**Lecture 1.**

**Introduction to basic microbiology. The pathogenic and opportunistic cocci (genus of *Staphylococcus, Streptococcus, Enterococcus* and *Neisseria*) and bacillus (genus of *Pseudomonas, Acinetobacter, Proteus* and *Klebsiella*)**

**The purpose of the lecture:** Introduction to specific microbiology, clinically important bacteria: pathogenic and opportunistic Gram-positive cocci, especially antibiotic-resistant forms (Staphylococcus (Methicilllin-resistant Staphylococcus aureus (MRSA), methicillin-resistant coagulase-negative staphylococcus), Strecoma); resistant enterococcus (VRE)), Gram-negative cocci (species Neisseria), pathogenic and opportunistic Gram-negative rodents (Pseudomonas, Acinetobacter, Proteus, Klebsiella species, their morpho-biological characteristics, pathogenic factors, diseases, microbiological diagnostics, specific treatment and provide information on prevention.

**Note.** In this lecture, the teacher should try to explain the importance of the properties of these microorganisms in the pathogenesis, microbiological diagnosis, treatment and prevention of diseases caused by them.

**Lecture plan:**

1. 1. Introduction to special microbiology, clinically important bacteria.

2. Pathogenic and opportunistic cocci:

- Gram-positive cocci: staphylococci, their morpho-biological characteristics, pathogenicity factors, diseases they cause, antibiotic-resistant forms (methicillin-resistant Staphylococcus aureus (MRSA), methicillin-resistant coagulase-negative staphylococcus (MRCNS)), microbiological diagnosis.

- Streptococci, their morpho-biological characteristics, pathogenicity factors, diseases they cause, microbiological diagnosis, specific treatment and prevention

- Enterococci, their morpho-biological characteristics, pathogenicity factors, diseases they cause, antibiotic-resistant forms (vancomycin-resistant enterococcus (VRE)), microbiological diagnosis.

- Gram-negative cocci: meningococci and gonococci, their morpho-biological characteristics, pathogenicity factors, diseases they cause, microbiological diagnosis, specific treatment and prevention.

3. Pathogenic and opportunistic Gram-negative bacteria:

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

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

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

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

**Staphylococcus** and Related Gram-Positive Cocci

STAPHYLOCOCCUS AUREUS

Trigger Words Coagulase, cytotoxins, exfoliative toxins, enterotoxins, toxic shock syndrome toxin, MRSA

*Biology and Virulence*

 Catalase-positive, gram-positive cocci arranged in clusters

 Species characterized by the presence of coagulase and protein A

 Virulence factors include structural components that facilitate adherence to host tissues and avoid phagocytosis, and a variety of toxins and hydrolytic enzymes

 Hospital- and community-acquired infections with MRSA are a significant worldwide Problem Epidemiology

 Normal flora on human skin and mucosal surfaces

 Organisms can survive on dry surfaces for long periods (because of thickened peptidoglycan layer and absence of outer membrane)

 Person-to-person spread through direct contact or exposure to contaminated fomites (e.g., bed linens, clothing)

 Risk factors include presence of a foreign body (e.g., splinter, suture, prosthesis, catheter), previous surgical procedure, and use of antibiotics that suppress the normal microbial flora

 Patients at risk for specific diseases include infants (scalded skin syndrome), young children with poor personal hygiene (impetigo and other cutaneous infections), patients with intravascular catheters (bacteremia and endocarditis) or shunts (meningitis), and patients with compromised pulmonary function or an antecedent viral respiratory infection (pneumonia)

 MRSA is now the most common cause of community-acquired skin and soft-tissue infections

*Diseases*

Diseases include toxin-mediated diseases (food poisoning, toxic shock syndrome, and scalded skin syndrome), pyogenic diseases (impetigo, folliculitis, furuncles, carbuncles, and wound infections), and other systemic diseases

**Diagnosis**

ᑏᑏMicroscopy useful for pyogenic infections but not blood infections or toxin-mediated infections

