



MICROBIOLOGY

- SHEET NO. **3**
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Asymptomatic bacteriuria has been briefly mentioned in the epidemiology of UTIs and we will further highlight its importance in this lecture/sheet.

ASYMPTOMATIC BACTERIURIA (ASB)

- Its diagnosis has 2 parts (clinical and microbiological):

REMEMBER: the diagnosis of asymptomatic bacteriuria should be based on culture of a urine specimen collected in a manner that **minimizes contamination**.

- **MICROBIOLOGICAL DIAGNOSIS**

- It tests for the presence of a certain number of CFU (colony forming units) in urine.

- **In asymptomatic women:** recent guidelines define it as 2 consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts $\geq 10^5$ cfu/ml (isolating the same bacterial strain in both specimens is important to eliminate the possibility of a contamination).

- **In men:** a *single*, clean-catch voided urine specimen with 1 bacterial species in a count $\geq 10^5$ cfu/ml can be identified as bacteriuria.

IN SIMPLE TERMS: MICROBIOLOGICAL DIAGNOSIS IS THE CUT OFF COUNT OF CFU IN URINE.

- **CLINICAL DIAGNOSIS**

- Indicates there should be no referable symptoms to the urinary tract, which means that the patient neither has cystitis nor pyelonephritis or prostatitis. There is no presence of symptoms, but there are bacteria in the urine.

*Similar to UTI, Escherichia coli remains the single most common organism isolated from bacteriuric women. But they found that this kind of E. coli has **fewer virulence characteristics** when compared to E. coli causing symptomatic infections. So, basically, a pathogen can exist in the urine without any presentation of symptoms mainly due to the few virulence characteristics present in the E. coli of this clinical entity.*

Important E.Coli virulence factors:
- fimbria/adhesions
- toxins
- flagella
- capsule

Why is asymptomatic bacteriuria important since there is no symptoms affecting the patient?

In certain cases, bacteriuria can have adverse outcomes. Those adverse outcomes can be prevented by antimicrobial therapy.

These certain cases in which bacteriuria should be screened for and treated are:

1. PREGNANCY: ASB can have devastating effects on the pregnancy. Thus, the first category of people who should be screened are pregnant women. Pregnant women should be

screened at least once early in the pregnancy. They should be treated if the results are positive. {FIRST GROUP THAT SHOULD BE SCREENED}.

Pregnant women with bacteriuria will have:

- 20-30 fold increased risk of developing pyelonephritis during pregnancy.
- Increased risk of premature pregnancy.
- Increased risk of infants of low birth weight.
- Preterm labor, preeclampsia.

2. PATIENTS UNDERGOING TRAUMATIC GENITOURINARY PROCEDURES: Most common example of this procedure is transurethral resection of the prostate (removing the prostate through the urethra). During this process, mucosal bleeding occurs. If the patient has ASB, the bacteria can move from the urine into the bloodstream through the damaged mucosa, which causes **bacteremia and sepsis**. Patients with ASB have a **high rate of post-procedure bacteremia and sepsis**.

In addition, advocate screening for ASB in another procedure in the urinary tract, renal implants, is needed because it can also cause mucosal damage.

Also in procedures like removing part of the kidney, dealing with urinary trauma in the ureter or urethra

TO SUM UP: Pregnancy and patients undergoing genitourinary procedures associated with mucosal bleeding (transurethral prostate resection and renal implants) should be screened and treated for asymptomatic bacteriuria.

No need to screen or treat ASB in patients who have catheters

CATHETER-ASSOCIATED URINARY TRACT INFECTION (CAUTI)

A clinical entity that is closely related to UTIs is CAUTI. We know that **the use of catheters** is a risk factor for developing UTIs, increases the chance of having bacteria in the urine without symptoms, and increases the chances of ascending UTIs in complicated UTIs.

Epidemiologically, **CAUTI/UTI is the most common type of healthcare-associated infection**. In an acute care hospital setting, more than 30% of infections are UTIs, and virtually all of those UTIs are associated with the presence of instrumentation, such as a catheter.

The source of microorganisms causing CAUTI can be **endogenous** (typically via meatal, rectal, or vaginal colonization), or **exogenous** (such as via contaminated hands of healthcare personnel or equipment).

How do we manage CAUTI?

