comment
Primary uropathogens		
Gram negative	*Escherichia coli*	70–95% of uncomplicated UTIs; the model bacteria in UTI research
	Proteus mirabilis, Klebsiella pneumoniae	2–5% of uncomplicated UTIs but increases in patients with complicating factors. May be associated with struvite stone formation
Gram positive	*Staphylococcus saprophyticus*	5–10% of uncomplicated UTIs, mostly in sexually active young women
	Enterococcus faecalis	Can cause uncomplicated sporadic UTI but is also associated with transplantations or catheter-associated infections
Secondary uropathogens		
Gram negative	*Pseudomonas aeruginosa*	Usually in complicated or hospital-acquired UTIs
	Serratia marcescens, Providencia stuartii *Citrobacter* spp *Enterobacter cloacae*	Uncommon uropathogens with low virulence, usually found in patients with compromised conditions
Gram positive	*Staphylococcus aureus*	Mostly in immunocompromised patients; can cause hematogenous UTI
Others	*Candida* spp	Usually associated with immunosuppression or after antibiotic treatment causing ecological disturbances

UTI = urinary tract infection.

Risk factors for UTI

- Non-modifiable
  - Age
  - Gender
  - Familiarity
  - Race
- Modifiable
  - reflux
  - phimosis
  - bladder function
  - voiding habits
  - Constipation and
  - fluid intake

Box 1. Risk factors for urinary tract infection in children.

- Poor urine flow, dysfunctional voiding and/or constipation
- Previous urinary tract infection
- Recurrent fever of uncertain origin
- Antenatally diagnosed renal abnormality or evidence of spinal lesion
- Family history of vesicoureteric reflux or renal disease
- Enlarged bladder and/or abdominal mass
- Poor growth
- High blood pressure

Bacterial factors

- Adherence factors
  - P fimbriae (E.coli)
  - Type 1 fimbriae
- Flagellation
  - bacterial dissemination to the upper urinary tract
- Lipopolysaccharide
  - Structural integrity and protection against host defence
- Toxins
  - Hemolysin (HlyA) – inhibitis chemotaxis and phagocytosis by PMNs
  - cytotoxic necrotizing factor 1 (CNF1) – apoptosis of epithelial celld, inhibits both chemotaxis and phagocytosis
- Biofilm
  - structured community of microorganisms encapsulated within a self-developed polymeric matrix adherent to a surface
  - protects the bacteria by being resistant to neutrophil migration

