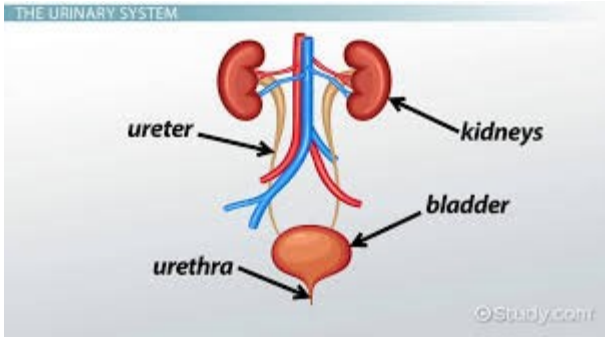
PATHOPHYSIOLOGY OF RENAL SYSTEM



Course Name: Pathophysiology

Course Code: 0520300

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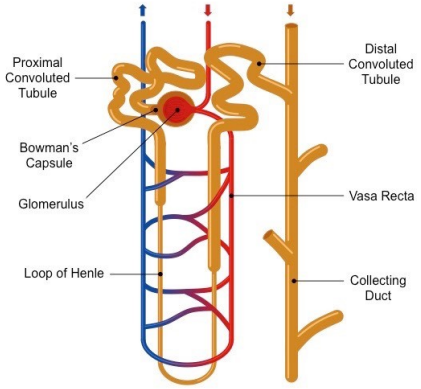
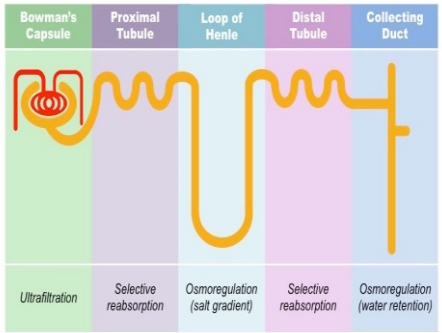
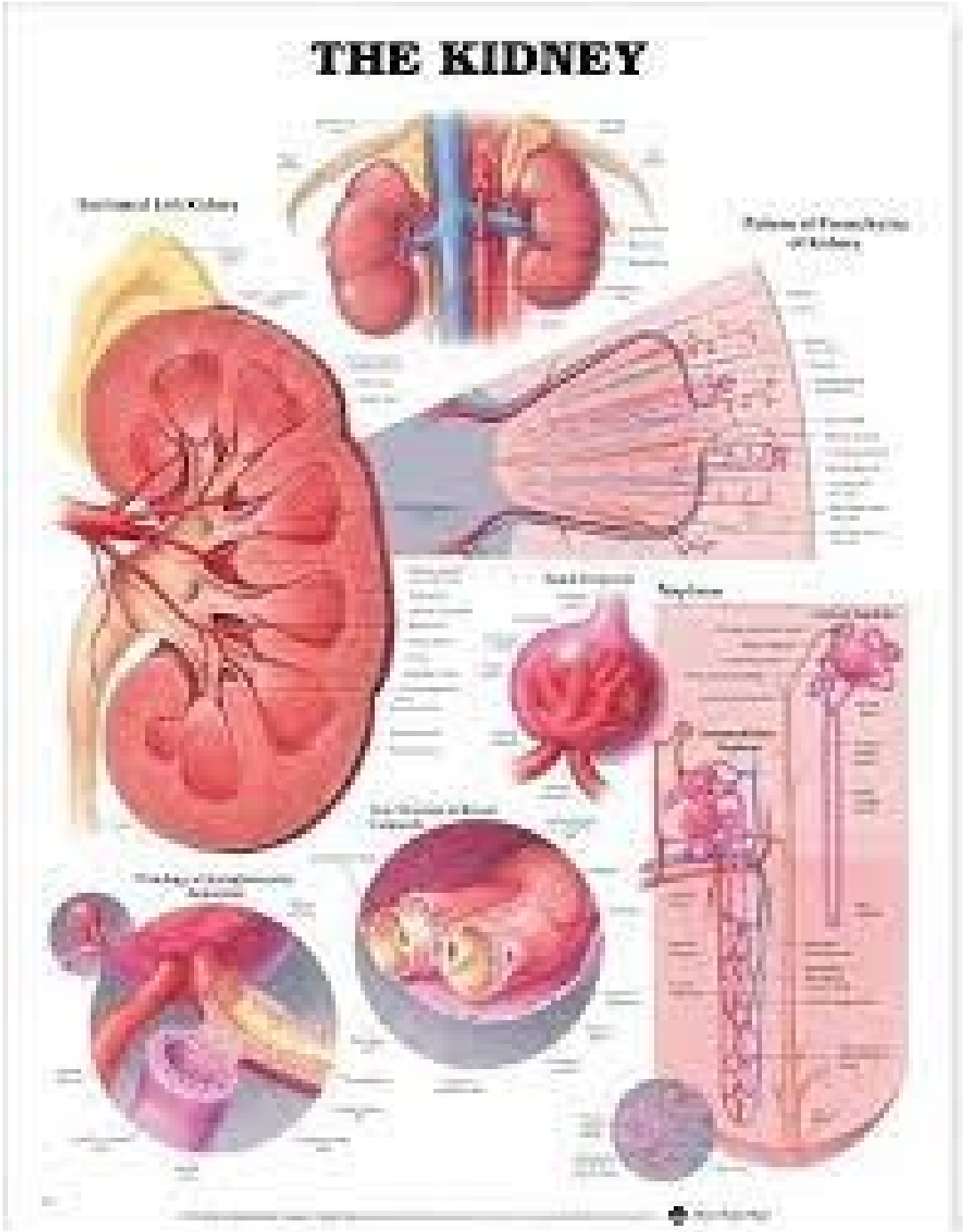
Kidney anatomy







