**Lecture 3.**

**Pathogenic anaerobes (genus of *Clostridium* and *Bacteroides*). The causative agents of zoonotic bacterial infections (genus of *Bruсella, Bacillus, Listeria, Yersinia, Francisella*)**

**The purpose of the lecture:** Morpho-biological characteristics of pathogenic and opportunistic anaerobes (species Clostridium and Bacteroides), causative agents of zoonotic infections (brucellosis, black ulcer, listeriosis, plague and tularemia), pathogenic factors, pathogenesis of diseases caused by these bacteria, basic clinical signs, , provide information on specific treatment and prevention principles.

**Lecture plan:**

**1. Anaerobic bacteria:**

- General characteristics of the genus Clostridium.

- The causative agents of gaseous anaerobic infection *(C.perfringens, C.novyi, C.septicum, C.histolyticum, C.sordellii),* morpho-biological characteristics, pathogenicity factors, pathogenesis of diseases caused by them, main clinical symptoms, microbiological diagnosis, specific treatment and prevention principles.

- the causative agent of tetanus, morpho-biological characteristics, pathogenicity factors, pathogenesis of diseases caused by it, main clinical signs, microbiological diagnosis, specific treatment and prevention principles.

- the causative agent of botulism, morpho-biological characteristics, pathogenicity factors, pathogenesis of diseases caused by it, main clinical signs, microbiological diagnosis, specific treatment and prevention principles.

- Clostridium difficile, characteristics. Its role in human pathology, microbiological diagnosis.

- Non-spore forming anaerobes. Genus Bacteroides (bacteroids), morpho-biological characteristics, role in pathology, principles of microbiological diagnosis.

**2. The causative agents of zoonotic infections:**

- Brucella. Classification, morpho-biological characteristics, pathogenicity factors. Pathogenesis. Principles of microbiological diagnosis, specific treatment and prevention.

- The causative agent of antrax. Morpho-biological features, pathogenicity factors, pathogenesis, clinical forms. Principles of microbiological diagnosis, specific treatment and prevention.

- The causative agent of listeriosis, morpho-biological characteristics, pathogenicity factors, pathogenesis of the disease, microbiological diagnosis.

- Yersinia. The causative agent of plague, morpho-biological characteristics, pathogenicity factors, diseases caused by it. Pathogenesis, microbiological diagnostics. Principles of specific treatment and prevention. Causes, characteristics, microbiological diagnosis of intestinal yersiniosis and pseudotuberculosis.

- The causative agent of tularemia. Morpho-biological characteristics, pathogenicity factors. The main clinical forms of the disease in humans. Microbiological diagnostics. Principles of specific treatment and prevention.

**Clostridium**

***CLOSTRIDIUM DIFFICILE***

**Trigger Words**

Spore former, fecal carriage, toxins A and B, antibiotic-associated diarrhea, pseudomembranous colitis

**Biology and Virulence**

Large anaerobic rod characterized by abundant spore formation, rapid growth, and production of volatile fatty acids

Most strains produce two toxins: an enterotoxin that attracts neutrophils and stimulates their release of cytokines, and a cytotoxin that increases permeability of the intestinal wall and subsequent diarrhea

Spore formation allows the organism to persist in the hospital environment and resist decontamination efforts

Resistance to antibiotics such as clindamycin, cephalosporins, and fluoroquinolones allows *C. difficile* to overgrow the normal intestinal bacteria in patients exposed to these antibiotics and produce disease

**Epidemiology**

Colonizes the intestines of a small proportion of healthy individuals (<5%)

Exposure to antibiotics is associated with overgrowth of *C. difficile* and subsequent disease (endogenous infection)

**Diseases**

Antibiotic-associated diarrhea: acute diarrhea generally developing 5 to 10 days after initiation of antibiotic treatment; may be brief and self-limited or more protracted with recurrent bouts of diarrhea

Pseudomembranous colitis: most severe form of *C. difficile* disease, with profuse diarrhea, abdominal cramping, and fever; whitish plaques (pseudomembranes) form over intact colonic tissue; can progress to death

**Diagnosis**

ᑏᑏ*C. difficile* disease is confirmed by detecting cytotoxin or enterotoxin or the toxin genes in the patient’s feces

**Treatment, Prevention, and Control**

The implicated antibiotic should be discontinued

Treatment with metronidazole or vancomycin should be used in severe disease; fecal transplants of colonic bacteria from healthy individuals can be used to treat recurrent disease

