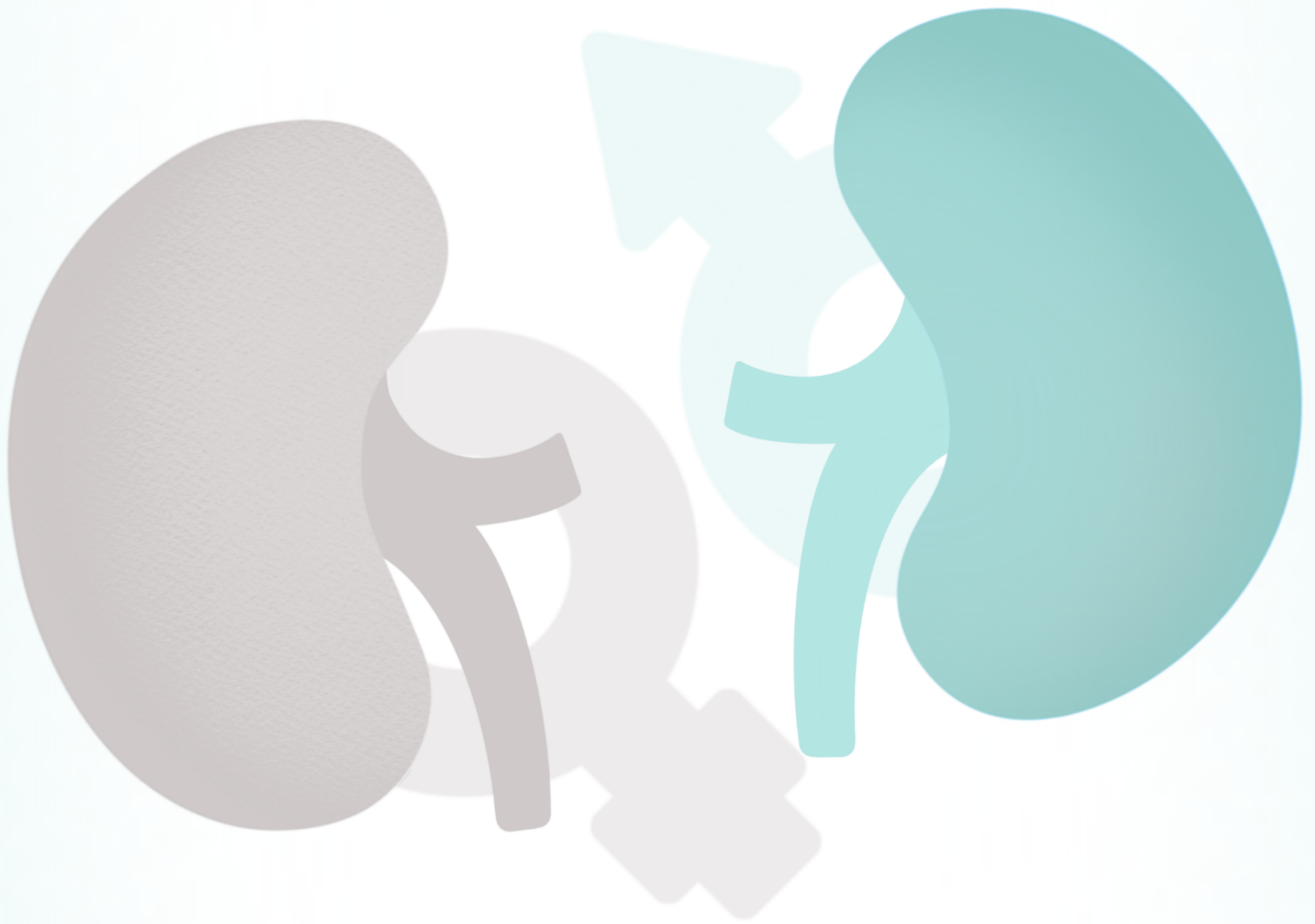


# G.U.S.

# Microbiology

1



Sheet: Sheet 1-UTIs.....

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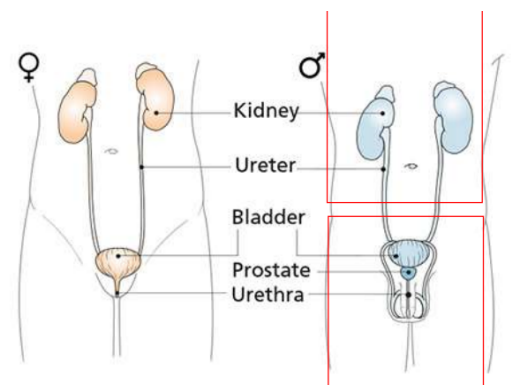
Doctor: Anas Abu Humaidan.....

