**Lecture 4.**

**The pathogenic bacteria including genus of *Corynebacterium, Bordetella, Haemophilus, Gardnerella, Legionella, Mycobacterium, Actinomyces* and *Nocardia***

**The purpose of the lecture:** To inform them about the morpho-biological characteristics of bacteria from the genera *Corynebacterium, Bordetella, Haemophilus, Gardnerella, Legionella, Mycobacterium, Actinomyces* and *Nocardia*, pathogenicity factors, pathogenesis, clinical signs, microbiological diagnosis, specific treatment and prevention principles of diseases caused by these bacteria.

**Lecture plan:**

1. Bacteria from the genus *Corynebacterium*. Morpho-biological characteristics of diphtheria causative agent. Pathogenicity factors. Mechanism of action of C.diphtheriae toxin. Pathogenesis of diphtheria. Microbiological diagnosis of diphtheria. Specific principles of prevention and treatment.

2. *Bordetellas*, classification, morpho-biological characteristics. Pertussis agents, their pathogenicity factors. Disease pathogenesis, microbiological diagnosis, specific prevention and treatment principles.

3. Hemophilic bacteria. *H.influenzae*, morpho-biological characteristics, pathogenicity factors. Role in human pathology. *H.ducreyi*, morpho-biological characteristics and microbiological diagnosis.

4. *Legionella*, morpho-biological characteristics, pathogenicity factors. Legionellosis pathogenesis, clinical forms, microbiological diagnosis.

5. *Gardnerella vaginalis*, morpho-biological characteristics, pathogenetic characteristics, microbiological diagnosis.

6. General characteristics, classification of bacteria from the genus *Mycobacterium*.

- Tuberculosis agents, morpho-biological characteristics, pathogenicity factors. Drug resistance. Multidrug-resistant (MDR), extensively drug-resistant (XDR), pandrug-resistant (PDR). Pathogenesis of the disease. Microbiological diagnostics. Specific prevention and treatment of tuberculosis. BCG vaccine.

- The causative agent of leprosy. Morpho-biological characteristics. Clinical forms of leprosy. Microbiological diagnostics.

7. *Actinomycetes*, classification, morpho-biological characteristics, pathogenicity factors. Pathogenesis, clinical forms and microbiological diagnosis of actinomycosis.

8. *Nocardia*, their role in human pathology.

***CORYNEBACTERIUM DIPHTHERIAE***

**Trigger Words**

Diphtheria toxin, pharyngitis, vaccine

**Biology and Virulence**

ᑏᑏGram-positive pleomorphic rods

ᑏᑏ The major virulence factor is the diphtheria toxin, an A-B exotoxin; inhibits protein synthesis

**Epidemiology**

ᑏᑏ Worldwide distribution maintained in asymptomatic carriers and infected patients

ᑏᑏ Humans are the only known reservoir, with carriage in oropharynx or on skin surface

ᑏᑏ Spread person to person by exposure to respiratory droplets or skin contact

ᑏᑏ Disease observed in unvaccinated or partially immune children or adults traveling to countries with endemic disease

ᑏᑏ Diphtheria is very uncommon in the United States and other countries with active vaccination programs

**Diseases**

ᑏᑏ Etiologic agent of diphtheria: respiratory and cutaneous forms

**Diagnosis**

ᑏᑏ Microscopy is nonspecific; metachromatic granules observed in *C. diphtheriae* and other corynebacteria

ᑏᑏ Culture should be performed on nonselective (blood agar) and selective (cysteine-tellurite agar, Tinsdale medium, colistin-nalidixic agar) media

ᑏᑏ Presumptive identification of *C. diphtheriae* can be based on the presence ofcystinase and absence of pyrazinamidase;definitive identification by biochemicaltests or species-specific genesequencing

ᑏᑏ Demonstration of exotoxin is performed by Elek test or polymerase chain reaction assay

**Treatment, Prevention, and Control**

ᑏᑏ Infections treated with diphtheria antitoxin to neutralize exotoxin, penicillin or erythromycin to eliminate *C. diphtheriae* and terminate toxin production, and immunization of convalescing patients with diphtheria toxoid to stimulate protective antibodies

ᑏᑏ Administration of diphtheria vaccine and booster shots to susceptible population

*Corynebacterium coryne-,* a club; *bakterion*, a small rod (a small,club-shaped rod)