Introduction

The kidney is a structurally complex organ that has evolved to carry out a number of important functions:

- Excretion of the waste products of metabolism
- Regulation of body water and salt
- Maintenance of acid balance
- Secretion of a variety of hormones and prostaglandins

Diseases of the kidney are as complex as its structure, but their study is facilitated by dividing them into those that affect its four components:

1-Glomeruli

2-Tubules

3-Interstitium

4-Blood vessels

Due to the large functional reserve capacity of the kidney, early signs of kidney disease are often missed, and much renal damage may occur before renal dysfunction becomes clinically apparent

The two most common syndromes associated with glomerular diseases, nephrotic and nephritic

Nephrotic syndrome

Characterized by the following:

- ***Proteinuria****,* with daily protein loss in the urine of 3.5 g or more in adults (said to be in the "nephrotic range")
- ***Hypoalbuminemia****,* with plasma albumin levels less than 3 g/dL

  → (low plasma osmotic pressure)
- ***Generalized edema****,* the most obvious clinical manifestation

  → (*anasarca is* a consequence of the drop in plasma colloid osmotic pressure as a result of hypoalbuminemia)
- ***Hyperlipidemia*** and lipiduria (lipid in the urine).

- **The nephrotic syndrome has diverse causes that share a common pathophysiology, a derangement in the capillary walls of the glomeruli that results in increased permeability to plasma proteins.**
- Podocyte injury is an underlying mechanism of proteinuria, and may be the result of nonimmune causes (as in minimal change disease and FSGS) or immune mechanisms (as in membranous nephropathy).

Nephritic syndrome

Characterized by the following:

- *Hematuria* (red cells and red cell casts in urine)
- *Proteinuria* (usually in the subnephrotic range) with or without edema
- *Azotemia (*elevation of blood urea nitrogen and creatinine)
- *Hypertension*

- **The nephritic syndrome usually has an acute onset and is caused by inflammatory lesions of glomeruli.**