ᑏᑏ Staphylococci grow rapidly when cultured on nonselective media

ᑏᑏ Selective media (e.g., chromogenic agar, mannitol-salt agar) can be used to recover *Staphylococcus aureus* in contaminated specimens

ᑏᑏNucleic acid amplification tests are useful for screening patients for carriage of methicillinsensitive *S. aureus* (MSSA) and MRSA

ᑏᑏ *S. aureus* is identified by biochemical tests (e.g., coagulase), molecular probes, or mass spectrometry

*Treatment, Prevention, and Control*

 Localized infections managed by incision and drainage; antibiotic therapy indicated for systemic infections

 Empirical therapy should include antibiotics active against MRSA strains

 Oral therapy can include trimethoprim sulfamethoxazole, doxycycline or minocycline, clindamycin, or linezolid; vancomycin is drug of choice for intravenous therapy, with daptomycin, tigecycline, or linezolid acceptable alternatives

 Treatment is symptomatic for patients with food poisoning (although the source of infection should be identified so that appropriate preventive procedures can be enacted)

 Proper cleansing of wounds and use of disinfectant help prevent infections

 Thorough hand washing and covering of exposed skin helps medical personnel prevent infection or spread to other patients

COAGULASE-NEGATIVE STAPHYLOCOCCI

Trigger Words Opportunistic, slime layer, subacute

*Biology and Virulence*

Catalase-positive, coagulase-negative, gram-positive cocci arranged in clusters Relatively avirulent, although production of a “slime” layer can allow adherence to foreign bodies (e.g., catheters, grafts, prosthetic valves and joints, shunts) and protection from phagocytosis and antibiotics

*Epidemiology*

 Normal human flora on skin and mucosal surfaces

 Organisms can survive on dry surfaces for long periods

 Person-to-person spread through direct contact or exposure to contaminated fomites,

although most infections are with the patient’s own organisms

 Patients are at risk when a foreign body is present

 The organisms are ubiquitous, so there are no geographic or seasonal limitations

*Diseases*

Infections include subacute endocarditis, infections of foreign bodies, and urinary tract infections

*Treatment, Prevention, and Control*

The antibiotics of choice are oxacillin (or other penicillinase-resistant penicillin) or vancomycin for oxacillin-resistant strains

Removal of the foreign body is often required for successful treatment

Prompt treatment for endocarditis or shunt infections is necessary to prevent further tissue damage or immune complex formation

*Important Staphylococci*

Organism Historical Derivation

Staphylococcus staphylé, bunch of grapes; coccus, grain or berry (grapelike cocci)

S. aureus aureus, golden (golden or yellow)

S. epidermidis epidermidis, outer skin (of the epidermis or outer skin)

S. lugdunensis Lugdunum, Latin name for Lyon, France, where the organism was first isolated

S. saprophyticus sapros, putrid; phyton, plant (saprophytic or growing on dead tissues)

*Common Staphylococcus Species and Their Diseases Organism Diseases*

Staphylococcus aureus Toxin mediated (food poisoning, scalded skin syndrome, and toxic shock syndrome), cutaneous (carbuncles, folliculitis, furuncles, impetigo, and wound infections), other (bacteremia, endocarditis, pneumonia, empyema, osteomyelitis, and septic arthritis) S. epidermidis *Bacteremia*; endocarditis; surgical wounds; opportunistic infections of catheters, shunts, and prosthetic devices

S. lugdunensis Endocarditis

S. saprophyticus Urinary tract infections

*Staphylococcus aureus*

Toxin-Mediated Diseases

*Scalded skin syndrome*: Disseminated desquamation of epithelium in infants; blisters with no organisms or leukocytes

*Food poisoning*: After consumption of food contaminated with heat-stable enterotoxin, rapid onset of severe vomiting, diarrhea, and abdominal cramping, with resolution within 24 hours