*C. diphtheriae-diphthera,* leather or skin (reference to theleathery membrane that forms initially on the pharynx)

*C. jeikeium- jeikeium* (species originally classified as group JK)

*C. urealyticum- urea*, urea; *lyticum*, lyse (capable of lysing urea; species rapidly hydrolyzes urea)

*Corynebacterium diphtheriae-* Diphtheria (respiratory, cutaneous); pharyngitis and endocarditis (nontoxigenic strains)

*C. jeikeium* (group JK) Septicemia, endocarditis, wound infections, foreign body (catheter, shunt, prosthesis) infections

*C. urealyticum* Urinary tract infections (including pyelonephritis and alkaline-encrusted cystitis), septicemia, endocarditis, wound infections

***BORDETELLA PERTUSSIS***

**Trigger Words**

Slow growing, whooping cough, pertussis toxin, person to person, vaccination

**Biology and Virulence**

ᑏ Very small gram-negative coccobacilli

ᑏᑏ Non-fermentative but can oxidize amino acids as an energy source

ᑏᑏ Strict aerobe

ᑏᑏ Growth in vitro requires prolonged incubation in media supplemented with

charcoal, starch, blood, or albumin

ᑏᑏ Adherence to eukaryotic cells mediated by pertactin, filamentous hemagglutinin, and fimbria; localized tissue destruction mediated by dermonecrotic toxin and tracheal cytotoxin; systemic toxicity produced by pertussis toxin

**Epidemiology**

ᑏᑏ Pertussis is a human disease with no known animal or environmental reservoir

ᑏᑏWorldwide distribution with a high prevalence in unvaccinated populations

ᑏᑏChildren younger than 1 year are at greatest risk for infection and mortality

ᑏᑏ In vaccinated populations, disease is observed in older children and young adults

ᑏᑏUnvaccinated individuals are at greatest risk for disease

ᑏᑏDisease spread person to person by infectious aerosols

**Diseases**

ᑏᑏ Pertussis characterized by three stages: catarrhal, paroxysmal, and convalescent

ᑏᑏ Most severe disease is in unvaccinated individuals, particularly children

**Diagnosis**

ᑏᑏMicroscopy is insensitive and nonspecific

ᑏᑏCulture is specific but insensitive

ᑏᑏNucleic acid amplification tests are the most sensitive and specific tests

ᑏᑏDetection of immunoglobulin (Ig)G or IgA can be used as a confirmatory test

**Treatment, Prevention, and Control**

ᑏᑏ Treatment with macrolide (i.e., azithromycin, clarithromycin) is effective in eradicating organisms and reducing length of infectious stage

ᑏᑏ Azithromycin is used for prophylaxis

ᑏᑏ Vaccines containing inactivated pertussis toxin, filamentous hemagglutinin,

and pertactin are effective

ᑏᑏ Pediatric vaccine administered in five doses (at ages 2, 4, 6, and 15 to 18 months, and between ages 4 and 6 years); adult vaccine administered at ages 11 to 12 years and between 19 to 65 years

***HAEMOPHILUS***

**Trigger Words**

Coccobacilli, type b, PRP, meningitis, chancroid, vaccine

**Biology and Virulence**

ᑏ Small, pleomorphic, gram-negative rods or coccobacilli

ᑏᑏ Facultative anaerobes, fermentative

ᑏᑏMost species require X and/or V factor for growth

ᑏᑏ*Haemophilus influenzae* subdivided serologically (types a to f) and biochemically (biotypes I to VIII)

ᑏᑏ*H. influenzae* type b is clinically most virulent (with PRP in capsule)

ᑏᑏ*Haemophilus* adhere to host cells via pili and nonpilus structures

**Epidemiology**

ᑏᑏ*Haemophilus* species commonly colonized in humans, although encapsulated

*Haemophilus* species, particularly *H.influenzae* type b, are uncommon members

of normal flora

ᑏᑏDisease caused by *H. influenzae* type b was primarily a pediatric problem; eliminated in immunized populations

ᑏᑏ*H. ducreyi* disease is uncommon in the United States

ᑏᑏWith the exception of *H. ducreyi,* which is spread by sexual contact, most *Haemophilus* infections are caused by the patient’s oropharyngeal flora (endogenous infections)

ᑏᑏ Patients at greatest risk for disease are those with inadequate levels of protective antibodies, those with depleted complement, and those who have undergone splenectomy