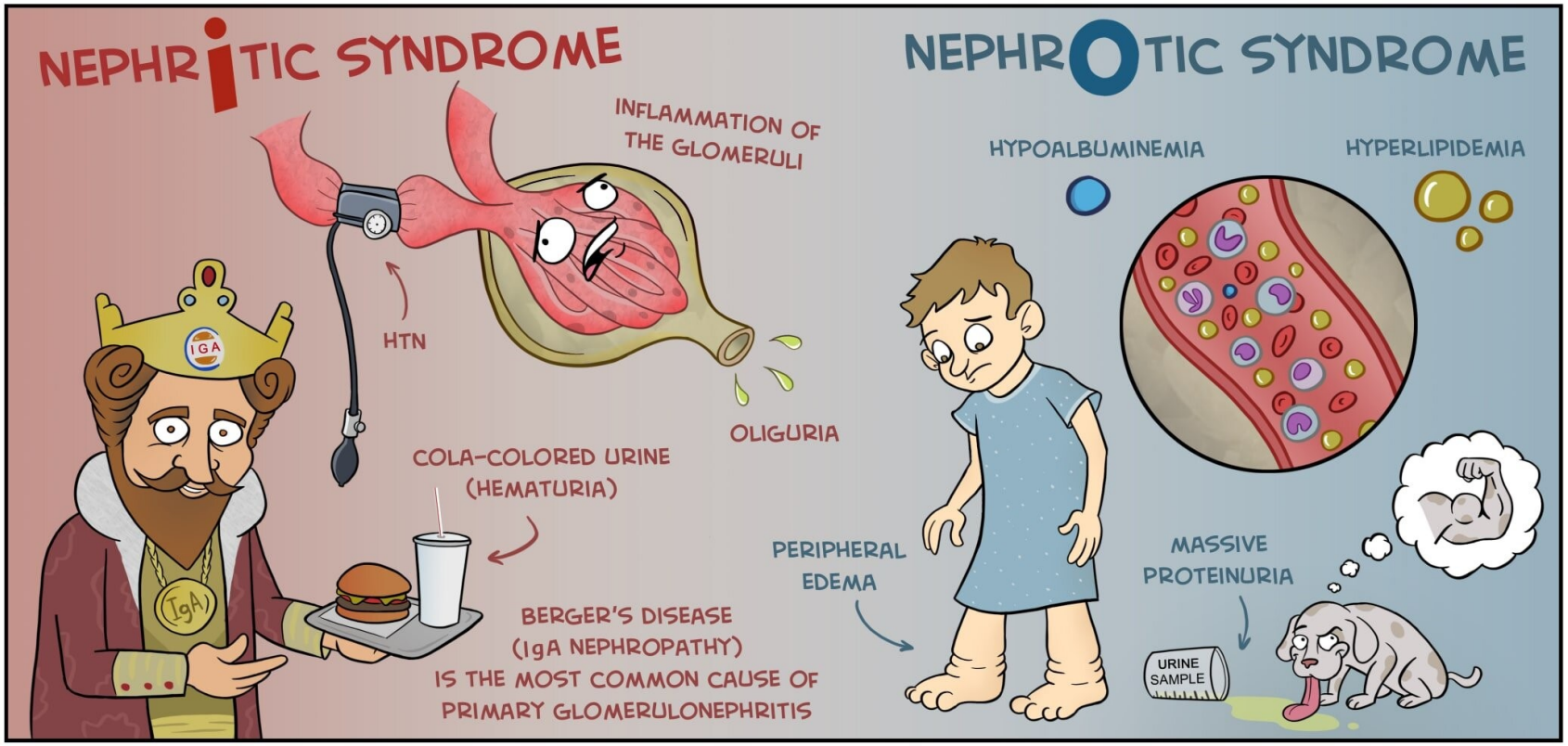
Nephritic syndrome(continued)

- The most common cause is immunologically mediated glomerular injury; lesions are characterized by proliferative changes and leukocyte infiltration.

- Acute post infectious glomerulonephritis typically occurs after streptococcal infection in children and young adults but may occur following infection with many other organisms

- May also be related to systemic conditions such as **lupus erythematosus** where there are excess levels of circulating antibodies or antigen–antibody complexes.

Nephritic VS Nephrotic



RENAL DISEASES

- *Asymptomatic hematuria:* or nonnephrotic proteinuria or a combination of the two is the typical clinical presentation of IgA nephropathy, Alport syndrome (inherited disorder causes deafness, progressive kidney damage and eye defects), or mild forms or early presentations of other glomerular diseases.

- *Rapidly progressive glomerulonephritis (RPGN*): results in rapid loss of renal function in a few days or weeks, typically in the setting of nephritic syndrome. If untreated, it leads to death from renal failure within a period of weeks to months.

- *Acute kidney injury :* refers to abrupt onset of renal dysfunction characterized by an acute increase in serum creatinine often associated with oliguria or anuria (decreased or no urine flow).