*Toxic shock*: multisystem intoxication characterized initially by fever, hypotension, and a diffuse, macular, erythematous rash; high mortality without prompt antibiotic therapy and elimination of the focus of infection

*Suppurative Infections*

*Impetigo*: localized cutaneous infection characterized by pus-filled vesicle on an erythematous base

*Folliculitis*: impetigo involving hair follicles

*Furuncles* or boils: large, painful, pus-filled cutaneous nodules

*Carbuncles*: Coalescence of furuncles with extension into subcutaneous tissues and evidence of systemic disease (fever, chills, bacteremia)

*Bacteremia and endocarditis*: Spread of bacteria into the blood from a focus of infection; endocarditis characterized by damage to the endothelial lining of the heart

*Pneumonia and empyema*: Consolidation and abscess formation in the lungs; seen in the very young and elderly and in patients with underlying or recent pulmonary disease; a severe form of necrotizing pneumonia with septic shock and high mortality is now recognized

*Osteomyelitis*: Destruction of bones, particularly the metaphyseal area of long bones

*Septic arthritis*: Painful erythematous joint with collection of purulent material in the joint space

*Coagulase-Negative Staphylococcus Species*

*Wound infections*: Characterized by erythema and pus at the site of a traumatic or surgical wound; infections with foreign bodies can be caused by S. aureus and coagulase-negative staphylococci

*Urinary tract infections*: Dysuria and pyuria in young sexually active women (S.saprophyticus), in patients with urinary catheters (other coagulase-negative staphylococci), or after seeding of the urinary tract by bacteremia (S. aureus)

*Catheter and shunt infections*: Chronic inflammatory response to bacteria coating a catheter or shunt (most commonly with coagulase-negative staphylococci)

*Prosthetic device infections*: Chronic infection of device characterized by localized pain and mechanical failure of the device (most commonly with coagulase-negative staphylococci)

***Streptococcus*** *pyogenes (Group A)*

Trigger Words Group A, pharyngitis, pyoderma, rheumatic fever, glomerulonephritis

*Biology and Virulence*

Rapidly growing gram-positive cocci arranged in chains; group-specific carbohydrate (A antigen) and type-specific proteins (M protein) in cell wall

Virulence determined by ability to avoid phagocytosis (mediated primarily by capsule, M and M- like proteins, and C5a peptidase), adhere to and invade host cells (M protein, lipoteichoic acid, and F protein), and produce toxins (streptococcal pyrogenic exotoxins, streptolysin S, streptolysin O, streptokinase, and DNAses)

*Epidemiology*

Transient colonization in upper respiratory tract and skin surface, with disease caused by recently acquired strains (before protective antibodies are produced)

Pharyngitis and soft-tissue infections typically caused by strains with different M proteins

Person-to-person spread by respiratory droplets (pharyngitis) or through breaks in skin after direct contact with infected person, fomite, or arthropod vector

Individuals at higher risk for disease include children 5 to 15 years old (pharyngitis); children 2 to 5 years old with poor personal hygiene (pyoderma); patients with soft-tissue infection (streptococcal toxic shock syndrome); patients with prior streptococcal pharyngitis (rheumatic fever, glomerulonephritis) or soft-tissue infection (glomerulonephritis)

*Diseases*

Responsible for suppurative diseases (pharyngitis, soft-tissue infetions, streptococcal toxic shock) and nonsuppurative diseases (rheumatic fever, glomerulonephritis)

**Diagnosis**

ᑏᑏMicroscopy is useful in soft-tissue infections but not pharyngitis or nonsuppurative complications

ᑏᑏDirect tests for the group A antigen are useful for the diagnosis of streptococcal pharyngitis

ᑏᑏ Isolates identified by catalase (negative), positive L-pyrrolidonyl arylamidase (PYR) reaction, susceptibility to bacitracin, and presence of group-specific antigen (group A antigen)