Relapse is common because antibiotics do not kill spores; a second course of therapy with the same antibiotic is usually successful, although multiple courses may be necessary

The hospital room should be carefully cleaned after the infected patient is discharged

***CLOSTRIDIUM PERFRINGENS***

**Trigger Words**

Spore former, myonecrosis, sepsis, food poisoning

**Biology and Virulence**

Large gram-positive rods with spores rarely observed

Distinct colony morphology and rapid growth

Produces many toxins and enzymes that lyse blood cells and destroy tissues, leading to diseases such as overwhelming sepsis, massive hemolysis, and myonecrosis

Produces a heat-sensitive enterotoxin that binds to receptors on the epithelium of the small intestine leading to loss of fluids and ions (watery diarrhea)

**Epidemiology**

Ubiquitous; present in soil, water, and intestinal tract of humans and animals

Type A strains are responsible for most human infections

**Diseases**

Food poisoning associated with contaminated meat products (beef, poultry, gravy) held at temperatures between 5° C and 60° C, which allows the organisms to grow to large numbers

Soft-tissue infections typically associated with bacterial contamination of wounds or localized trauma

**Diagnosis**

ᑏᑏ Reliably recognized in Gram-stained tissue specimens (large, rectangular, gram-positive rods)

ᑏᑏGrows rapidly in culture with characteristic colony morphology and hemolytic pattern

**Treatment, Prevention, and Control**

Rapid treatment is essential for serious infections

Severe infections require surgical debridement and high-dose penicillin therapy

Symptomatic treatment for food poisoning

Proper wound care and judicious use of prophylactic antibiotics will prevent most infections

***CLOSTRIDIUM TETANI***

**Trigger Words**

Spore former, environmental, neurotoxin, contaminated wounds, tetanus, vaccine

**Biology and Virulence**

Organism extremely oxygen sensitive, which makes detection by culture difficult

The primary virulence factor is tetanospasmin, which is a heat-labile neurotoxin that blocks release of neurotransmitters for inhibitory synapses (i.e., gamma-aminobutyric acid, glycine)

**Epidemiology**

Ubiquitous; spores are found in most soils and can colonize the gastrointestinal tract of humans and animals

Exposure to spores is common, but disease is uncommon, except in developing countries in which there is poor access to vaccine and medical care

Risk is greatest for people with inadequate vaccine-induced immunity

Disease does not induce immunity

**Diseases**

Disease is characterized by unrelenting

muscle spasms and involvement of the autonomic nervous system

**Diagnosis**

ᑏᑏDiagnosis is based on clinical presentation and not laboratory tests

ᑏᑏMicroscopy and culture are insensitive, and neither tetanus toxin nor antibodies are typically detected

**Treatment, Prevention, and Control**

Treatment requires the combination of wound debridement, antibiotic therapy (penicillin, metronidazole), passive immunization with antitoxin globulin, and vaccination with tetanus toxoid

Prevention through use of vaccination, consisting of three doses of tetanus toxoid followed by booster doses every 10 years

***CLOSTRIDIUM BOTULINUM***

**Trigger Words**

Spore former, environmental, neurotoxin, foodborne and infant botulism, no vaccine

**Biology and Virulence**

Multiple distinct botulinum toxins are produced, with human disease caused most commonly by types A and B; types E and F are also associated with human disease

Botulinum toxin prevents release of the neurotransmitter acetylcholine, blocking neurotransmission at peripheral cholinergic synapses, leading to a flaccid paralysis

**Epidemiology**

*C. botulinum* spores are found in soil worldwide Relatively few cases of botulism in prevalent in developing countries Infant botulism more common; associated with ingestion of contaminated soil or contaminated foods (particularly honey)

**Diseases**

Foodborne botulism is characterized by blurred vision, dry mouth, constipation, and abdominal pain, with progressive weakness of the peripheral muscles and flaccid paralysis

Infant botulism begins with nonspecific symptoms but progresses to flaccid paralysis

Other forms of botulism include wound botulism and inhalation botulism

**Diagnosis**

ᑏᑏDiagnosis of foodborne botulism is confirmed if toxin activity is demonstrated in the implicated food or in the patient’s serum, feces, or gastric fluid

ᑏᑏ Infant botulism is confirmed if toxin is detected in the infant’s feces or serum, or the organism cultured from feces

