Urogenital Tract / 3rd year
Urinary Tract Infections

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Urinary Tract Infections

ILOs

1. Define UTI
2. Classification
3. List the common bacteria causing UTI, including pathogenesis and host factors.
4. Define the major types of urinary tract infections such as: pyelonephritis, cystitis, urethritis, and asymptomatic bacteriuria
5. Describe the signs and symptoms
6. Outline the investigation of bacterial cystitis and pyelonephritis.
7. List the common classes of antimicrobials used to treat urinary tract infections.

Urinary Tract Infections

URINARY TRACT INFECTION (UTI)

- UTI results from the presence and multiplication of bacteria in one or more structures of the urinary tract with associated tissue invasion.
- This can give rise to a wide variety of clinical syndromes. These include:
- Upper UTI: acute and chronic pyelo-nephritis (kidney and renal pelvis)
- Lower UTI: cystitis (bladder), urethritis (urethra), epididymitis (epididymis) and prostatitis (prostate gland).
- Infection may spread to surrounding tissues (e.g. Perinephric abscess) or the bloodstream.

Urinary Tract Infections - Anatomy

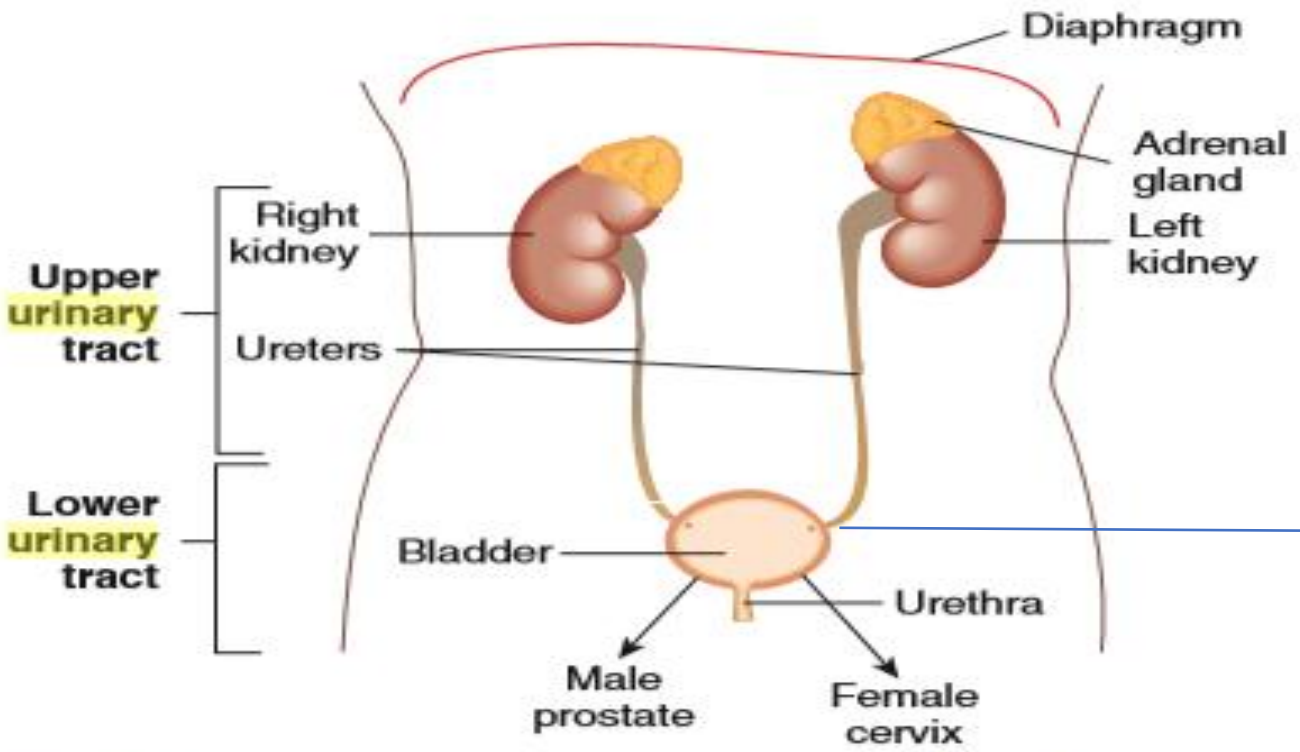


Figure 73-1 Overview of the anatomy of the urinary tract. (From Potter PH, Perry AG: *Fundamentals of nursing,* St. Louis, 1985, Mosby.)

BACTERIURIA

- Bacteriuria implies that bacteria may be grown from the urine, but the patient may or may not be symptomatic.

- Pregnant women should be offered routine screening for asymptomatic bacteriuria by midstream urine culture early in pregnancy.

- Identification and treatment of asymptomatic bacteriuria reduces the risk of preterm birth.

Epidemiology

- Approximately 10% of humans will have a UTI at some time during their lives.
- UTIs are also the most common hospital-acquired infection, accounting for as many as 35% of nosocomial infections (catheterization).
- UTIs are a leading cause of gram-negative sepsis in hospitalized patients
- The exact prevalence of UTIs is age and sex dependent.