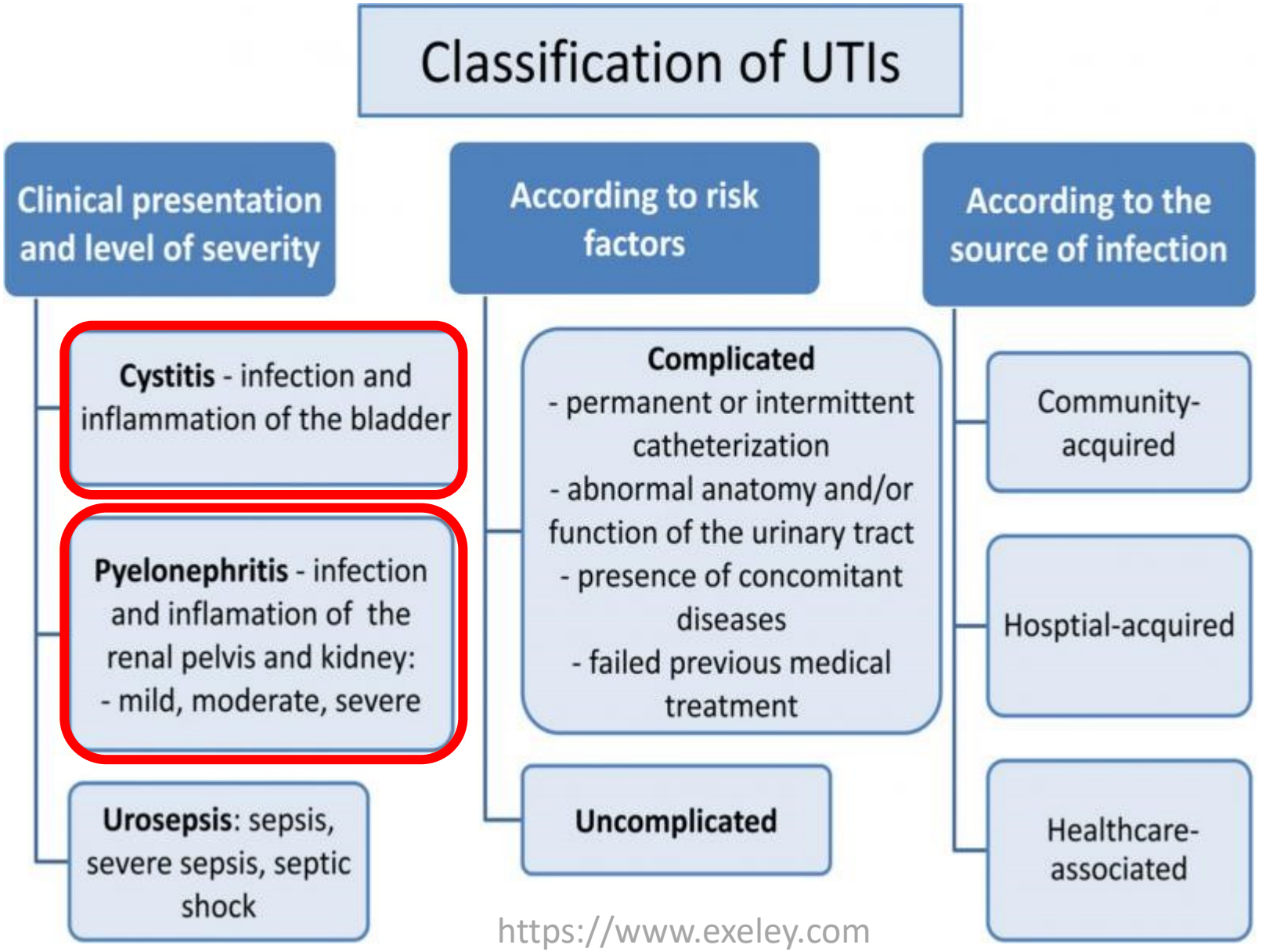
RENAL DISEASES (continued)

- *Chronic kidney disease :* results from progressive scarring in the kidney of any cause. It is characterized by various metabolic and electrolyte abnormalities such as hyperphosphatemia, dyslipidemia, and metabolic acidosis. However, it is often asymptomatic until the most advanced stages, when symptoms of uremia develop.
- *End-stage renal disease (ESRD):* is irreversible loss of renal function requiring dialysis or transplantation typically due to severe progressive scarring in the kidney from any cause.
- *Urinary tract infection (UTI):* is characterized by bacteriuria and pyuria (bacteria and leukocytes in the urine). It may be symptomatic or asymptomatic, and may affect the kidney (pyelonephritis) or the bladder (cystitis) only.
- *Nephrolithiasis:* refers to formation of stones in the collecting system and is manifested by renal colic and hematuria (without red cell casts).

Urinary Tract Infection (UTI)

- Generally caused by **bacteria**
- May occur in any of the **urinary tract structures**
- Occurs **most frequently in females** as well as senior citizens of both sexes

Classification of UTIs



https://www.exeley.com

Urinary tract infection (UTI)

1- Acute Cystitis → Inflammation of urinary bladder

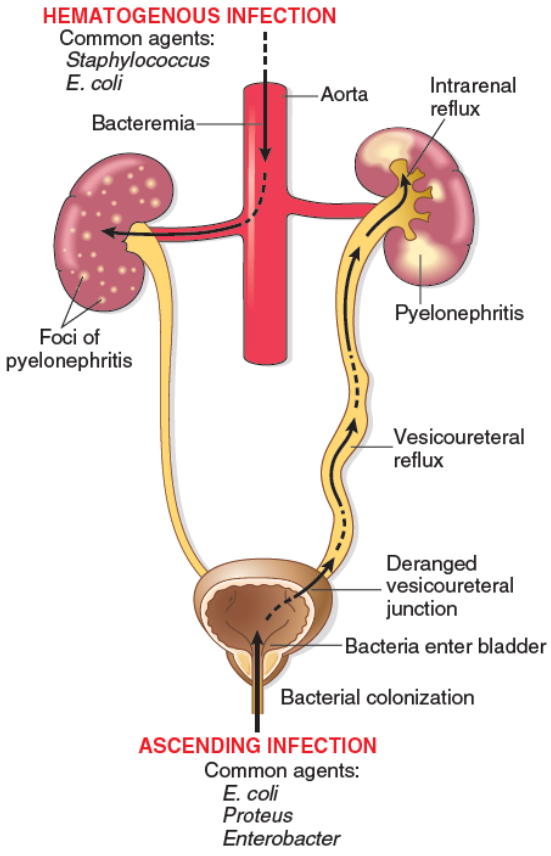
2- Pyelonephritis → Inflammation of interstitium of the kidney