ᑏᑏWound botulism is confirmed if toxin is detected in the patient’s serum or wound, or the organism cultured from the wound

**Treatment, Prevention, and Control**

Treatment involves the combination of administration of metronidazole or penicillin, trivalent botulinum antitoxin, and ventilatory support Spore germination in foods prevented by maintaining food at an acid pH, by high sugar content (e.g., fruit preserves), or by storing the foods at 4° C or colder

Toxin is heat labile; therefore, it can be destroyed by heating of food for 10

minutes at 60° C to 100° C

**Important Clostridia**

*Clostridium closter,* a spindle

*C. botulinum botulus,* sausage (the first major outbreak was associated with insufficiently smoked sausage)

*C. difficile difficile,* difficult (difficult to isolate and grow; refers to the extreme oxygen sensitivity of this organism)

*C. perfringens perfringens,* breaking through (associated with highly invasive tissue necrosis)

*C. septicum septicum,* putrefactive (associated with sepsis and a high mortality)

*C. tertium tertium,* third (historically, the third most commonly isolated anaerobe from war wounds)

*C. tetani tetani,* related to tension (disease caused by this organism characterized by muscle spasms)

**Pathogenic Clostridia and Their Associated Human Diseases**

***Clostridium difficile***

**Antibiotic-associated diarrhea:** acute diarrhea generally developing 5 to 10 days after initiation of antibiotic treatment (particularly clindamycin, penicillins, cephalosporins, fluoroquinolones); may be brief and self-limited or more protracted

**Pseudomembranous colitis:** most severe form of *C. difficile* disease, with profuse diarrhea, abdominal cramping, and fever; whitish plaques (pseudomembranes) over intact colonic tissue seen on colonoscopy

***Clostridium perfringens***

***Soft-Tissue Infections***

**Cellulitis:** localized edema and erythema with gas formation in the soft tissue; generally nonpainful

**Suppurative myositis:** accumulation of pus (suppuration) in the muscle planes, without muscle necrosis or systemic symptoms

**Myonecrosis:** painful, rapid destruction of muscle tissue; systemic spread with high mortality

***Gastroenteritis***

**Food poisoning:** rapid onset of abdominal cramps and watery diarrhea with no fever, nausea, or vomiting; short duration and self-limited

**Necrotizing enteritis:** acute, necrotizing destruction of jejunum, with abdominal pain, vomiting, bloody diarrhea, and peritonitis

***Clostridium tetani***

**Generalized tetanus:** generalized musculature spasms and involvement of the autonomic nervous system in severe disease (e.g., cardiac arrhythmias, fluctuations in blood pressure, profound sweating, dehydration)

**Localized tetanus:** musculature spasms restricted to localized area of primary infection

**Neonatal tetanus:** neonatal infection primarily involving the umbilical stump; very high mortality

***Clostridium botulinum***

**Foodborne botulism:** initial presentation of blurred vision, dry mouth, constipation, and abdominal pain; progresses to bilateral descending weakness of the peripheral muscles, with flaccid paralysis

**Infant botulism:** initially nonspecific symptoms (e.g., constipation, weak cry, failure to thrive) that progress to flaccid paralysis and respiratory arrest

**Wound botulism:** clinical presentation same as with foodborne disease, although the incubation period is longer and fewer gastrointestinal symptoms are reported

**Inhalation botulism:** rapid onset of symptoms (flaccid paralysis, pulmonary failure) and high mortality from inhalation exposure to botulinum toxin

***Non–Spore-Forming Anaerobic Bacteria***

***BACTEROIDES FRAGILIS***

**Trigger Words**

Pleomorphic gram-negative rod, capsule, abscess formation, drug resistance

**Biology and Virulence**

Anaerobic, pleomorphic, gram-negative rod

Surrounded by polysaccharide capsule

Lipopolysaccharide major cell wall component but without endotoxin activity

Polysaccharide capsule major virulence factor

Heat-labile metalloprotease toxin responsible for diarrheal disease

**Epidemiology**

Colonizes the gastrointestinal tract of animals and humans as a minor member of the microbiome; rare or absent from the oropharynx or genital tract of healthy individuals

Endogenous infections

**Diseases**

Associated with pleuropulmonary, intraabdominal, genital, and skin and soft-tissue infections characterized by abscess formation; bacteremia

