**LESSON 2.

Microbiology diagnosis of diseases, caused by Gram negative cocci (meningococci, gonococci), and opportunistic bacteria (klebsiella, proteus, acinetobacter, pseudomonas)**

**LESSON PLAN:**

• Classification of Gram-negative cocci

• Meningococci, morpho-biological characteristics, pathogenicity factors and diseases caused by it.

• Methods of microbiological diagnosis of meningococcal infections.

• Specific treatment and prevention of meningococcal infections.

• Gonococci, morpho-biological characteristics, pathogenicity factors and diseases caused by them.

• Microbiological diagnosis of acute and chronic gonorrhea.

• Specific treatment and prevention of gonorrhea.

• Common characteristics of opportunistic bacteria, main representatives. Their role in the occurrence of purulent-inflammatory diseases and healthcare-associated infections.

• Klebsiella genus, morpho-biological characteristics, pathogenicity factors, diseases they cause, antibiotic-resistant forms, microbiological diagnosis.

• Genus Proteus, morpho-biological characteristics, pathogenicity factors, diseases they cause, antibiotic-resistant forms, microbiological diagnosis.

• Acinetobacter genus, morpho-biological characteristics, pathogenicity factors, diseases they cause, antibiotic-resistant forms, microbiological diagnosis.

• Pseudomonas genus, morpho-biological characteristics, pathogenicity factors, diseases they cause, antibiotic-resistant forms, microbiological diagnosis.

***NEISSERIA GONORRHOEAE***

**Trigger Words**

Diplococci, gonorrhea, arthritis, ophthalmia

**Biology and Virulence**

ᑏᑏ Gram-negative diplococci with fastidious growth requirements

ᑏᑏ Growth best at 35° C-37° C in a humid atmosphere supplemented with CO2

ᑏᑏ Oxidase and catalase positive; acid produced from glucose oxidatively

ᑏᑏ Outer surface with multiple antigens: pili protein; Por proteins; Opa proteins; Rmp protein; protein receptors for transferrin, lactoferrin, and hemoglobin; lipooligosaccharide; immunoglobulin protease; β-lactamase

ᑏᑏ Refer to Table 23.2 for summary of virulence factors

**Epidemiology**

ᑏᑏ Humans are the only natural hosts

ᑏᑏ Carriage can be asymptomatic in women

ᑏᑏ Transmission is primarily by sexual contact

ᑏᑏ Almost 555,608 cases reported in United States in 2017 (true incidence of disease believed to be at least twice that); estimated 78 million new cases worldwide

ᑏᑏ Disease most common in blacks, people aged 15-24 years, residents of southeastern United States, people who have multiple sexual encounters

ᑏᑏ Higher risk of disseminated disease in patients with deficiencies in late components of complement

**Diagnosis**

ᑏᑏ Gram stain of urethral specimens is accurate for symptomatic males only

ᑏᑏ Culture is sensitive and specific but has been replaced with nucleic acid tests in most laboratories

**Treatment, Prevention, and Control**

ᑏᑏCeftriaxone with azithromycin is currently the treatment of choice, although high-level resistance to cephalosporins and azithromycin has been observed

ᑏᑏ For neonates, prophylaxis with 1% silver nitrate; ophthalmia neonatorum is treated with ceftriaxone

ᑏᑏ Prevention consists of patient education, use of condoms or spermicides with nonoxynol-9 (only partially effective), and aggressive follow-up of sexual partners of infected patients

ᑏᑏ Effective vaccines are not available

***NEISSERIA MENINGITIDIS***

**Trigger Words**

Diplococci, meningitis, meningococcemia, pneumonia, vaccine

**Biology and Virulence**

ᑏᑏ Gram-negative diplococci with fastidious growth requirements

ᑏᑏ Grows best at 35° C-37° C in a humid Atmosphere

ᑏᑏ Oxidase and catalase positive; acid produced from carbohydrates oxidatively

ᑏᑏ Outer surface antigens include polysaccharide capsule, pili, and lipooligosaccharides

ᑏᑏ Capsule protects bacteria from antibodymediated phagocytosis

ᑏᑏ Specific receptors for meningococcal pili allow colonization of nasopharynx and replication; posttranslational modification of the pili enhances host cell penetration and person-to-person spread

ᑏᑏ Bacteria can survive intracellular killing in the absence of humoral immunity

ᑏᑏ Endotoxin mediates most clinical manifestations

**Epidemiology**

ᑏᑏ Humans are the only natural hosts

ᑏᑏ Person-to-person spread occurs via aerosolization of respiratory tract secretions

ᑏᑏ Highest incidence of disease is in children younger than 1 year old, institutionalized people, and patients with late complement deficiencies

ᑏᑏ Endemic and epidemic disease most commonly caused by serogroups A, B, C, W135, X, and Y; pneumonia most commonly caused by serogroups Y and W135; serogroups A and W135 associated with disease in underdeveloped countries