- During the first year of life, UTIs are less than 2% in males and females. The incidence of UTIs among males remains relatively low after 1 year of age and untila pproximately 60 years of age when enlargement of the prostate interferes with emptying of the bladder.

Epidemiology

- The prevalence of bacteriuria in females increases gradually with time to as high as 10% to 20% in older women.
- The association of UTIs with sexual intercourse may also contribute to this increased incidence because sexual activity increases the chances of bacterial contamination of the female urethra.
- In pregnancy, as a result of anatomic and hormonal changes that favor development of UTIs, the incidence of bacteriuria increases during pregnancy. These infections can lead to serious infections in both mother and fetus.
- Other risk factors including DM, obstruction, instrumentation do increase the incidence

Anatomy

- In women:

✓Because of the shorter urethra in female, bacteria can reach the bladder more easily in the female host, thus urinary tract infections are primarily a disorder of women.

✓Sexual intercourse & lack of post coital voiding

✓ Diaphragm, spermicide use

✓Estrogen deficiency

- For men, the incidence of urinary tract infections increases after the age of 60, when the enlargement of the prostate interferes with the removal of urine from the bladder.

Urinary tract normal flora

- The urethra has resident microflora that colonize its epithelium in the distal portion; these organisms are lactobacilli, corynebacteria, and coagulase-negative staphylococci

- Potential pathogens, including gram-negative bacilli (primarily Enterobacteriaceae) and occasional yeasts, are also present as transient colonizers.

- All areas of the urinary tract above the urethra in a healthy human are sterile.

Urinary tract normal flora

- Urine is typically sterile, but noninvasive methods (MSU) for collecting urine must rely on a specimen that has passed through a contaminated milieu.

- Therefore, quantitative cultures for the diagnosis of UTIs have been used to discriminate among contamination and infection.

Urinary Tract Infections

Classification:

1- Community or hospital acquired (usually cath. associated)

2- Complicated and non-complicated:

❑Risk factors for complicated such as:

- Pregnancy
- Underlying diseases that predispose the kidney to infection
- (e.g., diabetes, sickle cell anemia)
- Kidney stones
- Structural or functional abnormalities of the urinary tract
- (e.g., a tipped bladder)
- Indwelling urinary catheters

Urinary Tract Infections

Community :

- *Escherichia coli* ,uropathogenic *E. coli* (UPEC), is by far the most frequent cause of uncomplicated community-acquired UTIs ; 75-90%
- Others are are Klebsiella, Staphylococcus saprophyticus, and enterococci.
- In more complicated UTIs, particularly in recurrent infections, the relative frequency of infection caused by *Proteus, Pseudomonas, Klebsiella, and Enterobacter* spp. increases

Urinary Tract Infections - bacteria

In HAI and complicated:

