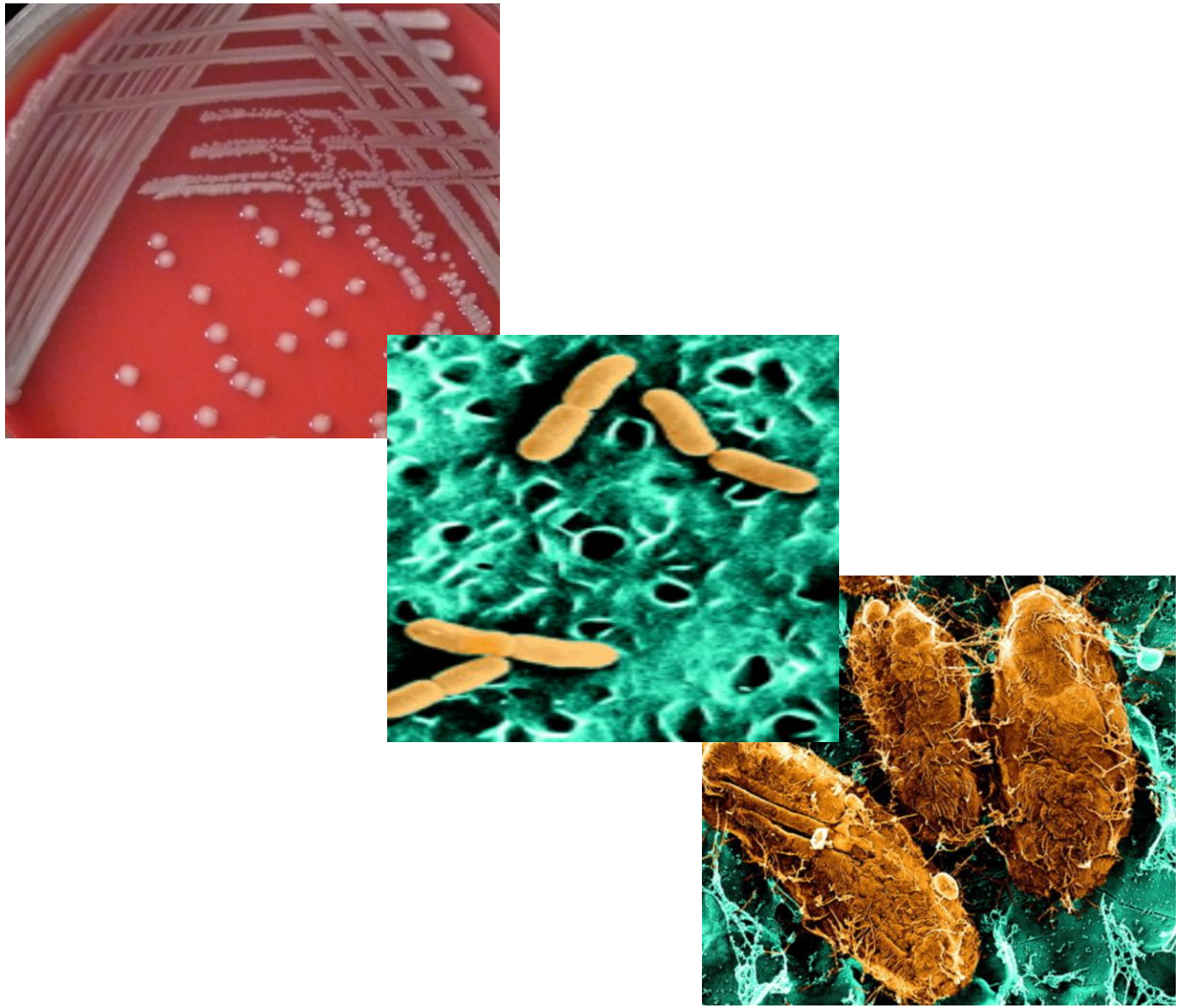
Microbiology of Urogenital system



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Lecture 2

How do UTI patients present?

The term urinary tract infection (UTI) encompasses a variety of clinical entities, including :

- **Asymptomatic bacteriuria (ASB)**
- **Cystitis**
- **Pyelonephritis.**
- **Prostatitis**