## Urinary tract infections (UTIs)

**Similar to CNS**, urinary tract should be a sterile environment (there shouldn't be any bacteria ) and when the bacteria reach the immune system there will be an exaggerated immune response and it's considered very harmful to the host. **Unlike CNS**, bacteria can commonly reach the urinary tract but in this situation the immune response can handle it properly by keeping the environment sterile and prevent the colonization of bacteria without an exaggerated response. This happens in several ways :

- ✓ The **bulk of flow of urine** through the bladder and micturition (contraction of the bladder) can work to **rinse away** and flush out non-attached or **weakly adherent** microbes from the bladder surface (mechanical form of defense).
- ✓ 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 by forming a harsh environment for bacteria (chemical form of defense).
- ✓ **Lactoferrin** within urine can scavenge essential iron away from incoming microbes (This protein binds ferrous and sequesters it which deprives the bacteria from the iron needed for their growth and survival ).
- ✓ A number of soluble and cell associated factors within the bladder, including **Tamm-Horsfall protein (THP)**, low molecular weight sugars, **secretory IgA**, and **uromucoid**, can act as **anti-adherence factors**, competitively inhibiting bacterial attachment to the bladder surface (secretory IgA are found at mucosal surfaces so they prevent the attachment of bacteria to the surface (by blockading epithelial receptors) because once the bacteria attach, they start colonizing then they can form an infection).

- Here you can see the gross anatomy of the male and female urinary system which consist of: Two kidneys, two ureters, a urinary bladder, a urethra, and a prostate gland (only in males).
- Notice the differences between male and female: males have prostate while females do not, the urethra of the male is quite longer than that in females, **that's why females get UTI's more than males.**



## Upper and lower UTIs

The disease	pyelonephritis	cystitis	prostitis	urethritis
The Location	kidney	bladder	prostate	urethra
The classification	Upper UTI	Lower UTI		

- ✓ There are certain symptoms associated with UTIs and if they are present, we can call it (**cystitis, prostatitis, pyelonephritis**) depending on where the bacteria are.
- ✓ If the symptoms are not present but there are bacteria in the urine, we call it **asymptomatic bacteriuria (ASB)**, we discover it by a routine urine examination where we can find the bacteria and the patient is not complaining about it.

## Epidemiology

### Epidemiology 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, males rarely face UTIs.
- About 20-30% of women who have one episode of UTI will have **recurrent episodes**.
- Early recurrence (within 2 weeks) is usually regarded as **relapse** rather than **reinfection** (if they happen after more than 2 weeks) 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.

### Epidemiology 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, and virtually all of them are caused by the usage of **catheters** (A tube inserted into the urethra up to the bladder to help excreting the urine) and we call them catheter associated UTIs (**CAUTI**).
- The source of microorganisms causing CAUTI can be **endogenous** (from our own microbiota) typically via metal, rectal or vaginal colonization, or **exogenous**, such as via contaminated hands of healthcare personnel or equipment.

➤ In preschool, school and reproductive age groups there is a **huge difference** in female to male ratio in relation with the UTIs and that is because of the anatomical differences between males and females (the shorter urethra in females make the UT of females more accessible to pathogens).

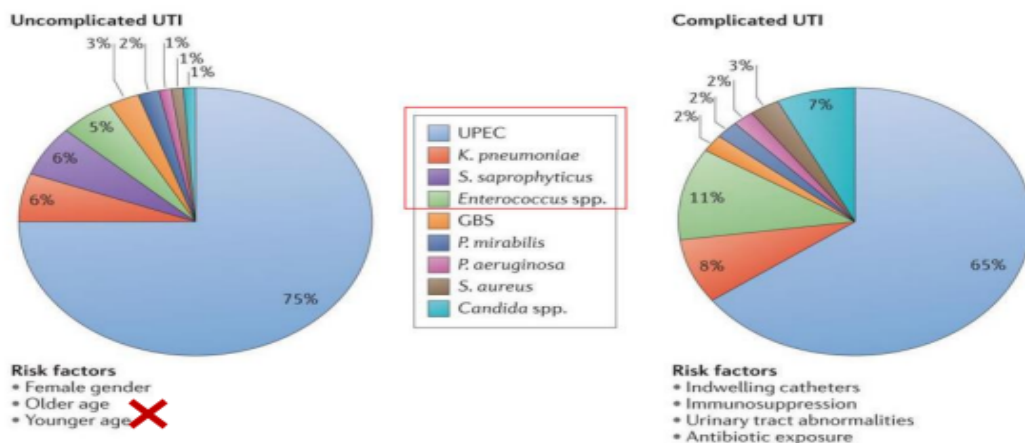
Age Group	Incidence (%)	Approximate Sex Ratio (Male:Female)
Neonatal	1.0	1.5:1.0
Preschool age	1.5-3.0	1:10
School age	1.2	1:30
Reproductive age	3-5	1:50
Geriatric	10-30	1:1.5