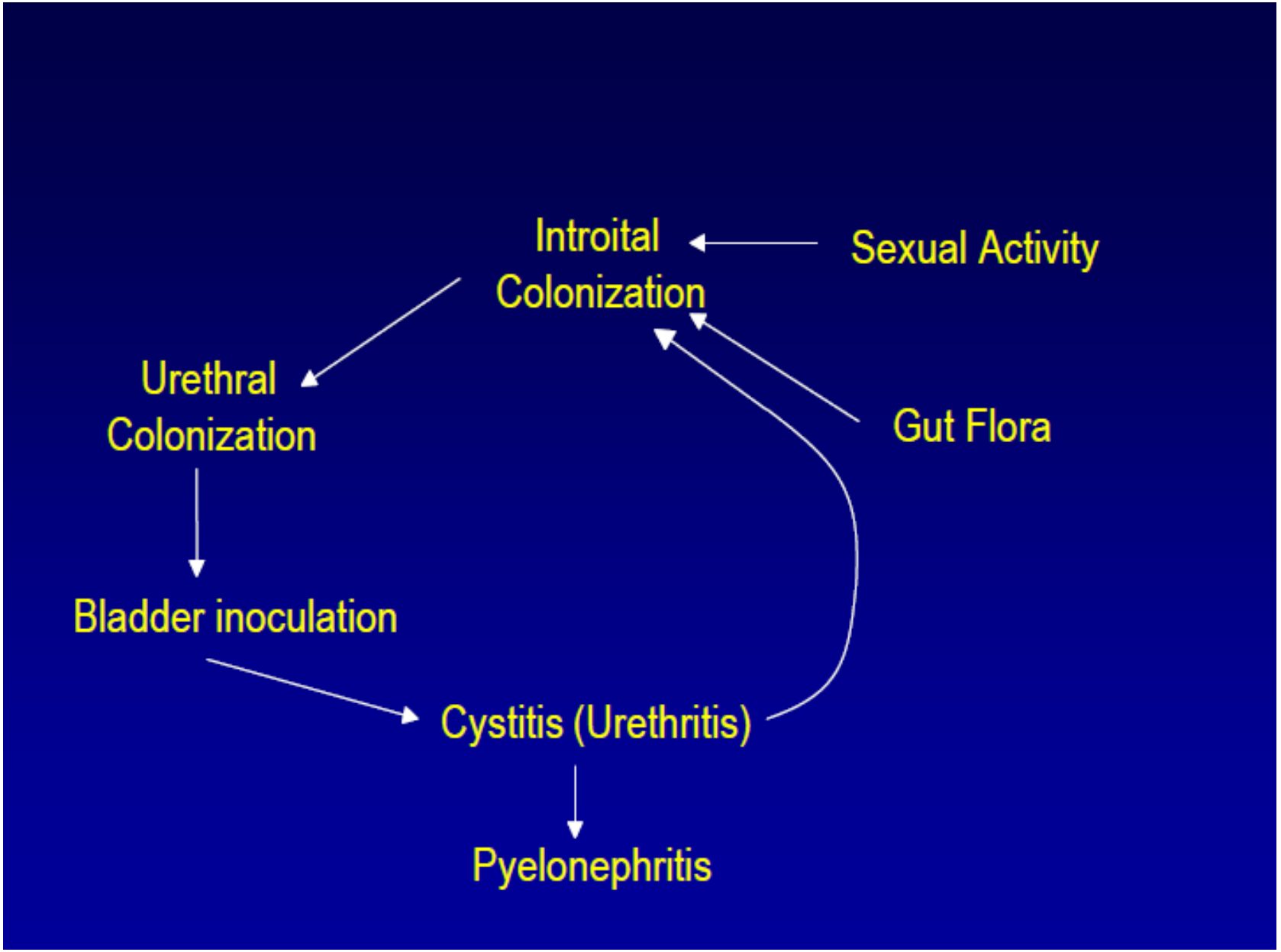
- *E. Coli* *30-35%*
- *Enterococcus* *20%*
- *Pseudomonas* *20%*
- *Klebsiella* *4-5%*
- *Proteus* *4-5%*
- *Staph saprophyticus* 4-5%
- Candida 2-3%
- Mixed and other 10%

Pathogenesis

- **Pathogenesis**
  - **Host Factors**
  - **Bacterial Factors**

- Route:

- Ascending Route 90 - 95%
  - Colonization of the genital area
  - Colonization of the urethra
  - Entry into the bladder and may ascend to kidneys
  - multiplication and Infection
- Hematogenous Route 5%


Introital Colonization
Sexual Activity
Urethral Colonization
Gut Flora
Bladder inoculation
Cystitis (Urethritis)
Pyelonephritis

Pathogenesis

Bacterial factors:

- Capsule: antiphagocytic
- Fimbria to bid to uroepithelium
- Motility
- Hemolysins that lyse the RBCs
- Siderophores to gather iron from the host

Pathogenesis

- Protection against infection is afforded by factors as:
- ✓ The constant flow of urine and regular bladder emptying – so obstruction of flow is risky
- ✓ Urine is a poor culture medium for many bacteria due to its acidity, high urea concentration and variable osmolality
- ✓ Vesicoureteral junction inhibits the backflow
- ✓ Defensin (antimicrobial peptides)and uromodulins (antiadherence factors)
- ✓ And, in men, possibly partly as a result of antibacterial activity of prostatic secretions.

Urinary Tract Infections - types

1 - Asymptomatic bacteriuria:

Screening and treatment for asymptomatic bacteriuria is recommended for:

- Pregnant women (because the risk of progression to severe symptomatic UTI and possible harm to the fetus)
- Males undergoing transurethral resection of the prostate or procedures for which mucosal bleeding is anticipated.

Urinary Tract Infections - types

2 - Urethritis

- Symptoms associated with urethritis (infection of the urethra) include dysuria (painful or difficult urination), and frequency Similar to those associated with lower UTIs

- Discharge may also exist

- *Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis* are common causes and considered sexually transmitted.

Urinary Tract Infections - types
3 – Cystitis

- Typically, patients with cystitis (infection of the bladder) complain of dysuria, frequency, and urgency (compelling need to urinate).

- These symptoms are due to inflammation of the bladder and multiplication of bacteria in the urine and urethra.

- Often, there is tenderness and pain over the area of the bladder.
- In some individuals, the urine is grossly bloody. The patient may note urine cloudiness and a bad odor.
- Because cystitis is a localized infection, fever and other signs of a systemic (affecting the body as a whole) illness are usually not present.

