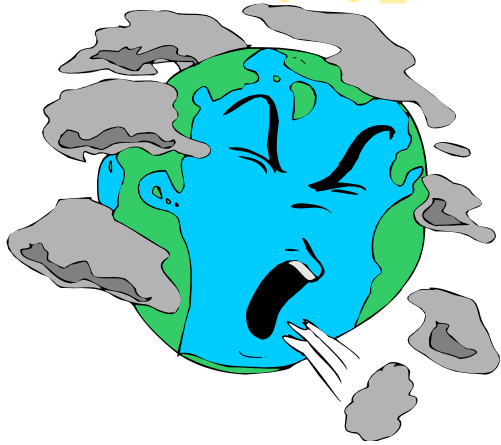


THE BORDETELLAE



Msc safaa abdul ameer

THE BORDETELLAE

There are several species of *Bordetella* :

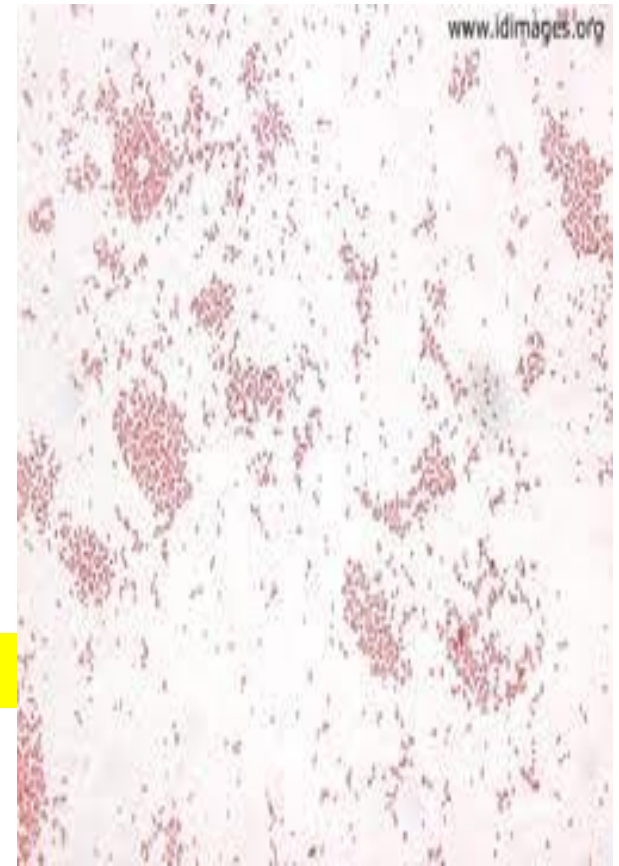
1- *Bordetella pertussis*, a highly communicable and important pathogen of humans, causes whooping cough (pertussis).

2- *Bordetella parapertussis* It can cause a milder pertussis-like disease in humans, but *Bordetella pertussis* is the most serious human pathogen in this genus



Bordetella pertussis

- The organisms are minute, gram-negative coccobacilli
- A capsule is present.
- aerobic, non-spore forming.
- Specific to Humans
- Colonizes the respiratory tract
- *B. pertussis* invades its human host through entry into the respiratory tract where it colonizes to cause whooping cough, also known as pertussis, which was at one time a very common and potentially life threatening infection for children



