Urinary Tract Infections (UTI) part (1)

Urogenital Tract Module

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Outlines

- Introduction
- Urinary Tract Defences
- Urinary tract infections pathophysiology
- Etiology
  - Pathogens: *E. coli, S. saprophyticus, P. mirabilis, K. pneumoniae*
  - Predisposing factors

UTI: Introduction

- Urinary tract infections (UTIs) are infections in any part of urinary system - the urethra, bladder, ureters, or kidneys.
- UTIs are the most common outpatient infections.
- Between 50% and 60% of adult women will have at least one UTI in their life, and close to 10% of postmenopausal women indicate that they had a UTI in the previous year.

UTI: Urinary Tract Defences

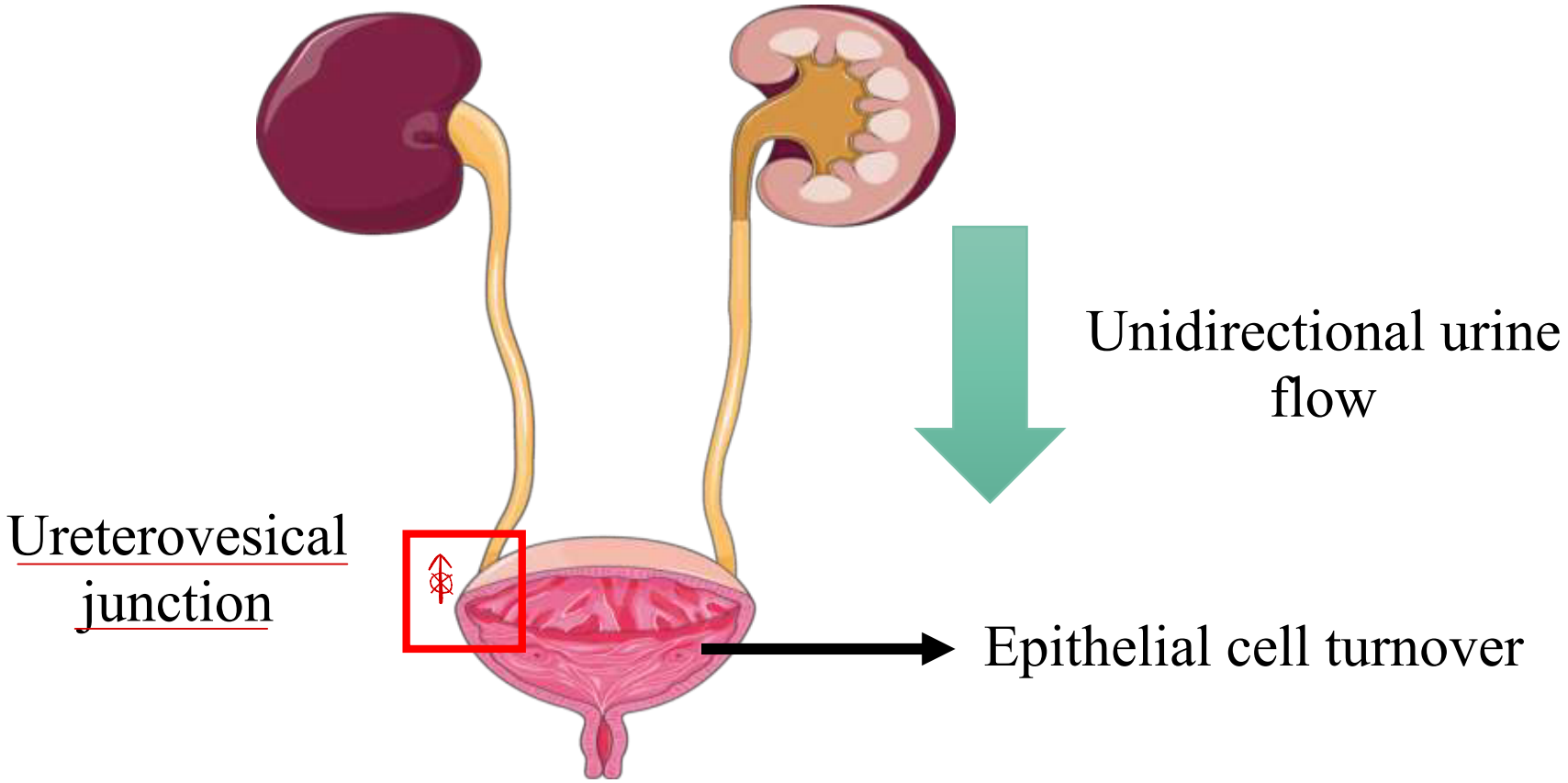
- The urinary tract is typically **a sterile environment**.
- Urinary tract employ several anatomical, physiological, and immunological defences to combat harmful microbes.

