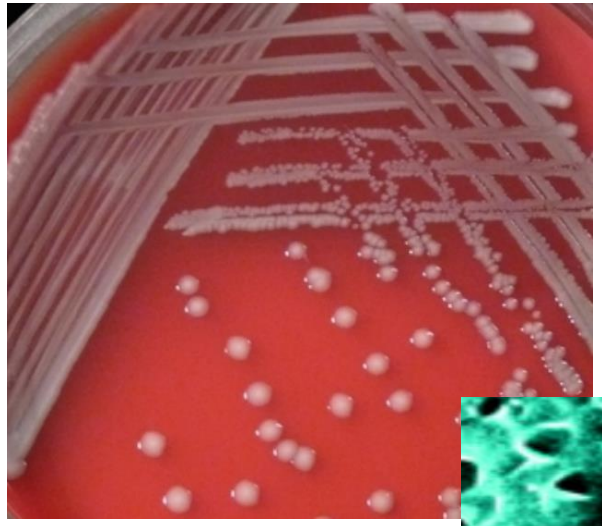
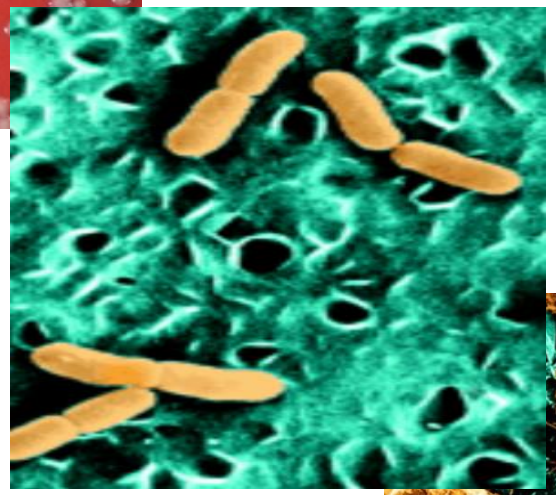
Microbiology of Urogenital system





Anas Abu-Humaidan
M.D. Ph.D.

Lecture 1

Overview

In this lecture, we will discuss the following regarding urinary tract infections (UTI):

- Urinary tract defenses.
- UTI clinical entities.
- UTI epidemiology and predisposing factors.
- UTI etiology and pathophysiology.

* اختي "إيمان" توجيهي، ادعولها :)

Urinary tract defenses

The urinary tract is typically a **sterile environment**, and bacterial colonization of the bladder epithelium does not go unchallenged. This happens in several ways:

- The bulk **flow of urine** through the bladder and micturition can work to **rinse away** non-attached or weakly adherent microbes from the bladder surface

- **Periurethral and Urethral microbiota**: lactobacilli, coagulase negative staph, corynebacterium and streptococci that form barriers against colonization. Changes in estrogen, low vaginal pH and cervical IgA affect colonization by normal flora.

- The **low pH and osmolarity** of urine can be **inhibitory** to bacterial growth, and the **salts**, **urea**, and **organic acids** present in urine can reduce bacterial survival

- **Lactoferrin** within urine can scavenge essential iron away from incoming microbes.

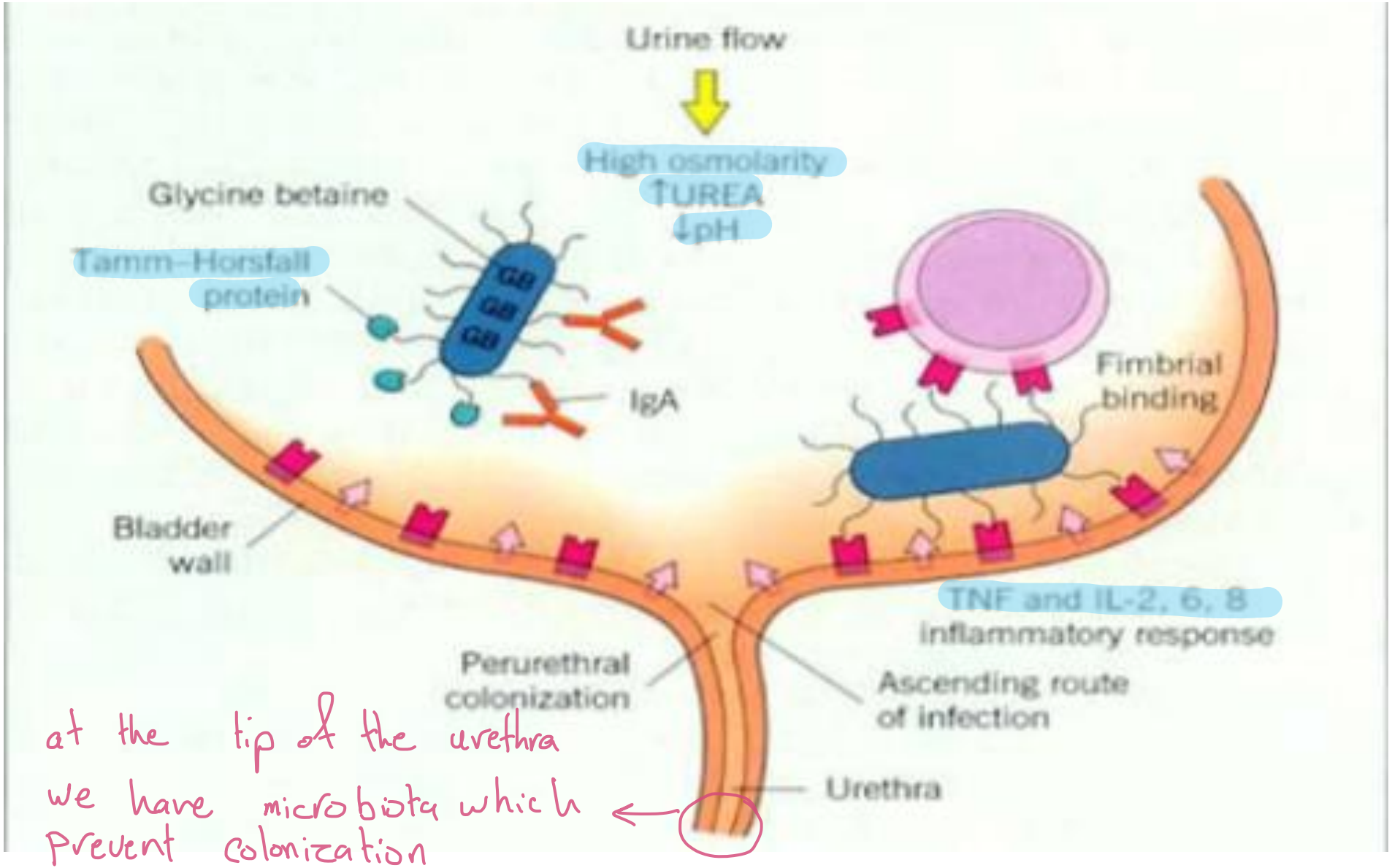
bacteria use siderophore to overcome th effect of lactoferin

Urinary tract defenses

- A number of soluble and cell associated factors within the bladder, including Tamm-Horsfall protein, low molecular weight sugars, **secretory IgA**, and uromucoid, can act as **anti-adherence factors**, competitively inhibiting bacterial attachment to the bladder surface

- **Bladder Epithelium** expresses Toll-like receptors (TLRs) that recognize bacteria and initiate immune/inflammatory response (PMNs, neutrophils, macrophages, eosinophils, NK cells, mast cells and dendritic cells). Adaptive immune response then predominates (T and B lymphocytes). **Induced exfoliation of cells** also occurs to allow excretion of bacterial colonization.