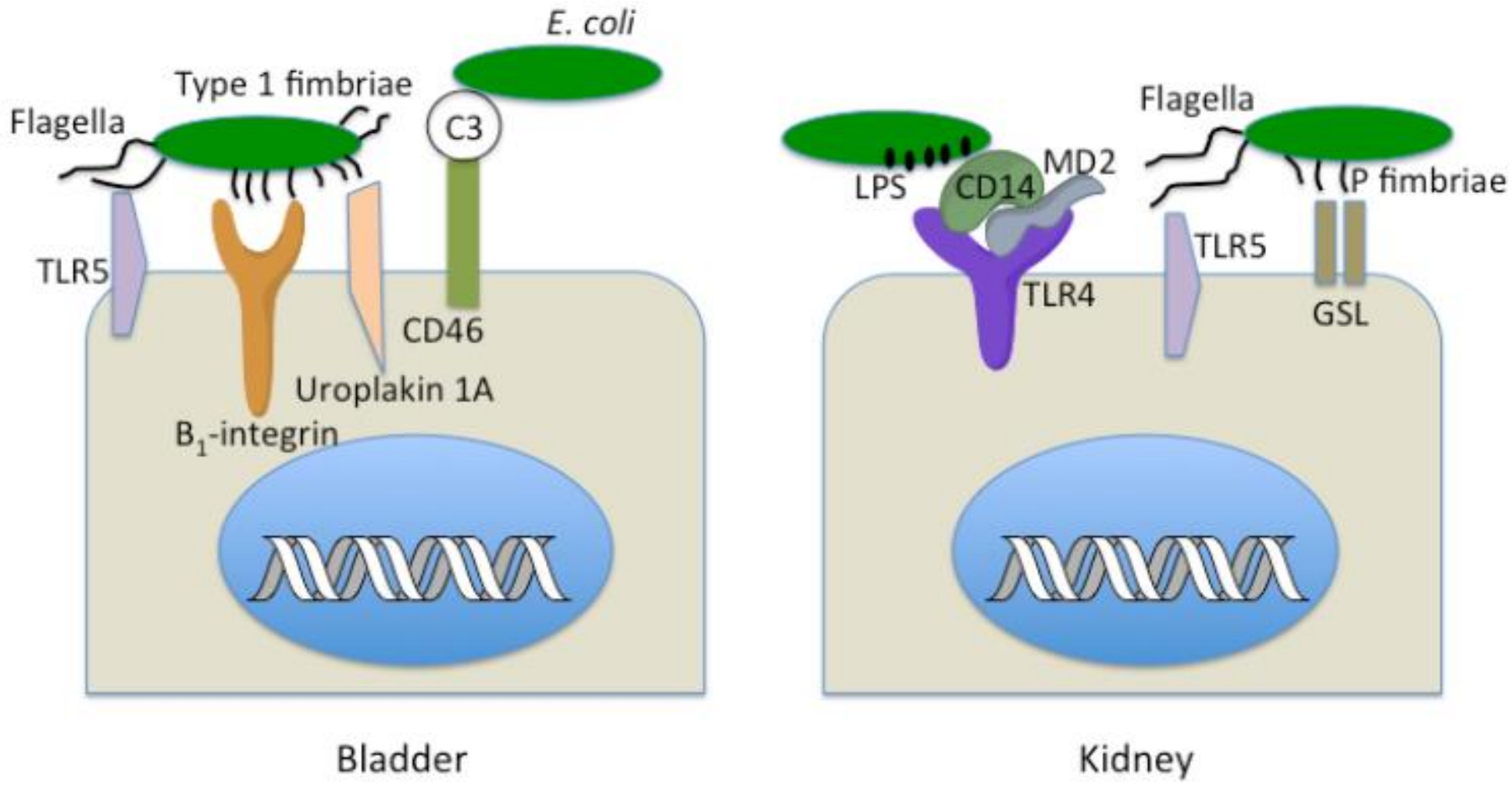


Figure 1. Attachment to urinary bladder cells (left) and renal epithelial cells (right) by uropathogenic *E. coli*.

Host factors

- High urine flow rate
- High voiding frequency
- Bactericidal effects of the bladder mucosa
- Secreted proteins that bind to fimbrial adhesins on the bacterial wall and
- The inflammatory response mediated by PMNs and cytokines

