Microbial Diseases of the Urinary and Reproductive System

Chapter 26
Introduction

• The urinary system regulates the chemical composition of the blood and excretes nitrogenous waste.
• The reproductive system produces gametes for reproduction and, in the female, supports the growing embryo.
• Microbial diseases of these systems can result from infection from an outside source or from opportunistic infection by members of the normal microbiota.
I. Structure of the Urinary System

- Urine is transported from the kidneys through ureters to the urinary bladder and is eliminated through the urethra.
- Valves prevent urine from flowing back to the urinary bladder and kidneys.
- The flushing action of urine and the acidity of normal urine have some antimicrobial value.
Overview of the anatomy of the urinary tract.
II. Structure and Function of the Reproductive System

- The female reproductive system consists of two ovaries, two uterine tubes, the uterus, the cervix, the vagina, and the external genitals. Note that the urethra is short and ends within the labia.
II. Structure and Function of the Reproductive System

- The male reproductive system consists of two testes, ducts, accessory glands, and the penis; seminal fluid and urine leaves the male body through the urethra.
III. Normal Microbiota of the Urinary and Reproductive Systems

• The urinary bladder and upper urinary tract are sterile under normal conditions.
• Lactobacilli dominate the vaginal microbiota during the reproductive years.
• The male urethra is normally sterile, except near the external opening.
Gram stain of *Lactobacillus* species illustrating gram-positive bacilli, singly and in chains. A few gram-negative staining bacilli are also present.
IV. Bacterial Diseases of the Urinary System

- Urethritis (urethra), cystitis (bladder), and ureteritis (ureters) are terms describing inflammations of tissues of the lower urinary tract.
- Pyelonephritis (kidney) can result from lower urinary tract infections (ascending) or from systemic bacterial infections (descending).
- Opportunistic gram-negative bacteria from the intestines often cause urinary tract infections.
- Nosocomial infections following catheterization occur in the urinary system. *E. coli* causes more than half of these infections.
- >100,000 orgs/ml, or more than 1000 bacteria/ml of one species, or 100 coliforms/ml of urine, indicates an infection. Inoculum = .001, so 10 colonies X 1000 = 10,000 orgs/ml, 100 colonies X 1000 = 100,000 orgs/ml.
- Treatment of urinary tract infections depends on the isolation and antibiotic sensitivity testing of the causative agents.
- Glomerulonephritis is an immune-complex disease of the kidneys.
Collection device to obtain urine by in and out, or straight, catheterization.
Method for inserting a calibrated loop into urine to ensure that the proper amount of specimen adheres to the loop.
Method for streaking with calibrated loop to produce isolated colonies and countable colony forming units.
Culture results illustrating some of the various interpretative guidelines. Growth of $>10^5$ CFU/mL of a lactose-fermenting gram-negative rod from a CCMS urine; only the organism with a colony count of $>10^4$ to $10^5$ CFU/mL would be worked up completely from a voided urine.
IV. Bacterial Diseases of the Urinary System

• A. Cystitis

  – Inflammation of the urinary bladder, or cystitis, is common in females.

  – Microorganisms at the opening of the urethra and along the length of the urethra, careless personal hygiene, and sexual intercourse contribute to the high incidence of cystitis in females.

  – Symptoms include dysuria (difficult urgent urination) and pyuria (leukocytes in the urine).

  – The most common etiologies are *E. coli* and *S. saprophyticus*. Trimethoprim-sulfamethoxazole clears cases quickly.
Fig. 93/94 - Infectious Disease

Left: Microscopy of urine showing presence of phagocytic neutrophils, red blood cells, and bacteria. This indicates acute infection of the urinary tract.

Right: Microscopy of urine showing a large number of squamous epithelial cells, bacteria and some pus cells. This is improperly collected urine (probably the forepart of urine carrying urethral epithelial cells and bacteria).
Novobiocin susceptibility test to differentiate coagulase-negative isolate from urine sample. Staphylococcus saprophyticus is resistant to novobiocin, depicted with no zone of inhibition around the disk.
IV. Bacterial Diseases of the Urinary System

• B. Pyelonephritis
  – Inflammation of the kidneys, or pyelonephritis, is usually a complication of lower urinary tract infections.
  – About 75% of pyelonephritis cases are caused by *E. coli*. Can be potentially life threatening so aggressive treatment is implemented.
IV. Bacterial Diseases of the Urinary System

• C. Leptospirosis: *Leptospira interrogans*
  – A disease of domestic and wild animals that can be spread by urine contaminated water to humans and cause liver and kidney disease.
  – Incubates 1-2 weeks, then headaches, chill, fever, and then maybe serious kidney (Weil’s disease) or liver
Leptospira interrogans. Note the tight coiling spirochetes.
Scanning electron micrograph of *Leptospira interrogans* from blood of a patient. The tight coils and bent ends are characteristic of this organism. x2500
V. Diseases of the Reproductive System

• A. Bacterial Diseases of the Reproductive System
  – Most diseases of the reproductive system are sexually transmitted diseases (STDs).
  – Most STDs can be prevented by the use of condoms and are treated with antibiotics.
V. Diseases of the Reproductive System

