MED437
KING SAUD UNIVERSITY

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MICROBIOLOGY
437

Cystitis

Important!
Doctor's Notes
Only found in females' slides
Only found in males' slides
Extra Notes

" I'm not telling you it's going to be easy. I'm telling you it's going to be worth it."

Objectives

- ➔ Define the term cystitis and recall who commonly gets cystitis.
- ➔ Describe the pathogenesis and risk factors of cystitis.
- ➔ List the most common causative organisms of cystitis
- ➔ Recall the different types of cystitis (infectious and non-infectious).
- ➔ Recognize that venereal diseases can present with cystitis.
- ➔ Describe the laboratory diagnostic of cystitis
- ➔ Recall the antimicrobial agents suitable for the treatment and prevention of cystitis.

Introduction and classification

Urinary Tract infection (UTI) divided into:

Upper UTIs:	Lower UTIs:
Acute pyelonephritis and chronic pyelonephritis.	1. **Cystitis** (infection of the bladder; superficial mucosal infections). 2. **Urethritis** (sexually transmitted pathogens)- urethritis in men & women. 3. **Prostatitis** and **Epididymitis**.

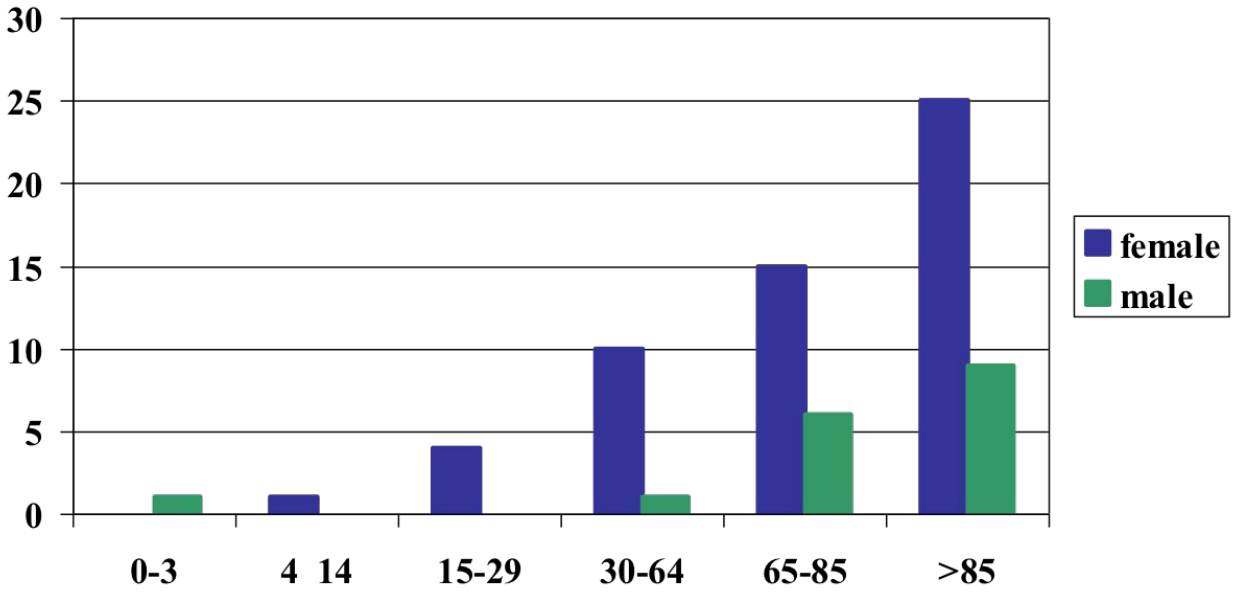
Bacteriuria:

1. Symptomatic bacteriuria: Patient presents with urinary symptoms and significant bacteriuria (10^5 or 100,000 bacteria/ml). (in healthy ppl urine is sterile so = 0)
2. Asymptomatic bacteriuria: the patient presents with significant bacteria in urine but without symptoms .

They are classified according to the factors that trigger the infection into:

- ➔ Uncomplicated UTI (first time getting infected → empirical therapy is possible so no predisposing factors).
- ➔ Complicated UTI (nosocomial UTI, relapses, structural or functional abnormalities).
  - ◆ Some kids have vesicoureteric reflux (congenital) which means that the valve b/w urethra and bladder isn't fully developed so it causes the contaminated urine to flow back to the kidney.

