Urinary tract infections

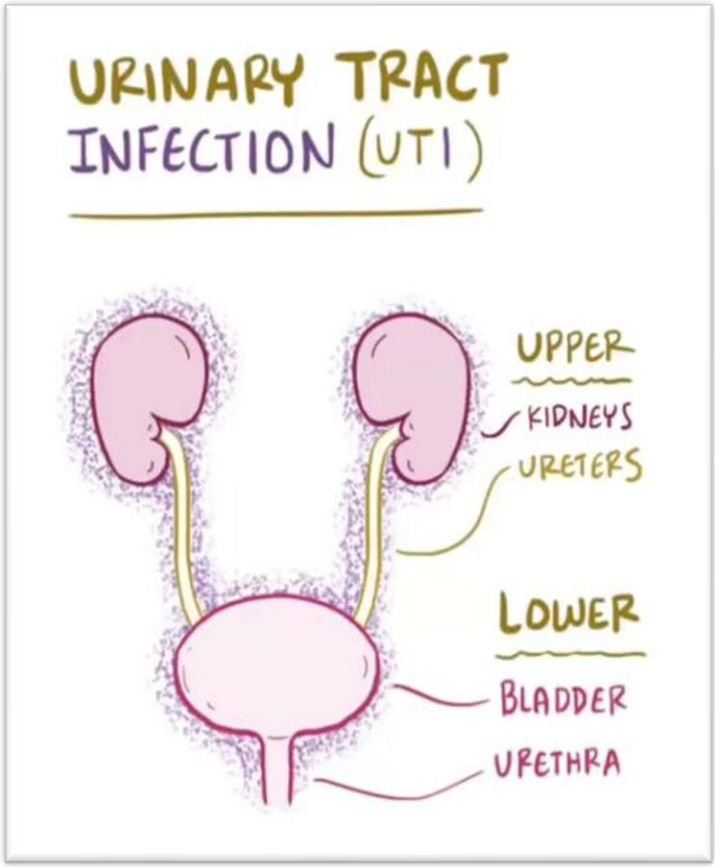
(Lectures 49,50)

Dr. Amany M. Nafeh

Assistant professor of Medical

Microbiology & Immunology

Faculty of Medicine Assiut University



Objectives:

1. **List the commonest causative agents (Pathogens) of UTI.**
2. **Recognize risk factors for UTI.**
3. **Explain the pathogenesis and microbiology of UTI.**
4. **Recognize classification of UTI.**
5. **Describe clinical manifestations of UTI.**
6. **Outline the laboratory diagnostic approach in different UTIs.**

Pathogens:

- **Urethritis**:

✓ Gonococcal urethritis caused by Neisseria gonorrhoeae

✓ Nongonococcal urethritis caused by Chlamydia trachomatis (50%), Ureaplasma urealyticum (20%), Mycoplasma hominis (5%), Trichomonas (1%), or herpes simplex

- **Cystitis :**

✓ E. coli in >80%; second are other (gram-negative bacilli) such as Proteus, Klebsiella, Enterobacter, Pseudomonas aeruginosa etc.; enterococci occasionally, and Staph. saprophyticus in young women

- **Pyelonephrites**:

✓ E. coli is most common pathogen; others include Klebsiella, Proteus, and Enterococcus. Patients who are immunosuppressed and subjected to indwelling catheters are more prone to Candida.

- **Other pathogens:**

✓ Staphylococci: S. aureus, S. epidermidis, S. saprophyticus.

✓ TB

✓ Leptospira.

- **Viruses:**

✓ adenovirus, mumps, HIV, cytomegalovirus can cause hemorrhagic cystitis in children and immunocompromised patients.

Epidemiology:

- **According to age:** UTI is more common in elderly, and infants.
- **According to sex:** UTI is more common in women.