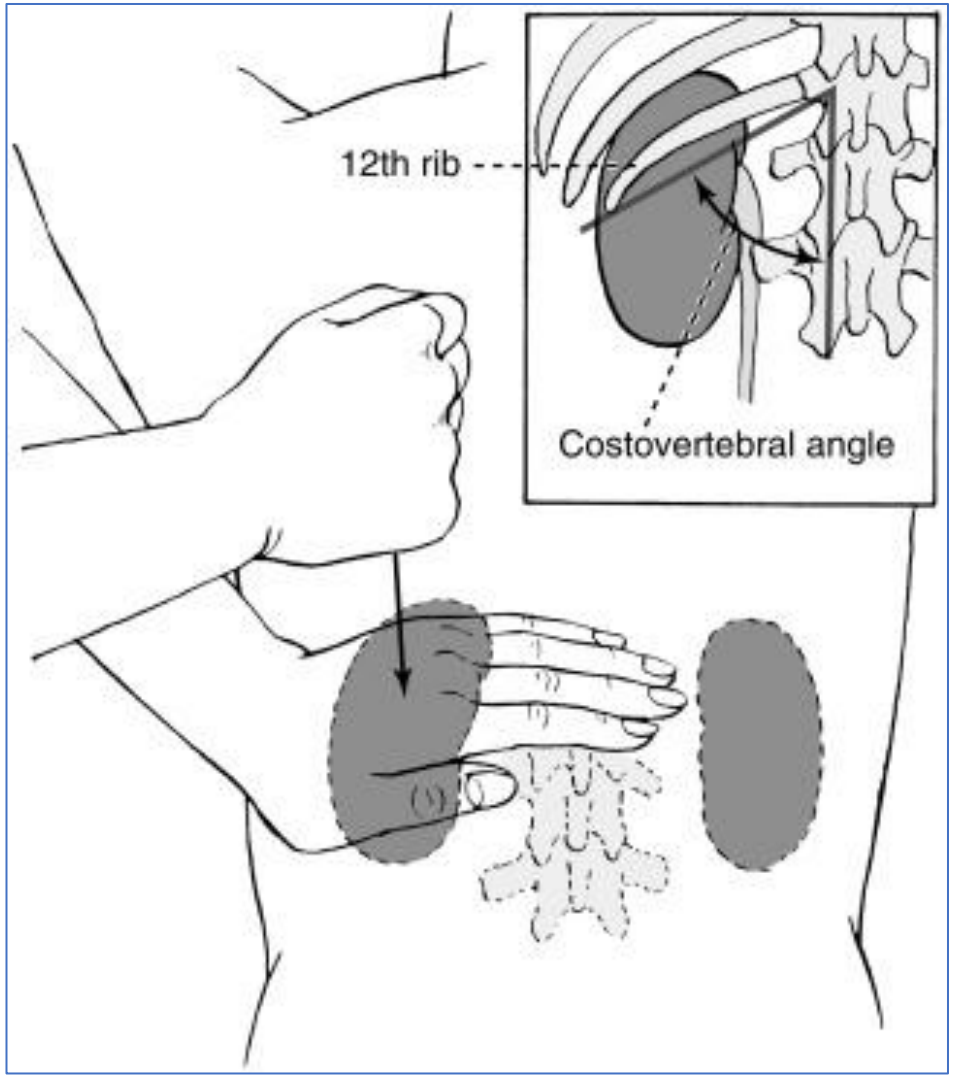
Cystitis and pyelonephritis

- The typical symptoms of **cystitis** are **dysuria**, urinary **frequency**, and **urgency**. **Nocturia**, **hesitancy**, suprapubic **discomfort**, and gross **hematuria** are often note as well.

- **Mild pyelonephritis** can present as **low-grade fever** with or without lower-back or **costovertebral-angle pain**.

- **Severe pyelonephritis** can manifest as **high fever**, **rigors**, **nausea**, vomiting, an **flank and /or loin pain**.

- Constitutional symptoms, such as **fever**, are mild or **absent in cystitis**, but commonly **found** in **pyelonephritis**.



Murphy's percussion test is also known as **costovertebral angle tenderness**

Cystitis and pyelonephritis

Clinical Features and Virulence Mechanisms in **Cystitis** and **Pyelonephritis**

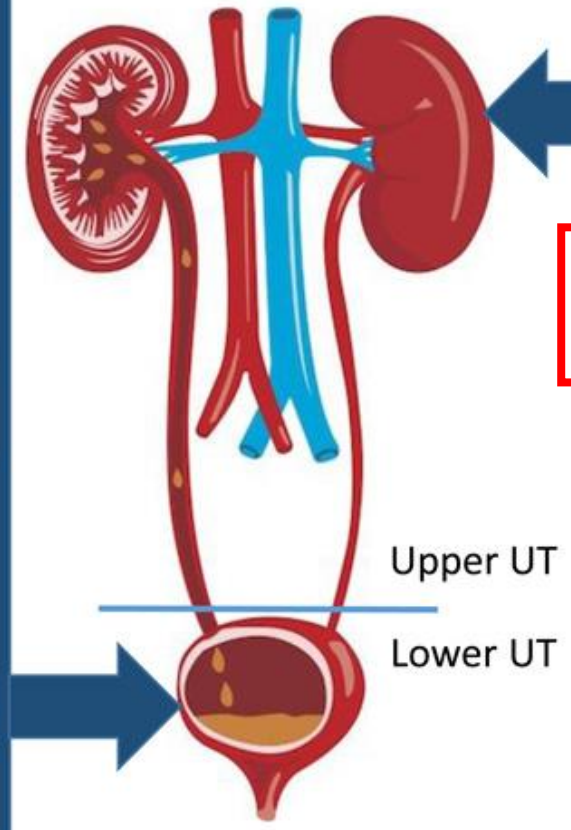
Cystitis

Risk factors
- Female sex, history of UTI
- Sexual activity
- Vaginal infection
- Diabetes, obesity, genetic susceptibility