- Kidney has **Local immunoglobulin/ antibody synthesis** in the kidney occurs in response toinfections (IgG, IgA)



at the tip of the urethra we have microbiota which prevent colonization

Bacterial entry

Bacteria ascending into the bladder through the urethra is the most common cause of UTIs.
There are several risk factors that may promote or encourage bacterial ascent:

Reduced Urine Flow

- outflow obstruction with incomplete bladder emptying (prostatic hyperplasia or foreign body)
- neurogenic bladder Cause incomplete bladder emptying
- inadequate fluid uptake
- voiding dysfunction

Facilitate Ascent

- catheterization (chronic or intermittent)
- urinary incontinence
- fecal incontinence
- residual urine with ischemia of bladder wall

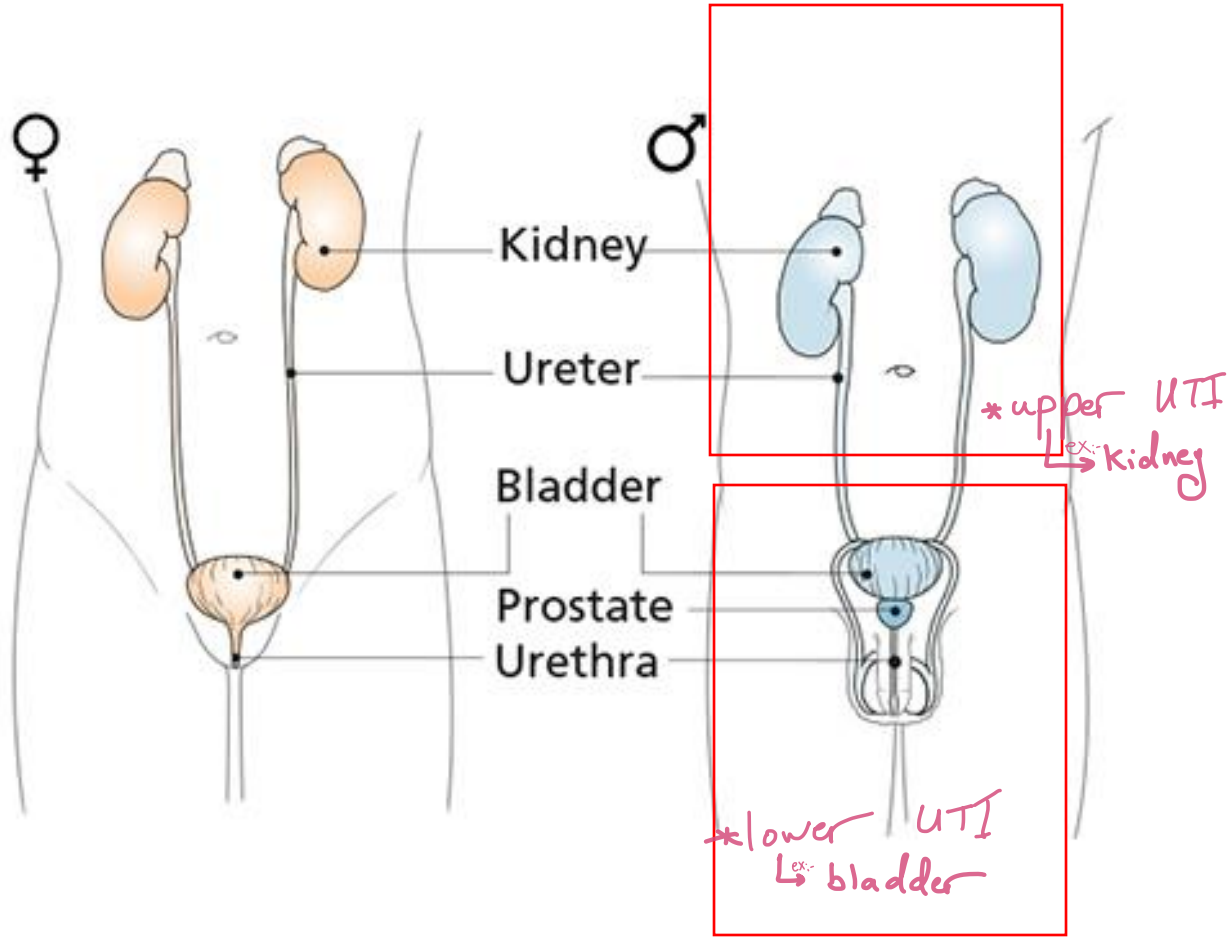
** UTI → (the most common route of infection) ascending route

* UTI are most common endogenous bacteria
↳ mostly from the GI

Definitions

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

- **Asymptomatic bacteriuria (ASB)**
- **Cystitis** = inflammation of the bladder
- **Prostatitis**
- **Pyelonephritis.**



Definitions

When discussing UTI's it is important to distinguish among the following terms:

Contamination
– organisms are introduced during collection or processing of urine. No health care concerns

Asymptomatic bacteriuria (Colonization)
– organisms are present in the urine but are causing no illness or symptoms. Depending on the circumstances, significance is variable, and the patient often does not require treatment

Infection (UTI)
– the combination of a pathogen(s) within the urinary system and symptomsand/or inflammatory response to the pathogen(s) requiring treatment

Definitions

→ if the question ask about young male
↳ it's not "uncomplicated" case :)

Uncomplicated UTI

– infection in a healthy, non-pregnant, pre-menopausal female patient with anatomically and functionally normal urinary tract

Complicated UTI → their pathogens are resistant to the antibiotics

– infection associated with factors increasing colonization and decreasing efficacy of therapy

Recurrent UTI

– occurs after documented infection that had resolved. Defined as **2 or more infections in 6 months, or > 3 infections in 12 months**

Reinfection UTI

– a new event with reintroduction of bacteria into urinary tract or by different bacteria

Persistent UTI

– UTI caused by same bacteria from focus of infection.

↳ not fully treated UTI, in which their symptoms are reduced for a while then they return

Epidemiology of UTIs in the community

- As many as **50–80%** of women in the general population **acquire at least one UTI during their lifetime**—uncomplicated cystitis in most cases.
- About **20–30%** of women who have had one episode of UTI will have **recurrent episodes**.
- Early recurrence (within 2 weeks) is usually regarded as relapse rather than reinfection and may indicate the need to evaluate the patient or a sequestered focus.
- Asymptomatic bacteriuria occurs in all age groups and does not necessarily result in clinical infection.
- Asymptomatic bacteriuria occurs in 1– 3% of non- pregnant women and 2– 9.5% of pregnant women.

Do we treat asymptomatic bacteriuria ?? NO, unless the patient-
① pregnant
② will have a surgery in their UG system

Epidemiology of UTIs in the hospital

- Urinary tract infections are the **most common type of healthcare-associated infection**, accounting for more than 30% of infections reported by acute care hospitals.

- Virtually all healthcare-associated UTIs are caused by instrumentation. (**Catheter-associated urinary tract infection** (CAUTI))

- 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.