A. Anatomical and Mechanical Defences

- Unidirectional urine flow: The bulk flow of urine can work to rinse away non-attached or weakly adherent microbes from the bladder surface
- Ureterovesical junction prevents vesicoureteral reflux
- Epithelial cell turnover: sloughing of infected cells

UTI: Urinary Tract Defences

A. Anatomical and Mechanical Defences



UTI: Urinary Tract Defences

B. Physiological and biochemical defences

- Frequent urination and high urinary volumes also reduce the risk of UTIs.
- Urine properties: Acidic pH, High osmolality and urea concentration → unfavourable conditions for bacteria
- Antimicrobial peptides: Urothelial cells have a key role in protecting the bladder from infection by producing antimicrobial peptides and proinflammatory cytokines
- The mucus layer lining the bladder wall serves as a mechanical barrier to bacterial infiltration and invasion.

Acidic PH

High osmolality

High urea concentration

Antimicrobial peptides

UTI: Urinary Tract Defences

anatomical → body
physiological → urine itself
immunological → innate
→ adaptive

C. Immune response

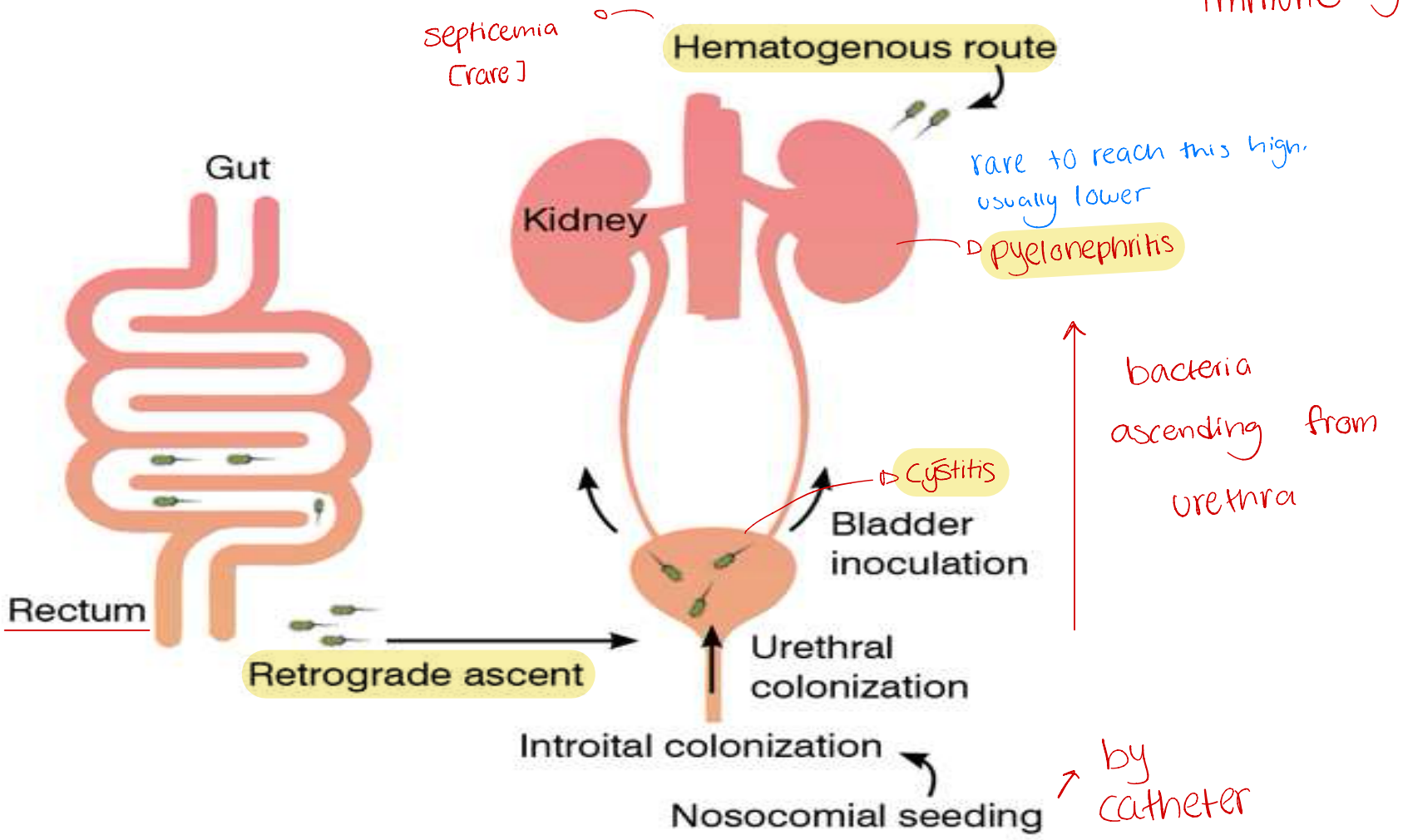
antigen / pathogen

1. Innate Immune Responses: Pattern Recognition Receptors (PRRs): Urothelial cells express Toll-like receptors that detect uropathogens like *E. coli*, initiating immune responses.