Prevalence As age increases the incidence of UTI increases especially in females of Bacteriuria in different age groups:



Cystitis

In women

- cystitis is common due to a number of reasons :
  - Short urethra
  - Pregnancy
  - Decreased estrogen production during menopause.

In men

- mainly due to persistent bacterial infection of the prostate.

In both sexes

- common risk factors are:
  - Presence of bladder stone
  - Urethral stricture
  - Catheterization of the urinary tract
  - Diabetes mellitus

Pathogenesis of Cystitis

- Due to frequent irritation of the mucosal surfaces of the urethra and the bladder.
- Infection results when bacteria ascends to the urinary bladder. These bacteria are residents or transient members of the perineal flora, and are derived from the large intestine flora.
- Toxins produced by uropathogens.
- **Conditions that create access to bladder:**
  - **Sexual intercourse** due to short urethral distance & **Uncomplicated UTI:** usually occurs in non pregnant, young sexually active females without structural or neurological abnormalities
- **Risk Factors: 1-** Catheterization of the urinary bladder/ instrumentation **2-** Structural abnormalities **3-** Obstruction
- **Haematogenous** through blood stream from other sites of infection (less common)

Etiologic agents

Most common cause (90%)	*E.coli* *(part of the enterobacteriaceae family)*
Other Enterobacteriaceae (gram -ve)	*Klebsiella pneumoniae* *Proteus spp*
Other gram -ve rods	*P.aeruginosa*
Gram +ve bacteria	*Enterococcus faecalis* *Group B streptococcus* *Staphylococcus saprophyticus (honeymoon cystitis)*
Fungi	Candida species
Venereal diseases (sexually transmitted)	Gonorrhea Chlamydia
Parasite	Schistosoma Haematobium in endemic areas causes hemorrhagic cystitis

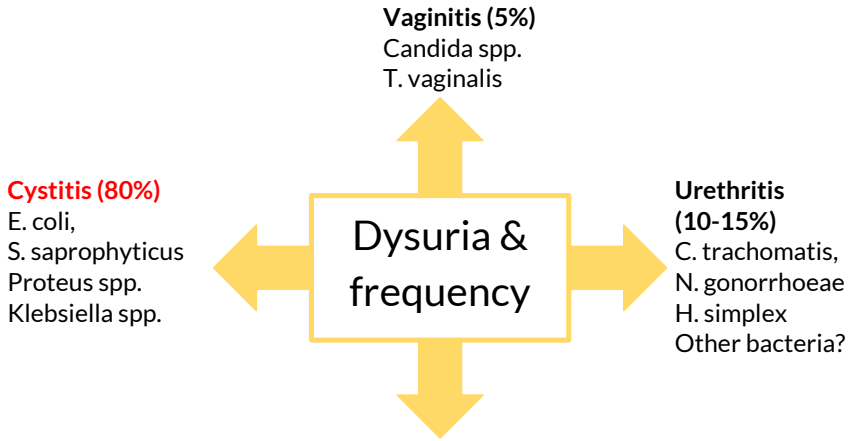
Pathogens involved

Uncomplicated UTI	**Complicated UTI** (% is not possible to judge, often multi-resistant strains)	**Special Cases**
E.coli (64%)	*E.coli*	S.epidermidis (normal flora of the skin)
Enterococcus spp (20%)	*Enterobacteriaceae*	S.saprophyticus
Enterobacteriaceae (16%)	*Pseudomonas spp*	Yeasts (Catheter related)
Pseudomonas spp (<1%)	*Acinetobacter spp*	Viruses (Adenovirus, Varicella)
S.aureus (<1%)		Chlamydia trachomatis

Clinical Presentation

Symptoms usually of acute onset, the patient will present with…

- ➔ Dysuria (painful urination)
- ➔ Frequency (frequent voiding)
- ➔ Urgency (an imperative call for toilet)
- ➔ Hematuria (blood in urine) in 50% of cases.
- ➔ Usually no fever.



So most of the patients that have dysuria is mainly because of cystitis and it's rarely due to other diseases.

How to differentiate between Cystitis and Urethritis?