ᑏᑏ Disease occurs worldwide, most commonly in the dry, cold months of the year

**Diagnosis**

ᑏᑏ Gram stain of cerebrospinal fluid is sensitive and specific but is of limited value for blood specimens (too few organisms are generally present, except in overwhelming sepsis)

ᑏᑏ Culture is definitive, but organism is fastidious and dies rapidly when exposed to cold or dry conditions

ᑏᑏ Tests to detect meningococcal antigens are insensitive and nonspecific

**Treatment, Prevention, and Control**

ᑏᑏ Breast-feeding infants have passive immunity (first 6 months)

ᑏᑏ Empirical treatment of patients with suspected meningitis or bacteremia should be initiated with ceftriaxone; if the isolate is penicillin susceptible, treatment can be changed to penicillin G

ᑏᑏ Chemoprophylaxis for contact with persons with the disease is with rifampin, ciprofloxacin, or ceftriaxone

ᑏᑏ For immunoprophylaxis, vaccination is an adjunct to chemoprophylaxis; it is used only for serogroups A, C, Y, and W135; no effective vaccine is available for serogroup B; vaccination for serogroup A has been introduced in Africa

*Important Neisseriaceae*

*Neisseria* Named after the German physician Albert Neisser, who originally described the organism responsible for gonorrhea

*N. gonorrhoeae gone,* seed; *rhoia,* a flow (a flow of seeds; reference to the disease gonorrhea)

*N. meningitidis meningis,* the covering of the brain; *itis,* inflammation (inflammation of the meninges as in meningitis)

*Eikenella* Named after M. Eiken, who first named the type species in this genus

*E. corrodens corrodens,* gnawing or eating (reference to the observation that colonies of this species pit [eat into] the agar)

*Kingella* Named after the American bacteriologist Elizabeth King

**Neisseriaceae: Clinical Summaries**

***Neisseria gonorrhoeae***

**Gonorrhea:** characterized by purulent discharge for involved site (e.g., urethra, cervix, epididymis, prostate, rectum) after a 2- to 5-day incubation period

**Disseminated infections:** spread of infection from genitourinary tract through blood to skin or joints; characterized by pustular rash with erythematous base and suppurative arthritis in involved joints

**Ophthalmia neonatorum:** purulent ocular infection acquired by neonate at birth

***Neisseria meningitidis***

**Meningitis:** purulent inflammation of meninges associated with headache, meningeal signs, and fever; high mortality rate unless promptly treated with effective antibiotics

**Meningococcemia:** disseminated infection characterized by thrombosis of small blood vessels and multiorgan involvement; small petechial skin lesions coalesce into larger hemorrhagic lesions

**Pneumonia:** milder form of meningococcal disease characterized by bronchopneumonia in patients with underlying pulmonary disease

*Virulence Factors in Neisseria gonorrhoeae*

**Pilin** Protein that mediates initial attachment to nonciliated human cells (e.g., epithelium of vagina, fallopian tube, and buccal cavity); interferes with neutrophil killing

**Por** protein Porin protein: promotes intracellular survival by preventing phagolysosome fusion in neutrophils

**Opa** protein Opacity protein: mediates firm attachment to eukaryotic cells

**Rmp** protein Reduction-modifiable protein: protects other surface antigens (Por protein, lipooligosaccharide) from bactericidal antibodies

**Transferrin-, lactoferrin-,** **and hemoglobinbinding proteins** Mediate acquisition of iron for bacterial metabolism

**LOS** Lipooligosaccharide: has endotoxin activity

**IgA1 protease** Destroys immunoglobulin A1 (role in virulence is unknown)

**β-Lactamase** Hydrolyzes the β-lactam ring in penicillin

**Pseudomonas *and Related Bacteria***

*PSEUDOMONAS AERUGINOSA*

**Trigger Words** Capsule, exotoxin A, opportunistic, nosocomial infections

*Biology and Virulence*

Small gram-negative rods typically arranged in pairs

Obligate aerobe; glucose oxidizer; simple nutritional needs

Mucoid polysaccharide capsule

Multiple virulence factors, including adhesins (e.g., flagella, pili, lipopolysaccharide, alginate capsule), secreted toxins and enzymes (e.g., exotoxin A, pyocyanin, pyoverdin, elastases, proteases, phospholipase C, exoenzymes S and T), and antimicrobial resistance (intrinsic, acquired, and adaptive)

*Epidemiology*

Ubiquitous in nature and moist environmental hospital sites (e.g., flowers, sinks, toilets, mechanical ventilation, and dialysis equipment)

No seasonal incidence of disease

Can transiently colonize the respiratory and gastrointestinal tracts of hospitalized patients, particularly those treated with broad-spectrum antibiotics, exposed to respiratory therapy equipment, or hospitalized for extended periods

 Patients at high risk for developing infections include neutropenic or immunocompromised patients, cystic fibrosis patients, and burn patients

*Diseases*

Diseases include infections of the respiratory tract, urinary tract, skin and soft tissues, ears, and eyes, as well as bacteremia and endocarditis