2. Adaptive Immune Responses: Secretory IgA: Produced by plasma cells binds to pathogens, preventing their adhesion and facilitating their removal via urine. } mucosa

UTI: Pathophysiology

how Pathogens evade the immune system



UTI: Pathophysiology

There are two potential routes:

Ascending infection

- Uropathogens (most commonly fecal flora) colonize periurethral area → ascend to bladder via urethra
- If pathogen reaches kidney via ureter → pyelonephritis or upper UTI
- Infection may occasionally enter blood → septicaemia

Hematogenous infection

- Bacteria in the bloodstream (bacteraemia) seed the kidneys via the renal arterial circulation (kidneys receive 20% to 25% of the cardiac output).
- The major causes of hematogenous infection are *S. aureus*, Salmonella species, *P. aeruginosa*, and Candida species.
- Rarely seen, usually in immunocompromised patients

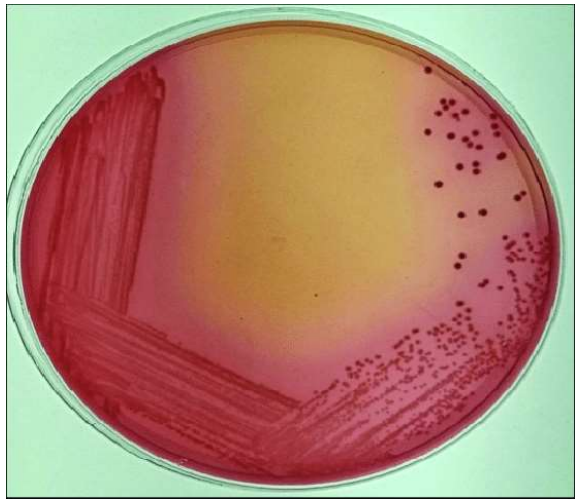
UTI: Etiology- Pathogens

E. coli

- *E. coli* is the leading cause of UTI (approx. 80%)
- Gram negative rod, facultative anaerobe, lactose fermenter.

most common

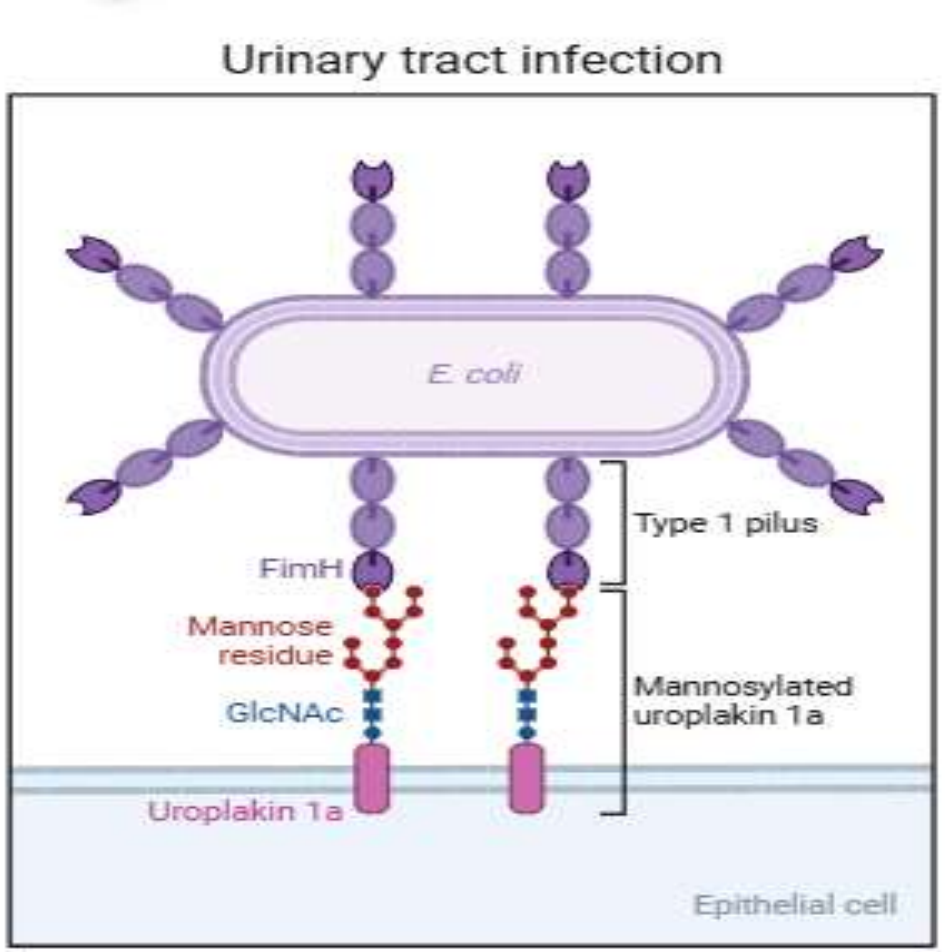
Pink color



UTI: Etiology- Pathogens

E. coli has virulence factors that aid in colonization, ascension, and invasion of the urinary tract:

- Type 1 fimbriae: attach to the uroepithelial cells (on the mannose residues of surface glycoproteins) → Prevent *E. coli* from being flushed out by the urine stream
- P fimbriae: Hair-like projections that interact with renal epithelial cells. It is important role in pyelonephritis