- ➔ Cystitis is of more acute onset
- ➔ More severe symptoms
- ➔ Pain, tenderness on the supra-pubic area.
- ➔ Presence of bacteria in urine (bacteriuria) (the usual bacteria like e.coli)
- ➔ Urethritis will also have bacteria in urine but it will be unusual bacteria like gonorrhea and chlamydia (sexually transmitted)
- ➔ Urine cloudy, malodorous and may be bloody

Differential diagnosis (types of Cystitis)

Traumatic Cystitis	Interstitial Cystitis	Eosinophilic Cystitis	Hemorrahagic Cystitis
In women. (During delivery might injure the bladder)	Unknown cause, may be due to autoimmune attack of the bladder.	Due to S. haematobium	Due to radiotherapy or chemotherapy.

Laboratory diagnosis of cystitis

Specimen collection

- Most important is clean catch urine Midstream Urine (MSU) to bypass contamination by preneal flora and must be before starting antibiotic.
- So we tell the patient when they collect the sample to wait after the first drop of urine & not collect it b/c it contains normal flora so they should collect the mid-drops b/c it contains the bacteria in the bladder and this is what we want
- Supra-pubic aspiration or catheterization may be used in children.
- Catheter urine should not be used for diagnosis of UTI.

Microscopic examination

- About 90% of patients have > 10 WBCs/cu.mm
- Gram stain of uncentrifuged sample is sensitive and specific.
- One organism per oil-immersion field is indicative of infection.
- Blood cells, parasites or crystals can be seen.

Chemical screening tests

- Urine dip stick–rapid, detects nitrites released by bacterial metabolism and leukocyte esterase from inflammatory cells.
- Not specific.

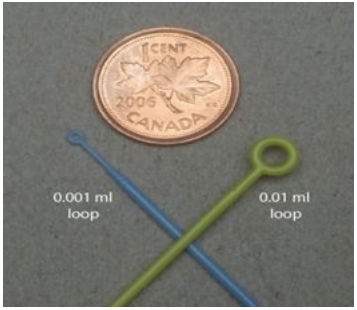
Urine culture

- Important to identify bacterial cause and antimicrobial sensitivity .
- Quantitative culture (to know the number of the bacteria) typical of UTI (>100,000 /cumm) Lower count (<100,000 or less eg. 1000/cumm) is indicative of cystitis if the patient is symptomatic.

Laboratory diagnosis of cystitis

For chemical screening

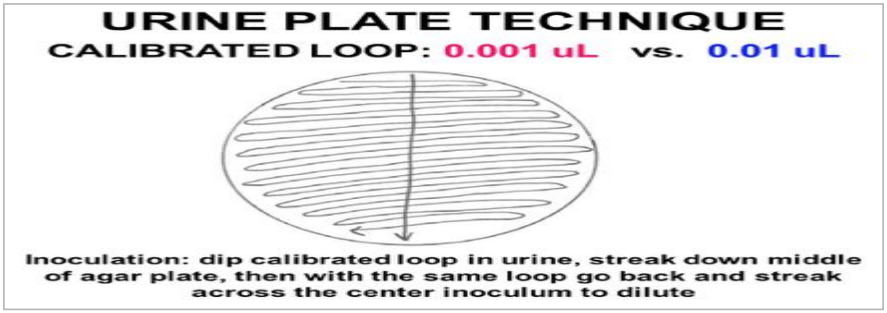
For quantitative urine culture



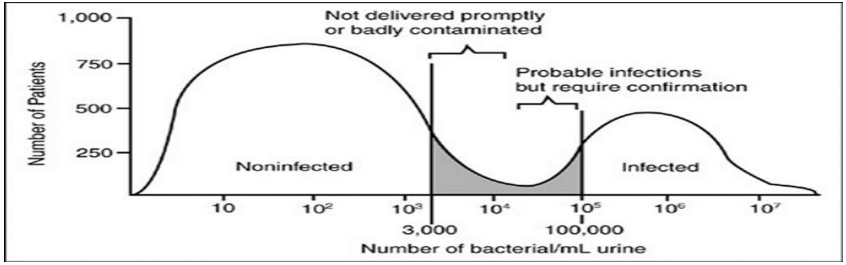
Urinalysis (sample collected after fluid therapy)

Specimen	Cystocentesis
Color	Yellow
Appearance	Cloudy
Specific gravity	1.014
pH	5.5
Protein	Trace
Glucose	3+
Ketones	1+
Bilirubin	1+
Blood	2+
Urobilinogen	0.2
Bacteria	Negative
Epithelial cells	0–3

Quantitative urine culture



➔ Using 0.001/ml loop:
- 1 colony = 1000 CFU/ml
- 100 colonies = 100,000 CFU/ml (CFU is colony forming unit)



Recurrent cystitis

- ➔ Three or more episodes of cystitis /year
- ➔ Requires further investigations such as Intravenous Urogram (**IVU**) or Ultrasound to detect obstruction or congenital deformity.
- ➔ Cystoscopy required in some cases.