- *Acute pyelonephritis* is a bacterial infection caused either by ascending infection as a result of reflux, obstruction, or other abnormality of the urinary tract, or much less commonly by hematogenous spread of bacteria; it is characterized by abscess formation in the kidneys, sometimes with papillary necrosis.
- *Chronic pyelonephritis* usually is associated with urinary obstruction or reflux; it results in scarring of the pelvicalyceal system and the interstitium of the involved kidney and gradual progression of chronic kidney disease.

Pathways of renal infection:

→ Hematogenous infection results from bacteremic spread.

→ More common is ascending infection, which results from a combination of urinary bladder infection, vesicoureteral reflux, and intrarenal reflux.



1- ACUTE CYSTITIS (lower UTI)

Inflammation of urinary bladder.

Signs and Symptoms: Presents as suprapubic pain, dysuria, urinary frequency, urgency. Systemic signs (eg, high fever, chills) are usually absent.

Risk factors: include female sex (short urethra), sexual intercourse, indwelling catheter, diabetes mellitus, impaired bladder emptying.

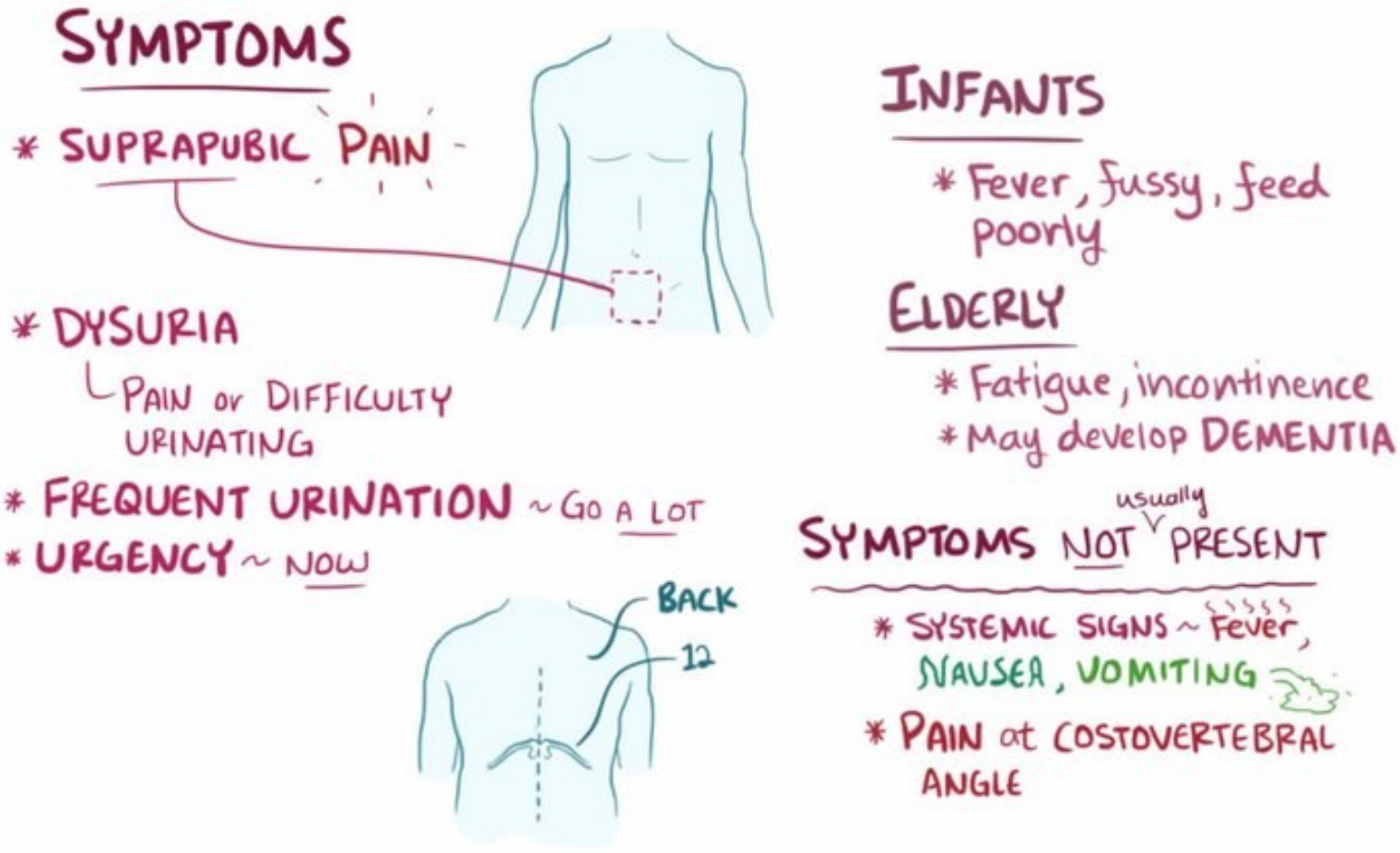
Causes:

- Escherichia Coli (*E coli:* most common)
- *Staphylococcus saprophyticus*—seen in sexually active young women (*E coli* is still more common in this group)
- *Klebsiella*
- *Proteus mirabilis*—urine has ammonia scent

Labs: ⊕ leukocyte esterase. ⊕ nitrites (indicates presence of Enterobacteriaceae). Sterile pyuria (pyuria with ⊖ urine cultures) could suggest urethritis by *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

Treatment: antibiotics (eg, TMP-SMX, nitrofurantoin).

1- ACUTE CYSTITIS (lower UTI)



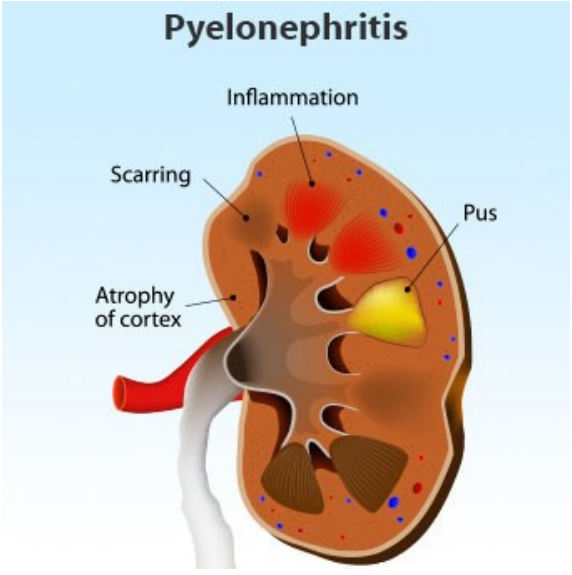
Causative microorganism: E. coli

2. PYELONEPHRITIS (UPPER UTI)

Pyelonephritis (from pyelo, "pelvis")→ Inflammation of the **kidneys**

Risk factors :

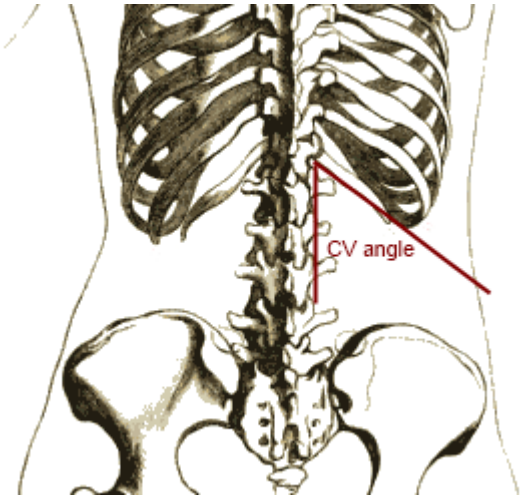
- **Sexual activity,** which can introduce bacteria into the urinary tract
- **Use of diaphragms and spermicides**, which alter the bacteria in a woman's urethra
- **Pregnancy:** because of changes in anatomy and physiology (a UTI can put the unborn child at risk and a doctor should be consulted immediately)
- **Increased age**
- **Poor hygiene**
- **Diabetes**



2. PYELONEPHRITIS (UPPER UTI)- *continued*

Symptoms of pyelonephritis

- Chills
- Fever
- Pain in your back, side, or groin
- Nausea
- Vomiting
- Cloudy, dark, bloody, or foul-smelling urine
- Frequent, painful urination
- **Costovertebral angle tenderness** (**CVAT)**