**Diagnosis**

ᑏᑏMicroscopy is a sensitive test for detecting *H. influenzae* in cerebrospinal fluid,

synovial fluid, and lower respiratory specimens but not from other sites

ᑏᑏCulture is performed using chocolate agar

ᑏᑏAntigen tests are specific for *H. influenzae* type b; therefore these tests are nonreactive for infections caused by other organisms

**Treatment, Prevention, and Control**

ᑏᑏ*Haemophilus* infections are treated with broad-spectrum cephalosporins, amoxicillin, azithromycin, doxycycline, or fluoroquinolones; susceptibility to

amoxicillin should be documented

ᑏᑏActive immunization with conjugated PRP vaccines prevents most *H.influenzae* type b infections

**Summaries** Clinically Significant Organisms *PRP,* Polyribitol phosphate.

 *Haemophilus - haemo,* blood; *hilos,* lover (“blood lover”; requires blood for growth on agar media)

*H. influenzae -* Originally thought to be the cause of influenza

*H. aegyptius - aegyptius,* Egyptian (observed by Robert Koch in 1883 in exudates from Egyptians with conjunctivitis)

*H. ducreyi -* Named after the bacteriologist Ducrey, who first isolated this organism

*Aggregatibacter aggregare, -* to come together; *bacter,* bacterial rod; rod-shaped bacteria that aggregate or clump together

*A. actinomycetemcomitans - comitans,* accompanying (“accompanying an

actinomycete”; isolates are frequently associated with *Actinomyces*)

*A. aphrophilus aphros, -* foam; *philos,* loving (“foam loving”)

*Pasteurella -* Named after Louis Pasteur

*P. multocida - multus,* many; *cidus,* to kill (“many-killing”; pathogenic for many species of animals)

*P. canis - canis,* dogs (isolated from the mouths of dogs)

***Haemophilus influenzae***

**Meningitis:** a disease primarily of unimmunized children characterized by fever, severe headache, and systemic signs

**Epiglottitis:** a disease primarily of unimmunized children characterized by initial pharyngitis, fever, and difficulty breathing, and progressing to cellulitis and swelling of the supraglottic tissues, with obstruction of the airways possible

**Pneumonia:** inflammation and consolidation of the lungs observed primarily in the elderly with underlying chronic pulmonary disease; typically caused by nontypeable strains

***Haemophilus aegyptius***

**Conjunctivitis:** an acute purulent conjunctivitis (“pink eye”)

***Haemophilus ducreyi***

**Chancroid:** sexually transmitted disease characterized by a tender papule with an erythematous base that progresses to painful ulceration with associated lymphadenopathy

***Aggregatibacter actinomycetemcomitans***

**Endocarditis:** responsible for subacute form of endocarditis in patients with underlying damage to the heart valve

***Aggregatibacter aphrophilus***

**Endocarditis:** as with *A. actinomycetemcomitans*

**Pasteurella multocida**

**Bite wound:** most common manifestation is infected cat or dog bite wound; particularly common with cat bites because the wounds are deep and difficult to disinfect

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***GARDNERELLA VAGINALIS***

*G vaginalis* is a serologically distinct organism isolated from the normal female genitourinary tract and also associated with vaginosis, so named because inflammatory cells are not present. In wet smears, this “nonspecific” vaginitis, or **bacterial vaginosis**, yields “clue cells,” which are vaginal epithelial cells covered with many Gram-variable bacilli, and there is an absence of other common causes of vaginitis such as trichomonads or yeasts. Vaginal discharge often has a distinct

“fishy” odor and contains many anaerobes in addition to *G vaginalis*. The pH of the vaginal secretions is greater than 4.5 (normal pH is <4.5). The vaginosis attributed to this organism is suppressed by metronidazole, suggesting an association with anaerobes. Oral metronidazole is generally curative.

Bacterial vaginosis is a common vaginal condition of women of reproductive age. It is associated with premature rupture of membranes and preterm labor and birth. Bacterial vaginosis has a complex microbiology; one organism, *Gardnerella vaginalis*, has been most specifically associated with the disease process.