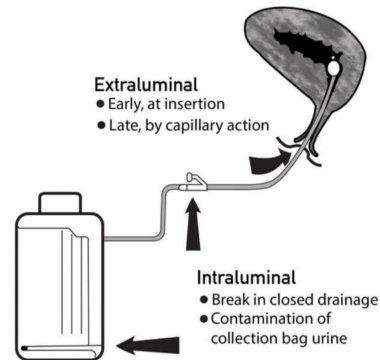
By removing or replacing the catheter. If a catheterized patient has a UTI, you should assume that there are bacteria found on this catheter. These bacteria found can persist on the catheter through the formation of biofilms which are difficult to eradicate. Therefore, you remove or replace the catheter. In addition, you start treatment with empirical IV

antibiotics based on local antibiotic susceptibility patterns (because they differ between regions) and previous infections.

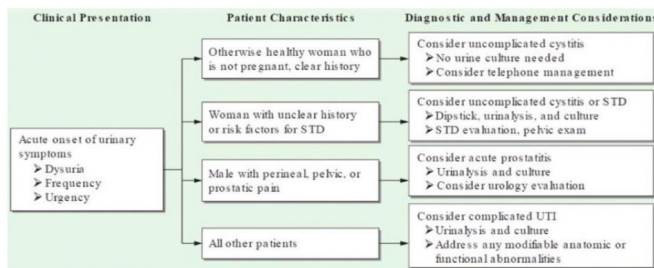
How do we minimize the risk of CAUTI?

Healthcare workers should follow septic techniques while placing the catheter. The catheter should be placed if there are clear indications. In cases of patients who require chronic indwelling catheters (long-term catheters), alternatives should be considered, such as intermittent catheterization.

• There are two ways through which bacteria can enter the body (routes of entry) via the urinary catheter. Potentially harmful bacteria may enter the bladder by either extraluminal or intraluminal routes. The extraluminal route refers to the outside of the catheter— i.e., between the catheter and the uroepithelial surface (urethral surface). The intraluminal route refers to bacteria entering through the inside of the catheter— e.g., when there is a break in the closed drainage system and/or when asepsis is defective. This can occur during specimen collection or when the bag is disconnected.



The following algorithms will help in the approach of a patient with a UTI. Focus on them:



1. Typical presentation of UTI (Dysuria, Frequency, Urgency), and the patient is a:

a) Healthy woman who is not pregnant, with a clear history (most common)

- Consider uncomplicated cystitis (if we rule out STDs and there are risk factors for UTI {female sex, sexual activity}, 90% it is cystitis).
- No need to do further laboratory tests.
- Give empiric therapy depending on local susceptibility pattern, most commonly given antibiotics are Nitrofurantoin or Trimethoprim-sulfamethoxazole for 3 days and follow up within a week or two (simple management).

b) Woman with unclear history and risk factor for STD

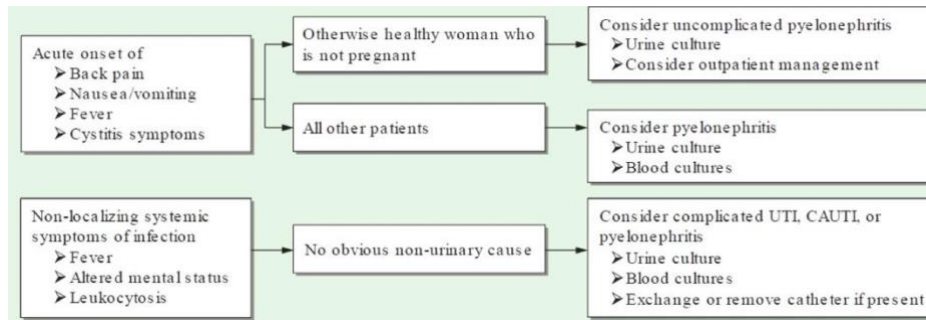
- Consider uncomplicated cystitis or STD.
- Perform some tests: dipstick, urinalysis and urine culture.
- STD evaluation: by asking for risk factors (unprotected sex and urethral discharge).
- Pelvic examination.

c) Male with perineal pain or prostatic pain

- Since the incidence of cystitis in males is very low compared to females, we should consider **acute prostatitis**.
- Urinalysis and culture.
- If there wasn't anything related to prostatitis, then consider a urology evaluation since acute cystitis is uncommon in males.

d) All other patients

- Consider complicated UTI.
- Urinalysis and culture.
- Address any modifiable anatomic or functional abnormalities.
- If there are risk factors that can lead to a complicated UTI, then we should try to address and modify those problems. For example, a patient presents with a urinary stone, which should be lysed.