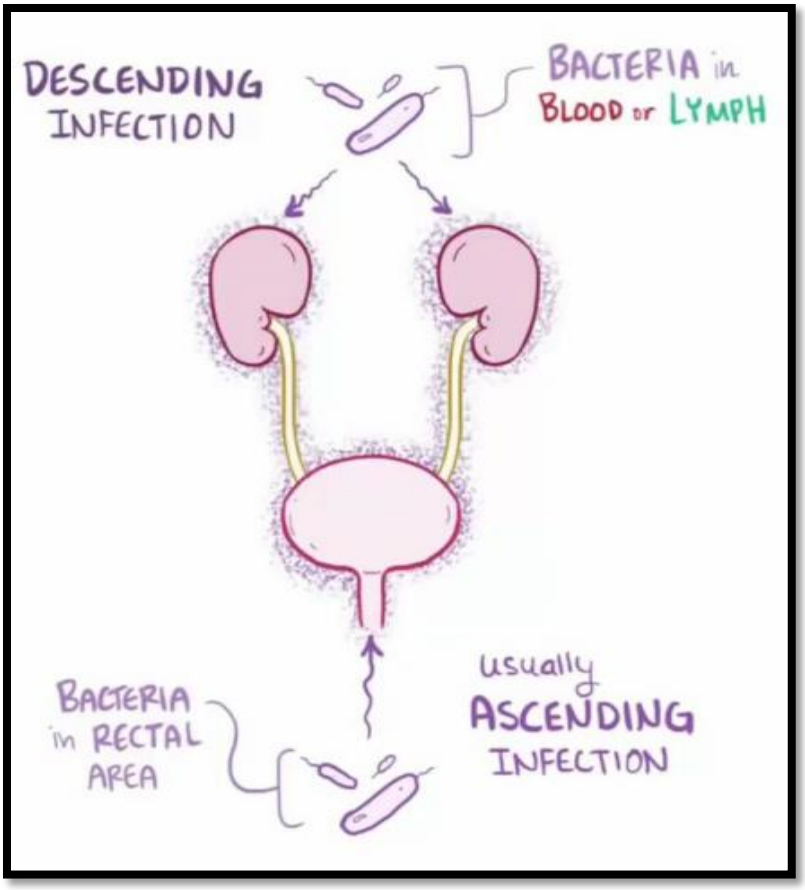
Mode of transmission:

1-Ascending route:

- In most cases bacteria ascends from the anus to the urethra **(urethritis)** especially with **E coli** or from the urethra to the bladder **(cystitis)**. Bacterial organisms can further ascend through the ureter and infect the kidney causing a renal parenchymal infection **(pyelonephritis).**

2-Descending route (through blood or lymph): Staph aureus, Candida, T.B, (rare)

3-Direct extension: from intestinal fistula.



Risk factors:

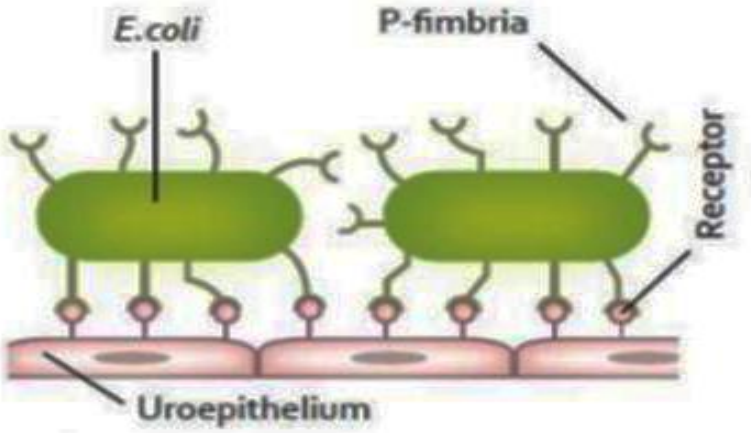
- Any cause of urinary stasis or any foreign body predisposes

Tumors/stones/strictures/prostatic hypertrophy/neurogenic bladder.