4– Pyelonephritis

- Pyelonephritis refers to inflammation of the kidney parenchyma, calices (cup-shaped division of the renal pelvis), and pelvis (upper end of the ureter that is located inside the kidney)

- Presentation includes :

✓fever and flank (lower back) pain and, frequently, lower tract symptoms (frequency, urgency, and dysuria)

✓Patients can also exhibit systemic signs of infection such as vomiting, diarrhea, chills, increased heart rate, and lower abdominal pain

✓Of significance, 40% of patients with acute pyelonephritis are bacteremic

Urinary Tract Infections - microbes

Enterobactericeae :Uropathogenic E. coli

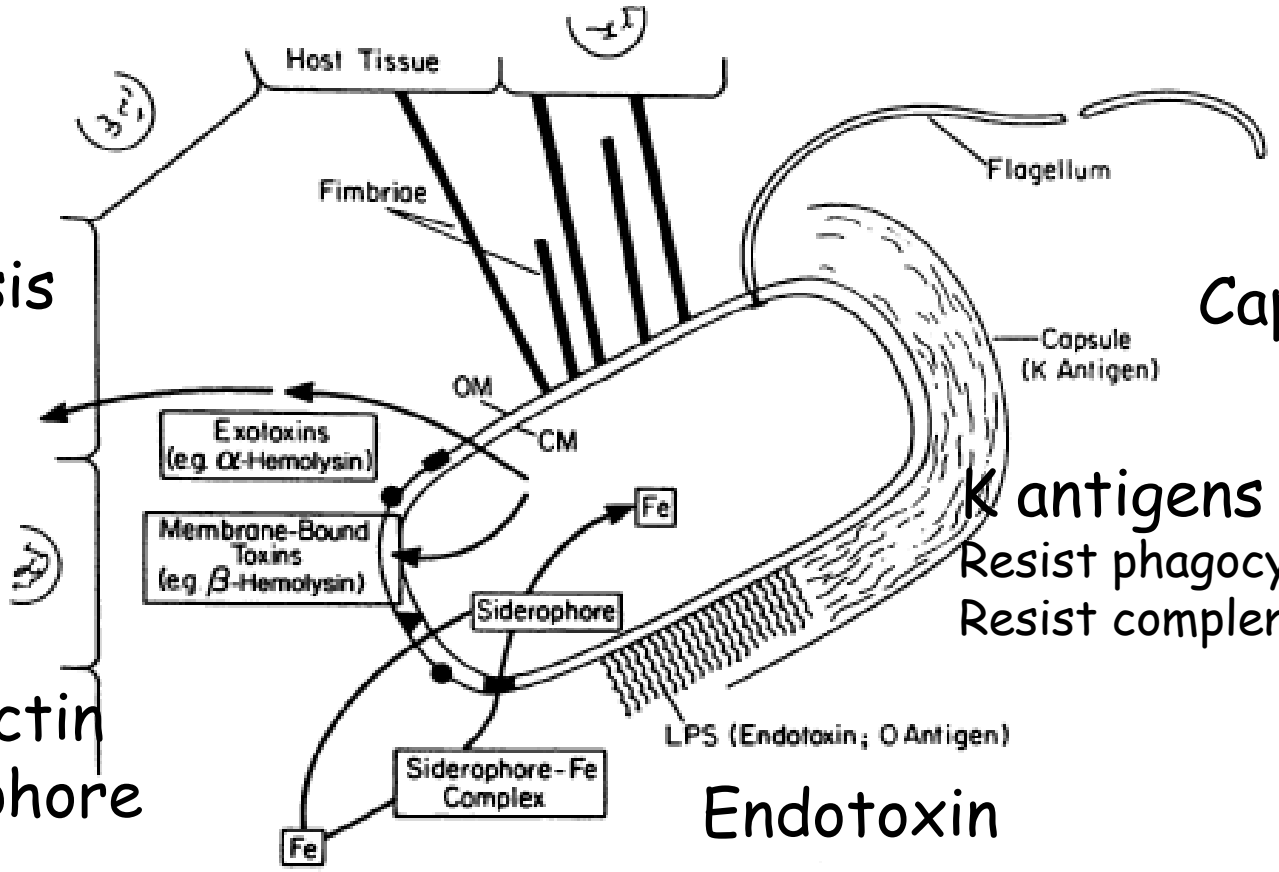
- Normal flora of the mouth and intestine
- Protects the intestinal tract from bacterial infection
- Assists in digestion
- Produces small amounts of vitamins B_{12} and K

- Colonizes newborns GI tract within hours after birth

- There are more than 700 different serotypes of *E. coli*
- Distinguished by different surface proteins and polysaccharides