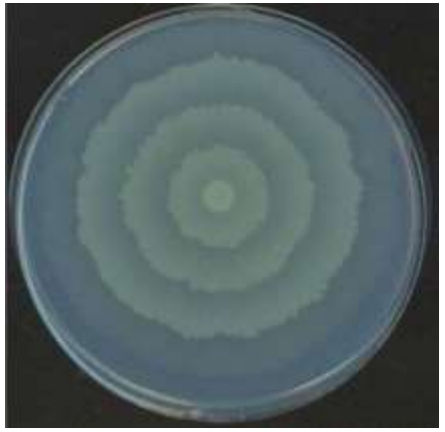
UTI: Etiology- Pathogens

- ***S. saprophyticus*:**
  - Gram-positive coccus belonging to the genus Staphylococcus.
  - Associated with UTIs in sexually active women.

catalase -
coagulase +

- ***Enterococcus faecalis*:** Gram-positive cocci, typically arranged in pairs and short chains .
  - *E. faecalis* is found in the large intestine in high concentrations
  - Associated with hospital-acquired infections frequently and with urinary catheterization or instrumentation
- ***Klebsiella pneumoniae*:** 3rd leading cause of UTI
  - Gram-negative, non-motile, encapsulated, lactose-fermenting, facultative anaerobic, rod-shaped bacterium.

UTI: Etiology- Pathogens



- ***Proteus mirabilis*:**
  - 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.

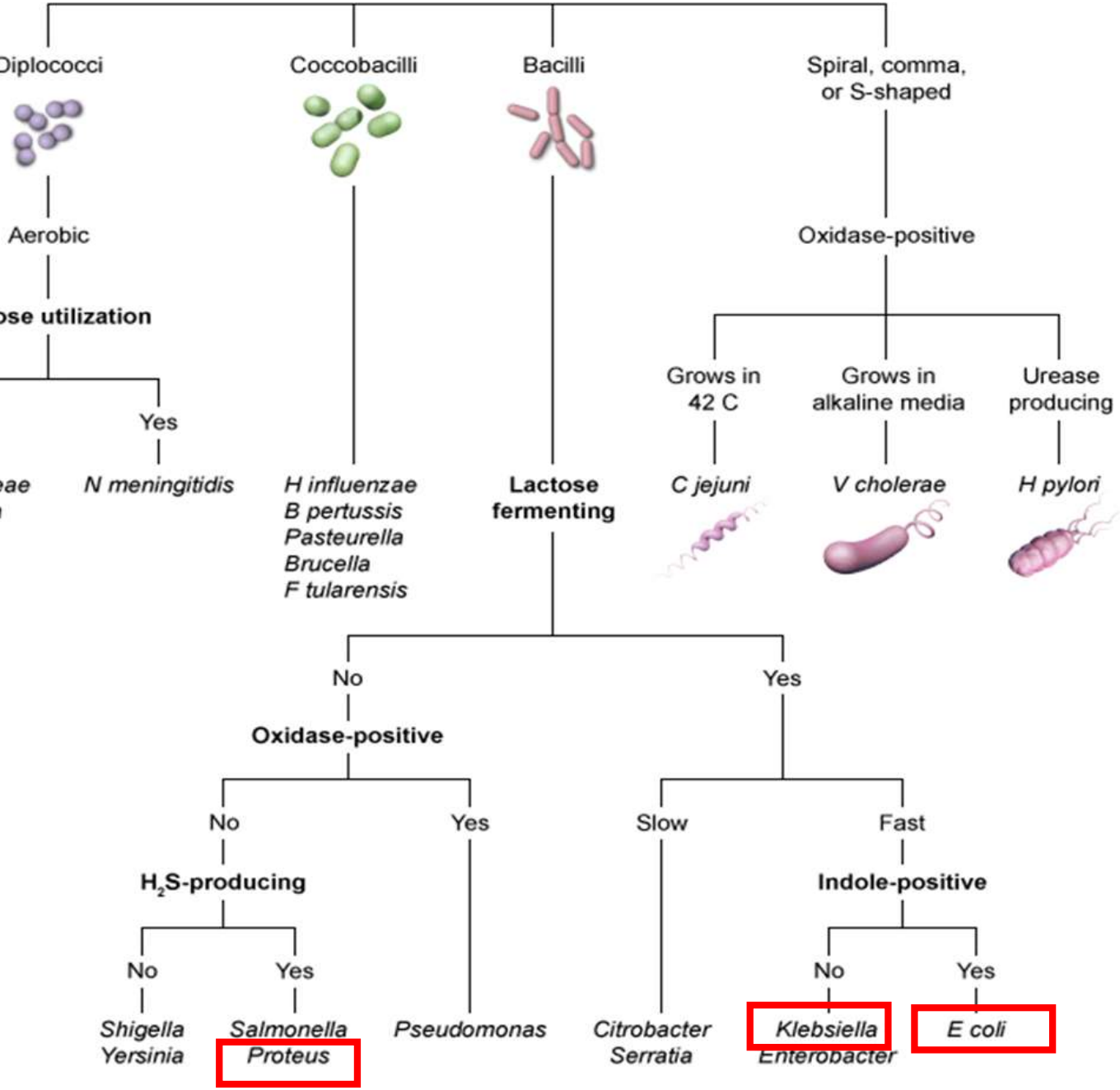
$$(NH_2)_2CO + 2\,H_2O \xrightarrow{\text{Urease}} CO_2 + H_2O + 2\,NH_3$$