- While in neonates and geriatrics **the ratio is almost equivalent.**
- The occurrence of UTIs in male neonates is equivalent or even more than females because males have more chances to have congenital abnormalities in the urinary tract which increases the chance of UTIs (certain abnormalities prevent the normal flow of urine and causes stasis, in turn, increases the probabilities of bacterial attachment and infection by impairing the normal mechanical defenses).
- In geriatrics, Males of old age most often develop benign prostatic hyperplasia (BPH) or hypertrophy so the prostate gets enlarged and blocks the flow of urine to the urethra and causes UTIs (a complicated infection) so stasis of urine disrupts the normal mechanical defense against infections.

Clinically, UTIs are categorized as uncomplicated and complicated:

- ✓ Uncomplicated UTIs happen **in previously healthy individuals** and have no structural or neurological UT abnormalities.
- ✓ Complicated UTIs are defined as UTIs associated with factors that compromise the urinary tract or host defense, 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.

## Etiological factors



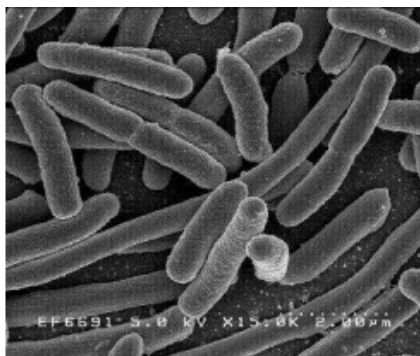
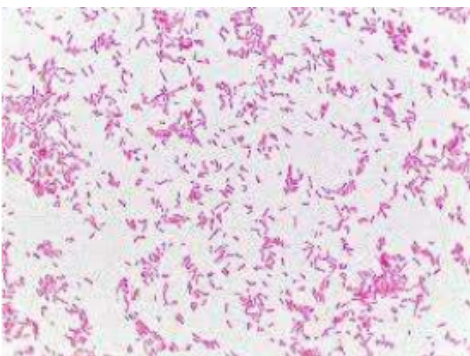
1. In both cases the most common causative pathogen is **uropathogenic E.coli (UPEC)**. Some strains of E.coli are part of the normal flora of GIT. UPEC is a strain of E.coli that has some virulence factors that enables it to cause UTIs.
2. **Klebsiella pneumoniae** another bacteria of the Enterobacteriaceae family
3. **Staphylococcus saprophyticus** (it is a Gram-positive coccus belonging to the coagulase negative genus) which is part of the microbiota of the skin along with staphylococcus epidermidis and others.
4. **Enterococcus species** (this type of bacteria is more common in complicated infection, so suspect this type of bacteria in catheterized patients who have UTI).

Here are some risk factors to UTIs:

- Complicated type: Immunosuppression, catheterization, congenital abnormalities in UT, antibiotic exposure.
- Uncomplicated type: female gender as healthy females have a 50% chance to have uncomplicated UTIs at certain age (other risk factors are mentioned in the figure above like older age and younger age).

## Uropathogenic E.coli (UPEC)

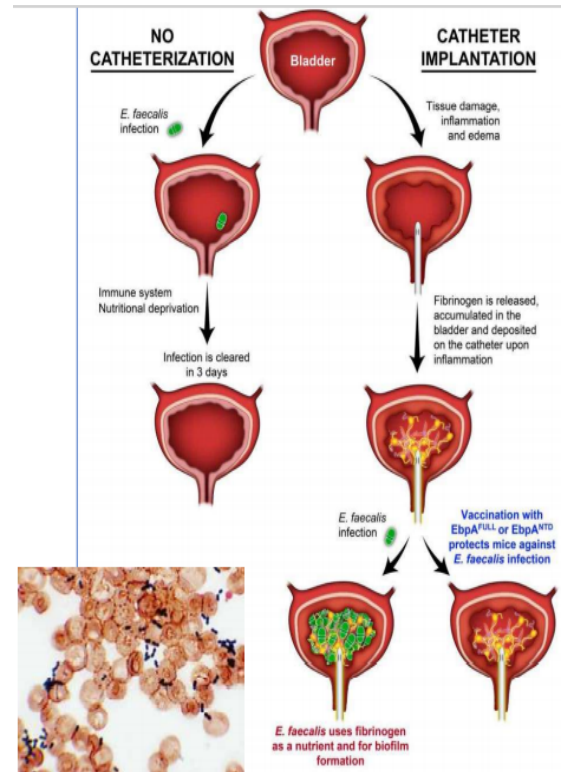
- ✓ It is a gram negative rod, facultative anaerobe.
- ✓ The optimum growth temperature is 37C.
- ✓ On nutrient agar, colonies are large, thick, greyish white, moist, smooth.
- ✓ E.coli and other facultative anaerobes constitute about 0.1% of gut microbiota.
- ✓ Some strains of E.coli gain certain virulence factors and cause UTIs (UPEC) while other strains are non- pathogenic and harmless and stay in the intestine.
- ✓ There is a subtype of E.coli can cause epidemic diarrheal diseases.