***BRUCELLA***

**Trigger Words**

Small coccobacilli, slow growing, zoonotic, undulant fever

**Biology and Virulence**

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

ᑏᑏ Strict aerobe; does not ferment carbohydrates

ᑏᑏ Requires complex media and prolonged incubation for in vitro growth

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

ᑏᑏ Smooth colonies associated with virulence

**Epidemiology**

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

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

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

ᑏᑏ Vaccination of herds has controlled disease in the United States

ᑏᑏ Most disease in the United States is reported in California and Texas in travelers from Mexico

ᑏᑏ Individuals at greatest risk for disease are people who consume unpasteurized

dairy products, people in direct contact with infected animals, and laboratory workers

**Diagnosis**

ᑏᑏMicroscopy is insensitive

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

ᑏᑏ 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**

ᑏᑏ 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

ᑏᑏHuman 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

***FRANCISELLA TULARENSIS***

**Trigger Words**

Small coccobacilli, slow growing, cysteine supplemented media, zoonotic, ulceroglandular, oculoglandular, pneumonic

**Biology and Virulence**

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

ᑏᑏ Strict aerobe; do not ferment carbohydrates

ᑏᑏ Antiphagocytic capsule

ᑏᑏ Intracellular pathogen resistant to killing in serum and by phagocytes

**Epidemiology**

ᑏᑏ 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

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

ᑏᑏ 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**

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

**Diagnosis**

ᑏᑏMicroscopy is insensitive

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

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

**Treatment, Prevention, and Control**

ᑏᑏGentamicin is the antibiotic of choice; fluoroquinolones (e.g., ciprofloxacin) and doxycycline have good activity; penicillins and some cephalosporins are ineffective

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

ᑏᑏ Live attenuated vaccine available but rarely used for human disease

***LEGIONELLA PNEUMOPHILA***

**Trigger Words**

Poor-staining slender rods, legionnaires disease, Pontiac fever, contaminated water, BCYE agar

**Biology and Virulence**

ᑏᑏ Slender, pleomorphic, non-fermentative, gram-negative rods

ᑏᑏ Stains poorly with common reagents

ᑏᑏNutritionally fastidious, with requirement for L-cysteine and enhanced growth with iron salts

ᑏᑏCapable of replication in alveolar macrophages (and in amebae in nature)

ᑏᑏ Prevents phagolysosome fusion

**Epidemiology**

ᑏᑏ Capable of sporadic, epidemic, and nosocomial infections

ᑏᑏ Commonly found in natural bodies of water, cooling towers, condensers, and water systems (including hospital systems)

ᑏᑏ Estimated to be as many as 18,000 cases of infection in United States annually

ᑏᑏ Patients at high risk for symptomatic disease include patients with compromised pulmonary function and patients with decreased cellular immunity (particularly transplant patients)

**Diseases**

ᑏᑏ Responsible for legionnaires disease and Pontiac fever

**Diagnosis**

ᑏᑏMicroscopy is insensitive

ᑏᑏAntigen tests are sensitive for *L. pneumophila* serogroup 1 but have poor sensitivityfor other serogroups and species

ᑏᑏCulture on buffered charcoal yeast extract agar is the diagnostic test of choice

ᑏᑏ Seroconversion must be demonstrated; this can take as long as 6 months to develop; positive serology may persist for months

ᑏᑏNucleic acid amplification assays are as sensitive and specific as culture

**Treatment, Control, and Prevention**

ᑏᑏ Macrolides (e.g., azithromycin, clarithromycin) or fluoroquinolones (e.g., ciprofloxacin, levofloxacin) are the treatment of choice

ᑏᑏ Decrease environmental exposure to reduce risk of disease

ᑏᑏ For environmental sources associated with disease, treat with hyperchlorination, superheating, or copper-silver ionization

**Important Miscellaneous Gram-Negative Rods**

*Bordetella -* Named after Jules Bordet, who first isolated the organism responsible for pertussis

*B. pertussis - per,* very or severe; *tussis,* cough (a severe cough)

*B. parapertussis - para,* resembling (resembling pertussis)

*B. bronchiseptica - bronchus,* the trachea; *septicus,* septic (an infected bronchus)

*B. holmesii -* Named after the microbiologist Barry Holmes

*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)

*Cardiobacterium hominis - cardia,* heart; *bakterion,* small rod; *hominis,* of man (small rod of the hearts of men; refers to the predilectionof this bacterium to cause endocarditis in humans)

*Francisella -* Named after the American microbiologist Edward Francis, who first described tularemia

*F. tularensis* subsp. *tularensis* (type A) - *tularensis,* pertaining to Tulare County, California, in which the disease was first described

*F. tularensis* subsp. *holarctica* (type B) - *holos,* whole; *arctos,* northern regions (reference to distribution in the arctic or northern regions)

*F. tularensis* subsp*. mediaasiatica - media,* middle; *asiatica,* Asian (pertaining to middle Asia)

*F. tularensis* subsp. *novicida - novus,* new; *cida,* to cut (a “new killer”)

*Legionella pneumophila - Legionella,* first recognized outbreak was at an American Legion convention; *pneumôn,* lung; *phila,* loving; *pneumophila,* lung-loving.