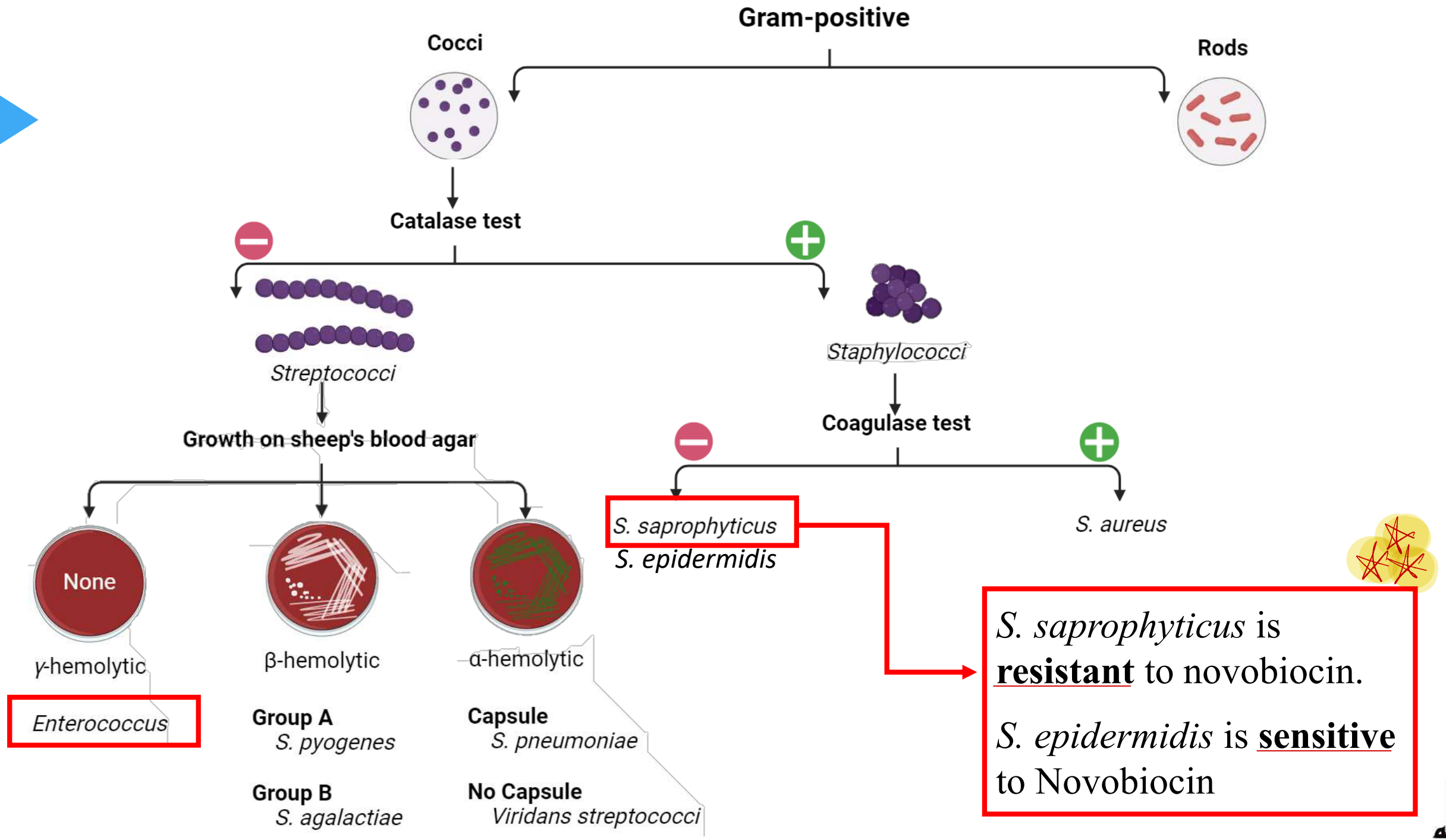
Urea — Carbon Dioxide — Water — Ammonia

acidic PH → protect [physiological]
alkaline PH → facilitate back inf

  - 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)