• B. Gonorrhea - *Neisseria gonorrhoeae*
  – *Neisseria gonorrhoeae* causes gonorrhea.
  – See as gram neg. diplococci within phagocytic cells. Survives poorly outside the body and requires special handling.
  – Gonorrhea is a common reportable communicable disease in the United States.
  – *N. gonorrhoeae* attaches to mucosal cells of the oral-pharyngeal area, genitals, eyes, and rectum by means of fimbriae.
  – Symptoms in males are painful urination and pus discharge. Blockage of the urethra and sterility are complications of untreated cases. **B. Gonorrhea - Neisseria gonorrhoeae**
  – Females might be asymptomatic unless the infection spreads to the uterus and uterine tubes (see pelvic inflammatory disease).
  – Gonorrhreal endocarditis, gonorrhreal meningitis, and gonorrhreal arthritis are complications that can affect both sexes if gonorrhreal infections are untreated.
  – Ophthalmia neonatorum is an eye infection acquired by infants during passage through the birth canal of an infected mother.
  – 1 % silver nitrate for G.C, Erythromycin for C. trachomatis, Tetracycline covers both G.C. and C. trachomatis
  – Gonorrhea is diagnosed by Gram stain, ELISA, or DNA probe.
  – Resistant: use fluoroquinolone (ciprofloxacin) + tetracycline for chlamydia.
Twenty-four hour growth of *Neisseria gonorrhoeae* on a JEMBEC plate streaked in a characteristic “Z” pattern.
Figure 14-5. A, Direct Gram-stained smear of male urethral discharge showing intracellular and extracellular gram-negative diplococci, which is diagnostic of *Neisseria gonorrhoeae*.
US incidence and distribution of gonorrhea.
Pus containing discharge from a male urethra with an acute case of gonorrhoea.
Gram stain smear from a patient with gonorrhea.
From 1944. Now cephalosporins are the first choice (ceftriaxone, cefixime)
Gonorrhea is also commonly known by the slang term "the clap".

One suggested etymology refers to a traditional treatment used to clear the blockage in the urethra from gonorrheal pus, where the penis would be "clapped" on both sides simultaneously.

It could also refer to the painful sting in the male urethra, which feels like the sting of a clap (as in clapping hands) when infected with the disease.

Yet another suggested source is from the old French word "clapier", meaning "brothel".

Another suggested source for the term is from a notorious 18th century keeper of a brothel, Margaret Clap (better known as "Mother Clap"), though perhaps her name itself was derived from the slang term.
V. Diseases of the Reproductive System

C. Nongonococcal Urethritis (NGU): *Chlamydia trachomatis*, *Ureaplasma urealyticum* and *Mycoplasma hominis*.

- Nongonococcal urethritis (NGU), or nonspecific urethritis (NSU), is any inflammation of the urethra not caused by *N. gonorrhoeae*.
- Most cases of NGU are caused by *Chlamydia trachomatis*.
- *C. trachomatis* infection is the most common STD.
- Symptoms of NGU are often mild or lacking, although uterine tube inflammation and sterility may occur.
- *C. trachomatis* can be transmitted to infant’s eyes at birth.
- Diagnosis is based on the detection of chlamydial DNA in urine.
- *Ureaplasma urealyticum* and *Mycoplasma hominis* also cause NGU.
- All are sensitive to tetracycline.
A direct smear with more than five PMNs per fluid but no bacteria may suggest nongonococcal urethritis (NGU).
Cytologic examination of endocervical specimen demonstrating inclusion bodies consistent with *Chlamydia trachomatis*. Papanicolaou stain.
V. Diseases of the Reproductive System

• D. Pelvic Inflammatory Disease (PID) - *N. gonorrhoeae, Chlamydia trachomatis*
  
  – Extensive bacterial infection of the female pelvic organs, especially of the reproductive system, is called pelvic inflammatory disease (PID).
  
  – PID is caused by *N. gonorrhoeae, Chlamydia trachomatis*, and other bacteria that gain access to the uterine tubes. Infection of the uterine tubes is called salpingitis.
  
  – 1 in 10 reproductive age women get PID. Can mitigate by using a barrier protection to prevent sperm migration.
  
  – PID can result in blockage of the uterine tubes and sterility and lead to ectopic pregnancy.
Salpingitis. A laproscopic photo shows an acutely inflamed right uterine tube and inflamed swollen fimbriae and ovary.
V. Diseases of the Reproductive System