**Diagnosis**

ᑏᑏCharacteristic Gram stain from clinical specimens

ᑏᑏGrows rapidly in cultures incubated anaerobically

ᑏᑏ Identified by biochemical tests, gene sequencing, or matrix-assisted laser desorption ionization mass spectrometry

**Treatment, Prevention, and Control**

 Resistant to penicillin and 25% of isolates resistant to clindamycin; uniformly susceptible to metronidazole and most strains to carbapenems and piperacillin tazobactam

**ANAEROBIC GRAM-POSITIVE COCCI**

*Anaerococcus - an,* without; *aer,* air; *coccus,* berry or coccus (anaerobic coccus)

*Atopobium - atopos,* uncommon; *bios,* life

*Finegoldia -* Named after the American microbiologist Sid Finegold

*Micromonas - micro,* tiny; *monas,* cell (tiny cell)

*Peptoniphilus - peptonum,* peptone; *philus,* loving (loving peptones, major source of energy)

*Peptostreptococcus - pepto,* cook or digest (the digesting streptococcus)

*Schleiferella -*Named after the German microbiologist K.H. Schleifer

**ANAEROBIC GRAM-POSITIVE RODS**

*Actinomyces - aktinos,* ray; *mykes,* fungus (ray fungus, referring to the radial arrangement of filaments in granules)

*Bifidobacterium - bifidus,* cleft; *bakterion,* small rod (a small clefted or bifurcated rod)

*Cutibacterium - cutis*, skin (skin bacteria)

*Eubacterium- eu,* good or beneficial (a beneficial rod, that is, a rod normally present)

*Lactobacillus - lacto,* milk (milk bacillus; organism originally recovered in milk; also, lactic acid is the primary metabolic product of fermentation)

*Mobiluncus - mobilis,* capable of movement or being active; *uncus,* hook (motile curved rod)

*Propionibacterium - propionicum,* propionic acid (propionic acid is the primary metabolic product of fermentation)

**ANAEROBIC GRAM-NEGATIVE COCCI**

*Veillonella -* Named after A. Veillon, the French bacteriologist who isolated the type species

**ANAEROBIC GRAM-NEGATIVE RODS**

*Bacteroides - bacter,* staff or rod; *idus,* shape (rod-shaped)

*Fusobacterium - fusus,* a spindle; *bakterion,* a small rod (a small, spindle-shaped rod)

*Porphyromonas - porphyreos,* purple; *monas,* unit (pigmented rods)

*Prevotella -* Named after the French microbiologist A.R.Prevot, a pioneer in anaerobic microbiology

**Anaerobic, Non–Spore-Forming, Gram-Positive Rods**

*Actinomyces* spp. Localized oral infections, actinomycosis (cervicofacial, thoracic, abdominal, pelvic, central nervous system)

*Cutibacterium (Propionibacterium)* spp. Acne, lacrimal canaliculitis, opportunistic infections

*Mobiluncus* spp. Bacterial vaginosis, opportunistic infections

*Lactobacillus* spp. Endocarditis, opportunistic infections

*Eubacterium* spp. Opportunistic infections

*Bifidobacterium* spp. Opportunistic infections

**Predominant Anaerobic Gram-Negative Bacteria Responsible for Human Disease**

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***BRUCELLA***

**Trigger Words**

Small coccobacilli, slow growing, zoonotic, undulant fever

**Biology and Virulence**

Very small gram-negative coccobacilli (0.5 × 0.6 to 1.5 μm)

Strict aerobe; does not ferment carbohydrates

Requires complex media and prolonged incubation for in vitro growth

Intracellular pathogen that is resistant to killing in serum and by phagocytes

Smooth colonies associated with virulence

**Epidemiology**

Animal reservoirs are goats and sheep *(B. melitensis);* cattle and bison *(B. abortus);* swine, reindeer, and caribou *(B. suis);* and dogs, foxes, and coyotes *(B. canis)*

Infects animal tissues rich in erythritol (e.g., breast, uterus, placenta, epididymis)

Worldwide distribution, particularly in Latin America, Africa, the Mediterranean basin, the Middle East, and Western Asia

Vaccination of herds has controlled disease

Most disease in travelers

ᑏᑏ Individuals at greatest risk for diseaseare people who consume unpasteurized dairy products, people in direct contact with infected animals, and laboratory workers