2. Presentation of the acute onset of back pain, nausea/vomiting, fever, flank pain and cystitis symptoms, and the patient is a:

a) Healthy woman who is not pregnant

- Consider uncomplicated pyelonephritis.
- Urine culture.
- Depending on how acutely ill the patient is, you can consider **outpatient management** (you send them home and give them the antibiotics). If the patient looks acutely ill, you admit them to the hospital and closely monitor their renal function.

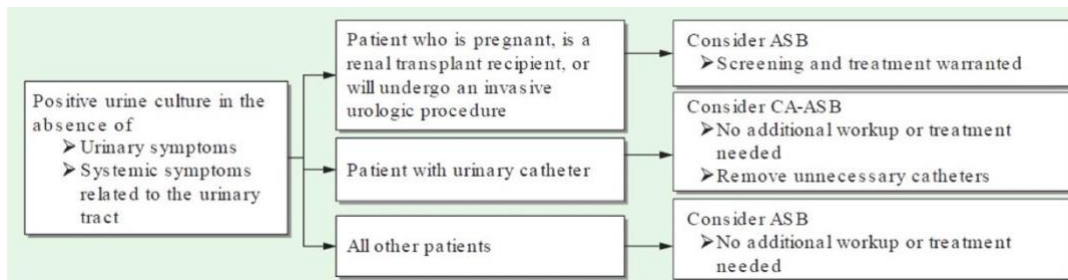
b) All other patients

- Consider pyelonephritis.
- Urine culture.
- Blood culture (*Since there is a predisposing factor that is leading the bacteria to go upstream into the kidney to cause pyelonephritis, the pathogen can often spread from the kidneys to the blood (and the other way around; the pathogen can be found in the blood and spreads to the kidneys), making blood cultures necessary*).

3. Non-localizing systemic symptoms of infection (fever, altered mental status, and leukocytosis) + there is **no obvious non-urinary cause**:

- Consider complicated UTI, CAUTI, or pyelonephritis.
- Urine culture.
- Blood culture.

- Exchange or change catheter if present. *(Most of these patients are elderly and present with altered mental status, and it is often associated with the presence of a catheter. If that is the case, we should exchange or remove the catheter.)*



4. Positive urine culture in the absence of urinary or systemic symptoms that are related to the urinary tract, and if the patient is:

a) Pregnant woman/renal transplantation recipient/will undergo an invasive urologic procedure (transurethral resection of the prostate)

- Consider ASB.
- Screening and treatment warranted.

b) Patient with urinary catheter

- Consider CA-ASB.
- Positive urine culture in the absence of symptoms: **no additional workup or treatment needed** because it is expected that a catheter will lead to or increase the chance of bacteriuria.
- Remove unnecessary catheters (bacteria form biofilms on the catheter).

c) All other patients

- Consider ASB.
- If you happen to accidentally find bacteria when examining the urine, **you don't need to do additional workup or treatment** according to the guidelines as there are no symptoms.

QUESTIONS COLLECTED FROM USLME TEST BANK BY THE PROFESSOR:

QUESTION: 23-year-old woman at **8 weeks gestation** comes to the clinic for her first antenatal visit. She reports no symptoms apart from some **mild nausea** which she is managing with small, frequent meals. **A urine sample is sent as part of the routine pregnancy panel.** Culture shows greater than **100,000 CFU/mL** of **gram- negative rods.** Failure to appropriately treat this condition will place this patient at an increased risk for?

ANSWER: An untreated urinary tract infection in pregnant patients is associated with an increased risk of several complications including: **pyelonephritis, preterm labor,** second-

trimester abortion, preeclampsia, maternal anemia, and chorioamnionitis. **Nitrofurantoin** or **trimethoprim** tend to be used first line for empiric treatment and are both safe in pregnancy.

REMEMBER: Screening for asymptomatic bacteriuria is part of a routine pregnancy panel.

QUESTION: A 25-year-old woman comes to the clinic because of urinary **frequency** and **dysuria** for the past 3 days. She is otherwise healthy and states that she is sexually active. Physical examination shows **suprapubic tenderness**. **Urinalysis** shows the presence of **leukocyte esterase and nitrites**. Which of the following is the most likely causative organism for her condition? **Leukocyte esterase → high sensitivity (not specific because it can present with other type of infections).**

Nitrates → high specificity for E.Coli but not very sensitive.

ANSWER: Escherichia coli is a gram-negative bacteria that is the most common pathogen found in community-acquired urinary tract infections.

