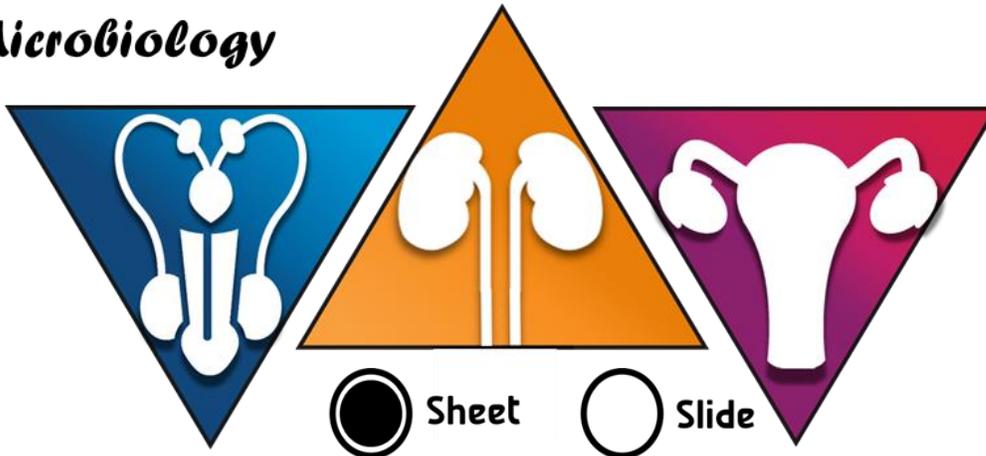




Urogenital system

Microbiology



Number: - Online 1

Done by: - Nadia Sweis

Corrected by: - Lojayn Salah

Doctor: - Anas

In the first lecture we talked about the epidemiology, etiology, and pathophysiology of UTIs. As for the second lecture, we discussed the clinical presentation, signs and symptoms of UTIs, along with a few specific clinical entities that are encompassed within the term Urinary Tract Infection (UTI). Such **clinical entities** include *cystitis*, *pyelonephritis*, *prostatitis* in men, and *asymptomatic bacteriuria (ASB)*. We had already briefly mentioned asymptomatic bacteriuria when we talked about the epidemiology of UTIs, and will further highlight its importance in this lecture.

Asymptomatic Bacteriuria (ASB)

First of all, how do we diagnose asymptomatic bacteriuria?

There are two criteria or parts involved in the diagnosis of ASB; a **microbiological** part and a **clinical** part.

The microbiological part tests for the presence of a certain number of colony forming units (CFU) of bacteria in the urine. For asymptomatic women, recent guidelines define it as *two* consecutive voided urine specimens with isolation of *the same bacterial strain* in counts of $\geq 10^5$ cfu/ml. Isolating the same bacterial strain in both specimens is important to eliminate the possibility of a contamination. Keep in mind that the diagnosis of asymptomatic bacteriuria should be based on culture of a urine specimen collected in a manner that minimizes contamination. For 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. So, to put it more simply, the microbiological part is basically just a cut off count of CFU in urine.

The clinical part indicates that there should be no referable symptoms to the urinary tract, which means that the patient neither has cystitis nor pyelonephritis or prostatitis. In other words, there are bacteria in the urine, but there are no symptoms.

Similar to UTIs, *Escherichia coli* remains the single most common organism isolated from bacteriuric women. But it was found that this kind of *E. coli* is characterized by **fewer virulence characteristics** than the *E. coli* that causes symptomatic infections. So it seems that a pathogen that has fewer virulence characteristics can exist in the urine without causing symptoms.

Even though asymptomatic bacteriuria doesn't have symptoms, it can still have adverse outcomes in certain cases. Those adverse outcomes can be prevented by antimicrobial therapy.

The first category of those few cases in which bacteriuria should be screened for and treated is pregnancy. Women identified with ASB in early pregnancy have a 20–30-fold increased risk of developing **pyelonephritis** during pregnancy. They might as well experience **premature delivery** and have **infants of low birth weight**.

Due to these devastating effects, pregnant women should be screened for bacteriuria by urine culture at least **once** in early pregnancy, and they should be treated if the results are positive.

The second category is patients who are going to undergo traumatic genitourinary procedures. The most common example on these procedures is the *transurethral resection of the prostate*; which means 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. So patients with ASB have a high rate of post-procedure bacteremia and sepsis.

Some also advocate screening for ASB in another procedure in the urinary tract, which is renal implants, since it can also lead to mucosal damage.

That sums up the two categories of patients that should be screened and treated for asymptomatic bacteriuria.

ASB or funguria should not be screened for or treated in patients with an indwelling urethral catheter.

Catheter-associated urinary tract infection (CAUTI)

A clinical entity that is closely related to UTIs is CAUTI. We have discussed the presence of catheters as a risk factor for developing UTIs. It also increases the chance of having bacteria in the urine without symptoms, and ascending UTIs in a complicated UTI.