**Diagnosis**

Microscopy is insensitive

Culture (blood, bone marrow, infected tissue if localized infection) is sensitive and specific if prolonged incubation is used (minimum of 3 days to 2 weeks)

Serology can be used to confirm the clinical diagnosis; fourfold increase in titer or single titer ≥1:160; high titers can persist for months to years

**Treatment, Prevention, and Control**

Recommended treatment is doxycycline combined with rifampin for a minimum of 6 weeks for nonpregnant adults; trimethoprim-sulfamethoxazole for pregnant women and for children younger than 8 years

Human disease is controlled by eradication of the disease in the animal reservoir through vaccination and serologic monitoring of the animals for evidence of disease, pasteurization of dairy products, and use of proper safety techniques in clinical laboratories working with this organism

*Brucella -* Named after Sir David Bruce, who first recognized the organism as a cause of “undulant fever”

*B. abortus - abortus,* abortion or miscarriage (this organism is responsible for abortion in infected animals)

*B. melitensis - melitensis,* pertaining to the Island of Malta (Melita), on which the first outbreak was recognized by Bruce

*B. suis - suis,* of the pig (a swine pathogen)

*B. canis - canis,* of the dog (a dog pathogen)

***BACILLUS ANTHRACIS***

**Trigger Words**

Spore former, capsule, edema toxin, lethal toxin, anthrax, bioterrorism

**Biology and Virulence**

ᑏ Spore-forming, nonmotile, nonhemolytic gram positive rods

ᑏᑏ Polypeptide capsule consisting of poly-D-glutamic acid observed in clinical specimens

ᑏᑏVirulent strains produce three exotoxins that combine to form edema toxin (combination of protective antigen and edema factor) and lethal toxin (protective antigen with lethal factor)

ᑏᑏ The polypeptide capsule inhibits phagocytosis of bacteria

**Treatment, Prevention, and Control**

ᑏᑏ Inhalation or gastrointestinal anthrax or bioterrorism-associated anthrax should be treated with ciprofloxacin or doxycycline, combined with one or two additional antibiotics (e.g., rifampin, vancomycin, penicillin, imipenem, clindamycin, clarithromycin)

ᑏᑏNaturally acquired cutaneous anthrax can be treated with amoxicillin

ᑏᑏVaccination of animal herds and people in endemic areas can control disease, but spores are difficult to eliminate from contaminated soils

ᑏᑏVaccination of animal herds and at-risk humans is effective, although the development of a less toxic vaccine is desired

ᑏᑏAlternative treatments interfering with the activity of anthrax toxins are under investigation

**Epidemiology**

ᑏᑏUbiquitous in soils throughout the world

ᑏᑏ People at risk include those who consume food contaminated with the bacterium (e.g., rice, meat, vegetables, sauces), those with penetrating injuries (e.g., to eye), those who receive intravenous injections, and immunocompromised patients exposed to *B.cereus*

**Diseases**

ᑏᑏCapable of causing gastrointestinal diseases (emetic and diarrheal forms), ocular infections, and an anthrax-like disease in immunocompetent patients

 **Diagnosis**

ᑏᑏOrganism is present in high concentrations in clinical specimens (microscopy typically positive) and grows readily in culture

ᑏᑏ Preliminary identification is based on microscopic (gram-positive rods) and colonial (nonhemolytic, adherent colonies) morphology; confirmed by demonstrating capsule and either lysis with gamma phage, a positive direct fluorescent antibody test for the specific cell wall polysaccharide, or positive nucleic acid amplification assay

**Epidemiology**

ᑏᑏ *B. anthracis* primarily infects herbivores, with humans as accidental hosts

ᑏᑏ Rarely isolated in developed countries but is prevalent in impoverished areas in which vaccination of animals is not practiced

ᑏᑏ The greatest danger of anthrax in industrial countries is the use of *B. anthracis* as an agent of bioterrorism

**Diseases**

ᑏᑏ Three forms of anthrax are recognized: cutaneous (most common in humans), gastrointestinal (most common in herbivores), and inhalation (bioterrorism)

***BACILLUS CEREUS***

**Trigger Words**

Spore former, enterotoxin, gastroenteritis, eye infections

**Biology and Virulence**

ᑏᑏ Spore-forming, motile, gram-positive rods

ᑏᑏ Heat-stable and heat-labile enterotoxin

ᑏᑏ Tissue destruction is mediated by cytotoxic enzymes, including cereolysin and phospholipase C