EXPLANATION: Frequency and dysuria indicate uncomplicated cystitis as a probable cause. Suprapubic tenderness indicates bladder pain. For some reason, the physician decided to do further workup (urinalysis), and the results reflect an inflammatory process that is taking place. Nitrites are produced from nitrates mostly by Enterobacteriaceae.

QUESTION: An **82-year-old woman** is sent from her nursing home to the emergency department because of concerns for **sepsis**. The patient has late-stage **Alzheimer's**, no known drug allergies, and an **indwelling Foley catheter**. The referral letter states that she has had **back pain, fevers, and tachycardia** for the past two days. Physical examination shows **costovertebral tenderness on the right**. Urinalysis is positive for protein, leukocyte esterase, and nitrates and shows greater than 50 WBC per high powered field. Laboratory studies show a leukocytosis. Which of the following is the next best step in the management of this patient? **With concerns of sepsis blood culture should be done.**

ANSWER: This patient has classic signs of urosepsis, most likely caused by a **catheter-associated urinary tract infection (CAUTI)**. While the culture is pending, the next best step is to **remove the indwelling Foley catheter** and then commence **empiric antibiotic therapy** according to local guidelines.

Costovertebral tenderness can be tested through Murphy's percussion test. You percuss at the costovertebral angle. Tenderness means kidney involvement. Urinalysis is positive for protein, leukocyte esterase, and

nitrites and shows greater than 50 WBC per high powered field: this indicates pyuria.

QUESTION: A 48-year-old woman comes to the emergency department because of **'burning, bloody urine'**. She has been urinating **more frequently** for the past 2 days, but she denies **polydipsia, vaginal discharge, back pain**, abdominal pain, **nausea, vomiting, or fevers**. Physical examination shows that she is afebrile, and her other vital signs are stable. Her abdomen is soft, non-tender and there is **no flank tenderness**. Urine dipstick is positive for leukocyte esterase and nitrites. What is the most appropriate initial treatment option?

ANSWER: Uncomplicated UTI is most commonly caused by Escherichia coli and **trimethoprim-sulfamethoxazole (TMP-SMX)** is the most common first line empiric antibiotic used for treatment whilst awaiting culture results. Nitrofurantoin can also be used.

Individualized treatment choice between nitrofurantoin, TMP-SMX, and ciprofloxacin (fluoroquinolone) depends largely on **clinical picture, allergy, tolerability, compliance and local community resistance patterns**

EXPLANATION: Burning, bloody urine (dysuria & hematuria) can happen as a sign of cystitis. No polydipsia (no excessive water intake) that might increase the frequency of urination. The patient clearly has no STD, no kidney involvement and no constitutional symptoms. You can directly diagnose this as an uncomplicated cystitis and start treatment, or you can do further workup like the dipstick test.

QUESTION: A 38-year-old woman comes to the office because of ongoing urinary **frequency, urgency, and dysuria**. Patient's medical history includes **recurrent urinary tract infections**, with about **four to six each year** for the last three years. She says that her symptoms typically resolve with antibiotic use but will return once she stops using the antibiotics. Urinalysis is performed and shows the following:

Urine Studies	Result
pH	9
Protein	0 mg/dL
Glucose	Negative
Blood	Negative
White blood cells	15-20 cells HPF
Leukocyte esterase	Positive
Epithelial cells	<5 cells HPF
Bacteria	Absent

What is the most likely underlying cause of this patient's recurrent urinary tract infections?

ANSWER: Recurrent urinary tract infections despite appropriate antibiotic use, and a **urinary pH >8** should clue you into a **urease producing organism** or a **struvite kidney stone**.

Struvite kidney stones or triple phosphate stones are composed of magnesium, ammonium and phosphate.

EXPLANATION: A woman who develops a UTI has a 20-30% chance of developing UTI again. The normal value of pH is around 4.5-5.5 so this is a rather alkaline pH (increase in the pH of urine). There is pyuria (15-20 WBCs per HPF; a value above 5 is abnormal). Leukocyte esterase is positive and epithelial cells are present, while bacteria are absent. Some bacteria produce enzymes like urease which breaks down urea and releases ammonia. This leads to an increase in the pH. With that change of pH, some ions will start to precipitate, like magnesium and calcium ions. Therefore, stones may be formed, such as struvite stones. The presence of those stones is probably causing the patient's recurrent UTIs. In this case, we do further testing to confirm the presence of the stone within the urinary tract. We manage it and give antibiotics.