Urovirulence Factors

Adherence
Fimbriae



Hemolysis
α
β

Capsule

K antigens
Resist phagocytosis
Resist complement proteins

Aerobactin
Siderophore

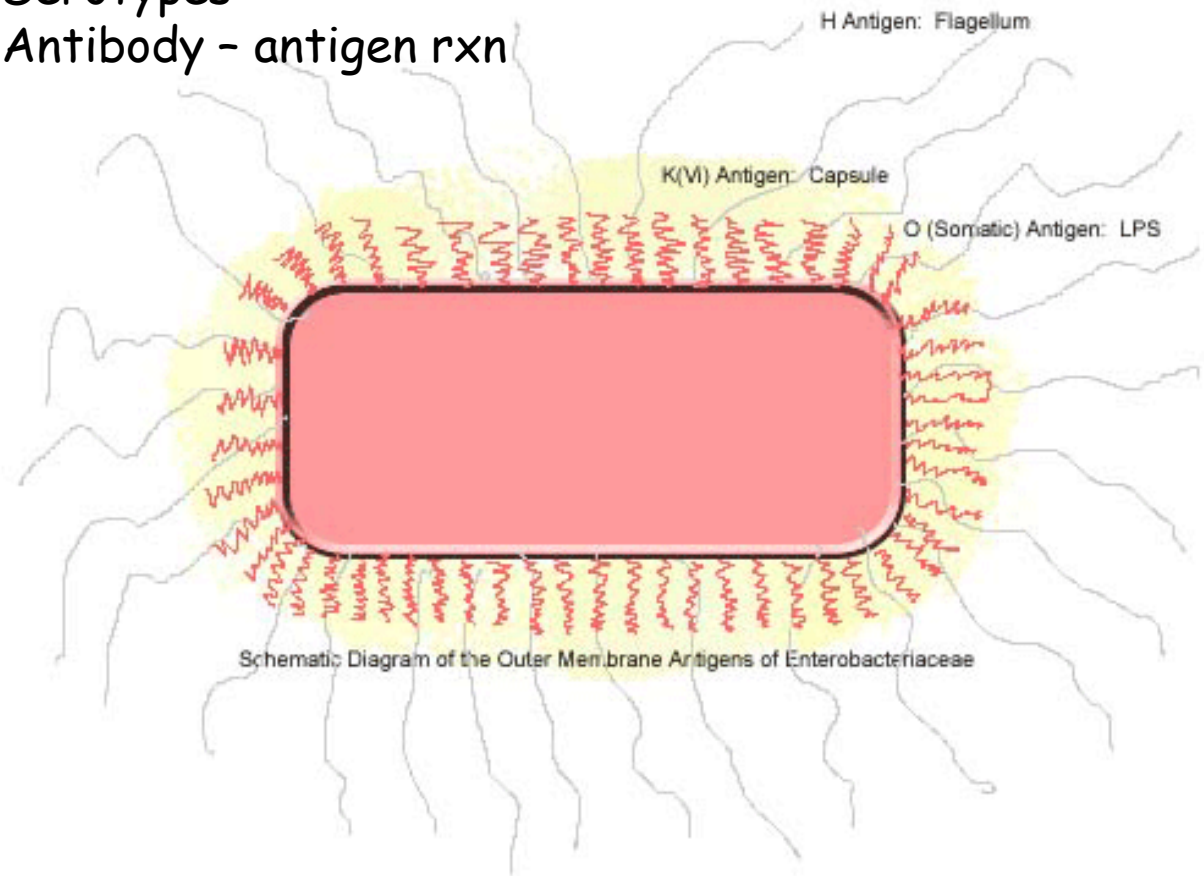
Endotoxin

FIG. 1. Schematic representation of an *E. coli* cell interacting with host tissue, highlighting features relevant to bacterial pathogenicity. Membrane proteins involved in transport, serum resistance, etc., are indicated by solid black circles, triangles, and rectangles. OM, Outer membrane; CM, cytoplasmic membrane; LPS, lipopolysaccharide. Adapted from reference 111, with permission from the publisher.

Many strains

Serotypes
Antibody – antigen rxn

- O antigen
  - Somatic (on LPS)
  - 171 antigens
- H antigen
  - Flagella
  - 56 antigens
- K antigen
  - Capsule and or fimbrial antigen
  - 80 antigens