**Treatment, Prevention, andControl**

ᑏᑏ Gastrointestinal infections are treated symptomatically

ᑏᑏ Ocular infectious or other invasive diseases require removal of foreign bodies and treatment with vancomycin, clindamycin, ciprofloxacin, or gentamicin

ᑏᑏ Gastrointestinal disease is prevented by proper preparation of food (e.g., foods should be consumed immediately after preparation or refrigerated)

 ***Important Bacillus Species***

*Bacillus-bacillum*, a small rod

*B. anthracis-anthrax*, charcoal, a carbuncle (refers to the black necrotic wound associated with cutaneous anthrax)

*B. cereus-cereus*, waxen, wax-colored (refers to colonies with a typical dull or frosted-glass surface)

***Bacillus* Diseases: Clinical Summaries**

***Bacillus anthracis***

**Cutaneous anthrax:** painless papule progresses to ulceration with surrounding vesicles and then to eschar formation; painful lymphadenopathy, edema, and systemic signs may develop

**Gastrointestinal anthrax:** ulcers form at site of invasion (e.g., mouth, esophagus, intestine), leading to regional lymphadenopathy, edema, and sepsis

**Inhalation anthrax:** initial nonspecific signs followed by rapid onset of sepsis with fever, edema, and lymphadenopathy (mediastinal lymph nodes); meningeal symptoms in half the patients, and most patients with inhalation anthrax will die unless treatment is initiated immediately

***Bacillus cereus***

**Gastroenteritis:** emetic form characterized by rapid onset of vomiting and abdominal pain and a short duration; diarrheal form characterized by a longer onset and duration of diarrhea and abdominal cramps

**Ocular infections:** rapid, progressive destruction of the eye after traumatic introduction of the bacteria into the eye

**Severe pulmonary disease:** severe anthrax-like pulmonary disease in immunocompetent patients

*Bacillus cereus* Food Poisoning



**Diagnosis**

ᑏᑏ Isolation of the organism in implicated food product or nonfecal specimens (e.g., eye, wound)

***LISTERIA MONOCYTOGENES***

**Trigger Words**

Coccobacilli, \_-hemolytic, meningitis, opportunistic, foodborne illness

**Biology and Virulence**

ᑏᑏ Gram-positive coccobacilli, often arranged in pairs resembling *Streptococcus pneumoniae*

ᑏᑏ Facultative intracellular pathogen that can avoid antibody-mediated clearance

ᑏᑏ Ability to grow at 4° C, in a wide pH range, and in the presence of salt can lead to high concentrations of the bacteria in contaminated foods

ᑏᑏ Virulent strains produce cell attachment factors (internalins), hemolysins (listeriolysin O, two phospholipase C enzymes), and a protein that mediates actindirected intracellular motility (ActA)

**Epidemiology**

ᑏᑏ Isolated in soil, water, and vegetation and from a variety of animals, including humans (low-level gastrointestinal carriage)

ᑏᑏ Disease associated with consumption of contaminated food products (e.g., contaminated milk and cheese, processed meats, raw vegetables [especially cabbage]) or transplacental spread from mother to neonate; sporadic cases and epidemics occur throughout the year

ᑏᑏ Neonates, elderly, pregnant women, and patients with defects in cellular immunity are at increased risk for disease

**Diseases**

ᑏᑏ Neonatal disease can result in in utero death or multiorgan abscesses, meningitis, and septicemia

ᑏᑏ Other diseases include influenza-like symptoms, self-limited gastroenteritis, and meningitis in patients with defects in cell-mediated immunity

**Diagnosis**

ᑏᑏ Microscopy is insensitive; culture may require incubation for 2 to 3 days or enrichment at I am not sure how to make the symbol for 4 degree C as in the sentence below.