Clinical symptoms
- Frequent and urgent urination
- Dysuria, suprapubic pain
- Nocturia, hematuria, malaise

Causative organisms
- UPEC
- *Klebsiella pneumoniae*
- *Staphylococcus saprophyticus*
- *Enterococcus faecalis*
- Others

Selected UPEC virulence factors
- Adhesins (Type 1 & other chaperone-usher pili)
- Toxins (HlyA, CNF1)
- Siderophores (aerobactin, enterobactin, yersiniabactin)
- Capsule



Pyelonephritis

Risk factors
- Diabetes
- HIV/AIDS
- Iatrogenic immunosuppression,
- Congenital or acquired urodynamic abnormalities

Clinical symptoms
- Back and/or flank pain
- Fever, chills, malaise
- Nausea, vomiting, anorexia

Causative organisms
- UPEC
- *Klebsiella pneumoniae*
- *Staphylococcus aureus*
- *Enterococcus faecalis*
- *Proteus* spp
- Others

Selected UPEC virulence factors
- Adhesins (Type 1 & P pili)
- Toxins (HlyA, CNF1)
- Siderophores (aerobactin, Iha, TonB siderophore receptor)
- Flagella

UTI diagnosis – History and self diagnosis

- The diagnosis of any of the UTI syndromes or ASB begins with a **detailed history.** (E.g. in women presenting with at least one symptom of UTI (dysuria, frequency, hematuria, or back pain) and without complicating factors, the probability of acute cystitis or pyelonephritis **is 50%**).

- If vaginal discharge and complicating factors are absent and risk factors for UTI are present, then the probability of UTI is close to **90%**, and no laboratory evaluation is needed before initiation of therapy.

- One significant concern is that **sexually transmitted disease**—that caused by Chlamydia trachomatis in particular—may be inappropriately treated as UTI.

UTI diagnosis – dipstick and urinalysis

- dipstick and urinalysis provide point-of -care information

Some points to consider:

- Only members of the **family Enterobacteriaceae** convert nitrate to nitrite.
- When **voiding frequently**, the dipstick test or nitrite is less likely to be positive.
- The **leukocyte esterase test** detects this enzyme in the host's polymorphonuclear leukocytes in the urine.
- A **negative dipstick test** is not sufficiently sensitive to rule out bacteriuria in pregnant women, in whom it is important to detect all episodes of bacteriuria.

Table 1. Urinalysis Results

Test	Usual Range	Indicators of Infection	Accuracy
Bacteria	Absent	Any amount	Low sensitivity,[a] high specificity[b]
Leukocyte esterase	Absent	Positive = pyuria, presence of WBCs in urine	High sensitivity, low specificity
WBC	<5	Pyuria: WBC >10	High sensitivity, low specificity
Nitrite	Absent	Positive = presence of bacteria that reduce nitrate	Low sensitivity, high specificity
RBC	<5	Hematuria common in infection	Low sensitivity, high specificity
Epithelial cells	<5	<5 = good urine sample	High epithelial cells indicate contamination with skin flora
pH	4.5-8	pH ↑ if urea-splitting organism (e.g., *Proteus mirabilis*) is present	Low specificity (there are many other causes of alkaline urine)

[a] *Sensitivity = likelihood of positive test when disease is present.*
[b] *Specificity = likelihood of negative test when disease is not present.*
Source: Reference 1.

UTI diagnosis – Urine culture

- The detection of bacteria in a **urine culture** is the diagnostic "**gold standard** " for UTI.

- Studies on women with symptoms of cystitis have found that a **colony count threshold of >10^2 bacteria/mL** is more sensitive (95%) and specific (85%) than a **threshold of 10^5/mL** for the diagnosis of acute cystitis in women.

- Urine specimens frequently become **contaminated** with the normal microbial flora of the distal urethra, vagina, or skin. Thus using Midstream Clean Catch Specimen or suprapubic aspiration might be needed.

culture **results** do not become available **until 24 h** after the patient's presentation. Identifying specific organism(s) can require an **additional 24 h**

- Antimicrobial therapy is warranted for **any symptomatic UTI**.
- The choice of antimicrobial agent and the onset and duration of therapy depend on **the site of infection** and the presence or absence of **complicating conditions**.
- Antimicrobial resistance among uropathogens **varies from region to region** and impacts the approach to empirical treatment of UTI.