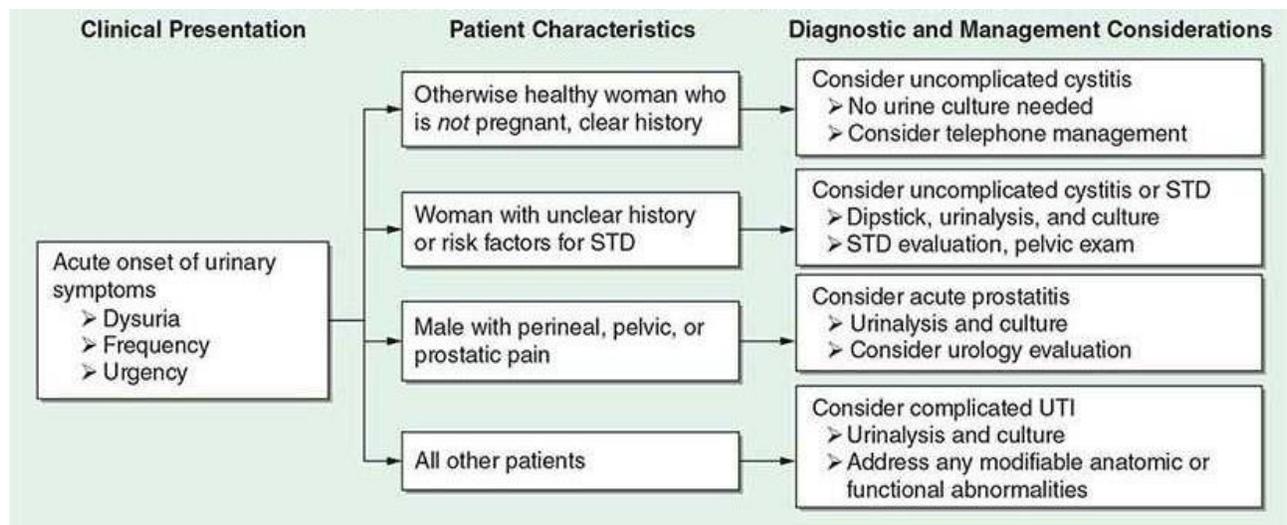
Epidemiologically, CAUTI is the most common type of healthcare-associated infection. In an acute care hospital setting, more than 30% of infections are UTIs, and virtually all of those UTIs are associated with the presence of instrumentation, such as a catheter.

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

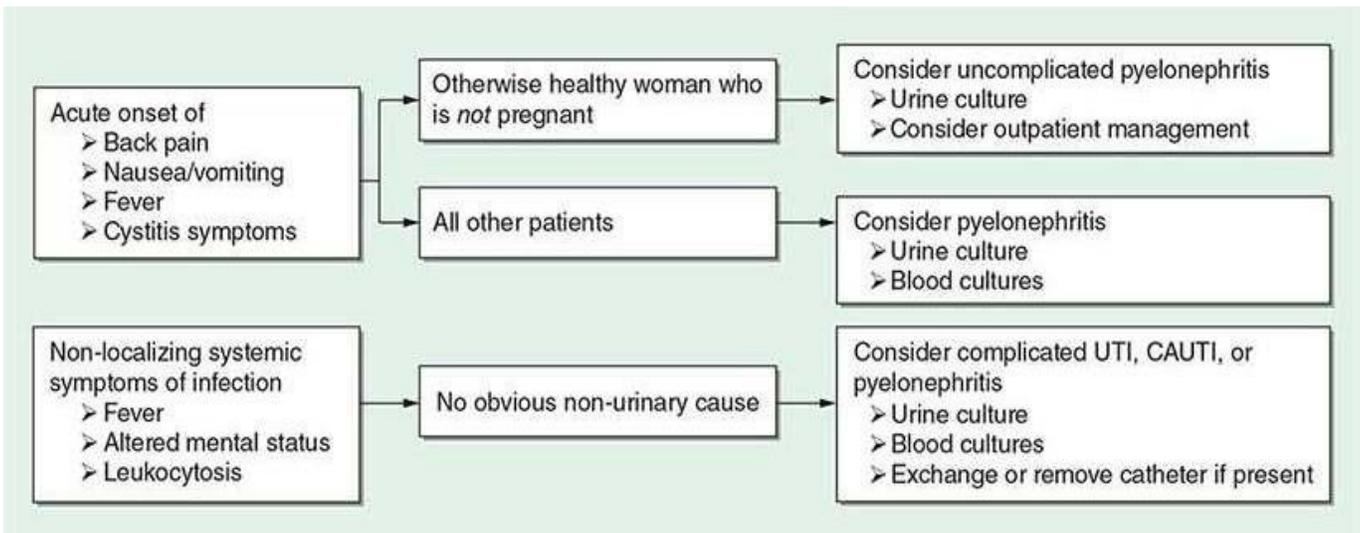
Management of CAUTI is through *removing or replacing* the catheter. If a catheterized patient has a UTI, you should suspect that there are bacteria on this catheter as well. The bacteria can persist on the catheter through the formation of biofilms that are hard to eradicate. Therefore, it is sensible to remove or replace the catheter, if possible. Patients should also be treated with **empirical IV antibiotics**, based on local antibiotic susceptibility patterns - since they differ between regions - and previous infections.