O18ac:H7:K1

18th O antigen

7th H antigen

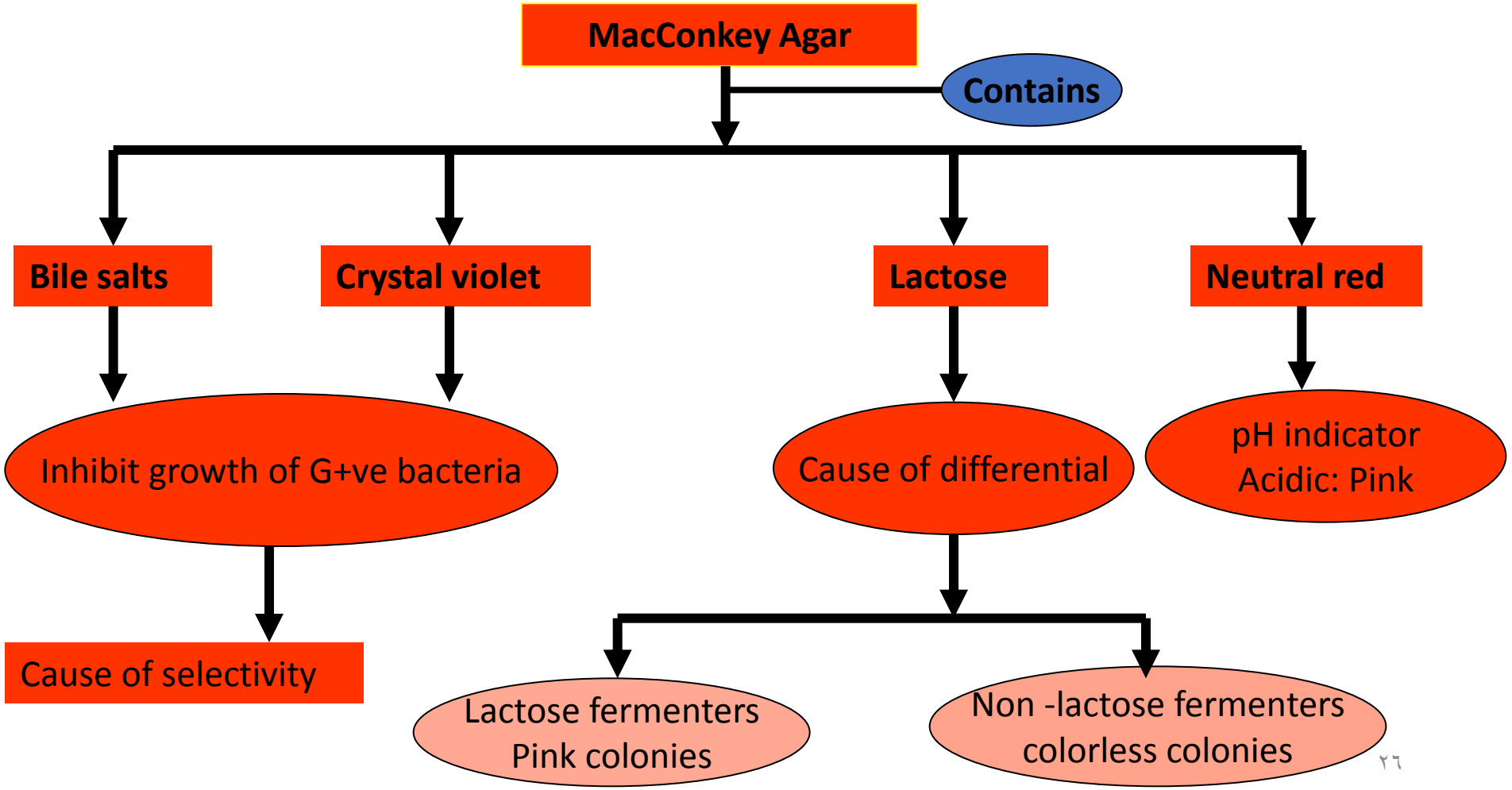
1st K antigen

Urinary Tract Infections

Enterobactericeae : Uropathogenic E. coli

- Gram negative rods
- Oxidase negative
- Catalase positive
- Reduce nitrate to nitrite
- Capsulated
- Motile
- Lactose fermenter

➢ **MacConkey agar is selective & differential medium for *Enterobacteriaceae***

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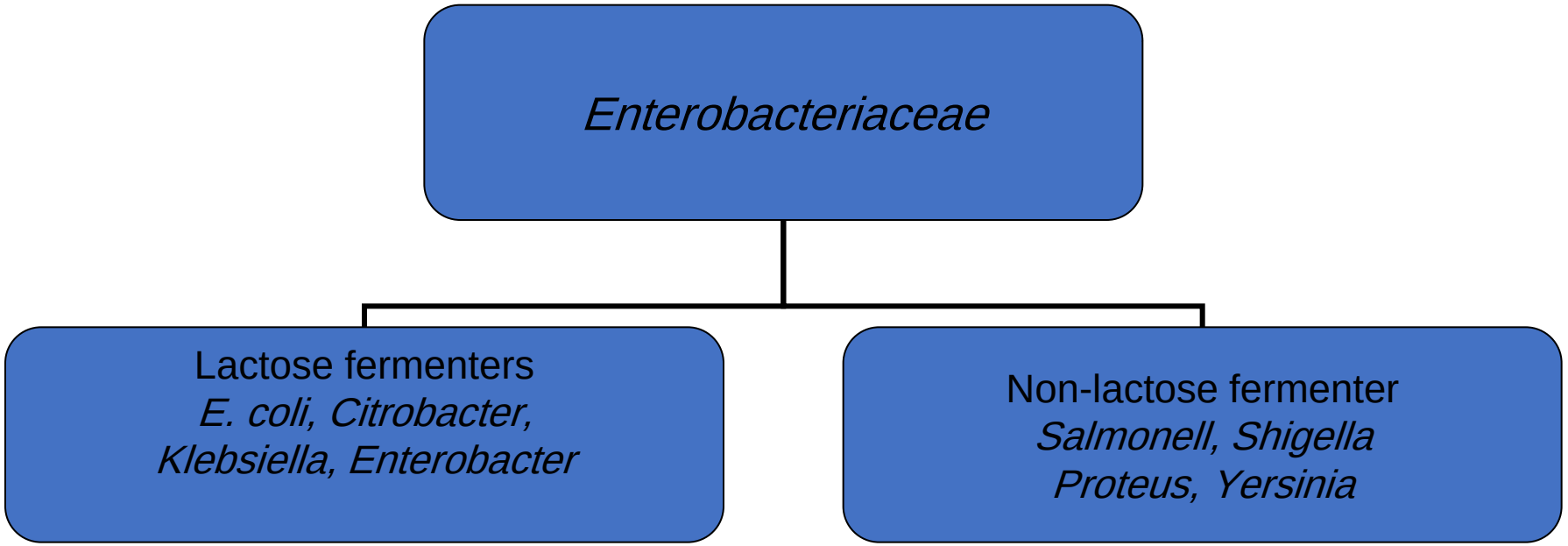