ᑏᑏAntistreptolysin O test is useful for confirming rheumatic fever or glomerulonephritis associated with streptococcal pharyngitis; anti DNase B test should be performed for glomerulonephritis associated with pharyngitis or soft-tissue infections

*Treatment, Prevention, and Control*

Penicillin V or amoxicillin used to treat pharyngitis; oral cephalosporin or macrolide for penicillin-allergic patients; intravenous penicillin plus clindamycin used for systemic infections

Oropharyngeal carriage occurring after treatment can be re-treated; treatment is not indicated for prolonged asymptomatic carriage because antibiotics disrupt normal protective flora

Starting antibiotic therapy within 10 days in patients with pharyngitis prevents rheumatic fever

For glomerulonephritis, no specific antibiotic treatment or prophylaxis is indicated

For patients with a history of rheumatic fever, antibiotic prophylaxis is required before procedures (e.g., dental) that can induce bacteremias leading to endocarditis

*Streptococcus agalactiae (Group B)*

Trigger Words Group B, neonatal disease, screening pregnant women

*Biology and Virulence*

Rapidly growing gram-positive cocci arranged in chains; group-specific carbohydrate (B antigen) and type-specific capsular carbohydrates (Ia, Ib, and II-VIII)

Virulence determined primarily by ability to avoid phagocytosis (mediated by capsule)

*Epidemiology*

Asymptomatic colonization of the upper respiratory tract and genitourinary tract

Early-onset disease acquired by neonates from mother during pregnancy or at time of birth

Neonates are at higher risk for infection if (1) there is premature rupture of membranes, prolonged labor, preterm birth, or disseminated maternal group B streptococcal disease, and (2) mother is without type-specific antibodies and has low complement levels

Women with genital colonization are at risk for postpartum disease

Men and nonpregnant women with diabetes mellitus, cancer, or alcoholism are at increased risk for disease

No seasonal incidence

*Diseases*

Responsible for neonatal disease (early-onset and late-onset disease with meningitis, pneumonia, and bacteremia), infections in pregnant women (endometritis, wound infections, and urinary tract infections), and other adults (bacteremia, pneumonia, bone and joint infections, and skin and soft-tissue infections)

**Diagnosis**

ᑏᑏMicroscopy useful for meningitis (cerebrospinal fluid), pneumonia (lower respiratory secretions), and wound infections (exudates)

ᑏᑏAntigen tests are less sensitive than microscopy and should not be used

ᑏᑏCulture most sensitive test; a selective broth (i.e., LIM) is needed for optimal detection of vaginal carriage

ᑏᑏ Polymerase chain reaction–based assays to detect vaginal carriage in pregnant women are commercially available; currently require use of enrichment broth for optimum sensitivity

ᑏᑏ Isolates identified by demonstration of group-specific cell wall carbohydrate or positive nucleic acid amplification test

*Treatment, Prevention, and Control*

Penicillin G is the drug of choice; empirical therapy with broad-spectrum antibiotics (broad-spectrum cephalosporin + aminoglycoside) used until specific pathogen identified; combination of penicillin and aminoglycoside is used in patients with serious infections; a cephalosporin or vancomycin is used for patients allergic to penicillin

For high-risk babies, penicillin is given at least 4 hours before delivery

No vaccine is currently available

*STREPTOCOCCUS PNEUMONIAE*

Trigger Words Diplococci, capsule, pneumonia, meningitis, vaccine

*Biology and Virulence*

Elongated gram-positive cocci arranged in pairs (diplococci) and short chains; cell wall includes teichoic acid rich in phosphorylcholine (C polysaccharide), which is required for the activity of an autolytic enzyme, amidase

Virulence determined by ability to colonize oropharynx (surface protein adhesions), spread into normally sterile tissues (pneumolysin, immunoglobulin [Ig]A protease), stimulate local inflammatory response (teichoic acid, peptidoglycan fragments, pneumolysin), and evade phagocytic killing (polysaccharide capsule)

Responsible for pneumonia, sinusitis and otitis media, meningitis, and bacteremia