Table 1 Incidence of Urinary Tract Infection According to Age and Sex

Age Group	Incidence (%)	Approximate Sex Ratio (Male:Female)
Neonatal	1.0	1.5:1.0
Preschool age	1.5-3.0	1:10
School age	1.2	1:30
Reproductive age	3-5	1:50
Geriatric	10-30	1:1.5

هون بتقارب النسبة بين الذكور والاناث ←

*انه في بهاي المرحلة اختلاف بين الذكور والاناث ⊕ في كل الذكور وهاي مغاير نفس في كل الاناث

* why there's an increase in males ratio?
Due to the impaired urine flow

الكبار بالعمر (فوق 70)

هون بتقارب النسبة بين الذكور والاناث ←

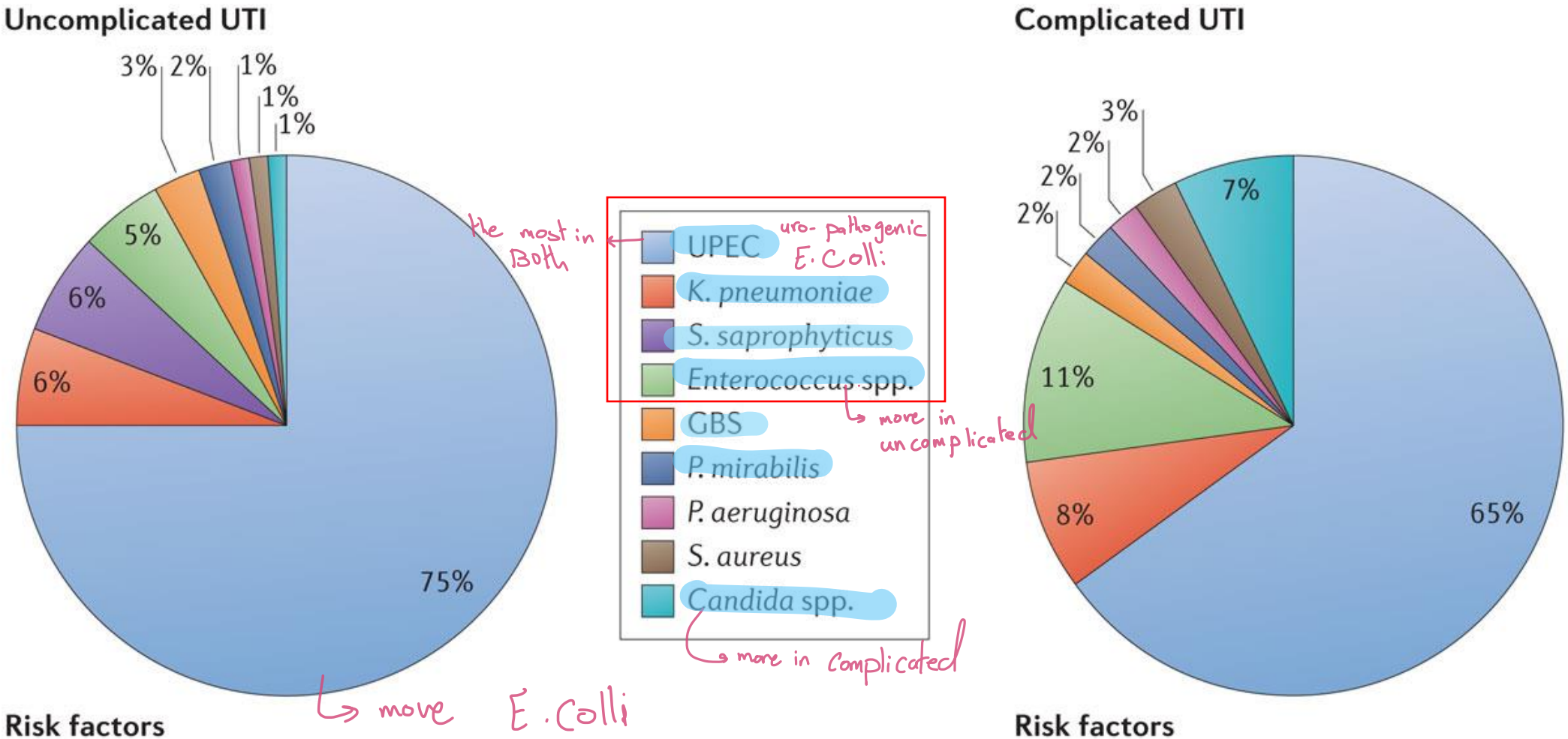
Clinical categories of UTIs

Clinically, UTIs are categorized as uncomplicated or complicated:

- **Uncomplicated UTIs** typically affect individuals who are otherwise healthy and have **no structural or neurological urinary tract abnormalities**

- **Complicated UTIs** are defined as UTIs associated with factors that compromise the urinary tract or host defence, including **urinary obstruction**, **urinary retention** caused by neurological disease, **immunosuppression**, renal failure, renal transplantation, pregnancy and the **presence of foreign bodies** such as calculi or indwelling catheters .

Etiology of UTIs



the most in Both

uro-pathogenic E. Coli:

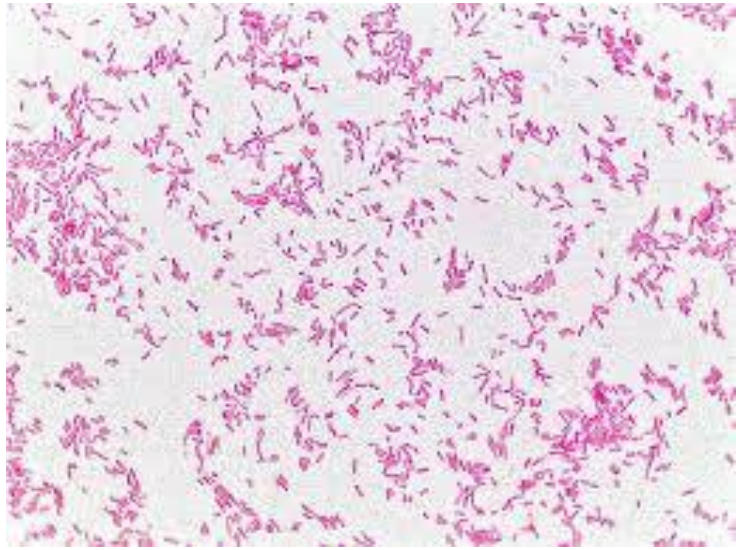
more in uncomplicated

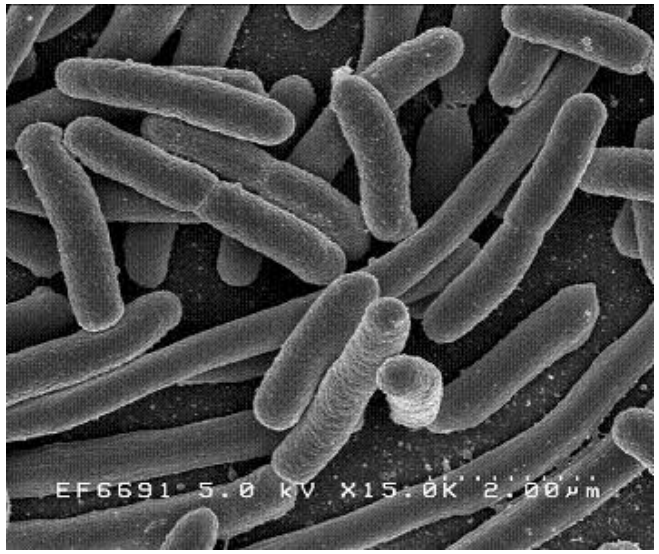
more in Complicated

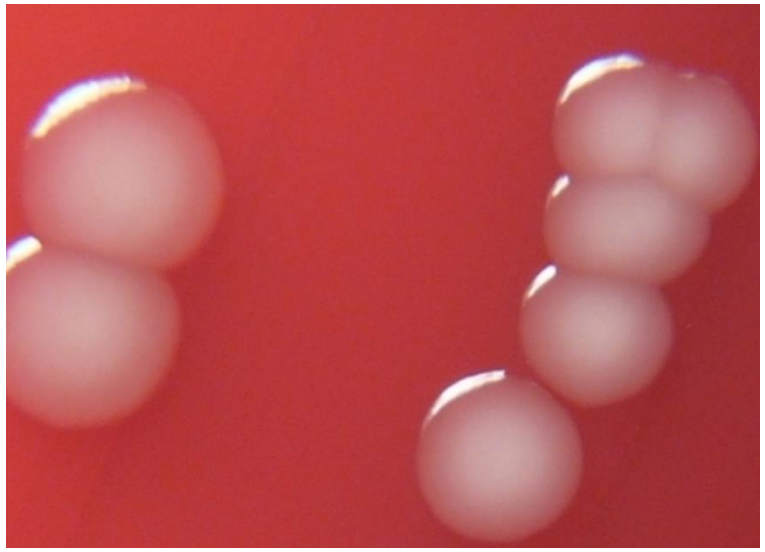
move E. Colli

Cause Resistance pathogen

Uropathogenic *E.coli* (UPEC)







- A **gram negative rod**, facultative anaerobe. The optimum growth temperature is 37°C. On Nutrient agar, colonies are large, thick, greyish white, moist, smooth.

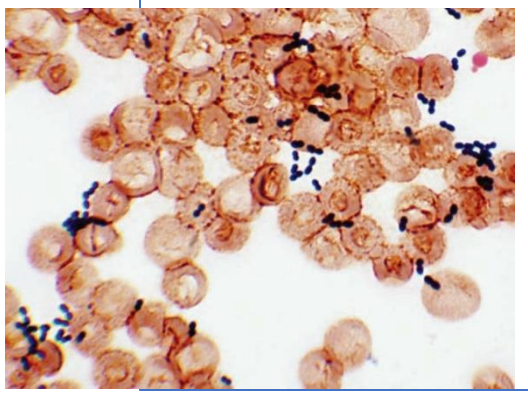
- E. coli and other facultative anaerobes constitute about 0.1% of **gut microbiota**.

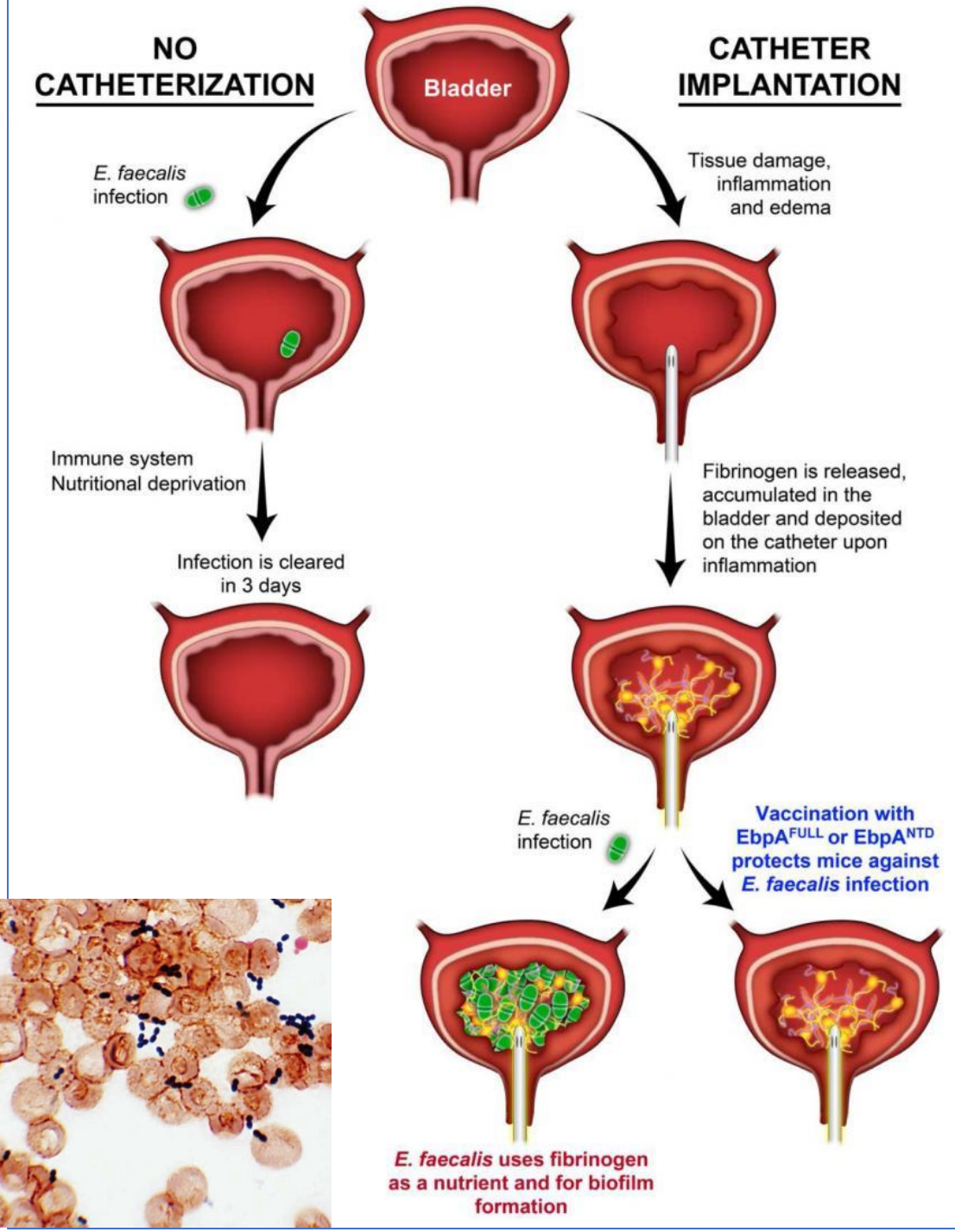
Enterococcus faecalis + staph. are the only gram positive bacteria causing UTI

- The enterococci are gram-positive cocci, typically arranged in **pairs and short chains** .

- *E. faecalis* is found in the **large intestine** in high concentrations (e.g., 10^5 to 10^7 organisms per gram of feces) and in the **genitourinary tract**.

- enterococci are one of the most common causes of infections acquired in the hospital **(nosocomial infection).** The **urinary tract is the most common site of enterococcal** infections, and infections are **frequently associated with urinary catheterization or instrumentation .**