Table 1. Antibiotics for non-pregnant women aged 16 years and over

Antibiotic[1]	Dosage and course length[2]
First choice[3]	
Nitrofurantoin – if eGFR ≥45 ml/minute	50 mg four times a day or 100 mg modified-release twice a day for 3 days
Trimethoprim – if low risk of resistance and not used in the past 3 months	200 mg twice a day for 3 days
Second choice (no improvement in lower UTI symptoms on first choice taken for at least 48 hours, or when first choice not suitable)[3,4]	
Nitrofurantoin – if eGFR ≥45 ml/minute and not used as first choice	50 mg four times as day or 100 mg modified-release twice a day for 3 days
Pivmecillinam	400 mg initial dose, then 200 mg three times a day for a total of 3 days
Fosfomycin	3 g single dose sachet

UTI treatment

- Antimicrobial therapy is warranted for **any symptomatic UTI**.

- The choice of antimicrobial agent and the onset and duration of therapy depend on **the site of infection** and the presence or absence of **complicating conditions**.

- Antimicrobial resistance among uropathogens **varies from region to region** and impacts the approach to empirical treatment of UTI.

TABLE 33-1

TREATMENT STRATEGIES FOR ACUTE UNCOMPLICATED CYSTITIS

DRUG AND DOSE	ESTIMATED CLINICAL EFFICACY, %	ESTIMATED BACTERIAL EFFICACY,[a] %	COMMON SIDE EFFECTS
Nitrofurantoin, 100 mg bid × 5–7 d	84–95	86–92	Nausea, headache
TMP-SMX, 1 DS tablet bid × 3 d	90–100	91–100	Rash, urticaria, nausea, vomiting, hematologic abnormalities
Fosfomycin, 3-g single-dose sachet	70–91	78–83	Diarrhea, nausea, headache
Pivmecillinam, 400 mg bid × 3–7 d	55–82	74–84	Nausea, vomiting, diarrhea
Fluoroquinolones, dose varies by agent; 3-d regimen	85–95	81–98	Nausea, vomiting, diarrhea, headache, drowsiness, insomnia
β-Lactams, dose varies by agent; 5- to 7-d regimen	79–98	74–98	Diarrhea, nausea, vomiting, rash, urticaria

Research Article

Urinary Tract Infection in South Jordanian Population

Khaled M. Khleifat , Muayad M. Abboud , Sharaf S. Omar and Jafar H. Al-Kurishy

The result of different examination test suggest that the *Escherichia coli* is responsible for the large proportion of infection (53.24%), followed by other strains like *Enterococcus faecalis* (24.05%), *Proteus* sp. (19.537%), *Staphylococcus aureus* (19.206%), *Staphylococcus epidermidis* (7.8%), *Staphylococcus saprophyticus* (13.2%), *Klebsiella* sp. (11.96%), *Enterobacter* sp. (5.128%), *Pseudomonas aeruginosa* (3.4%), *Citrobacter* sp. 1.92% and *Serratia marcescens* (0.8%).