- Sexual intercourse in women ("honeymoon cystitis")
- Catheters are a major cause, and the risk is directly related to the length of catheterization (3–5% per day).
- Women > men (due to short urethra).
- More common in childhood.
- Pregnancy, Postmenopausal (decrease in estrogen).
- Immunocompromised patients.
- Diabetes mellitus.

Bacterial Virulence Factors:

1- Enhanced adherence (Increased adhesion) of uropathogenic *E coli* to receptors on uroepithelial cells by type 1 pili and P fimbria



2- Capsular polysaccharide antigen with antiphagocytic activity: e.g.Klebseilla.

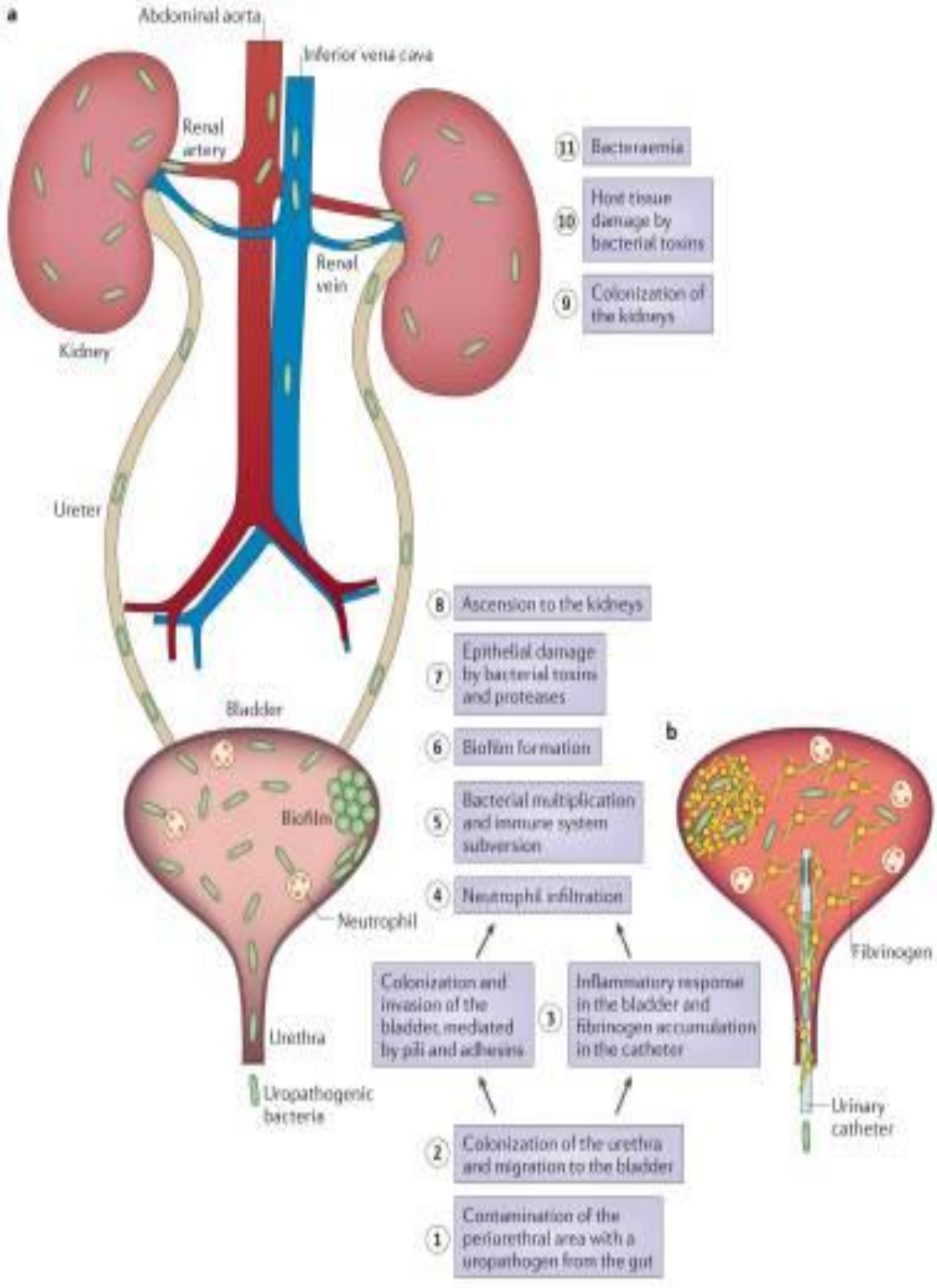
3- Flagella- enhanced motility e.g..*E.coli*