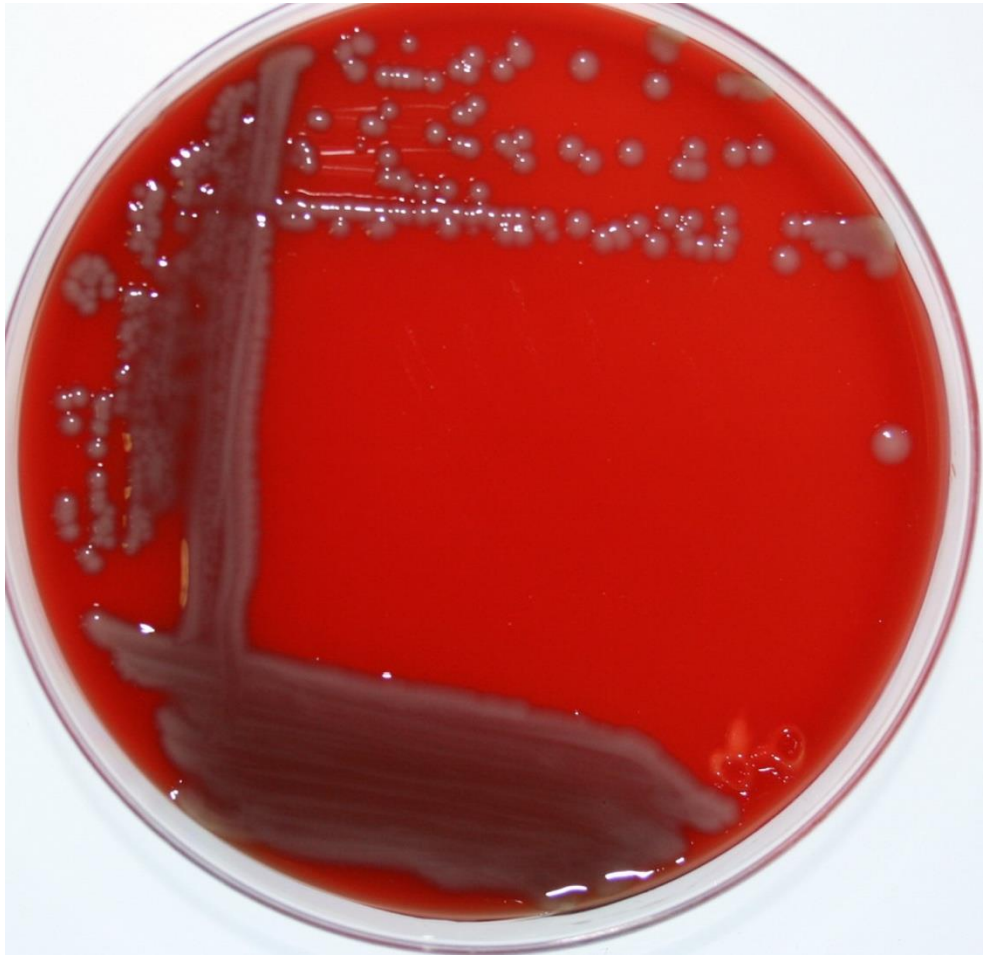




Klebsiella pneumoniae

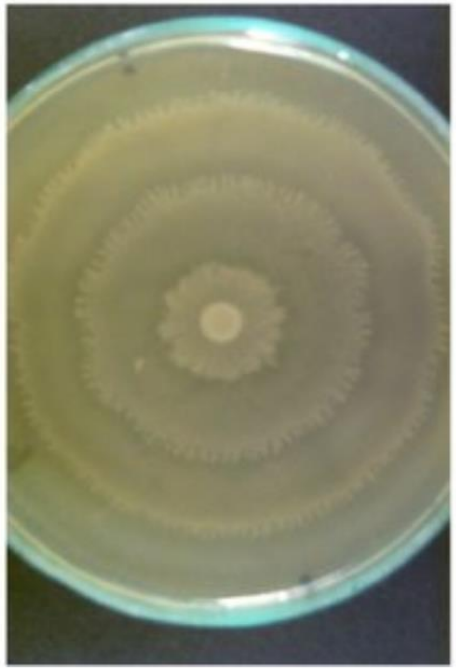
- *Klebsiella* species are routinely found in the human nose, mouth, and gastrointestinal tract as normal flora.

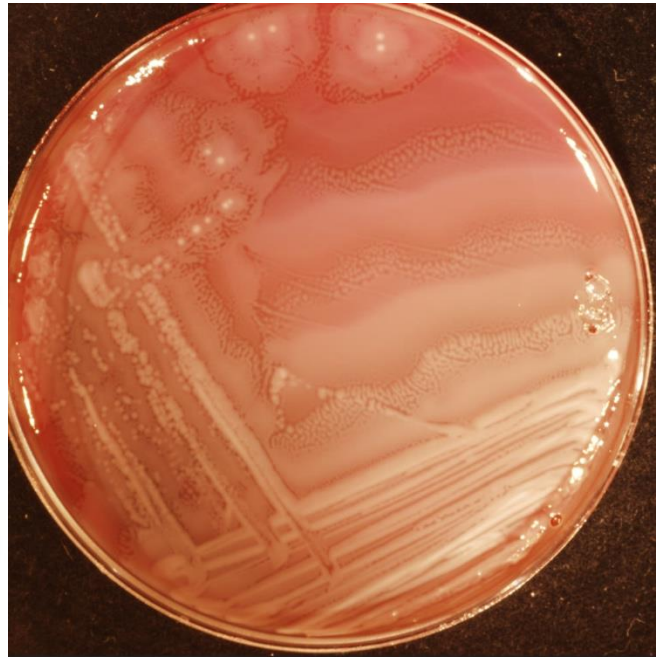
- The ability of *K. pneumoniae* to **colonize the hospital environment**, including carpeting, sinks, flowers, and various surfaces, as well as the skin of patients and hospital staff, has been identified as a major factor in the spread of **hospital-acquired infections**



Proteus mirabilis

Proteus mirabilis is a **Gram-negative**, facultatively anaerobic, **rod-shaped** bacterium. It shows **swarming motility** and **urease** activity.





A direct result of **urease** activity and ammonia generation is an **increase in local pH**. In the urinary tract alkaline pH leads to precipitation of calcium and magnesium ions and the formation of **urinary stones** composed of magnesium ammonium phosphate (**struvite**) and calcium phosphate (**apatite**)

$$(NH_2)_2CO + 2\,H_2O \xrightarrow{\text{Urease}} CO_2 + H_2O + 2\,NH_3$$

Urea — Carbon dioxide — Water — Ammonia

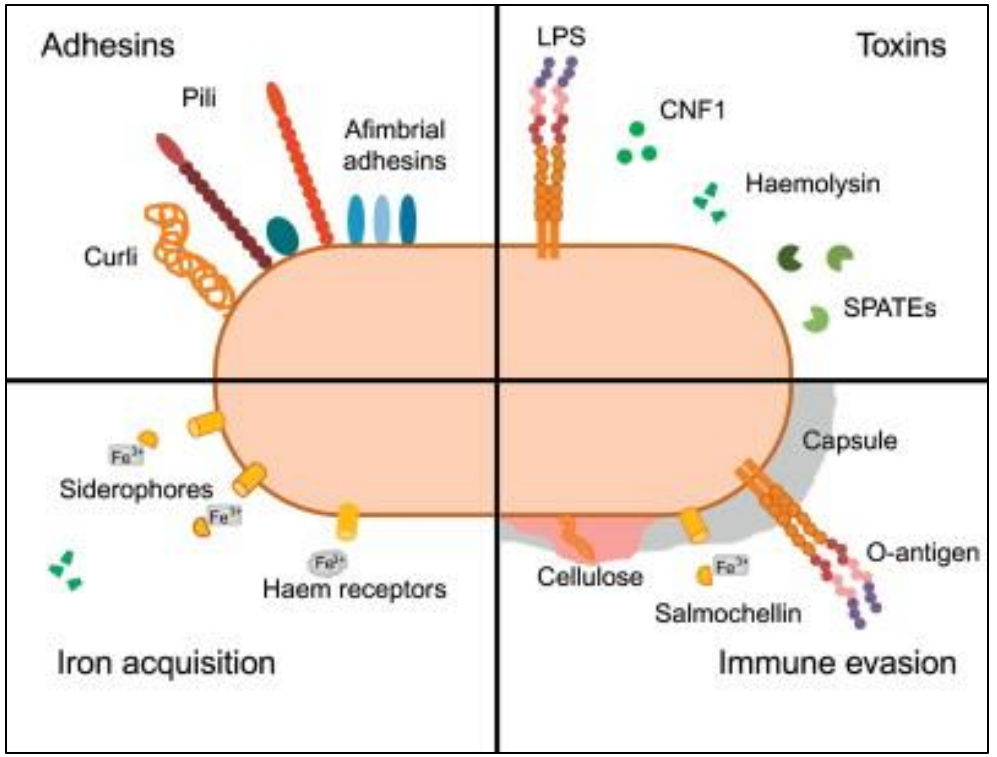
* most of the pathogen are part of the enterobacteriaceae

Some important acronyms in antimicrobial resistance

- Antimicrobial resistance **(AMR)**
- Multidrug resistant **(MDR)**
- Extensively drug-resistant **(XDR)**
- **ESKAPE** is an acronym comprising the scientific names of six **highly virulent** and **antibiotic-resistant** bacterial pathogens including Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp. The acronym is sometimes extended to ESKAPEE to include Escherichia coli.