ᑏᑏ Characteristic properties include motility at room temperature, weak this should be the Greek symbol for beta-hemolysis, and growth at 4° C and at high-salt concentrations

**Treatment, Prevention, and Control**

ᑏᑏ The treatment of choice for severe disease is penicillin or ampicillin, alone or in combination with gentamicin

ᑏᑏ People at high risk should avoid eating raw or partially cooked foods of animal origin, soft cheese, and unwashed raw vegetables

***YERSINIA***

**Trigger Words**

Bubonic plague, pneumonic plague, gastroenteritis, transfusion sepsis

**Biology and Virulence**

Gram-negative, facultatively anaerobic rods

Fermenter; oxidase negative

Lipopolysaccharide consists of somatic O polysaccharide, core polysaccharide (common antigen), and lipid A (endotoxin)

*Y. pestis* is covered with a protein capsule

Some species (e.g., *Y. enterocolitica*) can grow at cold temperatures (e.g., can grow to high numbers in contaminated refrigerated food or blood products)

Virulence: refer to Box 25.2; capsule on *Y. pestis* is antiphagocytic; *Y. pestis* is resistant to serum killing; *Yersinia* with genes for adherence, cytotoxic activity, inhibition of phagocytic migration and engulfment, and inhibition of platelet aggregation

**Epidemiology**

*Y. pestis* is a zoonotic infection, with humans the accidental host; natural reservoirs include rats, squirrels, rabbits, and domestic animals

Disease is spread by flea bites or direct contact with infected tissues or person to person by inhalation of infectious aerosols from a patient with pulmonary disease

Other *Yersinia* infections are spread through exposure to contaminated food products or blood products *(Y.enterocolitica)*

Colonization with other *Yersinia* species can occur

**Diseases**

*Y. pestis* causes bubonic plague (most common) and pulmonary plague, both having a high mortality rate; other *Yersinia* species cause gastroenteritis (acute watery diarrhea or chronic diarrhea) and transfusion-related sepsis; enteric disease in children may manifest as enlarged mesenteric lymph nodes and mimic acute appendicitis

**Diagnosis**

Organisms grow on most culture media; prolonged storage at 4° C can selectively enhance isolation

**Treatment, Prevention, and Control**

*Y. pestis* infections are treated with streptomycin; tetracyclines, chloramphenicol, or trimethoprim-sulfamethoxazole can be administered as alternative therapy

Enteric infections with other *Yersinia* species are usually self-limited; if antibiotic therapy is indicated, most organisms are susceptible to broad-spectrum cephalosporins, aminoglycosides, chloramphenicol, tetracyclines, and trimethoprim-sulfamethoxazole

Plague is controlled by reduction of the rodent population and vaccination of individuals at risk

Other *Yersinia* infections are controlled by proper preparation of food products

***FRANCISELLA TULARENSIS***

**Trigger Words**

Small coccobacilli, slow growing, cysteine supplemented media, zoonotic, ulcerous-glandular, oculo-glandular, pneumonic

**Biology and Virulence**

Very small gram-negative coccobacilli (0.2 × 0.2 to 0.7 μm)

Strict aerobe; do not ferment carbohydrates

Antiphagocytic capsule

Intracellular pathogen resistant to killing in serum and by phagocytes

**Epidemiology**

Wild mammals, domestic animals, birds, and fish, and blood-sucking arthropods are reservoirs; rabbits, cats, hard ticks, and biting flies are most commonly associated with human disease; humans are accidental hosts

A total of 239 cases were seen in 2017, although the actual number may be much higher

Infectious dose is small when exposure is by arthropod, through skin, or by inhalation; large numbers of organisms must be ingested for infection by this route

**Diseases**

Clinical symptoms and prognosis determined by route of infection: ulceroglandular, oculoglandular, glandular, typhoidal, oropharyngeal, gastrointestinal, pneumonic

**Diagnosis**

Microscopy is insensitive

Culture on cysteine-supplemented media (e.g., chocolate agar, buffered charcoal yeast extract agar) is sensitive if prolonged incubation is used

fold increase in titer or single titer ≥1:160; high titers can persist for months to years

**Treatment, Prevention, and Control**

Gentamicin is the antibiotic of choice; fluoroquinolones (e.g., ciprofloxacin) and doxycycline have good activity; penicillin’s and some cephalosporins are ineffective

Disease prevented by avoiding reservoirs and vectors of infection; clothing and gloves are protective

Live attenuated vaccine available but rarely used for human disease

***Francisella tularensis***

**Ulceroglandular tularemia:** painful papule develops at the site of inoculation that progresses to ulceration; localized lymphadenopathy

**Oculoglandular tularemia:** after inoculation into the eye (e.g., rubbing eye with a contaminated finger), painful conjunctivitis

develops, with regional lymphadenopathy

**Pneumonic tularemia:** pneumonitis with signs of sepsis develops rapidly after exposure to contaminated aerosols; high mortality

unless promptly diagnosed and treated