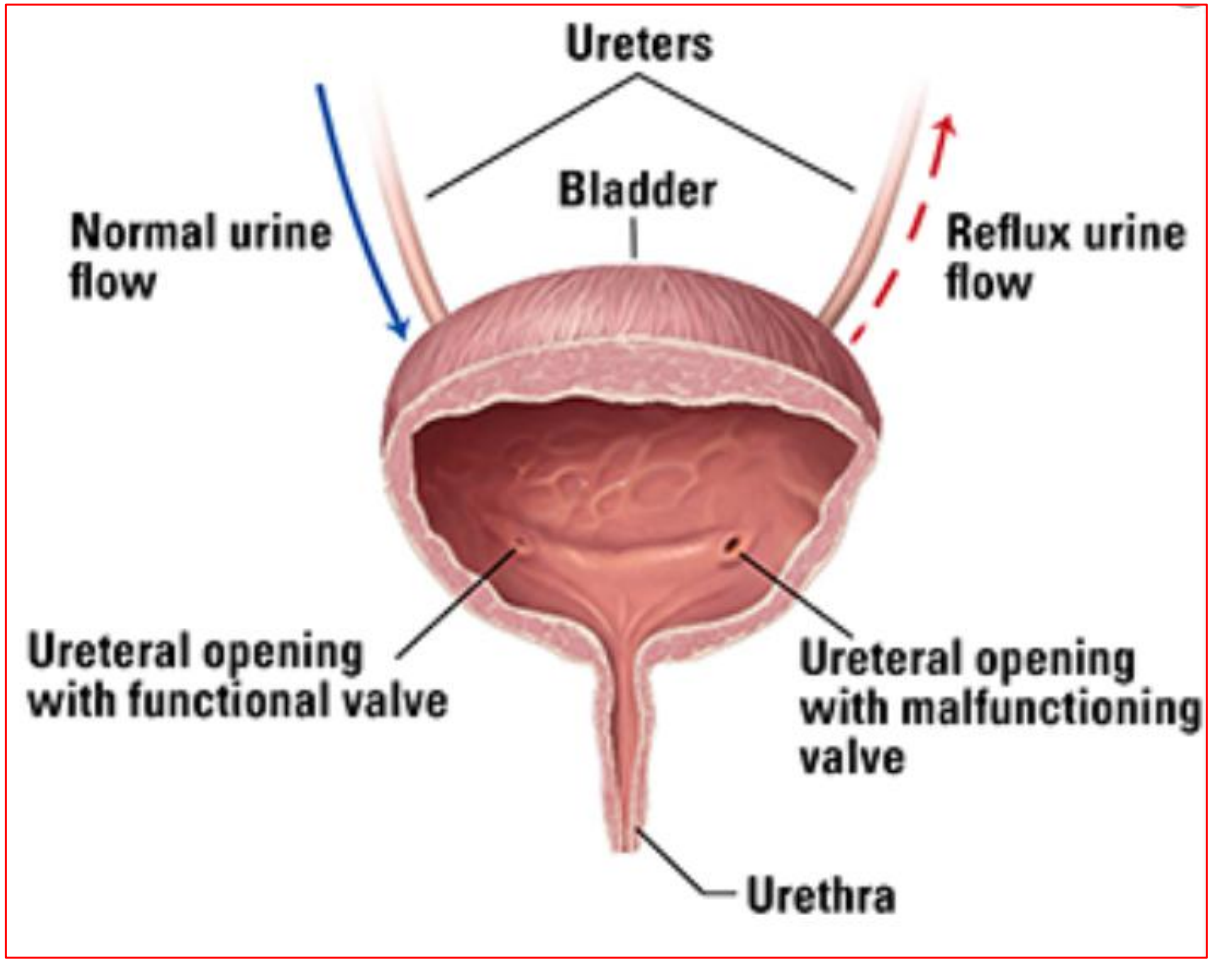
For the treatment of urinary tract infection the antibiotic Ciprofloxacin (5 µg disk-1) was found to be most effective antimicrobial agents against all isolated bacteria strains, while Oxacillin (1 µg disk-1) was found to be the least effective.

Complications of pyelonephritis

- A single episode of acute pyelonephritis in an adult woman can lead to **renal scarring.**

- Pyelonephritis becomes potentially fatal when secondary conditions develop such as **emphysematous pyelonephritis** (20–80% mortality rate), **perinephric abscess** (20– 50% mortality rate), or **sepsis**.

- **Chronic pyelonephritis** might develop following acute pyelonephritis in childhood in the context of (**vesico-ureteric reflux**) VUR.



Complications of pyelonephritis

- **Emphysematous pyelonephritis:** A severe, necrotizing, acute, multifocal bacterial nephritis, with extension of the infection through the renal capsule. Gas is found in the renal substance and perinephric space. Often happens in diabetics.

- Diagnosis is confirmed by **CT scan**.

- Treatment involves **antibiotics**, **drainage**, **nephrectomy**.

- Mortality is high (around 60%)