Virulance factors in UPEC (many factors are shared with other bacteria causing UTI)

- adhesive **fimbriae**, which enable bacteria to adhere avidly to specific receptors on the urothelium.
- **flagella** that enable bacteria to swim along the urinary tract including ‘upstream’ from the bladder to the kidneys.
- **toxins**, such as haemolysin and cytotoxic necrotizing factor, which disrupt the epithelial barrier and enable access to the underling tissue
- **siderophores**, which enable bacteria to chelate iron that is important for growth
- expression of cell surface **capsules**, which enable them to resist the bactericidal actions of complement and phagocytic cells



Pathophysiology of UTIs

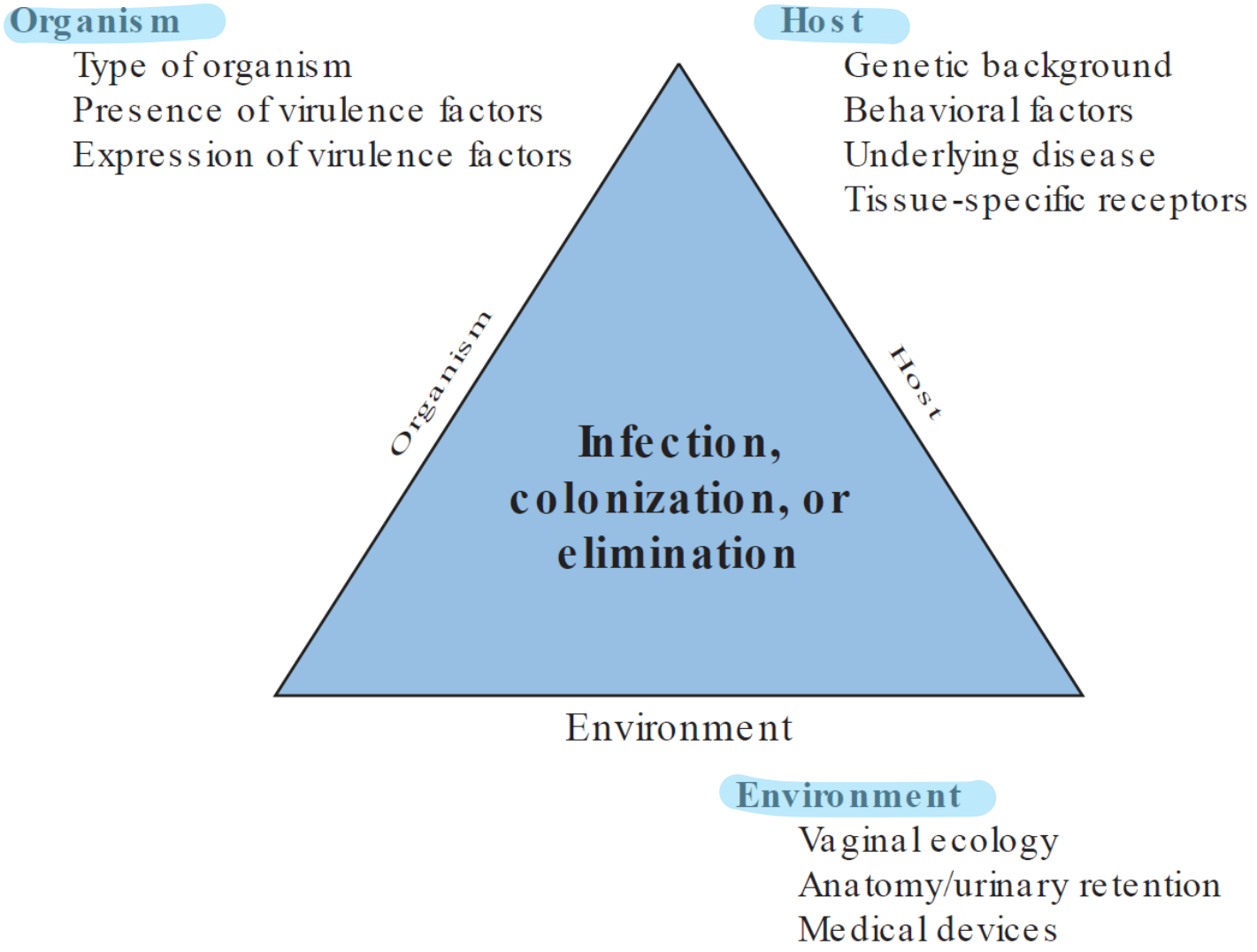


FIGURE 33-1
Pathogenesis of urinary tract infection. The relationship among specific host, pathogen, and environmental factors determines the clinical outcome.