*Streptobacillus moniliformis - streptos,* twisted or curved; *bacillus,* rod; *monile,* necklace; *forma,* shape (twisted, necklace-shaped bacillus; refers to the pleomorphic morphology of the bacteria)

**Clinical Summaries**

***Bordetella pertussis***

**Pertussis:** after a 7- to 10-day incubation period, disease is characterized by the catarrhal stage (resembles the common cold), progressing to the paroxysmal stage (repetitive coughs followed by inspiratory whoops), then the convalescence stage (diminishing paroxysms and secondary complication)

***Bordetella parapertussis:*** produces a milder form of pertussis

***Bordetella bronchiseptica:*** primarily a respiratory disease of animals but can cause bronchopneumonia in humans

***Bordetella holmesii:*** uncommon cause of sepsis

***Brucella***

**Brucellosis:** initial nonspecific symptoms of malaise, chills, sweats, fatigue,

myalgias, weight loss, arthralgias, and fever; can be intermittent

(undulant fever); can progress to systemic involvement (gastrointestinal

tract, bones or joints, respiratory tract, other organs)

***Brucella melitensis:*** severe, acute systemic disease, with complications common

***Brucella abortus:*** mild disease with suppurative complications

***Brucella suis:*** chronic, suppurative, destructive disease

***Brucella canis:*** mild disease with suppurative complications

***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

***Legionella pneumophila***

**Pontiac fever:** self-limited febrile disease with chills, myalgias, malaise, and headache but no evidence of pneumonia

**Legionnaires disease:** severe pneumonia with acute onset of fever, chills, nonproductive cough, and headache progressing to multilobar consolidation of the lungs and multiorgan failure

**Clinical presentation of *Bordetella pertussis* disease.**



***MYCOBACTERIUM TUBERCULOSIS***

**Trigger Words**

Acid-fast, lipid-rich cell wall, intracellular, purified protein derivative (PPD), drug-resistant

**Biology and Virulence**

ᑏ Weakly gram-positive, strongly acid-fast, aerobic rods

ᑏᑏ Lipid-rich cell wall, making the organism resistant to traditional stains, disinfectants, detergents, common antibacterial antibiotics, and host immune response

ᑏᑏ Capable of intracellular growth in alveolar macrophages

ᑏᑏ Disease primarily from host response to infection

**Epidemiology**

ᑏᑏ Worldwide; one-fourth of the world’s population is infected with this organism

ᑏᑏ A total of 10.4 million new cases each year and 1.6 million deaths

ᑏᑏ Disease most common in India, Pakistan, sub-Saharan Africa, South Africa, China, and Eastern Europe

ᑏᑏ 9272 new cases in the United States in 2016

ᑏᑏ Populations at greatest risk for disease are foreign born or travelers to endemic countries, immunocompromised patients (particularly those with HIV infection), drug or alcohol abusers, homeless persons, and individuals exposed to diseased patients

ᑏᑏ Humans are the only natural reservoir

ᑏᑏ Person-to-person spread by infectious aerosols

**Diseases**

ᑏᑏ Primary infection is pulmonary

ᑏᑏ Dissemination to anybody site occurs most commonly in immunocompromised patients

**Diagnosis**

ᑏᑏ Tuberculin skin test and interferon (IFN)-γ release tests are sensitive markers for exposure to the organism

ᑏ Microscopy and culture are sensitive and specific

ᑏᑏ Nucleic acid amplification tests are important where culture is not available and microscopy is inaccurate for detection of *M. tuberculosis* in clinical specimens

ᑏᑏ Identification most commonly made using species-specific molecular probes, sequencing, or mass spectrometry

**Treatment, Prevention, and Control**

ᑏᑏ Prolonged treatment with multiple drugs is required to prevent development of drug-resistant strains