Enterobacteriaceae
Lactose fermenters
E. coli, Citrobacter,
Klebsiella, Enterobacter
Non-lactose fermenter
Salmonell, Shigella
Proteus, Yersinia

Proteus

1. *P. vulgaris*.
2. *P.mirabilis*.

- Proteus species are found in soil and water, and are normal inhabitants of the intestine in man.
- They cause infections only when they leave the intestine.
- They cause UTI, otitis media, wound infections, pneumonia and bacteraemia.

- Gram negative bacilli, and highly motile.
- Fucultative anaerobes.

- Due to their high motility, they give colonies which swarm (swarming phenomenon) as successive waves of trunslucent growth

- On MacConkey's agar, the m.o. Appear as NLF growth, with fishy bad odour.

- They are urease +ve and can Hydrlyse urea to produces ammonia & CO_2.

- Ammonia can increase the pH of urine (alkalinization) and then precipitate Ca & PO_4 leading to stone formation.

Pseudomonas aeruginosa

- Most are saprophytes found widely in aquatic environments
- *Major cause of nosocomial infections*
- *Usually multidrug resistant*

- Oxidase positive aerobic gram negative bacteria
- Motile 1-2 flagella
- Pigmented colonies with cut grass or grape like smell

➢blue pigment, *pyocyanin, and the yellow–green* fluorescent pigment *pyoverdin*

- Virulence:
- Protease, LPS, pigments production
- Exopolysaccharide (Alginate like)which is responsible for the mucoid colonial phenotype

Fig. 28.3 Alcohol extraction of alginate from mucoid *Ps. aeruginosa*.

- Infections:

- Wide range of Community and hospital acquired including UTI

- Diagnosis:

Selective media containing acetamide

Commercial kits

PCR

- Treatment:

Follow lab sensitivity

- **Enterococcus:**
- Gram positive cocci
- As indicated by the name, members of the genus *Enterococcus have their natural habitat in the human* intestines.
- The species most commonly associated with human disease are *E. faecalis and E. faecium.*
- The diseases with which they are associated are:
- urinary tract infection, infective endocarditis, biliary tract infections, suppurative abdominal lesions, peritonitis.
- *E. faecalis and E. faecium are important causes of wound and urinary tract infection in hospital*
- Bacteraemia carries a poor prognosis as it often occurs in patients with major underlying pathology and in those who are immunocompromised.
- Treatment: Vancomycin but resistance increasing , Linezolid

Diagnosis – urine analysis and culture

SPECIMEN COLLECTION

Prevention of contamination by normal vaginal, perineal, and anterior urethral flora is the most important consideration for collection of a clinically relevant urine specimen.

1- Clean-Catch Midstream Urine

- The least invasive procedure
- Good patient education is essential
- Clean the periurethral area well with a mild detergent to avoid contamination.
- The patient begin to void, and then collect a midstream urine sample.

2- In and out catheterized urine…

3- Suprapubic bladder aspiration…

✓**Transport immediately or fridge for max 24 hrs**

Microscopic examination:

•Approximately 90% of patients with acute symptomatic UTI have pyuria (that is, 10 white cells/mm3 of urine) but is not specific.

• A more sensitive and specific procedure is a Gram stained smear of uncentrifuged urine. The presence of at least one organism per oil-immersion field is almost always indicative of bacterial infection.

•Absence of WBCs and bacteria makes the diagnosis unlikely, but does not rule it out.