Pathophysiology of UTIs

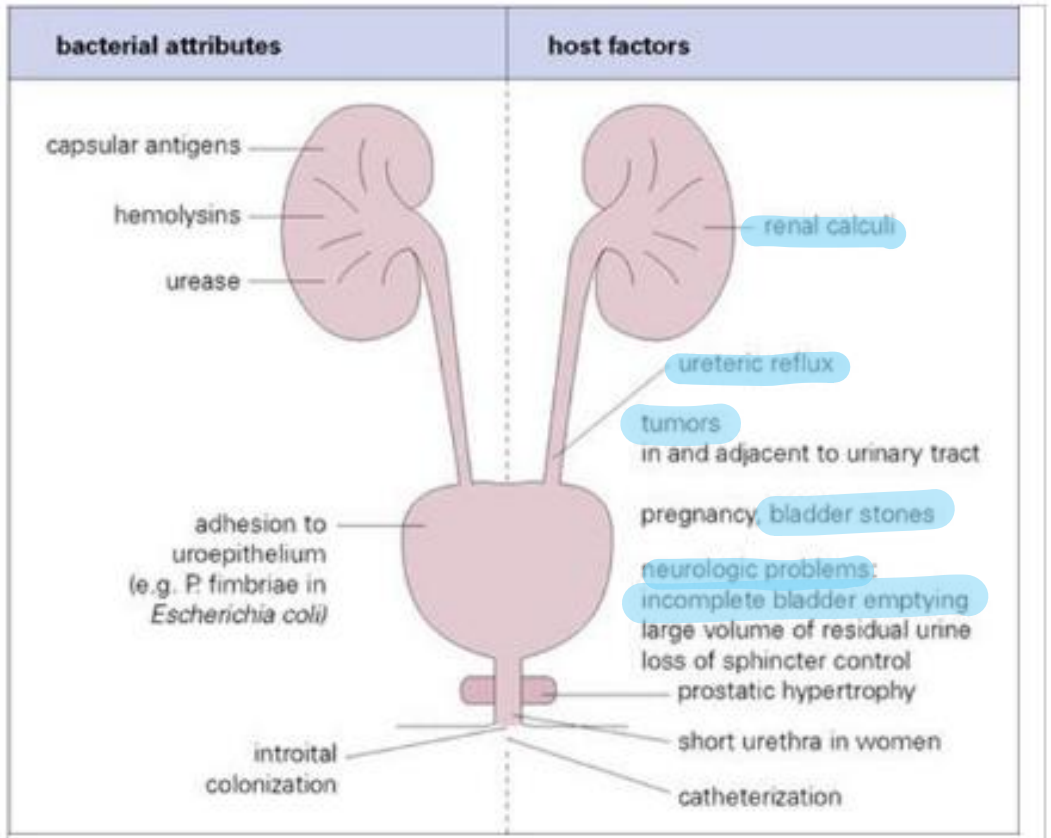
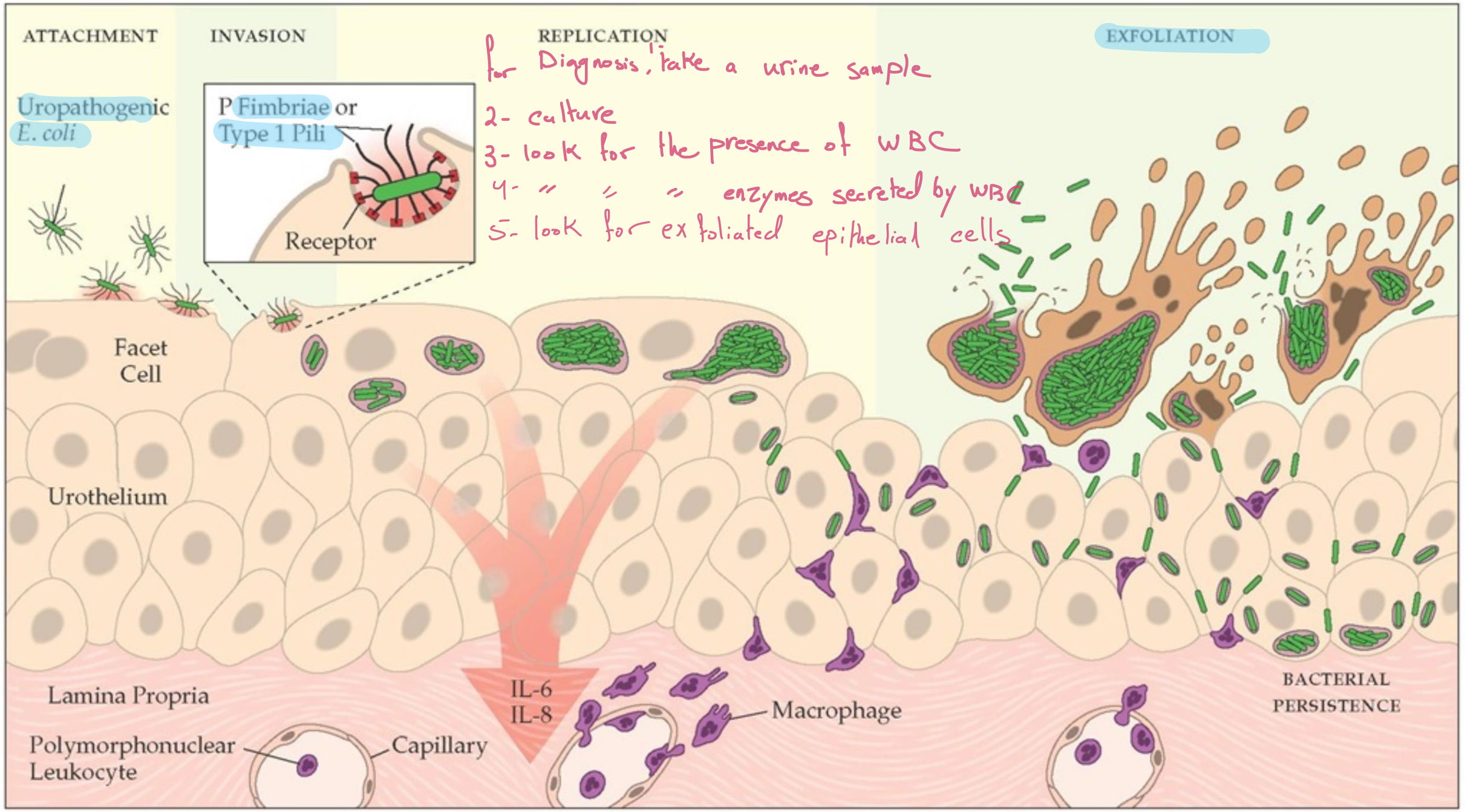


Figure 4. Bladder (Medical Microbiology, 2017)


ATTACHMENT
INVASION
REPLICATION
EXFOLIATION
for Diagnosis, take a urine sample
2- culture
3- look for the presence of WBC
4- " " " enzymes secreted by WBC
5- look for exfoliated epithelial cells
Uropathogenic
E. coli
P Fimbriae or
Type 1 Pili
Receptor
Facet
Cell
Urothelium
Lamina Propria
IL-6
IL-8
Macrophage
BACTERIAL
PERSISTENCE
Polymorphonuclear
Leukocyte
Capillary

Pathophysiology of UTIs

المعلومات من تسجيل 2021، ما ذكرها الدكتور لافتنل ولكن في عليها أسئلة من Past paper خاصة رقم 1, 5