*Epidemiology*

Most infections are caused by endogenous spread from the colonized nasopharynx or oropharynx to distal site (e.g., lungs, sinuses, ears, blood, meninges); person-to-person spread through infectious droplets is rare

Colonization is highest in young children and their contacts

Individuals with antecedent viral respiratory tract disease or other conditions that interfere with bacterial clearance from respiratory tract are at increased risk for pulmonary disease

Children and the elderly are at greatest risk for meningitis

People with hematologic disorder (e.g., malignancy, sickle cell disease) or functional asplenia are at risk for fulminant sepsis

Although the organism is ubiquitous, disease is more common in cool months

**Diagnosis**

ᑏᑏ Microscopy is highly sensitive, as is culture, unless the patient has been treated with antibiotics

ᑏᑏ Antigen tests for pneumococcal C polysaccharide are sensitive with cerebrospinal fluid (meningitis) but not with urine (meningitis, pneumonia, other infections)

ᑏᑏ Nucleic acid–based tests are the tests of choice for the diagnosis of meningitis, particularly in patients who have been

treated with an antibiotic

ᑏᑏ Culture requires use of enriched-nutrient media (e.g., sheep blood agar); organism susceptible to many antibiotics, so culture can be negative in partially treated patients

ᑏᑏ Isolates identified by catalase (negative), susceptibility to optochin, and solubility in bile

*Treatment, Prevention, and Control*

Penicillin is the drug of choice for susceptible strains, although resistance is increasingly common

Vancomycin combined with ceftriaxone is used for empirical therapy; monotherapy with a cephalosporin, fluoroquinolone, or vancomycin can be used in patients with susceptible isolates

Immunization with 13-valent conjugated vaccine is recommended for all children younger than 2 years; a 23-valent polysaccharide vaccine is recommended for adults at risk for disease

***ENTEROCOCCUS***

Trigger Words Diplococci, gastrointestinal carriage, drug resistant, urinary tract infections, peritonitis

*Biology and Virulence*

Gram-positive cocci arranged in pairs and short chains (morphologically similar to S.pneumoniae)

Cell wall with group-specific antigen (group D glycerol teichoic acid)

Virulence mediated by ability to adhere to host surfaces and form biofilms and by antibiotic resistance

*Epidemiology*

Colonizes the gastrointestinal tracts of humans and animals; spreads to other mucosal surfaces if broad-spectrum antibiotics eliminate the normal bacterial population

Cell wall structure typical of gram-positive bacteria, which allows survival on environmental surfaces for prolonged periods

Most infections endogenous (from patient’s bacterial flora); some caused by patient-to- patient spread

Patients at increased risk include those hospitalized for prolonged periods and treated with broad-spectrum antibiotics (particularly cephalosporins, to which enterococci are naturally resistant)

*Diseases*

Diseases include urinary tract infections, peritonitis (usually polymicrobic), wound infections, and bacteremia with or without endocarditis

**Diagnosis**

ᑏᑏMicroscopy is useful in soft-tissue infections but not pharyngitis or nonsuppurative complications

ᑏᑏDirect tests for the group A antigen are useful for the diagnosis of streptococcal pharyngitis

ᑏᑏ Isolates identified by catalase (negative), positive l-pyrrolidonyl arylamidase (PYR) reaction, susceptibility to bacitracin, and presence of group-specific antigen (group A antigen)

ᑏᑏAntistreptolysin O test is useful for confirming rheumatic fever or glomerulonephritis associated with streptococcal pharyngitis; anti-DNase B test should be performed for glomerulonephritis associated with pharyngitis or soft-tissue infections

*Treatment, Prevention, and Control*

Therapy for serious infections requires combination of an aminoglycoside with a cell wall–active antibiotic (penicillin, ampicillin, or vancomycin); newer agents used for antibiotic-resistant bacteria include linezolid, daptomycin, tigecycline, and quinupristin/dalfopristin