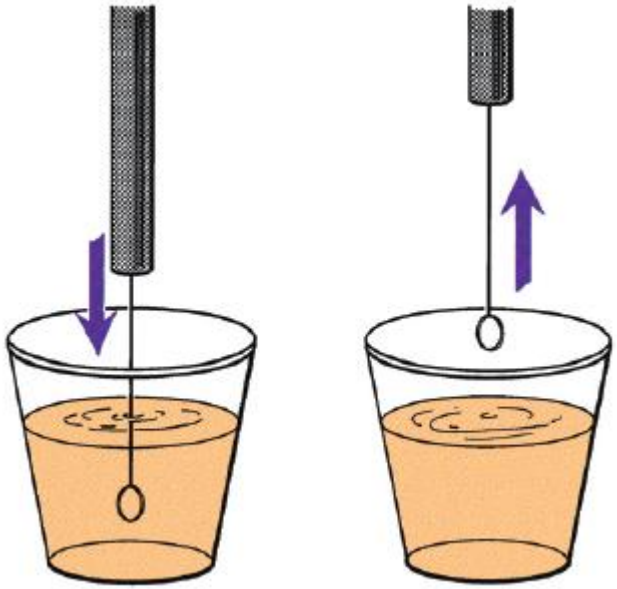
Chemical Screening Tests

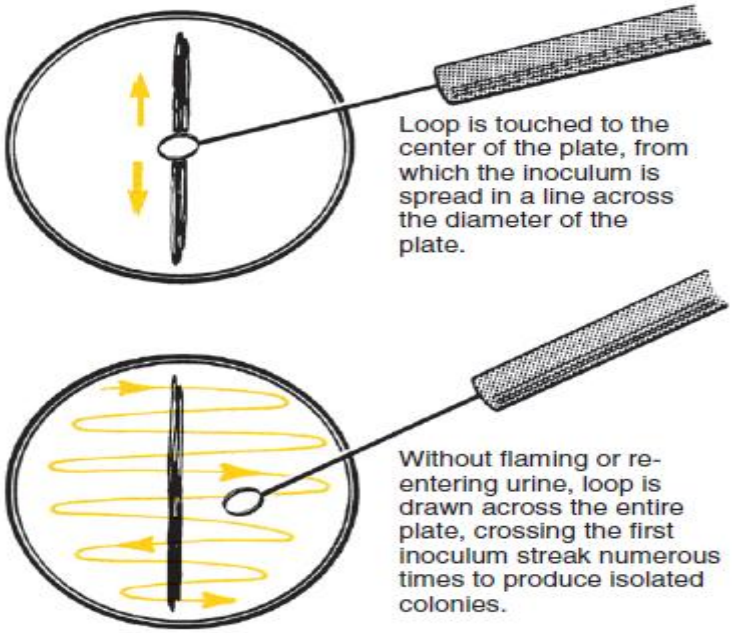
•leukocyte esterase from inflammatory cells and nitrite produced from urinary nitrates by bacterial metabolism.

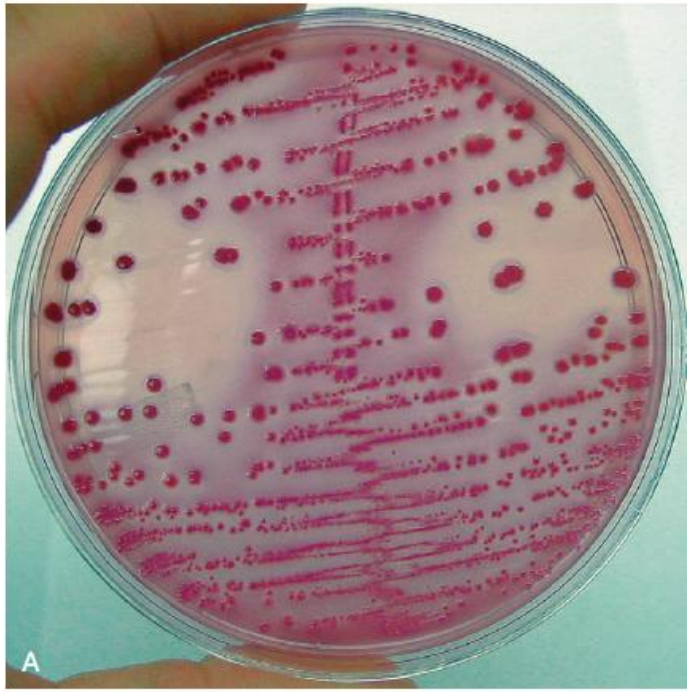
•sensitivity and specificity of these products are similar to that of microscopic examination. Like microscopic examination, they do not reliably detect bacteriuria below the level of 10^5 organisms/mL.

Urine culture

- Using 0.001 ml calibrated loop the urine is cultured on CLED and MacConkey agar
- Incubated at 37 ^{o}C for 24 hours
- The bacterial growth is counted and identified
- Each colony = 10^3 cfu
- ✓ More than 10^5 is UTI in CCMS
- ✓ Less than 10^5 is most likely contaminant or can be cystitis (look for symptoms)
- IN OTHER METHODS ANY IS SIGNIFICANT




Loop is touched to the center of the plate, from which the inoculum is spread in a line across the diameter of the plate.
Without flaming or re-entering urine, loop is drawn across the entire plate, crossing the first inoculum streak numerous times to produce isolated colonies.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TREATMENT

- The treatment of UTI is best guided by the results of cultures and antimicrobial susceptibility tests.

- In simple isolated instances of cystitis in a young woman, the etiology is often assumed to be *E. coli*
- Trimethoprim alone or in combination with sulfamethoxazole, a fluoroquinolone, OR nitrofurantoin are the agents most commonly used
- 3-5 Days duration
- Longer course 14 days if complicated
- Route: oral or IV depending on whether upper, lower, simple orcomplicated
- Cranberry juice