In order to minimize the risk of CAUTI, healthcare workers should follow aseptic techniques while placing the catheter. The catheter should only be placed if there are clear indications. In the case of patients who require chronic indwelling catheters (or long-term catheters), alternatives should be considered, such as intermittent catheterization.

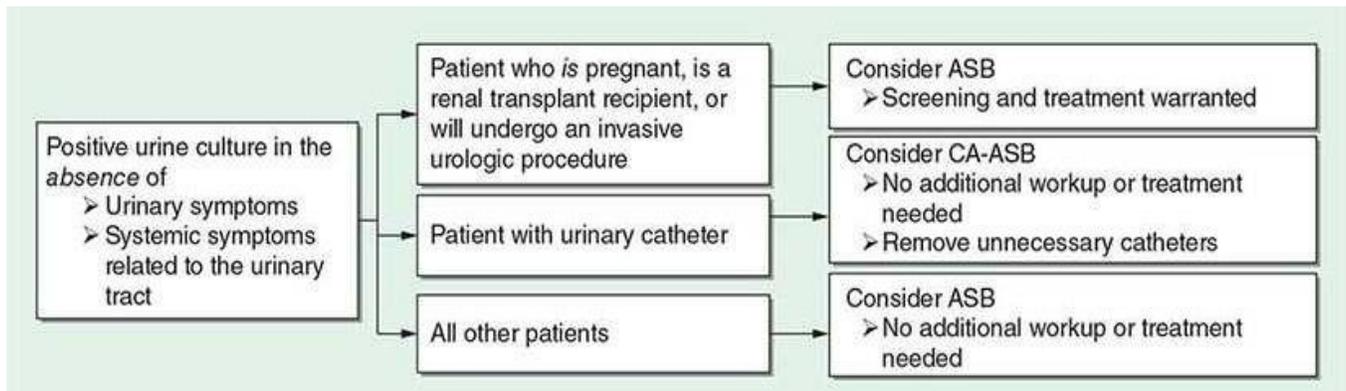
The following algorithms are important and help approach the patients with UTIs. Study them well.



- An otherwise healthy woman: The most common patient that you will probably face. Remember that if we exclude STDs and there are risk factors for a UTI, such as a sexually active female for example, there is a 90% chance that we're dealing with a case of cystitis, and we can diagnose it by history alone. We do not need to do any further laboratory tests in this case, and we give empiric therapy depending on local susceptibility patterns. We usually give Nitrofurantoin or Trimethoprim-sulfamethoxazole for 3 days and follow up within a week or two (simple management).
- If history is unclear: We can do point-of-care tests, such as dipstick, urinalysis, and culture. STD evaluation is done through asking for risk factors like unprotected sex for example, or looking for other signs like urethral discharge. Evaluation is needed, but we are still most likely dealing with an uncomplicated cystitis. You give antibiotics and follow up as well.
- We said that the incidence of uncomplicated cystitis in males is very low compared to females. Therefore, we consider acute prostatitis when a male presents with these symptoms, especially in the presence of perineal, pelvic, or prostatic pain. In the absence of prostatic symptoms, consider a urology evaluation, since acute cystitis is a bit uncommon in males.
- 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 can present with a urinary stone, which should be lysed.



- In the case of back pain, which includes costovertebral tenderness and flank pain, and constitutional symptoms such as nausea and vomiting, we should suspect pyelonephritis. Depending on how acutely ill the patient is, you can consider outpatient management (you send them home and give them the antibiotics), and if the patient looks acutely ill, you admit them to the hospital and closely monitor their renal function. Blood cultures should be done in certain cases along with the urine 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.
- When the patient has constitutional symptoms that are unrelated to the urinary tract, but no non-urinary cause can be identified, UTIs should be considered. Basically because they are quite prevalent, and are the most common infection in a healthcare setting. Accordingly, you do the necessary tests. 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.



- Remember that invasive urologic procedures include transurethral resection of the prostate.
- A patient with urinary catheter and 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. Unnecessary catheters are removed since bacteria form biofilms on them.
- In all other patients, 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

Q: A 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.¹ 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?

A: 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.

¹ screening for asymptomatic bacteriuria is part of a routine pregnancy panel

Q: 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?

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

Further 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. Nitrites are produced from nitrates mostly by enterobacteriaceae.

Q: 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 tenderness² on the right. Urinalysis is positive for protein, leukocyte esterase, and nitrates and shows greater than 50 WBC per high powered field³. Laboratory studies show a leukocytosis. Which of the following is the next best step in the management of this patient?

A: 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.

² This can be tested through Murphy's percussion test. You percuss at the costovertebral angle. Tenderness means kidney involvement.

³ This indicates Pyuria.

Q: 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?

A: 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**

Further 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.

Q: 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:

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

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

A: 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.

Further explanation: We said that 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.

“A flower does not think of competing to the flower next to it. It just blooms.”