Treatment of cystitis

- ➔ Empiric treatment commonly used depending on the knowledge of common organism and sensitivity pattern. (if the patient has no predisposing illness i will give him antibiotics for 3 days only)
- ➔ Treatment best guided by susceptibility pattern of the causative bacteria.
- ➔ Common agents:
  - ◆ Ampicillin, Ampicillin-Clavulanic acid , Cephradine, Ciprofloxacin, Norfloxacin, Gentamicin or TRM-SMX.

Duration of treatment: **three days** for uncomplicated cystitis
10-14 days for complicated and recurrent cystitis.

Prophylaxis required for recurrent cases by Nitrofurantoin or TRM-SMX.

Prevention : drinking plenty of water and prophylactic antibiotic.

Dr's Notes

- Uncomplicated UTI happens mainly to females
- If a male gets UTI then we have to look for the cause.
- postmenopausal women are at higher risk. Why? they start to have changes within their normal flora along with their hormones.
- To differentiate between urethritis and cystitis:
  - pain and tenderness along the suprapubic area are not commonly seen in urethritis.
  - cystitis is more severe than urethritis. More importantly urethritis is associated with discharge.
- Eosinophilic cystitis can be caused infectious "Schistosoma haematobium" and non-infectious.
- We should always obtain midstream urine not the initial stream because the initial maybe contaminated with microbes within the distal urethra.
- when we do urine culture we do a specific type which is Quantitative culture.
- A 25 year old women visited a clinic because of burning pain during urination, increased frequency, urgency for 1 day and suprapubic pain. He also complained about blood-stained debris at the end of urination.
- **Q1) diagnosis?** uncomplicated UTI particularly cystitis.
  - طيب لو غيرناها وقلنا ان عندها fever and flank pain the answer will be pyelonephritis.
- **Q2/ which sample will you collect?** mid-stream urine. If she was a child then mainly suprapubic aspiration or catheter if there's no other choice.
- **Q3/ lab work-up**
- 1-urine-dip (urine analysis) tells us about the nitrites and leukocyte esterase
- 2- urine microscopy which tells you about the bacteria and the presence of WBC or RBC but mainly WBC
- 3- urine culture. What type of culture? Quantitative urine culture
- **Q4/ what is the source of infection?** ascending infection mainly from the GIT
- **Q5/ mention general three risk factors:**
  - short urethra for female
  - Catheterization
  - structural abnormalities.

Common causative agents:

Microorganism	notes
E.coli gram – rod lactose fermenter bacilli	E. coli is the most causative agent of in all types of patients of cystitis whether the patient is normal, diabetic, or sexually active
Staph saprophyticus gram + cocci in clusters, catalase + coagulase – novobiocin resistant	Seen mostly in sexually active females.
Neisseria gonorrhoeae: gram – diplococci metabolizes glucose only	Commonly seen in sexually active female A teenager complains of pain during sexual intercourse and irregular intermenstrual bleeding. She has also begun to experience lower abdominal pain. A pelvic exam reveals a yellow mucopurulent discharge, during the exam, the cervix begins to bleed. Gram stain of discharge reveals Gram intracellular diplococci. The teenager reports that she has been sexually active with several partners over the last year. One of her partners, a male, comes to the same clinic complaining of dysuria and profuse yellow urethral discharge.
Enterococcus faecalis: gram + cocci, catalase -	
Staph epidermidis: gram + cocci in clusters, catalase + coagulase –	Can be the causative agents in patients with catheters.