4- Production of hemolysin (a membrane damaging toxin), e.g. *E.coli* induces pore formation in cell membrane

5- Production of urease and changing the PH into alkaline is correlated with pyelonephritis and stones e.g. Proteus.

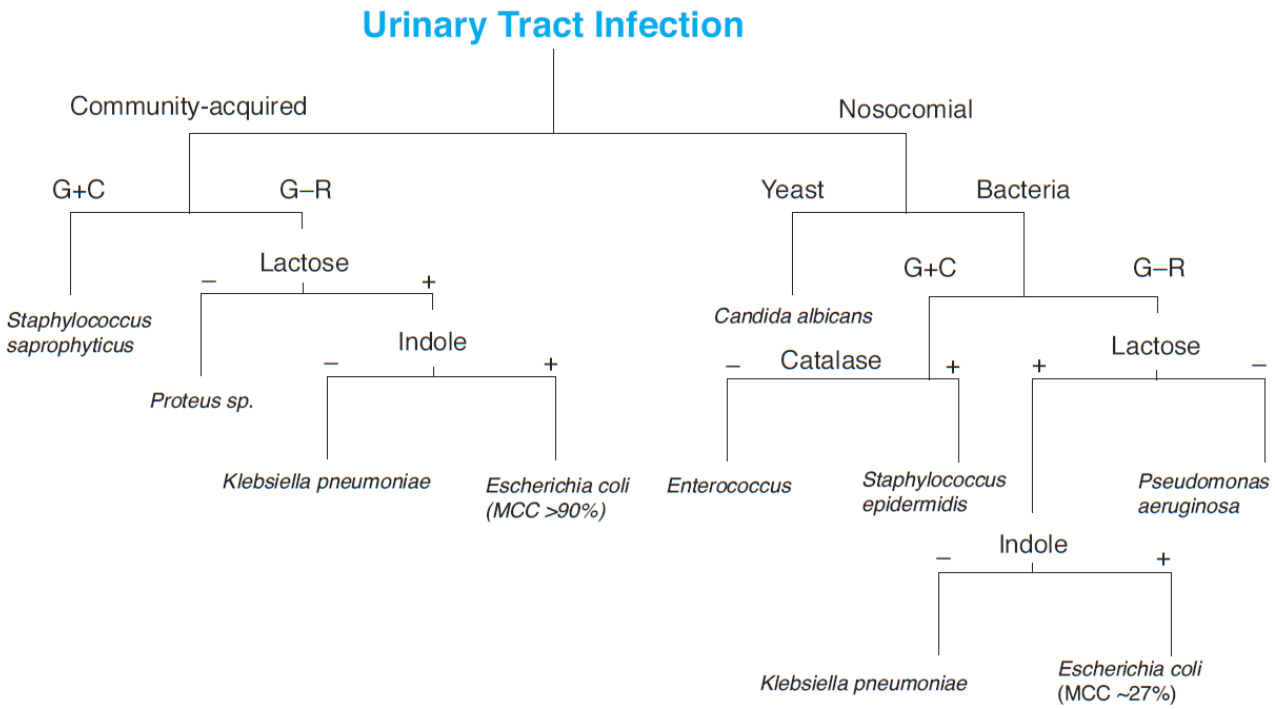
Pathogenesis of urinary tract infections (UTIs):