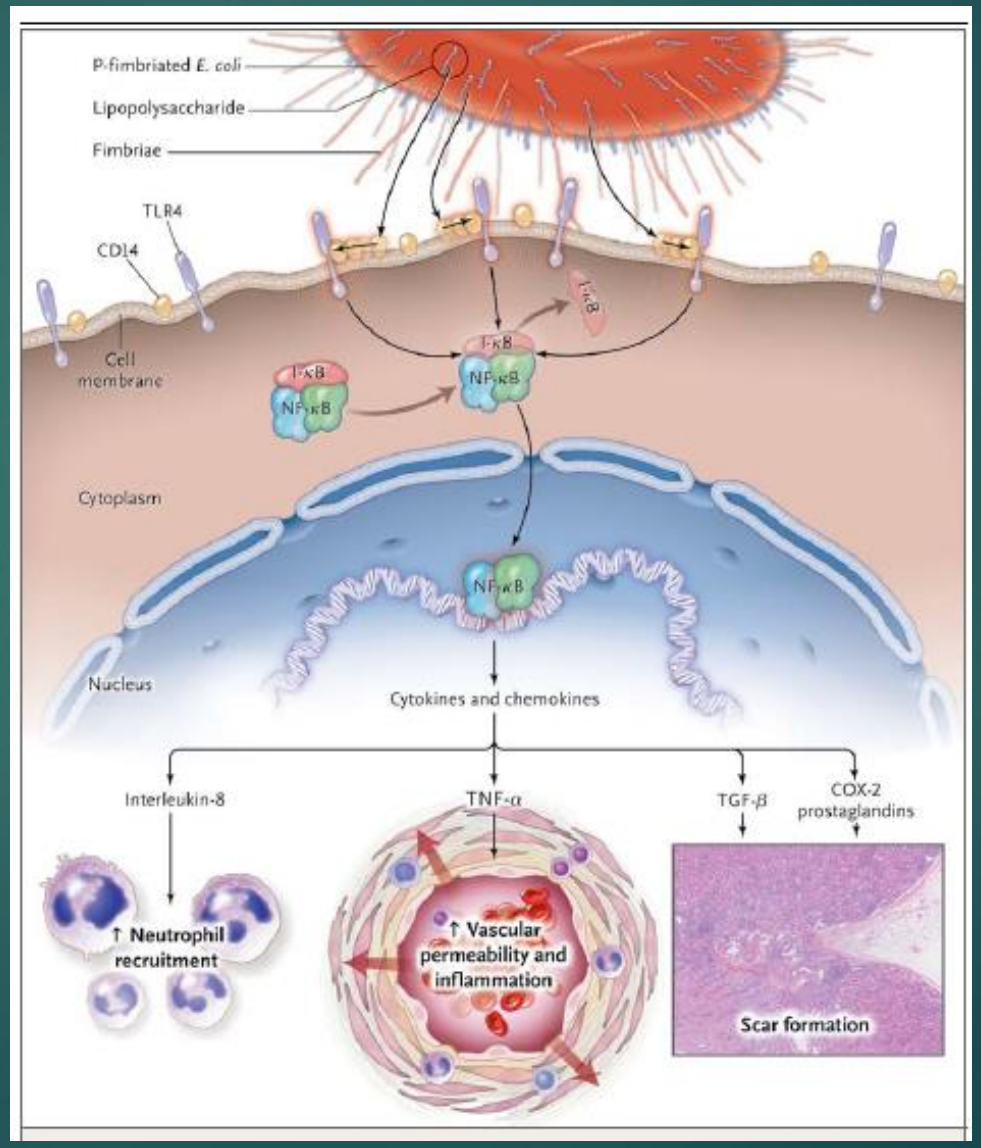
Pathogenesis

- Ascending route
  - Most uropathogens originate in the rectal flora and enter the bladder via the urethra
- Hematogenous route
  - Infection of the renal parenchyma by blood-borne organisms occurs in humans, albeit less commonly than by the ascending route
- Lymphatic route
  - There is little evidence to support a lymphatic spread of infection to the urinary tract with any regularity.

Pathophysiology of UTI and scar formation

- Urinary tract is germ free
- Certain bacteria have features that favour infection e.g. E.coli have P fimbriae that facilitate attachement to uroepithelium
- In presence of kidney malformation, inadequate urine flow, incomplete voiding of bladder even non attaching bacteria can cause infection
- When bacteria invade the kidney, localized inflammation develops, triggering the innate immune system through multiple pathways
- If a renal parenchymal infection is limited in extent and duration, full recovery can occur but continued inflammation may lead to scarring

Pathophysiology of UTI and scar formation



Age group		Symptoms and signs Common →		Rare
<3 months		Fever Vomiting Lethargy Irritability	Poor feeding Failure to thrive	Abdominal pain Jaundice Haematuria Offensive urine
≥3 months	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