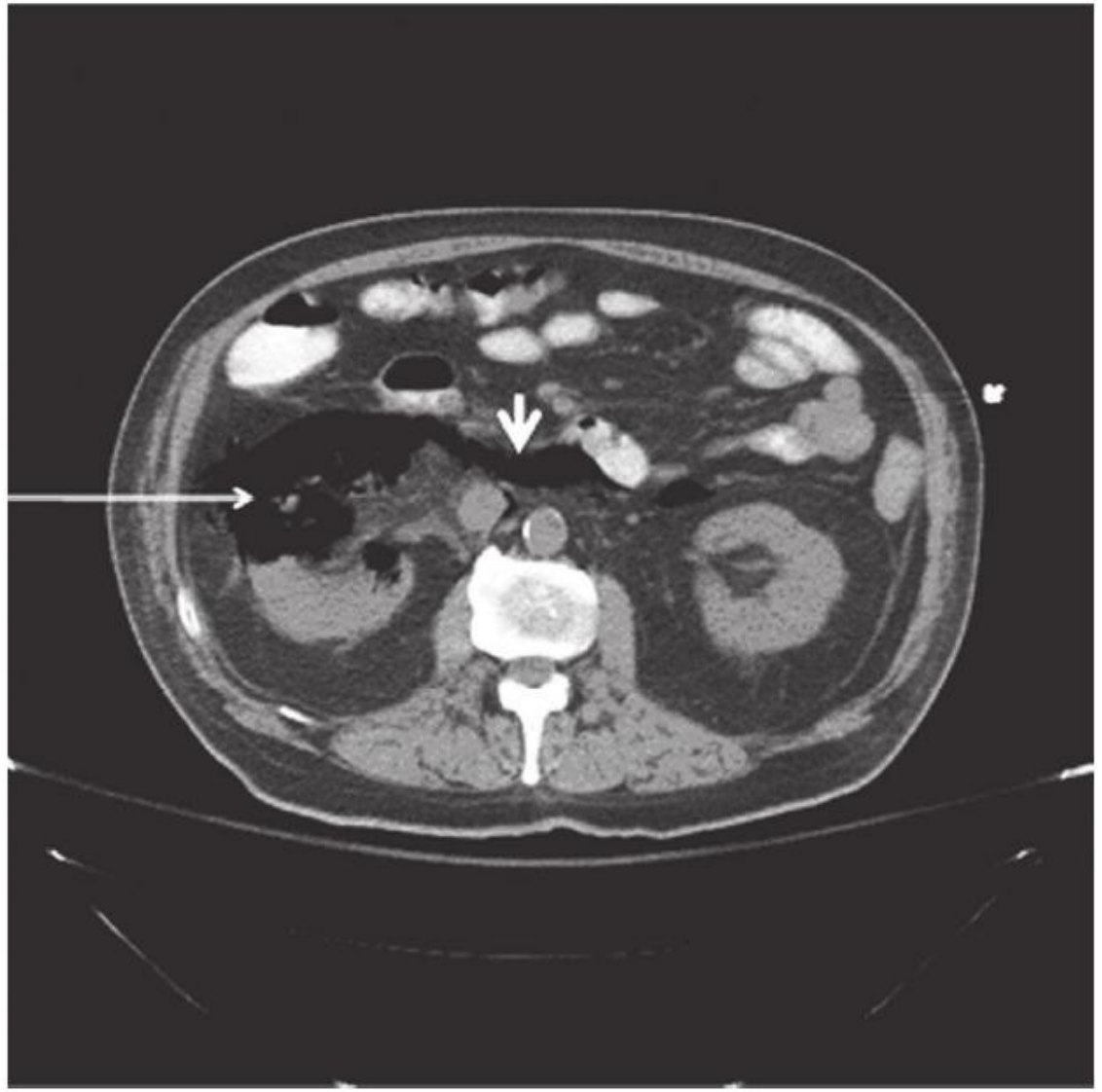


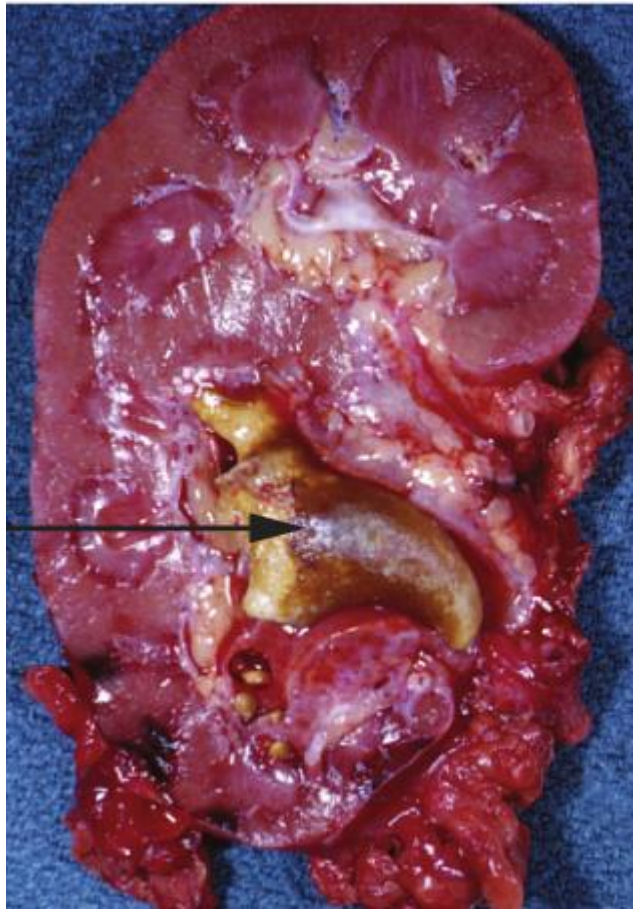
FIGURE 33-2
Emphysematous pyelonephritis. Infection of the right kidney of a diabetic man by Escherichia coli, a gas-forming, facultative anaerobic uropathogen, has led to destruction of the renal parenchyma (arrow) and tracking of gas through the retroperitoneal space (arrowhead).