Antibiotic resistance to each of these drugs is becoming increasingly common, and infections with many isolates (particularly Enterococcus faecium) are not treatable with anyantibiotics

Prevention and control of infections require careful restriction of antibiotic use and implementation of appropriate infection-control practices

*Important Streptococci and Enterococci*

Organism Historical Derivation

Streptococcus - streptus, pliant; coccus, grain or berry (a pliant berry or coccus; refers to the appearance of long, flexible chains of cocci)

S. agalactiae - agalactia, want of milk (original isolate [called S.mastitidis] was responsible for bovine mastitis)

S. anginosus - anginosus, pertaining to angina

S. constellatus - constellatus, studded with stars (original isolate embedded in agar with smaller colonies surrounding the large colony; satellite formation does not occur around colonies on the surface of an agar plate)

S. dysgalactiae - dys, ill, hard; galactia, pertaining to milk (loss of milk secretion; isolates associated with bovine mastitis)

S. gallolyticus - gallatum, gallate; lyticus, to loosen (able to digest or hydrolyze methyl gallate)

S. intermedius - intermedius, intermediate (initial confusion about whether this was an aerobic or an anaerobic bacterium)

S. mitis - mitis, mild (incorrectly thought to cause mild infections)

S. mutans - mutans, changing (cocci that may appear rodlike, particularly when initially isolated in culture)

S. pneumoniae - pneumon, the lungs (causes pneumonia)

S. pyogenes - pyus, pus; gennaio, beget or producing (pus producing; typically associated with formation of pus in wounds)

S. salivarius - salivarius, salivary (found in the mouth in saliva)

Enterococcus - enteron, intestine; coccus, berry (intestinal coccus)

E. faecalis - faecalis, relating to feces

E. faecium - faecium, of feces

E. gallinarum - gallinarum, of hens (original source was intestines of domestic fowl)

E. casseliflavus - casseli, Kassel’s; flavus, yellow (Kassel’s yellow)

Catalase-Negative, Gram-Positive Cocci and Their Diseases

*Organism Diseases*

Abiotrophia Bacteremia, endocarditis (native and prosthetic valves), nosocomial brain abscesses and meningitis, eye infections

Aerococcus Bacteremia, endocarditis, urinary tract infections Enterococcus Bacteremia, endocarditis, urinary tract infections, peritonitis, wound infections

Granulicatella Bacteremia, endocarditis (native and prosthetic valves), eye infections

Lactococcus Bacteremia in immunocompromised patients, endocarditis (native and prosthetic valves), urinary tract infections, osteomyelitis Leuconostoc Opportunistic infections, including bacteremia, wound infections, central nervous system infections, and peritonitis

Pediococcus Opportunistic infections, including bacteremia in severely immunocompromised patients

*Classification of Common β-Hemolytic Streptococci* Group

Representative

*Species Diseases*

**A**- S. pyogenes Pharyngitis, skin and soft-tissue infections, bacteremia, rheumatic fever, acute glomerulonephritis

S. anginosus group Abscesses

**B**- S. agalactiae Neonatal disease, endometritis, wound infections, urinary tract infections, bacteremia, pneumonia, skin and soft-tissue infections

**C**- S. dysgalactiae Pharyngitis, acute glomerulonephritis

F, G- S. anginosus group Abscesses

S. dysgalactiae Pharyngitis, acute glomerulonephritis

*Classification of Viridans Group of Streptococcus* Group Representative

***Species - Diseases***

Anginosus S. anginosus, S. constellatus, S. intermedius

Abscesses in brain, oropharynx, or peritoneal cavity

Mitis S. mitis, S. pneumoniae, S. oralis

Subacute endocarditis; sepsis in neutropenic patients; pneumonia; meningitis

Mutans S. mutans, S. sobrinus

Dental caries; bacteremia

Salivarius S. salivarius Bacteremia; endocarditis

Bovis S. gallolyticus subsp. gallolyticus, subsp. Pasteurianus

Bacteremia associated with gastrointestinal cancer (subsp. gallolyticus); meningitis (subsp. pasteurianus)