1+5: the most common

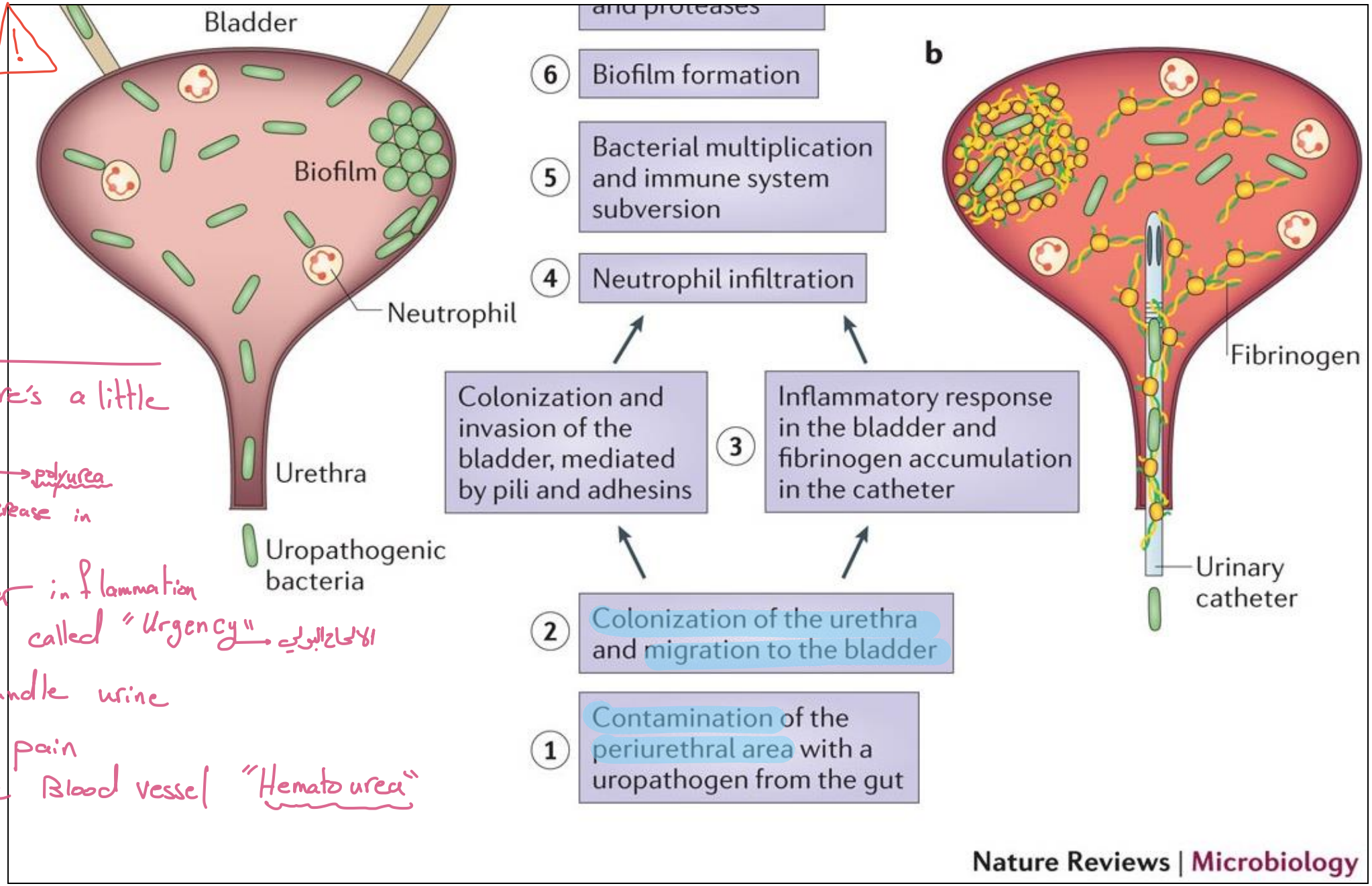
① increase the frequency of urination BUT there's a little amount of urea
↳ it differ from diabetes → polyurea because their is an increase in the amount of urine

② Due to bladder inflammation there is somthing called "Urgency" الالحاح البولي
↳ they can't handle urine

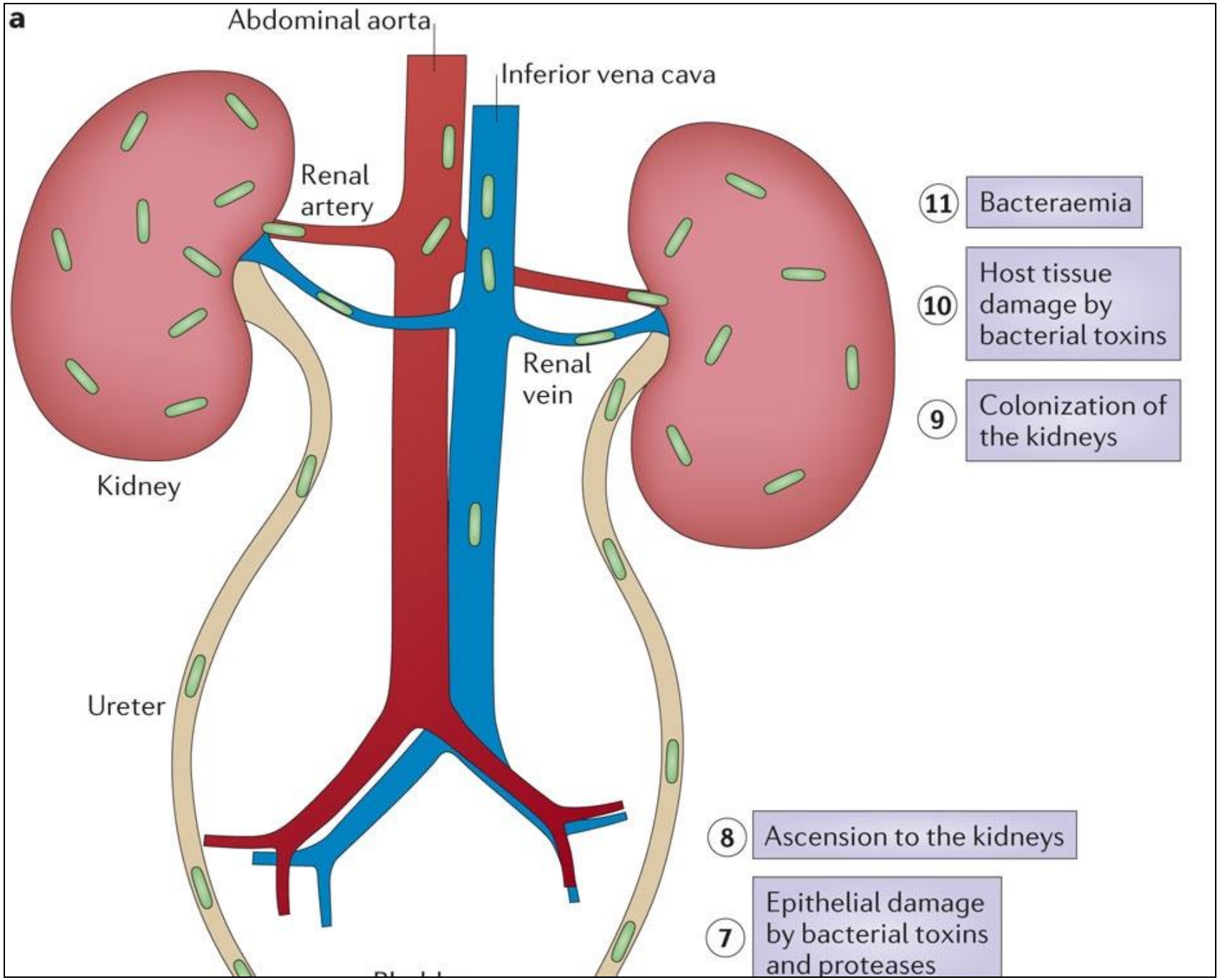
③ supra pelvic pain

④ Damage to the Blood vessel "Hematourea"

⑤ dysurea



Pathophysiology of UTIs



- الاسئلة من كيتش دقيقة
→ from chat GPT

1.What is the most common pathogen responsible for UTIs in women? a) Escherichia coli b) Klebsiella pneumoniae c) Staphylococcus aureus d) Streptococcus pyogenes
Answer: a) Escherichia coli
2.Which age group is most commonly affected by UTIs? a) Infants and toddlers b) Adolescents c) Young adults d) Older adults
Answer: d) Older adults
3.Which gender is more prone to develop UTIs? a) Males b) Females c) Both genders are equally affected d) It depends on the age group
Answer: b) Females
4.Which anatomical factor increases the risk of developing UTIs in women? a) Shorter urethra b) Longer urethra c) Narrower urethra d) Wider urethra
Answer: a) Shorter urethra
5.Which condition is a risk factor for recurrent UTIs? a) Hypertension b) Diabetes mellitus c) Hypothyroidism d) Asthma
Answer: b) Diabetes mellitus
6.What is the most common mode of transmission for UTIs? a) Airborne transmission b) Direct contact transmission c) Vector-borne transmission d) Foodborne transmission
Answer: b) Direct contact transmission
7.What is the most common site of infection in UTIs? a) Kidneys b) Bladder c) Ureters d) Urethra
Answer: d) Urethra

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