Summary

Urinary Tract infection Classified into:	**Upper UTIs:** **Cystitis:** infection of the bladder **Urethritis:** sexually transmitted **Prostatitis and Epididymitis**	**Complicated UTI:** nosocomial UTI, relapses, structural or functional abnormalities	
	Lower UTIs: Acute and chronic pyelonephritis	**Uncomplicated UTI:** occurs in non pregnant, young sexually active females	
Risk factors:	**Women:** 1-short urethra. 2-pregnancy. 3-decreased estrogen production during menopause.	**Men:** persistent bacterial infection of the prostate.	**In both sexes:** 1- bladder stone. 2-Urethral stricture 3-Catheterization 4-DM
Pathogenesis:	frequent irritation of the mucosal surface when bacteria ascends to the urinary bladder		
Etiologic agents	**Gram -ve:** **E.coli** - Klebsiella pneumoniae - Proteus spp - P.aeruginosa	**Gram +ve:** Enterococcus faecalis Group B streptococcus *Staphylococcus saprophyticus* (honeymoon cystitis)	**Special cases:** S. epidermidis Yeasts (catheter related) Viruses (Adenovirus, Varicella) Chlamydia trachomatis

Clinical presentation:	➔ Dysuria ➔ Frequency ➔ Urgency ➔ Hematuria ➔ no fever	**Differentiate between cystitis and urethritis: Cystitis is**	acute onset - more sever symptoms Pain, tenderness on the <u>supra-pubic area</u> Bacteriuria, Urine cloudy, malodorous and may be bloody
Types of cystitis	1.**Traumatic cystitis** in women 2.**Interstitial cystitis** (may be due to autoimmune attack of the bladder) 3.**Eosinophilic cystitis** due to *S. haematobium* 4.**Hemorrhagic cystitis** due to radiotherapy or chemotherapy.		
Laboratory diagnosis of cystitis	1-Specimen collection: - Midstream urine (MSU) before starting antibiotic. -Supra-pubic aspiration or catheterization (for children). <u>Catheter urine should not be used for diagnosis of UTI.</u>	2- Microscopic examination: > 10 WBCs /cu.mm Blood cells, parasites or crystals can be seen	3- Chemical screening tests: Urine dipstick: detects <u>nitrites</u> released by bacterial metabolism and leukocyte esterase from inflammatory cells. <u>Not specific.</u> 4-Urine culture:<u>Quantitative culture</u>
Treatment	Ampicillin, Ampicillin-Clavulanic acid , Cephradine, Ciprofloxacin, Norfloxacin, Gentamicin or TRM-SMX	**complicated and recurrent cystitis:** 10-14 days	**Uncomplicated cystitis:** Empiric treatment - for 3 days
Prophylaxis	required for recurrent cases by Nitrofurantoin or TRM-SMX.	**Prevention**	drinking plenty of water and prophylactic antibiotic.

MCQs

1- A 28 years female presented with tenderness in the supra-pubic area with pain during urination, 3 days after her wedding. urinalysis showed presence of bacteria. Which of the following bacteria is most likely to be found?
A- E.coli
B-P.aeruginosa
C-Staphylococcus saprophyticus
D-Enterococcus spp

2-Type of non-infection cystitis which occurs due to Schistosoma haematobium?
A-Traumatic cystitis
B-Interstitial cystitis.
C-Eosinophilic cystitis
D-Hemorrhagic cystitis.

3- A 40 male with history of recurrent cystitis, doctor prescribed him prophylactic drug . Which one of these did he prescribe ?
A- Ampicillin
B-Nitrofurantoin
C-Gentamicin
D-Cephradine

4-urinalysis was required for diagnosis, how should Specimen be collected ?
A-Catheter urine.
B-MSU after antibiotic.
C-MSU before antibiotic.

5- Urine dipstick detect nitrites released by ?
A-leukocyte esterase
B-bacterial toxins.
C-bacteria.
D-bacterial metabolism and leukocyte esterase.

1-C
2-C
3-B
4-C
5-D

SAQ

A mother noticed that her 7 years daughter cries every time she has to use the bathroom, although she uses the bathroom almost 8 time she has not urinated much. The mother described the urine as smelly and cloudy. The daughter temperature is 37.3c, no significant past history.

- ➔ What lab test would you order?
  - Microscopic examination
  - Urine culture
  - Urine dipstick
- ➔ How can we collect urine for this patient?
  - Supra-pubic aspiration or catheterization
- ➔ What kind of urine culture will you perform? What is the importance of urine culture?
  - Quantitative culture, important to identify bacterial cause and antimicrobial sensitivity .
- ➔ What is your differential diagnosis?
  - Cystitis
- ➔ The most likely etiologic agents?
  - E.COLI
- ➔ Based on your diagnosis, why are women are more likely to develop this disease?
  - 1-short urethra.
  - 2-pregnancy.
  - 3-decreased estrogen production during menopause.

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