ᑏᑏ Isoniazid (INH), ethambutol, pyrazinamide, and rifampin for 2 months followed by 4-6 months of INH and rifampin or alternative combination drugs

ᑏᑏ Prophylaxis for exposure to tuberculosis can include INH for 6-9 months or daily rifampin for 4 months; pyrazinamide and ethambutol or levofloxacin are used for 6-12 months after exposure to drugresistant *M. tuberculosis*

ᑏᑏ Immunoprophylaxis with bacillus Calmette-Guérin (BCG) in endemic countries

ᑏᑏ Control of disease through active surveillance, prophylactic and therapeutic intervention, and careful case monitoring

***MYCOBACTERIUM LEPRAE***

**Trigger Words**

Acid-fast, leprosy, nonculturable, skin test

**Biology and Virulence**

ᑏᑏ Weakly gram-positive, strongly acid-fast rods

ᑏᑏ Lipid-rich cell wall

ᑏᑏUnable to be cultured on artificial media

ᑏᑏ Disease primarily from host response to infection

**Epidemiology**

ᑏᑏ 200,000 new cases were reported in 2016, with most cases in India, Brazil, and Indonesia

ᑏᑏ 178 new cases reported in the United States in 2015

ᑏᑏ Lepromatous form of disease, but not the tuberculoid form, is highly infectious

ᑏᑏ Person-to-person spread by prolonged exposure to respiratory secretions of an untreated, infected person

**Diseases**

ᑏᑏ Tuberculoid (paucibacillary) and lepromatous (multibacillary) forms of leprosy

**Diagnosis**

ᑏᑏ Microscopy is sensitive for the lepromatous form but not the tuberculoid form

ᑏᑏ Skin testing is required to confirm tuberculoid leprosy

ᑏᑏCulture is not useful

**Treatment, Prevention, and Control**

ᑏᑏ Tuberculoid form is treated with rifampicin and dapsone for 6 months; clofazimine is added to this regimen for treatment of the lepromatous form, and therapy is extended to a minimum of 12 months

ᑏᑏ Disease is controlled through prompt recognition and treatment of infected people

***MYCOBACTERIUM AVIUM* COMPLEX**

**Trigger Words**

Acid-fast, pulmonary infections, AIDS, prophylaxis

**Biology and Virulence**

ᑏᑏ Weakly gram-positive, strongly acid-fast aerobic rods

ᑏᑏ Lipid-rich cell wall

ᑏᑏ Disease primarily from host response to infection

**Epidemiology**

ᑏ Worldwide distribution, but disease is seen most commonly in countries where tuberculosis is less common

ᑏᑏ Acquired primarily through ingestion of contaminated water or food; inhalation of infectious aerosols is believed to play a minor role in transmission

ᑏᑏ Patients at greatest risk for disease are those who are immunocompromised (particularly patients with acquired immunodeficiency syndrome [AIDS]) and those with long-standing pulmonary disease

**Diseases**

ᑏᑏ Disease includes asymptomatic colonization, chronic localized pulmonary disease, solitary nodule, or disseminated disease, particularly in patients with AIDS

**Diagnosis**

ᑏᑏ Microscopy and culture are sensitive and specific

**Treatment, Prevention, and Control**

ᑏᑏ Infections treated for prolonged period with clarithromycin or azithromycin combined with ethambutol and rifabutin

ᑏᑏ Prophylaxis in AIDS patients who have a low CD4 cell count consists of clarithromycin or azithromycin or rifabutin, and such treatment has greatly reduced the incidence of disease

***NOCARDIA***

**Trigger Words**

Modified acid-fast, filamentous, bronchopulmonary or cutaneous disease, opportunistic

**Biology and Virulence**

ᑏᑏ Gram-positive, partially acid-fast, filamentous rods; cell wall with mycolic acid

ᑏᑏ Strict aerobe capable of growth on most nonselective bacteria, fungal, and mycobacterial media; however, prolonged incubation (2 days or more) may be required

ᑏᑏ Virulence associated with ability to avoid intracellular killing

ᑏᑏ Catalase and superoxide dismutase inactivate toxic oxygen metabolites (e.g.,hydrogen peroxide, superoxide)

ᑏᑏ Cord factor prevents intracellular killing in phagocytes by interfering with fusion of phagosomes with lysosomes