Physical findings

- CVA tenderness
- Abdominal tenderness
- Suprapubic tenderness
- Palpable bladder
- Dribbling, poor stream or straining on voiding

Diagnosis

- Urine dipstick
  - Leukocyte esterase
  - Nitrite
  - Blood
  - Protein
- Urine microscopy

- Urine culture

Urine dipstick

- LE is most sensitive for diagnosis of UTI
- Nitrite is more specific but less sensitive
- Blood and Protein have poor sensitivity and specificity

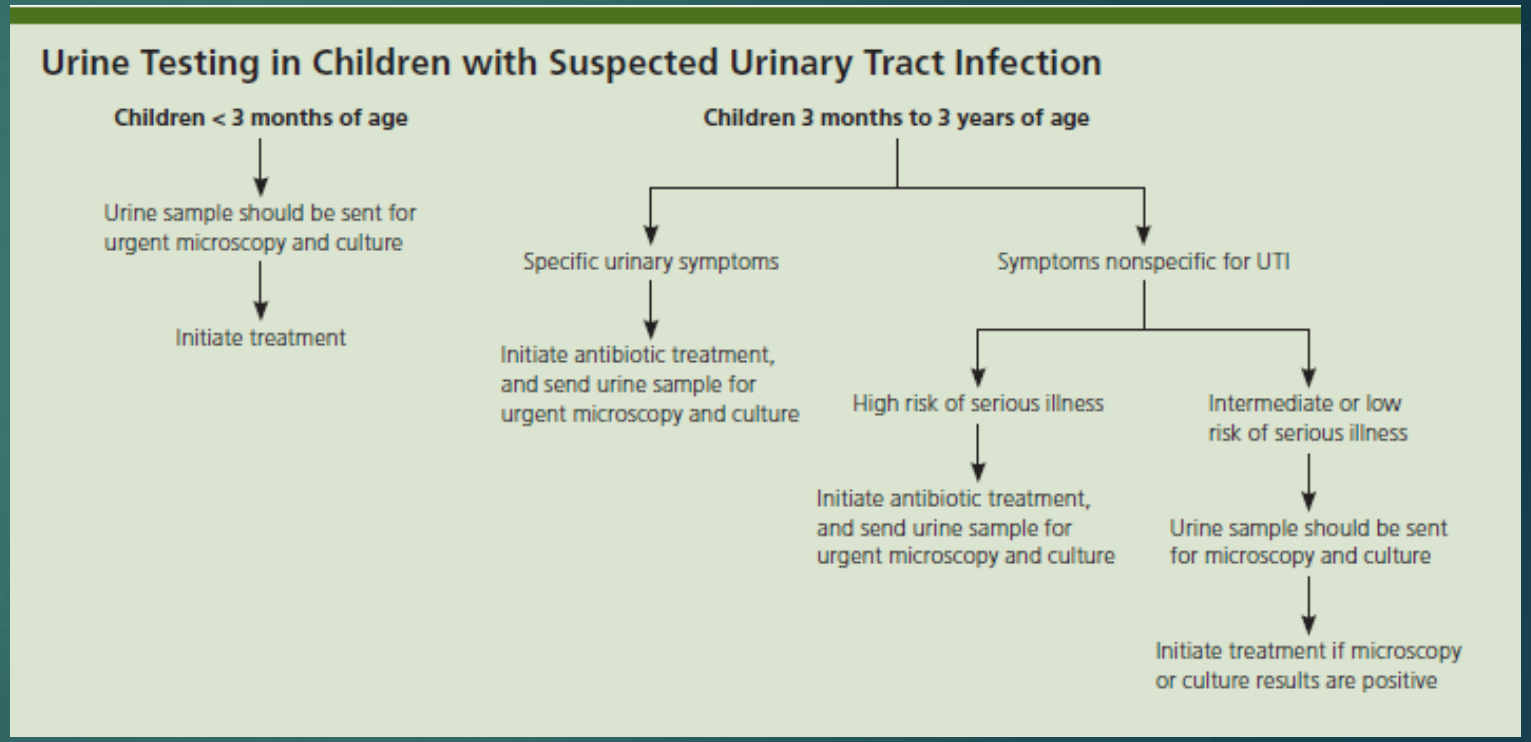
	SENSITIVITY	SPECIFICITY	PROBABILITY OF UTI
Nitrite	53%	98%	75%
bacteria on microscopy	81%	83%	35%
Leukocyte on microscopy	73%	81%	30%
Leukocyte esterase	83%	78%	30%
Leukocyte or nitrite	93%	72%	27%
Blood	47%	78%	19%
Protein	50%	76%	19%