**Diagnosis**

ᑏᑏGrows rapidly on common laboratory media

ᑏᑏ Identified by colonial characteristics (e.g., \_-hemolysis, green pigment, grapelike odor) and simple biochemical tests (e.g., positive oxidase reaction, oxidative utilization of carbohydrates

*Treatment, Prevention, and Control*

Combined use of effective antibiotics (e.g., aminoglycoside and \_-lactam antibiotics) frequently required; monotherapy is generally ineffective and can select for resistant strains

Hospital infection-control efforts should concentrate on preventing contamination of sterile medical equipment and nosocomial transmission; unnecessary use of broad-spectrum antibiotics can select for resistant organisms

**Important Non fermentative Gram-Negative Rods**

*Acinetobacter - akinetos,* unable to move; *bactrum,* rod (nonmotile rods)

*A. baumannii - baumannii,* named after the microbiologist Baumann

*Burkholderia -Burkholderia,* named after the microbiologist Burkholder

*B. cepacia - cepacia,* like an onion (original strains isolated from rotten onions)

*B. mallei - mallei,* the disease glanders

*B. pseudomallei - pseudes,* false; *mallei* (refers to the fact this species closely resembles *B. mallei*)

*Moraxella - Moraxella,* named after the Swiss ophthalmologist Morax, who first recognized the species

*M. catarrhalis - catarrhus,* downflowing or catarrh (refers to inflammation of the respiratory tract mucus membranes)

*Pseudomonas - pseudes,* false; *monas,* a unit (refers to Gram-stain appearance of pairs of organisms that resemble a single cell)

*P. aeruginosa - aeruginosa,* full of copper rust or green (refers to blue and yellow pigments produced by this species that appear green)

*Stenotrophomonas - stenos,* narrow; *trophos,* one who feeds; *monas,* unit (refers to observation that these are narrow bacteria that require few substrates for growth)

*S. maltophilia - malt,* malt; *philia,* friend (friend of malt)

**Clinical Summaries for Nonfermentative Gram-Negative Rods**

*Pseudomonas aeruginosa*

*Pulmonary infections***:** range from mild irritation of the bronchi (tracheobronchitis) to necrosis of the lung parenchyma (necrotizing bronchopneumonia)

*Primary skin infections***:** opportunistic infections of existing wounds (e.g., burns) to localized infections of hair follicles (e.g.,associated with immersion in contaminated waters such as hot tubs)

*Urinary tract infections***:** opportunistic infections in patients with indwelling urinary catheters and after exposure to broad-spectrum antibiotics (selects for these antibiotic-resistant bacteria)

*Ear infections***:** can range from mild irritation of external ear (“swimmer’s ear”) to invasive destruction of cranial bones adjacent to the infected ear

*Eye infections***:** opportunistic infections of mildly damaged corneas

*Bacteremia***:** dissemination of bacteria from primary infection (e.g., pulmonary) to other organs and tissues; can be characterized by necrotic skin lesions (ecthyma gangrenosum)

***Burkholderia*** *cepacia***Complex**

*Pulmonary infections***:** most worrisome infections are in patients with chronic granulomatous disease or cystic fibrosis, in whom infections can progress to significant destruction of pulmonary tissue

*Opportunistic infections***:** urinary tract infections in catheterized patients; bacteremia in immunocompromised patients with contaminated intravascular catheters

*Burkholderia pseudomallei*

*Pulmonary infections***:** can range from asymptomatic colonization to abscess formation (melioidosis)

*Stenotrophomonas maltophilia*

*Opportunistic infections***:** a variety of infections (most commonly bacteremia and pneumonia) in immunocompromised patients previously exposed to broad-spectrum antimicrobial therapy

*Acinetobacter* Species

*Pulmonary infections***:** opportunistic pathogen in patients receiving respiratory therapy

*Wound infections***:** traumatic (e.g., resulting from military conflicts) and nosocomial wounds

*Moraxella catarrhalis*

***Pulmonary infections*:** tracheobronchitis or bronchopneumonia in patients with chronic pulmonary diseases

***Klebsiella*** *pneumoniae*

*klebsiella,* named after Klebs; *pneumoniae,* inflammation of the lungs

*K. oxytoca - oxus,* acid; *tokos,* producing; acid producing (refers to biochemical properties)

***Proteus*** *mirabilis - proteus,* a god able to change himself into different shapes; *mirabilis,* surprising; refers to pleomorphic colony forms

***Citrobacter*** *freundii - citrus,* lemon; *bacter,* a rod; citrate-utilizing rod; *freundii,* named after Freund

 *Citrobacter - koseri koseri,* named after Koser *E.*

***Enterobacter*** *cloacae -* enteron, intestine; bacter, a small rod; *cloacae,* of a sewer; originally isolated in sewage

***Serratia*** *marcescens - serratia,* named after Serrati; *marcescens,* becoming weak, fading away; originally believed not virulent