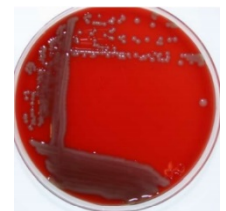
## Enterococcus faecalis

- ✓ 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, and as we said it is a common cause of complicated UTIs (**By the insertion of a catheter**).
- ✓ 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** (complicated UTI). It's resistant to many antibiotics.
- ✓ If this bacteria manages to reach the bladder, the urinary flushing and normal immune system will help in its clearance, while if there is a catheter inserted to the urethra this will offer a surface for the bacteria to adhere to it, also the insertion of a catheter damages the tissue leading to **the release of fibrinogen** which is considered a good factor for the bacteria to attach and adhere, then the bacterial growth begins causing UTI.
- ✓ Pass antibiotic-resistance genes to other bacteria by horizontal gene transfer either by conjugation of plasmid or transformation with naked DNA, *S. aureus* specifically MRSA gets its resistance to vancomycin from *Enterococcus faecalis*, in certain settings both bacteria are found at the same place and *S. aureus* will acquire genes of resistance from Enterococci.



## 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.
- ✓ It is becoming problematic now because it causes hospital-acquired infections.
- ✓ Antibiotic resistant which is another problem.
- ✓ Pass antibiotic-resistance genes to other bacteria by horizontal gene transfer either by conjugation or transformation with naked DNA.





5. expression of cell surface **capsules**, which enable them to resist the bactericidal actions of complement and phagocytic cells.
  6. Certain **surface antigens** that help in immune evasion, and **antigen switching mechanism** in some G<sup>-ve</sup> Enterobacteriaceae which makes it unrecognizable by immune system.
- If E.coli acquires these virulence factors by a mutation or through horizontal gene transfer it will become uropathogenic (UPEC) and it will be able to cause UTIs.

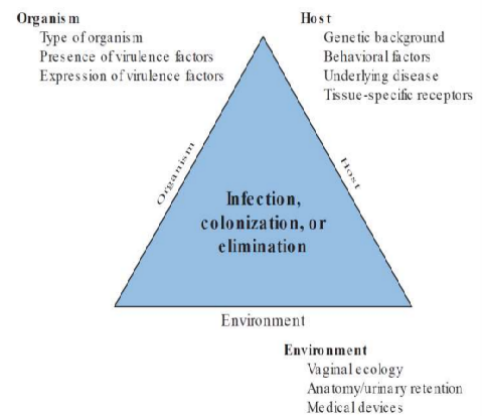
### The triad of infection (this triad is applied to any sort of infection)

- We have 3 things that act together in order to generate the final result of infection, colonization, or elimination of the bacteria. Elements/factors of this triad are:

1. Factors in the organism, most importantly the existence and the expression of virulence factors.

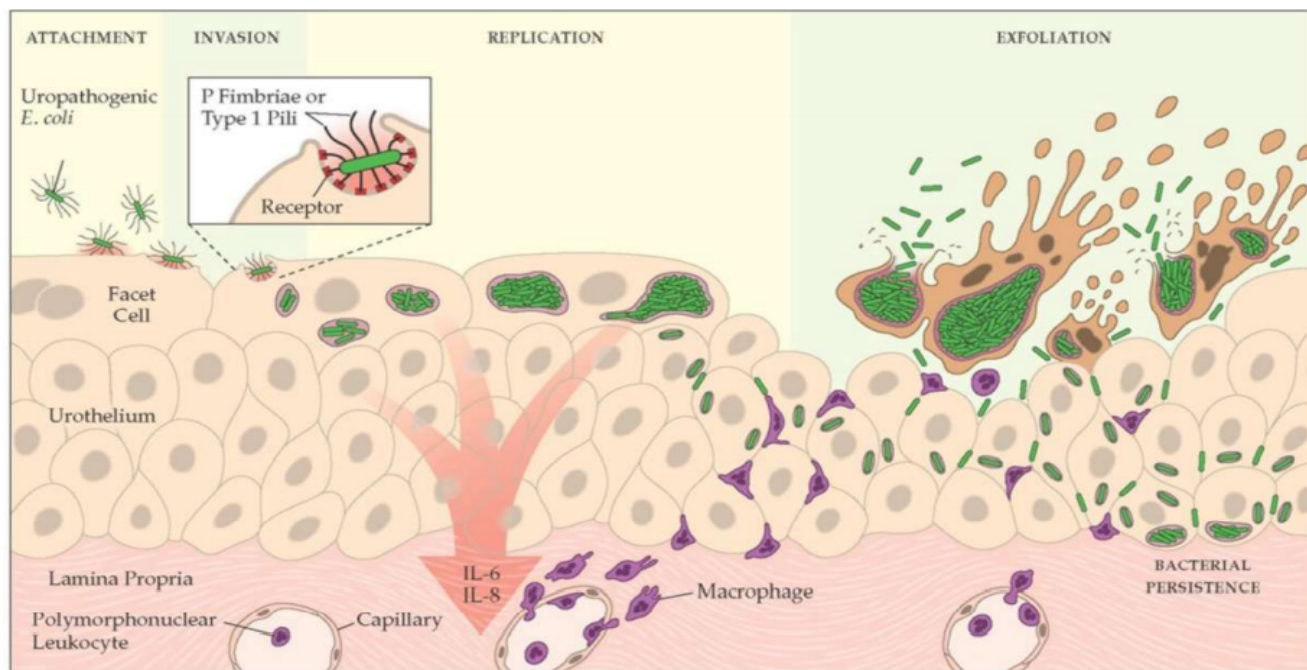
2. Host factors, which include:

- ✓ **The immune response.** Ex: immunocompromised patients are more likely to get UTIs.
- ✓ **Behavioral factors** related to the host; sexual intercourse is an independent factor that increases the risk of UTIs. Also, multiple sexual partners increase the risk of UTIs.
- ✓ **Genetic background:** certain people have a higher risk of having UTIs. It's found that females who have UTIs their daughters or mothers also have a higher chance of getting UTIs.



- There are certain proteins that the bacteria can adhere to and hence adhere to the epithelium or the absence of certain protein leads to decrease clearance of the Bacteria which will affect the final outcome mentioned before (the presence or absence of these proteins is genetically determined).
3. The environment in which this interaction takes place, for example, patients with indwelling bladder catheters are predisposed to UTIs. Also, females vaginal ecology plays a role.





-now let us dig deeper to see how the infection takes place:

1. We have the bacteria with the most important virulence factor; the fimbriae attaching to the epithelial cells.

2. Then the bacteria go inside the cell where they start the replication (within the uroepithelium). This will lead to two outcomes:

a. if the bacteria gets to the inside of the cell → the cell will recognize the bacteria by pattern recognition molecules and starts secreting cytokines like IL-6 and IL-8 .

b. another outcome is that the cell will die either because of necrosis ; (there is too many bacteria inside it which will blow it up) or the cell commits itself to die by apoptosis (programmed cell death). They are mechanisms by which the uroepithelium tries to eliminate the bacteria.

3. Infiltration of immune cells which will also try to clear the infection but the bacterium in certain cases can persist in pockets hidden away which will then cause a relapse of the infection. (Symptoms will disappear & the infection recurs within two weeks) .

\*remember that the main source of uropathogenic E .coli is the gut, it reaches the urethra through the anus & perineum (it is difficult for the bacterium to reach the male urethra than that in female due to the anatomical differences).

The professor read this diagram as it shows the pathophysiology of UTI in steps: (these steps are required, study them from the figure in the next page ) Notes regarding the figure: -

biofilm is composed of proteins, macromolecules, DNA and sugars that the bacteria secrete in order to make this thin layer (film) which helps the bacteria to keep in protection from defense mechanisms of host and also from antibiotics.

-In the case of complicated UTI where we have a catheter for example, it is easier for the bacteria to get attached to fibrinogen and the surface of the catheter and form an infection ,later on the bacteria can even ascend up through ureters to the kidney and cause upper urinary tract infection or it can reach the blood causing bacteremia.