Gram-negative bacteria




Gram-positive
Cocci
Rods
Catalase test
Streptococci
Staphylococci
Growth on sheep's blood agar
Coagulase test
None
γ-hemolytic
Enterococcus
β-hemolytic
Group A
S. pyogenes
Group B
S. agalactiae
α-hemolytic
Capsule
S. pneumoniae
No Capsule
Viridans streptococci
S. saprophyticus
S. epidermidis
S. aureus
S. saprophyticus is resistant to novobiocin.
S. epidermidis is sensitive to Novobiocin

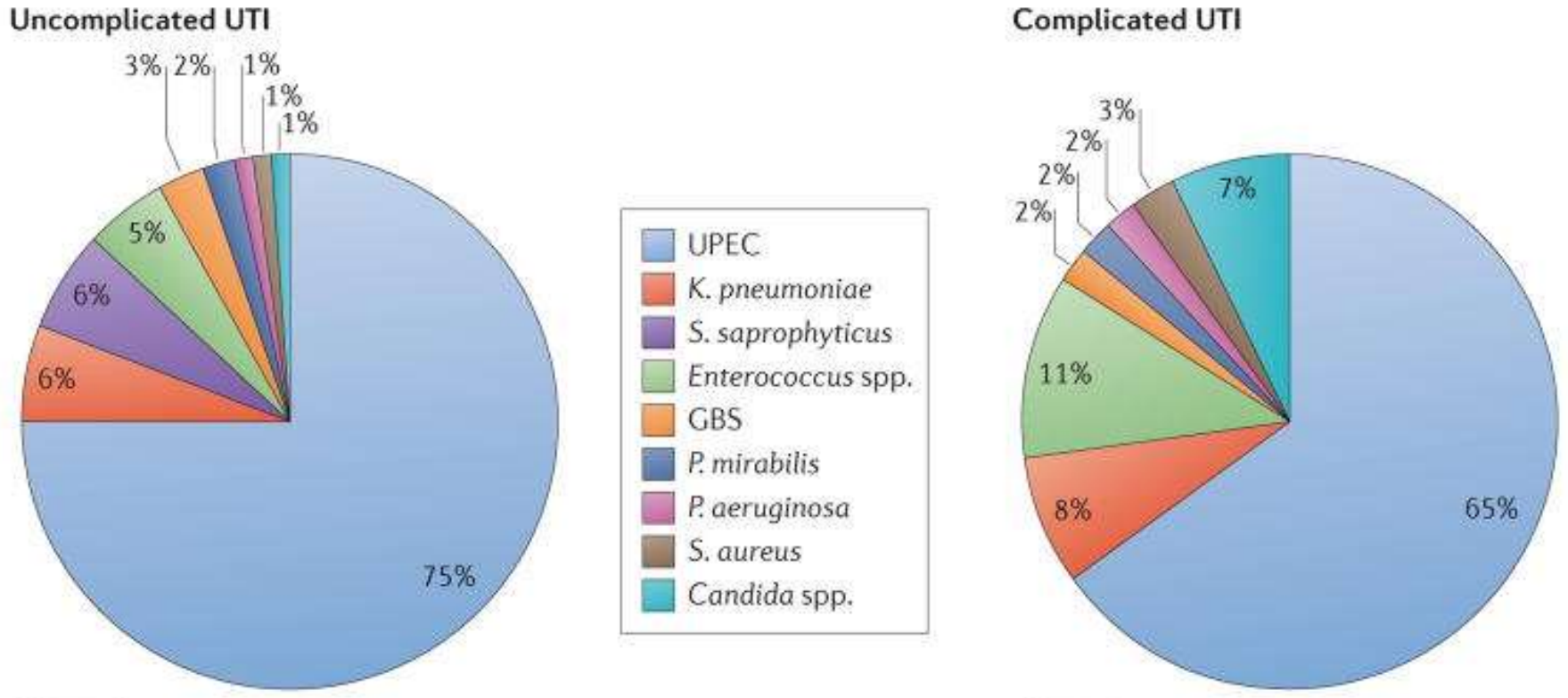
UTI: Etiology- Pathogens

Other causes

- Viruses: Rare cause (Adenovirus, cytomegalovirus)
  - Immunocompromised patients and children are particularly susceptible to viral UTIs.
- Fungi: rare cause (usually Candida species).