- Begins when uropathogens contaminate the periurethral area (step 1)
- Bacteria able to colonize the urethra. Subsequent migration to the bladder (step 2)
- Expression of pili and adhesins results in colonization and invasion (step 3).
- Host inflammatory responses, including neutrophil infiltration begin to clear extracellular bacteria (step 4)
- Some bacteria evade the immune system, that result in resistance to neutrophils, and these bacteria undergo multiplication (step 5)
- Biofilm formation (step 6).
- These bacteria produce toxins and proteases that induce host cell damage (step 7)
- bacterial survival and ascending to the kidneys (step 8).
- Kidney colonization (step 9)
- Bacterial toxin production and host tissue damage (step 10).
- UTIs can progress to bacteraemia, If left untreated (step 11).


a
Abdominal aorta
Inferior vena cava
Renal artery
Renal vein
Kidney
Ureter
Bladder
Biofilm
Neutrophil
Urethra
Uropathogenic bacteria
11 Bacteraemia
10 Host tissue damage by bacterial toxins
9 Colonization of the kidneys
8 Ascension to the kidneys
7 Epithelial damage by bacterial toxins and proteases
6 Biofilm formation
5 Bacterial multiplication and immune system subversion
4 Neutrophil infiltration
3 Inflammatory response in the bladder and fibrinogen accumulation in the catheter
Colonization and invasion of the bladder mediated by pili and adhesins
2 Colonization of the urethra and migration to the bladder
1 Contamination of the periurethral area with a uropathogen from the gut
b
Fibrinogen
Urinary catheter

Classification:

- Lower UTI: cystitis, urethritis, prostatitis
- Upper UTI: pyelonephritis, intra-renal abscess, perinephric abscess (usually late complications of pyelonephritis)
- Uncomplicated UTI – Infection in a structurally and neurologically normal urinary tract. Simple cystitis of short (1-5 day) duration
- Complicated UTI – Infection in a urinary tract with functional or structural abnormalities (ex. indwelling catheters and renal calculi). Cystitis of long duration or hemorrhagic cystitis.
- Community Acquired: 80% are due to E.coli.
- Nosocomial infection or hospital acquired: is due to E coli, Pseudomonas, Enterococcus species. It is the fourth most common nosocomial infection and mostly commonly caused by indwelling urinary catheters



Characteristics of bacteria causing UTI:

A. Gram negative bacilli:

Escherichia coli:

Distinguishing Features:

1. Gram-negative rod.
2. Facultative anaerobic, oxidase negative.
3. E. coli is a lactose fermenter: colonies with metallic green sheen on EMB.

Virulence:

1. Pili (adherence to uroepithelium)
2. Haemolysin. .
3. Flagella- enhanced motility .
4. X -adhesins .

PROTEUS:

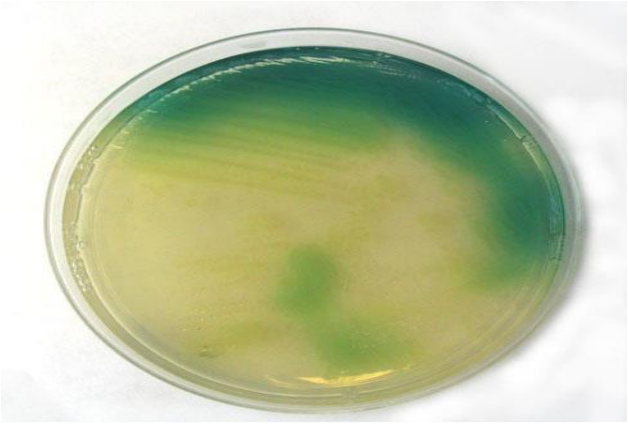
Distinguishing Features:

1. Gram-negative rods, non-lactose fermenting
2. Highly motile; "swarming" motility on surface of blood agar
3. Urease produced
4. Facultative anaerobe (Enterobacteriaceae), oxidase negative

Pathogenesis:

1. Urease raises urine pH to cause kidney stones (staghorn renal calculi)
2. Motility may aid entry into bladder
3. Endotoxin causes fever and shock when septicemia occurs

Pseudomonas aeruginosa:

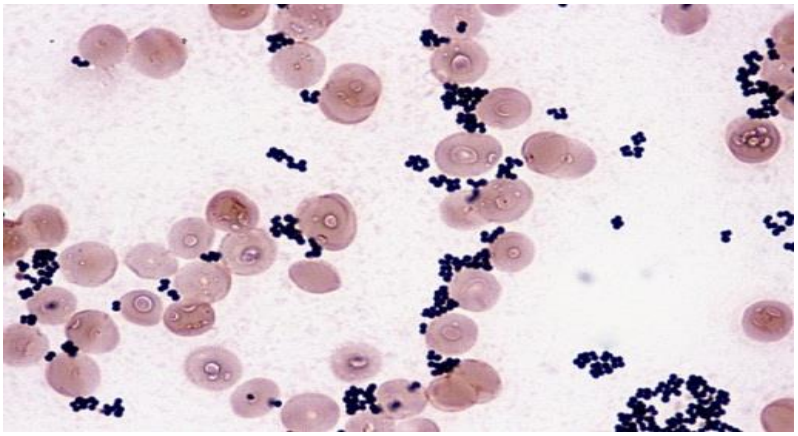


Distinguishing Features:

1. Oxidase-positive, Gram-negative rods, nonfermenting
2. Pigments: pyocyanin (blue-green) and fluorescein
3. Grape-like odor
4. Non–lactose fermenting colonies on EMB or MacConkey
5. Biofilm, Slime layer
6. Associated with nosocomial infection and urinary catheterization.

B. Staphylococci:

STAPHYLOCOCCUS:



1. Gram-positive cocci in clusters
2. Catalase positive (streptococci are catalase negative)

3. Species of Medical Importance:

- S. aureus
- S. epidermidis
- S. saprophyticus

Coagulase negative Staphylococci:

S. epidermidis:

1. Coagulase (-); gram (+) cocci
2. Novobiocin sensitive
3. Infections of catheters/shunts

S. saprophyticus:

1. Coagulase (-), gram (+) cocci
2. Novobiocin resistant

Clinical manifestation

URETHRITIS

Symptoms include purulent urethral discharge, dysuria, urgency, and frequent urination. Disseminated gonococcal infection can cause purulent arthritis alone or arthritis-dermatitis. Urethral swabs from men (vagina or cervix from women) is the best test.

CYSTITIS

Common presenting symptoms include dysuria, frequency, urgency, and suprapubic pain. Hematuria is less common. On exam, there is suprapubic tenderness but no flank tenderness.

Diagnosis:

- Urinalysis (most important test) looking for WBCs >10 or urine dipstick positive for leukocyte esterase and nitrites
- Nitrites are indicative of gram-negative infection.
- Complicated UTI is UTI with co-morbid conditions, e.g., DM, pregnancy, kidney transplant, stones or anatomic abnormality, catheterization, recent antibiotics, or recent hospitalization. UTI in males is also considered complicated.

- Urine culture with >100,000 colonies of bacteria per mL of urine confirmatory but not always necessary with characteristic symptoms and a positive urinalysis. Obtain cultures if complicated UTI, recurrent UTI, or patient is pregnant.

ACUTE BACTERIAL PYELONEPHRITIS

Clinical findings:

Chills,fever, flank pain, nausea, vomiting, costovertebral angle tenderness, increased frequency in urination, and dysuria.

Diagnosis:

Clean-catch urine for urinalysis, culture, and sensitivity. In most cases, >100,000 bacteria/mL of urine.

Routine imaging is not required, but if there is no improvement in 48–72 hours or complications are suspected (obstruction, renal, or perinephric abscess), consider U/S or CT.