Urine testing based on child's age (NICE 2007)

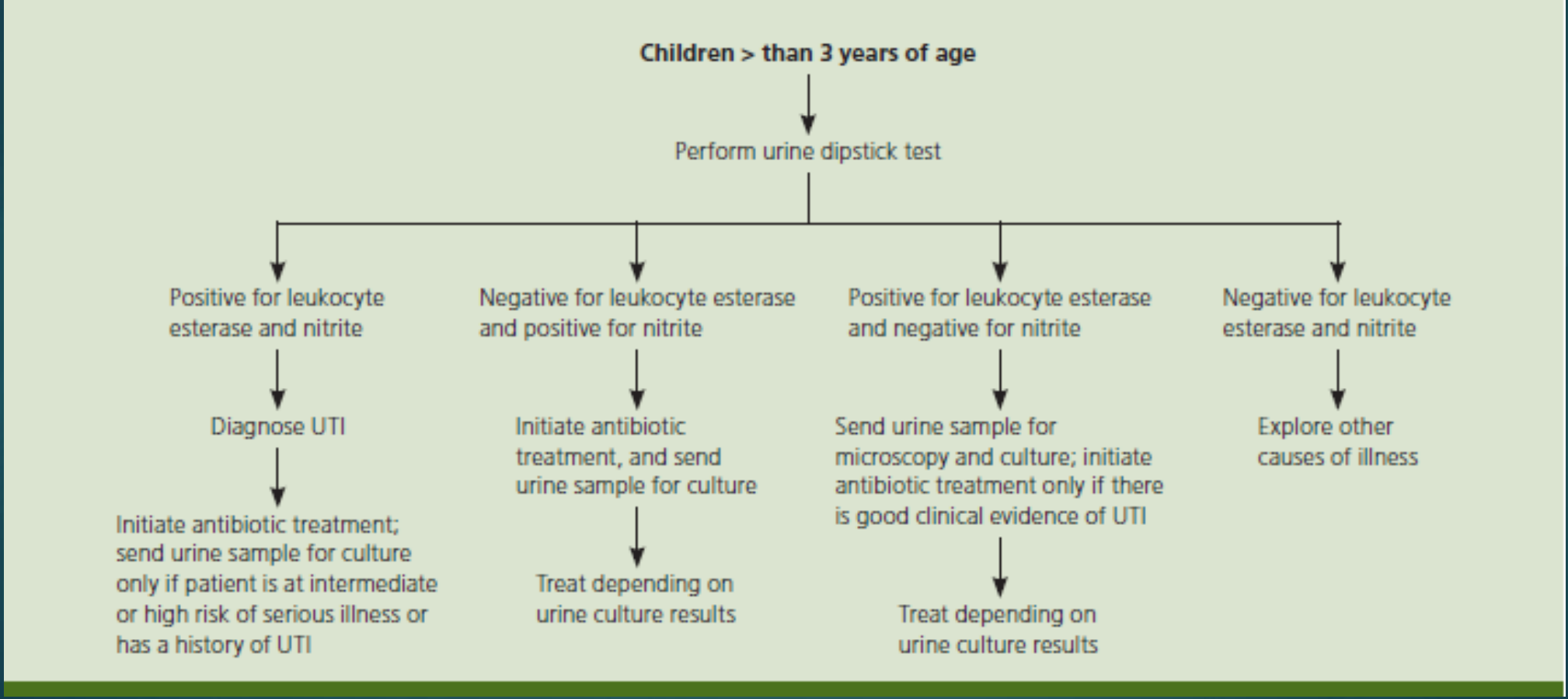
Children younger than 3 years

- Microscopy and
- Urine culture

(Not urine dipstick)