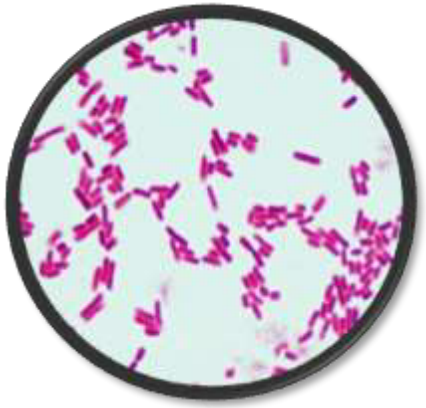
↑ hematogenous in Immunocompromised

UTI: Etiology- Pathogens



(UPEC): uropathogenic *Escherichia coli* >

UTI: Etiology- Pathogens

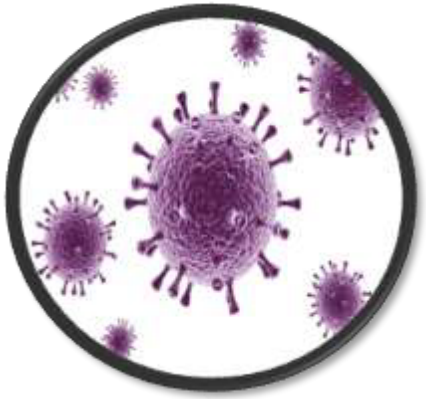


E. coli

S. saprophyticus

K. pneumoniae

P. mirabilis



Viruses

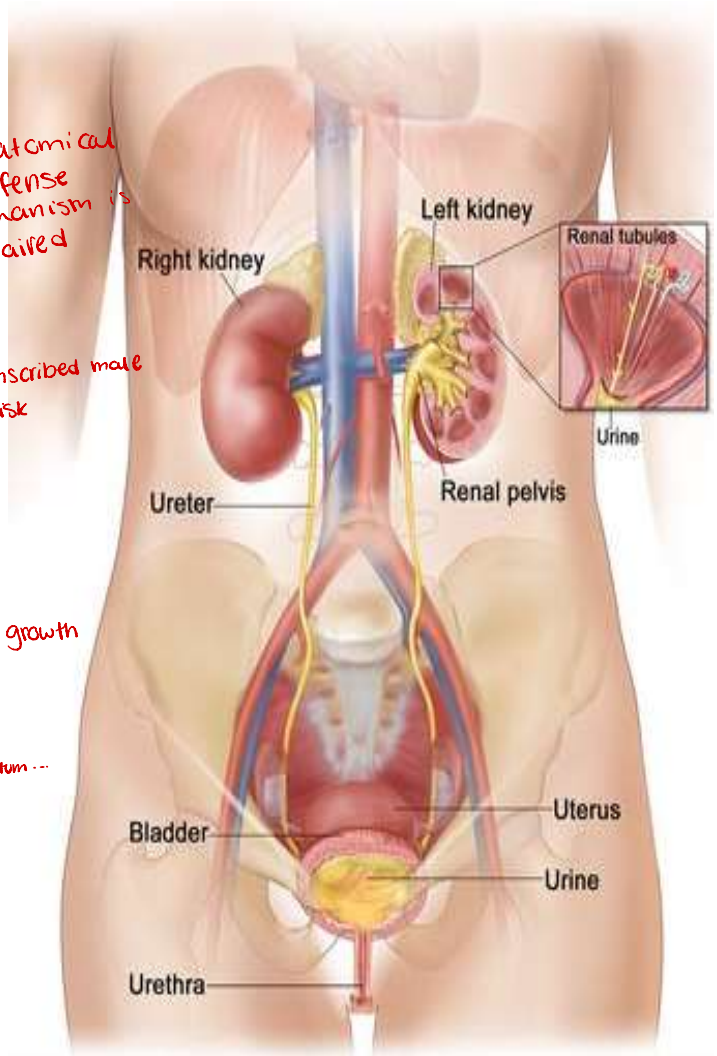
Fungi

risk factors

UTI: Etiology- Predisposing Factors

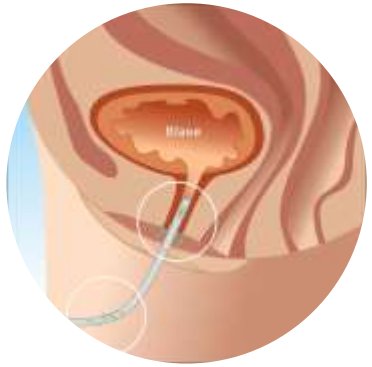
Host-dependent factors

- Structural or functional abnormalities of the urinary tract
  - ex: ⊗ uni-directional flow
  - anatomical defense mechanism is impaired
- Gender F > M
  - ⊕ uncircumscribed male ↑↑ risk
  - urethra short & in close proximity
- Pregnancy
  - hormonal change + urine stasis
- Post menopause → lactobacillus growth disturbance
- Chronic constipation
  - stool in rectum...
- Prior conditions
  - diabetes