Complications of pyelonephritis

- **Xanthogranulomatous pyelonephritis,** A rare, serious, debilitating illness characterized by a chronic inflammatory mass originating in the renal parenchyma.

- Gross appearance: mass of yellow tissue composed of **lipid- laden macrophages** and inflammatory cells regional **necrosis**, and **haemorrhage**.

- Often associated with infection by *Proteus, E. coli*, or *Pseudomonas* spp. in the context of chronic obstruction.



A large staghorn calculus (arrow) is seen obstructing the renal pelvis and calyceal system. The lower pole of the kidney shows areas of hemorrhage and necrosis with collapse o cortical areas.

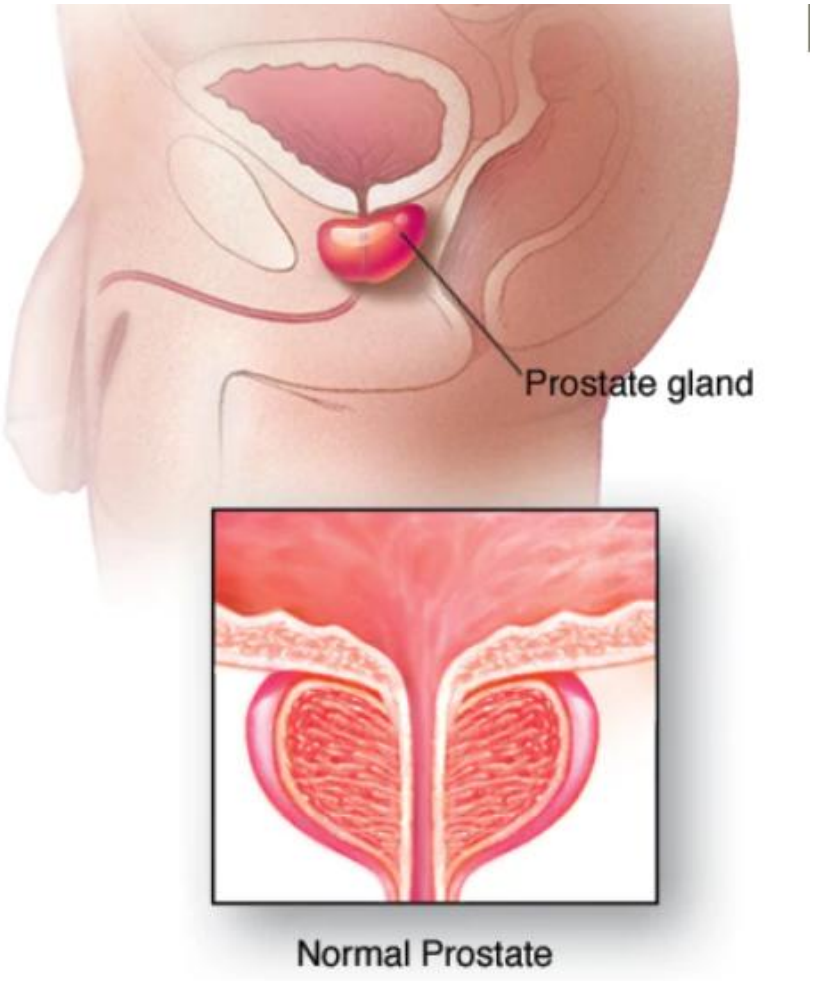
Prostatitis

- Up to 50% of men will experience symptoms of prostatitis at some time in their lives. However, **actual bacterial infections of the prostate account for a minority of these cases**

- Prostatitis includes both infectious an non-infectious abnormalities of the prostate gland.

- **Acute bacterial prostatitis** presents as **dysuria**, **frequency**, and **pain** in the prostatic pelvic or perineal area. Fever and chills are usually present, an symptoms of bladder outlet obstruction are common.

- Chronic/ recurrent bacterial prostatitis occurs in young and middle- aged men. Risk factors include **previous acute prostatitis**, history of prior **manipulation** of the urinary tract, diabetes, smoking.



Bacterial prostatitis/ management

- The pathogens associated with acute prostatitis **reflect the spectrum of organisms causing cystitis**, urethritis, and deeper genital tract infections (such as epididymitis). Thus, gram-negative infections, especially with **Enterobacterales**, are the most common.

- The presence of typical symptoms of prostatitis should prompt digital rectal exam, and the finding of an **edematous and tender prostate on physical exam** in this setting usually establishes the diagnosis of acute bacterial prostatitis.