Urine testing based on child's age (NICE 2007) cont'd



Confirming UTI

- A clean catch urine (CCU) sample should be obtained for culture
- If urine cannot be collected via non-invasive method, catheter sample(CS) or suprapubic aspiration (SPA) should be used
- Reference standard is single organisms culture from specimen obtained via
  - Suprapubic aspirate (any growth)
  - Catheter specimen (>10,000 cfu/ml)
  - Clean-catch, mid-stream urine (>100,000cfu/ml)

Acute UTI management by

Under 3 months old or very ill	• **Refer + admit for adequate fluid and nutrition,** • **Urine mc&s to lab + renal function tests check,** • **Start broad spectrum IV antibiotics Cephalosporin or Aminoglycoside** • **Then according to urine culture results**
Older children Acute pyelonephritis/Upper UTI – temp > 38^{o}C, loin pain, vomiting	• Appropriate urine to lab • Oral antibiotics according to local sensitivities • **Amoxil/Clavulanic acid** or **Cefuroxime** X 7 days. If ill: IV Antibiotics X 48hrs(as above) then oral X 5 days
Older children Cystitis/lower UTI	• Appropriate urine to lab • Oral antibiotic X 3-5 days • Review if still unwell after 48 hours

Aim of further investigation

- Localisation of infection
  - Confirm acute pyelonephritis (power doppler/DMSA)
- Detection of anatomical abnormalities that may be amenable to surgery
- Prediction of renal scarring & detection of VUR
- Detection of renal scarring

NICE 2007 Recommendation

Table 6 Recommended imaging schedule for infants younger than 6 months

Test	Responds well to treatment within 48 hours	Atypical UTIa	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

[a] See box 1 for definition

[b] If abnormal consider MCUG

[c] In an infant or child with a non-*E. coli*-UTI, responding well to antibiotics and with no other features of atypical infection, the ultrasound can be requested on a non-urgent basis to take place within 6 weeks

Table 7 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 UTIa	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]

[a] See box 1 for definition

[b] While MCUG should not be performed routinely it should be considered if the following features are present:

- dilatation on ultrasound
- poor urine flow
- non-*E. coli*-infection
- family history of VUR.

[c] In an infant or child with a non-*E. coli*-UTI, responding well to antibiotics and with no other features of atypical infection, the ultrasound can be requested on a non-urgent basis to take place within 6 weeks

Table 8 Recommended imaging schedule for children 3 years or older

Test	Responds well to treatment within 48 hours	Atypical UTI[a]	Recurrent UTI[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

Imaging NICE 2007 Recommendation

- Ultrasound scan is required on diagnosis of all atypical infection
- Those with recurrent infection ultrasound is reserved for those <6 mo
- For older children scan should be done within 6 weeks
- DMSA in recurrent Uti and atypical infections after 4-6 mo in <3 yr
- MCUG in both recurrent and atypical infections in children <6 mo and older if there is poor urine flow, non-E. coli infection, urinary tract dilatation on ultrasound and family history of VUR

Summary

- Urinary tract infection is a common infection worldwide
- Timely and appropriate evaluation should be undertaken to make diagnosis and treat UTI to prevent renal scarring, ESRD and minimize cost
- NICE guideline clearly outlines the recommendations in management of UTI although there are still areas of controversies in the management of UTI
- Children under 6mo and those with recurrent UTI or atypical infection are special group need early treatment and further evaluation

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Thank you!