E. Syphilis - *Treponema pallidum*

- Syphilis is caused by *Treponema pallidum*, a spirochete that has not been cultured in vitro. Laboratory cultures are grown in cell cultures.
- Other strains cause tropical skin disease, yaws.
- *T. pallidum* is transmitted by direct contact and can invade intact mucous membranes or penetrate through breaks in the skin.
- Coiled like metal spring axial filaments assists in penetrating tissue.
- Primary lesion: a small, hard-based chancre at the site of infection. The bacteria then invade the blood and lymphatic system, and the chancre spontaneously heals.
- Secondary stage: The appearance of a widely disseminated rash on the skin and mucous membranes. Spirochetes are present in the lesions of the rash.
- The patient enters a latent period after the secondary lesions spontaneously heal.
- Tertiary stage: At least 10 years after the secondary lesion, lesions called gummas can appear on many organs.
- Congenital syphilis, resulting from *T. pallidum* crossing the placenta during the latent period, can cause neurological damage in the newborn.
- *T. pallidum* is identifiable through darkfield microscopy of fluid from primary and secondary lesions.
- Many serological tests, such as VDRL (Veneral Disease Research Lab), RPR (Rapid plasma reagin), and FTA-ABS, can be used to detect the presence of antibodies against *T. pallidum* during any stage of the disease.
Treponema pallidum from tissue section, Levadit’s stain
Penile syphilitic chancre caused by *Treponema pallidum*. 
Secondary syphilis lesions.
The US incidence and distribution of primary and secondary syphilis.

*First 26 weeks of 2005

(a) Incidence of syphilis in the United States from 1942 through the first 26 weeks of 2005

(b) Geographical distribution of cases in 2004

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Progression of syphilis through clinical recognized stages.

(a) Chancre of primary stage on a male in genital area.

(b) Lesions of secondary syphilis rash on a palm; any surface area of the body may be afflicted with such lesions.

(c) Gummas of tertiary stage on the back of an arm; gummas such as these are rarely seen today in the era of antibiotics.

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VI. Viral Diseases of the Reproductive System

• A. Genital Herpes –dsDNA *Family Herpesviridae* Herpes simplex virus type 2 (HSV-2)
  – Herpes simplex virus type 2 (HSV-2) causes genital herpes.
  – Symptoms of the infection are painful urination, genital irritation, and fluid-filled vesicles.
  – Neonatal herpes is contracted during fetal development or birth. It can result in neurological damage or infant fatalities.
  – The virus might enter a latent stage in nerve cells. Vesicles reappear following trauma, stress, and hormonal changes.
  – Genital herpes is associated with cervical cancer.
  – The drug acyclovir has proven effective in treating the symptoms, but it does not cure the disease.
Vesicles of genital herpes on a penis.
Herpes genitalis lesion
VI. Viral Diseases of the Reproductive System

• B. Warts - *Papillomavirus* dsDNA Family: *Papillomaviridae Genus: Papillomavirus*
  
  - Papillomaviruses cause genital warts (condylomas). Vary in appearance from smooth and flat to projecting and cauliflowerlike.
  
  - A few serotypes (mainly 16 and 18) of papillomaviruses that cause genital warts have been associated with cancer of the cervix (or rarely the penis). Visible warts are usually caused by types 6 and 11.
  
  - Pap smears are used to monitor for cancer of the cervix. Tests to identify cancerous serotypes are available.
  
  - Gardasil and Cervarix vaccines!
A case of genital warts.
Condyloma acuminatum.
VI. Viral Diseases of the Reproductive System

• C. AIDS - HIV *Human immunodeficiency virus 1*, RNA retro, *Family: Retroviridae* Genus: *Lentivirus*
  
  – AIDS is a sexually transmitted disease that degrades the immune system (see Chapter 19, pp. 545-552). Male to female transfer is more likely than the reverse.

  – Lesions from other STDs may facilitate the transfer of HIV.
Schematic illustration of human immunodeficiency virus (HIV).
Fig. 183
Sexually Transmitted Diseases - Kaposi’s sarcoma (a human herpes virus induced tumor), a consequence of immunodeficiency caused by the HIV virus. Well-developed skin lesions often have a pigmented ring around them (left).
VII. Fungal Disease of the Reproductive System

A. Candidiasis - *Candida albicans*, a yeast

- *Candida albicans* causes and vulvovaginal candidiasis, or yeast infection, in females. 75% of all women experience at least one case. Uncommonly a cause of NGU in males.
- Vulvovaginal candidiasis is characterized by lesions that produce itching and irritation, yellow cheesy discharge, yeasty or no odor.
- Predisposing factors are oral contraceptives/pregnancy, diabetes, and broad-spectrum antibacterial chemotherapy.
- Diagnosis is based on observation of the fungus and its isolation from lesions.
- Topical application of clotrimazole and miconazole is the treatment.
Fig. 132
Microbiology of Infectious Disease - Gram stain of *Candida albicans*.
VIII. Protozoan Disease of the Reproductive System

A. Trichomoniasis – *Trichomonas vaginalis*
   - *Trichomonas vaginalis* causes trichomoniasis when the pH of the vagina increases.
   - May be a normal inhabitant of female vagina & male urethra in small numbers, but the infections is generally passed by sexual contact.
   - Protozoa outgrow normal flora in increased pH
   - Diagnosis is based on observation of the protozoa in purulent discharges from the site of infection.
   - In females discharges are profuse, greenish/yellow and have bad odor, leading to irritation and itching. *Males are generally asymptomatic.*
   - *Metronidazole is treatment both sex partners.*
*Trichomonas vaginialis* adhering to the surface of an epithelial cell in a cell culture preparation.
Fig. 122 - Microbiology of Infectious Disease

*Trichomonas vaginalis* in vaginal swab prep.
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