Other factors

- Postcoital cystitis
- Catheter-associated UTI
  - enterococcus

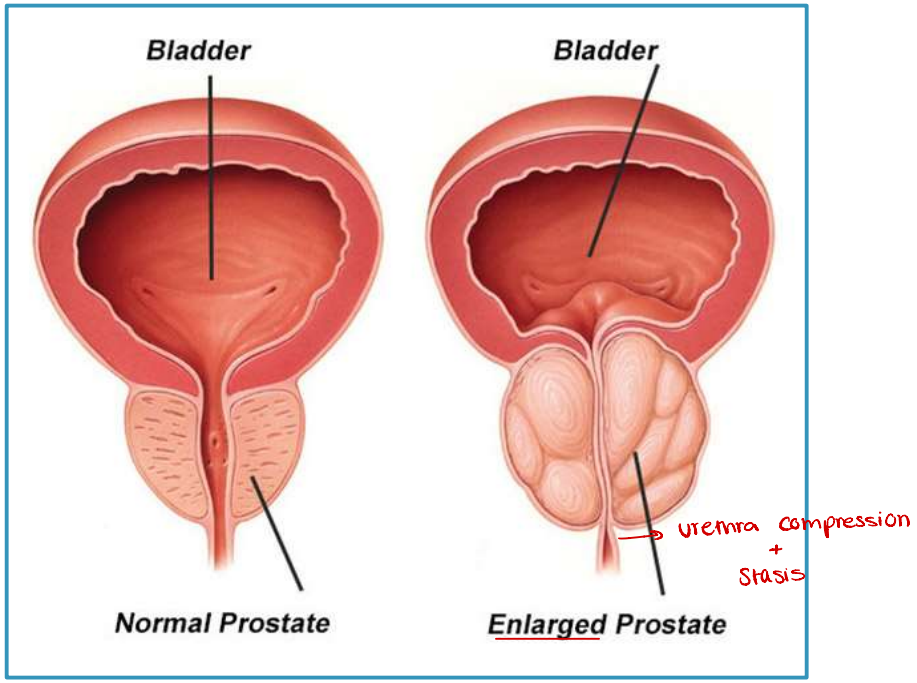


UTI: Etiology- Predisposing Factors

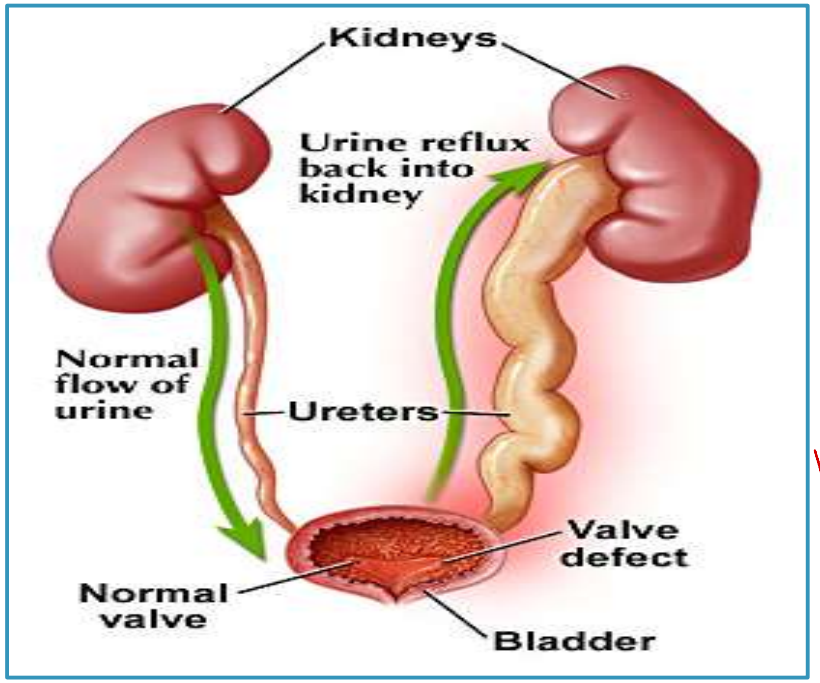
- Structural or functional abnormalities of the urinary tract Prevent bladder emptying and/or result in urinary stasis
- Examples include:
  - Benign prostatic hyperplasia
  - Congenital malformations causing vesicoureteral reflux
  - Neurogenic bladder
  - Urinary tract calculi

UTI: Etiology- Predisposing Factors

Examples of Structural or functional abnormalities of the urinary tract



Benign prostatic hyperplasia



Urine back flow bladder → kidney

Vesicoureteral reflux

UTI: Etiology- Predisposing Factors

- Sex:
  - Female individuals: anatomically predisposed because **the urethra is shorter** and anal and genital regions are in close proximity → bacteria spreading from the anal region → colonization of vagina → ascending UTIs.
  - Male individuals: higher risk in uncircumcised male infants
- Pregnancy: hormonal changes during pregnancy → urinary stasis and vesicoureteral reflux → increased risk of UTIs
- Post menopause: ↓ oestrogen → ↓ vaginal lactobacilli → ↑ vaginal pH → ↑ colonization by *E. coli*
- Postcoital cystitis (honeymoon cystitis): a lower urinary tract infection that occurs in women after recent sexual activity, which can cause irritation of the urethra and facilitate bacterial entry into the urethra (e.g., from the genital and/or anal region).

- A 24-year-old female presents to your office with burning urination, urgency and frequency. She is sexually active. Urine cultures show catalase-positive, gram-positive cocci. The organism responsible for this patient's symptoms is most likely to be:

S. saprophyticus

A. Coagulase positive
B. B. Haemolytic
C. Novobiocin resistant
D. DNase positive
E. E. Yellow pigment producer