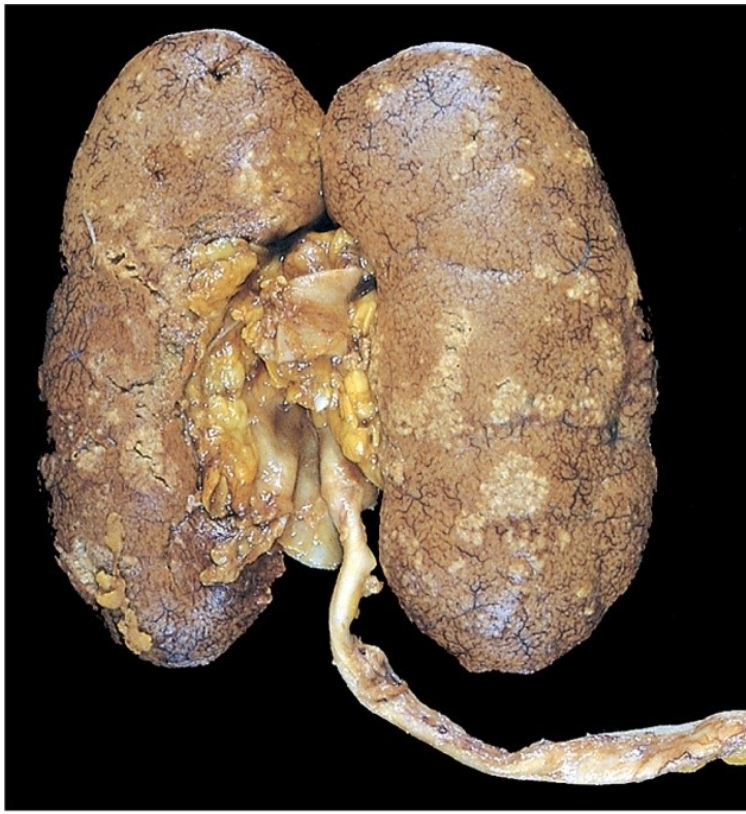
Causative microorganisms:

Escherichia Coli (E.Coli: most common) , Pseudomonas aeruginosa, Staphylococcus, Klebsiella

A- Acute Pyelonephritis

The **cortical surface** is **studded** with focal pale **abscesses**, more numerous in the upper pole and middle region of the kidney; the lower pole is relatively unaffected.

Between the abscesses there is dark congestion of the renal surface.

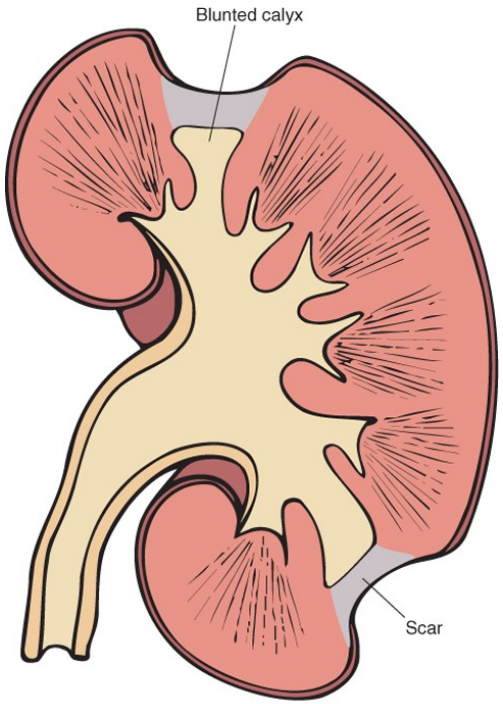


B- Chronic Pyelonephritis

- **Chronic pyelonephritis** implies **recurrent kidney infections**, usually is associated with urinary obstruction or reflux; results in scarring of the involved kidney, and gradual **renal insufficiency**.

→ Typical coarse scars of chronic pyelonephritis associated with vesicoureteral reflux.

→ The scars are usually located at the upper or lower poles of the kidney and are associated with underlying blunted calyces.