Glomerulonephritis (GN)

Glomerular diseases are the most common cause of chronic kidney disease .Most glomerular diseases are also called **glomerulonephritis** (GN) or inflammation of the glomerulus, often as the result of an autoimmune (immune complex) which is the most well

characterized mechanism of post streptococcual **glomerulonephritis** (GN) caused by streptococcus pyogenes (throat and skin infection).

GN may be classified as follows:

- Primary disease without systemic illness (e.g., membranous GN, IgA nephropathy)
- Secondary disease due to systemic illness (e.g., post-infectious GN, diabetic nephropathy, lupus nephritis)

Diagnosis:

Using clinical evaluation and specific serologies, but the definitive diagnosis is usually made by **renal biopsy**, especially when there is heavy proteinuria or renal insufficiency.

Leptospirosis (Weil's disease)

Leptospirosis is a rare bacterial disease that is contracted by contact with the urine of rodents. It is caused by bacteria of the genus Leptospira.

- Renal and liver failure
- Myositis
- Serology with ELISA

Laboratory diagnosis:

URINALYSIS:

Specimen:

- Midstream urine (MSU) is necessary to avoid contamination with vaginal or perineal skin flora and must be before starting antibiotic.
- Suprapubic aspiration or urinary catheter aspiration collected in sterile container can also be performed if a clean catch cannot be obtained without contamination (e.g., in children who are not toilet trained.)

1-Dip stick urine test:

Urease positivity:

Urine pH > 7 (alkaline) suggest Proteus mirabilis infections.

Protein:

Proteinuria may be caused by glomerular or tubular disease

Nitrites:

Gram-negative bacteria reduce nitrate to nitrite, which is a marker of urinary infection.

2-Urinalysis with microscopy:

Examination of wet preparation:

white blood cells (WBCs), red blood cells (RBCs),casts, crystals, yeasts, eggs and bacteria (in fresh urine only)

Gram staining:

When bacteria or WBCs (pus cells) are seen in wet preparation.

White blood cells (WBC):

May be due to pyelonephritis, cystitis, or intrarenal inflammation . If due to bacterial infection, the WBC should be accompanied by visible bacteria, but this may not be the case with all microorganisms (e.g., TB).WBCs count is ≥ 10 WBC/high power field (hpf)

Heme and red blood cells:

(RBC) Red cells can be found in the urine from any cause of disease in the urologic system. Hematuria is also from infections such as cystitis or prostatitis. Proteinuria and **RBC casts** are pathognomonic for glomerulonephritis.

Diagnostic criteria for UTI:

- **Pyuria:** ≥ 5-10 WBC/ hpf
- **Bacteriuria:**

  presence of bacteria on Gram stain (most commonly, gram-negative rods)
- **Leukocyte casts** :

  should be absent in lower UTIs (cystitis), however it is a diagnostic finding of an upper UTIs (e.g., pyelonephritis)

3-Urine culture: Culture on specific media.

Bacteriuria:

By itself, the isolated finding of bacteria in the urine is of very limited significance. The most important exception is in pregnant women, since 30% of those with bacteriuria progress to pyelonephritis.

- Negative culture is associated with TB, viruses, and recent antibiotic treatment.
- Diagnostic criteria for UTI:

✓ Significant bacteriuria defined as ≥ 10^5 colony forming units (CFU)/mL serves to confirm a UTI.

✓ Any bacteriuria in urine from a suprapubic aspiration of the bladder is abnormal.

4- Antibiotic sensitivity tests in case of recurrent infections

Test your knowledge:

Which of the following statements about infection-related acute glomerulonephritis is false?

1. Viral infections are most commonly implicated
2. It is post-streptococcal glomerulonephritis
3. It is associated with *Streptococcus pyogenes* throat and skin infections
4. It's main mechanism is immune complexes deposition

References:

Kaplan Medical **USMLE® STEP 1, 2021**

Pages: 205, 232, 233, 246, 252.

Kaplan Medical **USMLE® STEP 2, 2021**

Pages: 573, 574, 586, 587, 588, 589, 590, 640, 644, 645, 668, 669.