- In order to establish the microbial etiology, a urine Gram stain and culture should be obtained in all men suspected of having acute prostatitis. Gram stain of the urine, if positive, can be used as a guide to initial therapy

- Treatment of acute prostatitis includes antimicrobial therapy and supportive measures to reduce symptoms. Rarely, more invasive intervention is indicated to manage complications.

Further reading:

- Oxford handbook of infectious diseases and microbiology-

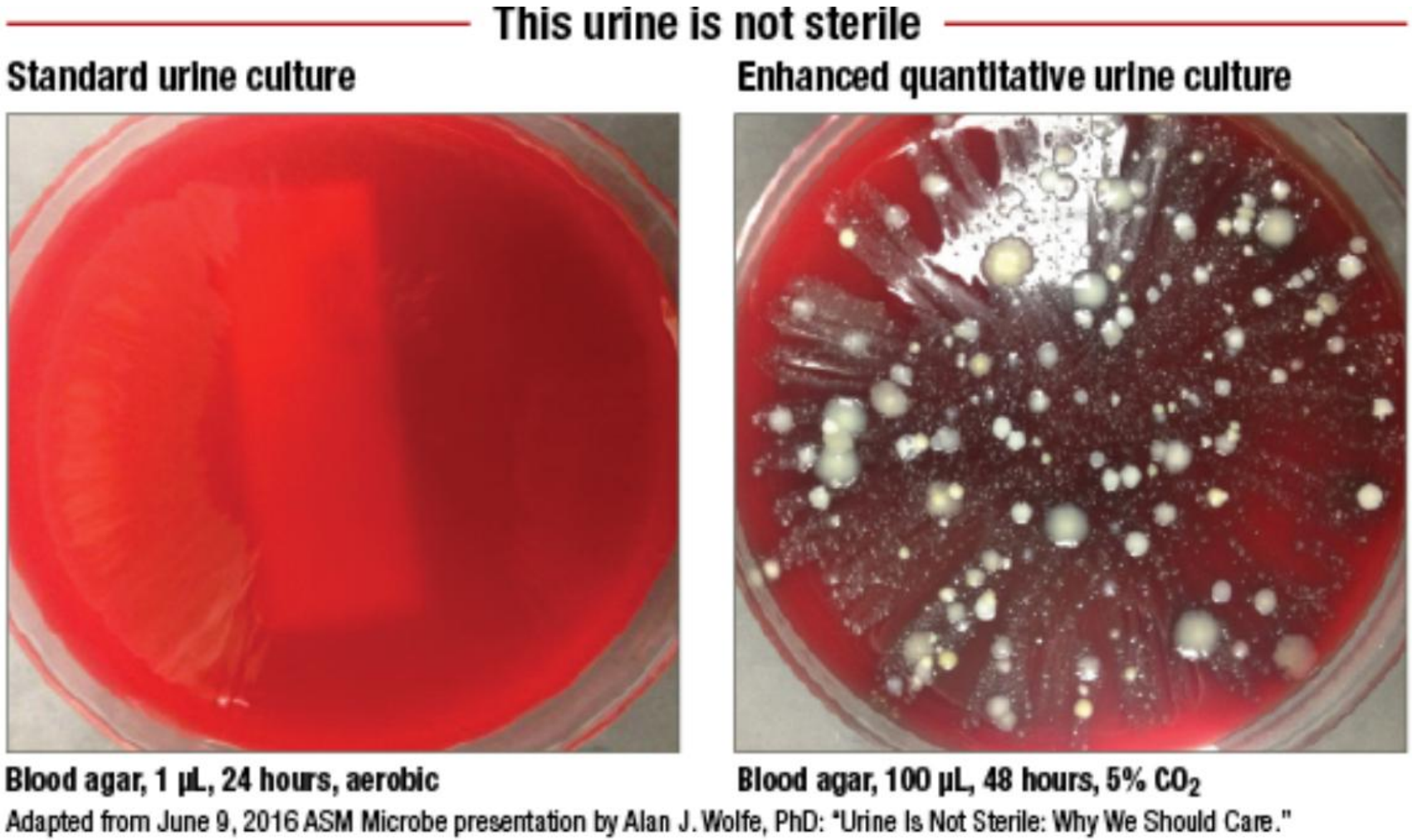
Part4: Clinical syndroms

Chapter 17 Urinary tract infections

- Harrison's Infectious Diseases 3rd Edition

SECTION III Infections in organ systems

Chapter 33



"I thought, like everybody thought, that urine was sterile except when there's an infection," he says. The Loyola team tried more than two dozen different combinations of atmospheric conditions, media, incubation times, and urine volumes before arriving at the streamlined EQUC. The process of studying each of these and seeing under which conditions the uropathogens grew best took about a year.

The Clinical Urine Culture: Enhanced Techniques Improve Detection of Clinically Relevant Microorganisms
Journal of clinical microbiology 2016