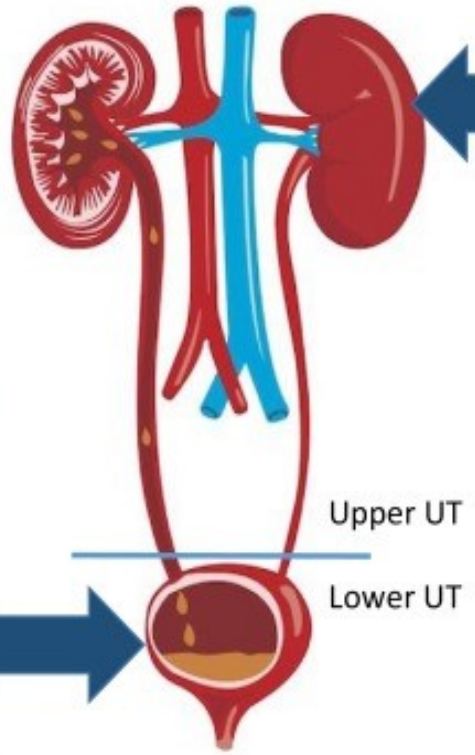
Cystitis

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

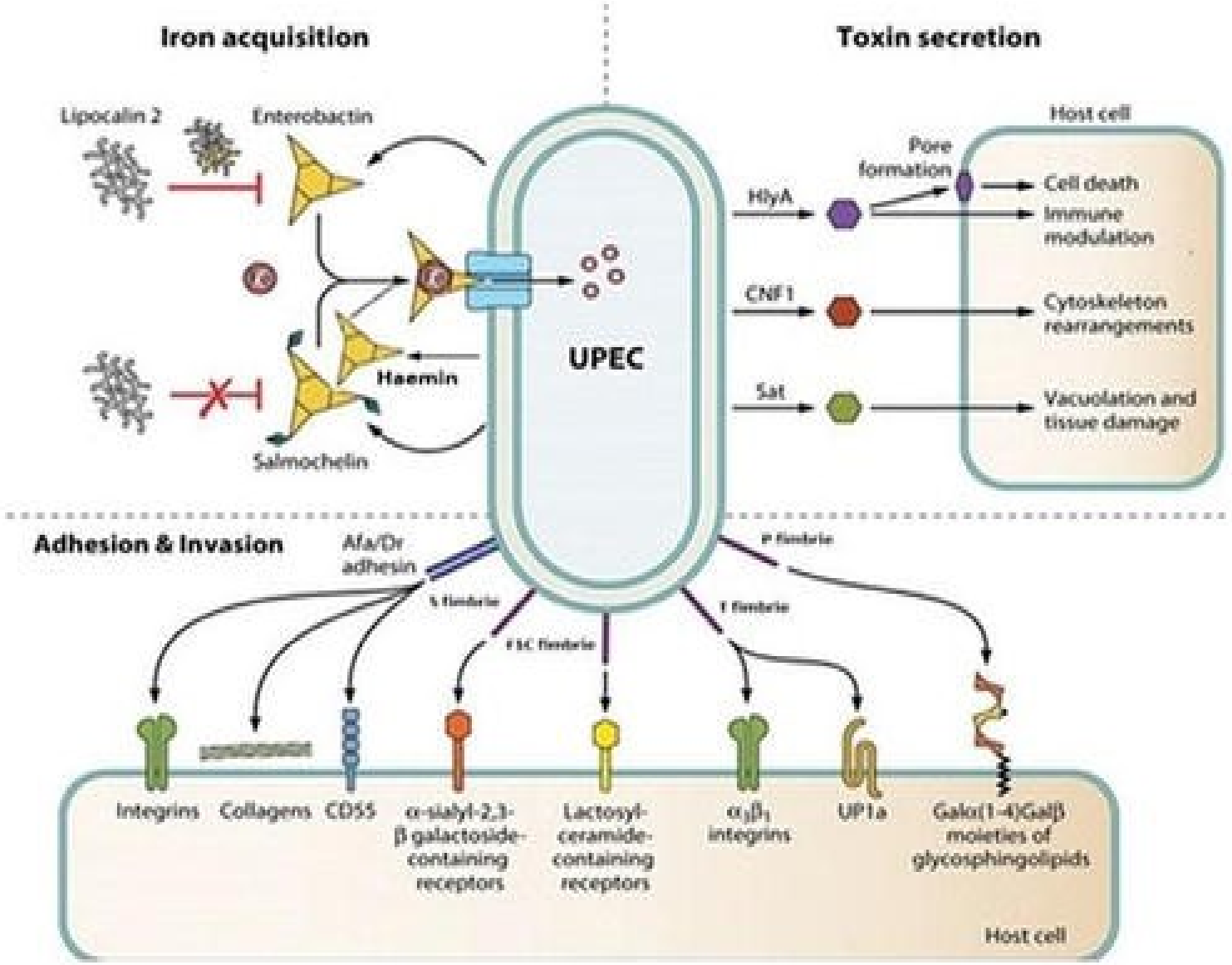
Clinical symptoms
- Back and/or flank pain
- Fever, chills, malaise
- Nausea, vomiting, anorexia

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

UPEC= Uropathogenic *Escherichia coli*

Trends in Molecular Medicine



UPEC= Uropathogenic *Escherichia coli* → *WHY?? Virulence factors*