**Epidemiology**

ᑏᑏ Worldwide distribution in soil rich with organic matter

ᑏᑏ Exogenous infections acquired by inhalation (pulmonary) or traumatic introduction (cutaneous)

ᑏᑏ Opportunistic pathogen causing disease most commonly in immunocompromised patients with T-cell deficiencies (transplant recipients, patients with malignancies, patients infected with the human immunodeficiency virus [HIV], patients receiving corticosteroids)

**Diseases**

ᑏᑏ Primary disease most commonly bronchopulmonary (e.g., cavitary disease) or primary cutaneous infections (e.g.,mycetoma, lymphocutaneous infection, cellulitis, subcutaneous abscesses)

ᑏᑏ Dissemination most commonly to central nervous system (e.g., brain abscesses) or skin

**Diagnosis**

ᑏᑏ Microscopy is sensitive and relatively specific when branching, partially acidfast organisms are seen

ᑏᑏ Culture is slow, requiring incubation for up to 1 week; selective media (e.g., buffered charcoal yeast extract agar) may be required for isolating *Nocardia* in mixed cultures

ᑏᑏ Identification at the genus level can be made by the microscopic and macroscopic appearances (branching, weakly acid-fast rods forming colonies with aerial hyphae)

ᑏᑏ Identification at the species level requires genomic analysis for most isolates or mass spectrometry

**Treatment, Prevention, and Control**

ᑏᑏ Infections are treated with antibiotics and proper wound care

ᑏᑏ Trimethoprim-sulfamethoxazole (TMP-SMX) used as initial empirical therapy for cutaneous infections in immunocompetent patients; therapy for severe infections and cutaneous infections in immunocompromised patients should include TMP-SMX plus amikacin for pulmonary or cutaneous infections and TMP-SMX plus imipenem or a cephalosporin for central nervous system infections; prolonged treatment (up to 12 months) is recommended

ᑏᑏ Exposure cannot be avoided because nocardiae are ubiquitous

***Important Acid-Fast Bacteria***

*Mycobacterium - myces,* a fungus; *bakterion,* a small rod (fungus-like rod)

*M. abscessus - abscessus,* of abscesses (causes abscess formation)

*M. avium - avis,* of birds (causes tuberculosis-like illness in birds)

*M. chelonae - chelone,* a tortoise (initial source)

*M. fortuitum - fortuitum,* casual, accidental (refers to the fact that this is an opportunistic pathogen)

*M. haemophilum - haema,* blood; *philos,* loving (blood loving; refers to requirement for blood or hemin for in vitro growth)

*M. intracellulare - intra,* within; *cella,* small room (within cells; refers to the intracellular location of this and all mycobacteria)

*M. kansasii - kansasii,* of Kansas (where the organism was originally isolated)

*M. leprae lepra,* of leprosy (the cause of leprosy)

*M. marinum - marinum,* of the sea (bacterium associated with contaminated freshwater and saltwater)

*M. tuberculosis - tuberculum,* a small swelling or tubercle; *osis* (characterized by tubercles; refers to the formation of tubercles in the lungs of infected patients)

*Nocardia* Named after the French veterinarian Edmond No card

*Rhodococcus - rhodo,* rose or red colored; *coccus,* berry (red colored coccus)

*Gordonia -* Named after the American microbiologist Ruth Gordon

*Tsukamurella -* Honoring the Japanese microbiologist Michio Tsukamura, who first described the original isolate of this genus

***Classification of Selected Acid-Fast Bacteria Pathogenic for Humans***

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***Clinical and Immunologic Manifestations of Leprosy***

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***Diseases of Selected Pathogenic Actinomycetes***

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**Nocardiosis: Clinical Summaries**

**Bronchopulmonary disease:** indolent pulmonary disease with necrosis and abscess formation; dissemination to central nervous

system or skin is common

**Mycetoma:** chronic destructive progressive disease, generally of extremities, characterized by suppurative granulomas, progressive

fibrosis and necrosis, and sinus tract formation

**Lymphocutaneous disease:** primary infection or secondary spread to cutaneous site, characterized by chronic granuloma formation and erythematous subcutaneous nodules, with eventual ulcer formation

**Cellulitis and subcutaneous abscesses:** granulomatous ulcer formation with surrounding erythema but minimal or no involvement of the draining lymph nodes

**Brain abscess:** chronic infection with fever, headache, and focal deficits related to the location of the slowly developing abscess(es)