Ungrouped S. suis Meningitis; bacteremia; streptococcal toxic shock syndrome

***Streptococcus pyogenes (Group A)***

*Suppurative Infections*

*Pharyngitis*: reddened pharynx with exudates generally present; cervical lymphadenopathy can be prominent

*Scarlet fever:* diffuse erythematous rash beginning on the chest and spreading to the extremities; complication of streptococcal pharyngitis

*Pyoderma*: localized skin infection with vesicles progressing to pustules; no evidence of systemic disease

*Erysipelas*: localized skin infection with pain, inflammation, lymph node enlargement, and systemic symptoms

*Cellulitis*: infection of the skin that involves the subcutaneous tissues

*Necrotizing fasciitis*: deep infection of skin that involves destruction of muscle and fat layers

*Streptococcal toxic shock syndrome*: multiorgan systemic infection resembling staphylococcal toxic shock syndrome; however, most patients are bacteremic and with evidence of fasciitis

*Other suppurative diseases*: variety of other infections recognized including puerperal sepsis, lymphangitis, and pneumonia

***Nonsuppurative Infections***

*Rheumatic fever:* characterized by inflammatory changes of the heart (pancarditis), joints (arthralgias to arthritis), blood vessels, and subcutaneous tissues

*Acute glomerulonephritis*: acute inflammation of the renal glomeruli with edema, hypertension, hematuria, and proteinuria

***Streptococcus agalactiae (Group B)***

Early-onset neonatal disease: within 7 days of birth, infected newborns develop signs and symptoms of pneumonia, meningitis, and sepsis

Late-onset neonatal disease: more than 1 week after birth, neonates develop signs and symptoms of bacteremia with meningitis

Infections in pregnant women: most often present as postpartum endometritis, wound infections, and urinary tract infections; bacteremia and disseminated complications may occur

Infections in other adult patients: most common diseases include bacteremia, pneumonia, bone and joint infections, and skin and soft-tissue infections

***Other β-Hemolytic Streptococci***

Abscess formation in deep tissues: associated with S. anginosus group

Pharyngitis: associated with S. dysgalactiae; disease resembles that caused by *S.pyogenes*; can be complicated with acute glomerulonephritis

***Viridans Streptococci***

*Abscess formation in deep tissues*: associated with S. anginosus group

*Septicemia in neutropenic patients*: associated with S. mitis group

*Subacute endocarditis*: associated with S. mitis and S. salivarius groups

*Dental caries*: associated with S. mutans group

*Malignancies of gastrointestinal tract*: associated with S. bovis group (S. gallolyticus subsp. gallolyticus)

*Meningitis*: associated with *S.gallolyticus subsp. pasteurianus, S.suis, and S.mitis* group

***Streptococcus pneumoniae***

*Pneumonia*: acute onset with severe chills and sustained fever; productive cough with blood-tinged sputum; lobar consolidation

*Meningitis*: severe infection involving the meninges, with headache, fever, and sepsis; high mortality and severe neurologic deficits in survivors

*Bacteremia*: more common in patients with meningitis than with pneumonia, otitis, media, or sinusitis; overwhelming sepsis in asplenic patients

*Enterococcus faecalis and Enterococcus faecium*

*Urinary tract infection*: dysuria and pyuria, most commonly in hospitalized patients with an indwelling urinary catheter and receiving broad-spectrum cephalosporin antibiotics

*Peritonitis*: abdominal swelling and tenderness after abdominal trauma or surgery; patients typically are acutely ill and febrile and have positive blood cultures; typically, a polymicrobic infection

*Bacteremia*: associated with either a localized infection or endocarditis

*Endocarditis*: infection of the heart endothelium or valves; associated with persistent bacteremia; can present acutely or chronically

****Characteristics of Medically Important Streptococci**

***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