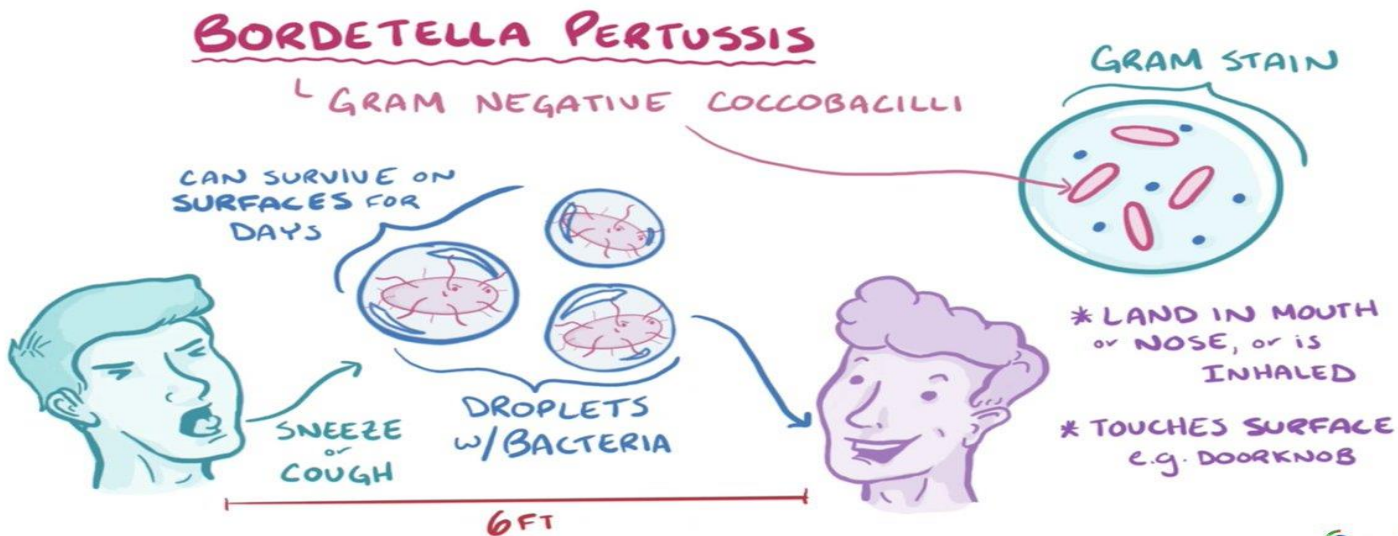
Spread

- Pertussis is highly contagious
- Pertussis is generally transmitted from person to person via respiratory droplets, but direct contact with respiratory secretions from infected individuals may also lead to the disease.
- 90% of nonimmune household contacts acquire the disease
- Adolescents and adults are the major source of infection in unvaccinated children
- Infants and young children are infected by older siblings who have mild to asymptomatic disease.





Spread

Freshly contaminated articles (such as clothing) from the infected person can also contain infectious respiratory secretions, allowing pertussis to be passed indirectly from the infected person to a susceptible host who comes in direct contact with these items.



Pathogenesis, Pathology and Virulence factors

- *B. pertussis* invades the human host through the inhalation of respiratory droplets  adheres to the ciliated epithelium of the respiratory tract but do not invade the underlying tissue.
- It was believed that *B. pertussis* was an entirely extracellular pathogen, but it has recently been shown that *B. pertussis* can invade aveolar macrophages.
-  This pathogen can multiply rapidly on the mucosal membrane of the upper respiratory tract, producing adhesions that allow it to colonize by adhering to the ciliated epithelium.

Pathogenesis, Pathology and Virulence factors



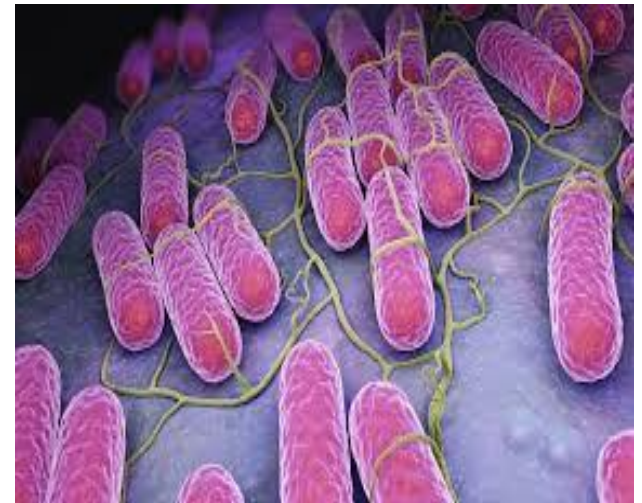
- *B. pertussis* must survive within the hostile environment of its human host by producing a variety of virulence factors in an attempt to evade or counter the immune system of the host as it tries to clear the infection.
- *B. pertussis* survives for only brief periods outside the human host. There are no vectors.
- Transmission is largely by the respiratory route from early cases and possibly via carriers.

Pathogenesis, Pathology and Virulence factors

- *B pertussis* produces a number of **virulence** factors that are involved in the pathogenesis of disease. Adhesions such as:
 1. filamentous hemagglutinin
 2. agglutinogens
 3. peractin
 4. fimbriae
- a number of toxins including:**
 - a. pertussis toxin
 - b. adenylate cyclase toxin (ACT)
 - c. tracheal cytotoxin
 - d. dermonecrotic toxin (DNT)
 - e. heat-labile toxin
 - f. lipopolysaccharide coat that acts as an endotoxin and can aid colonization by agglutinating human cells.

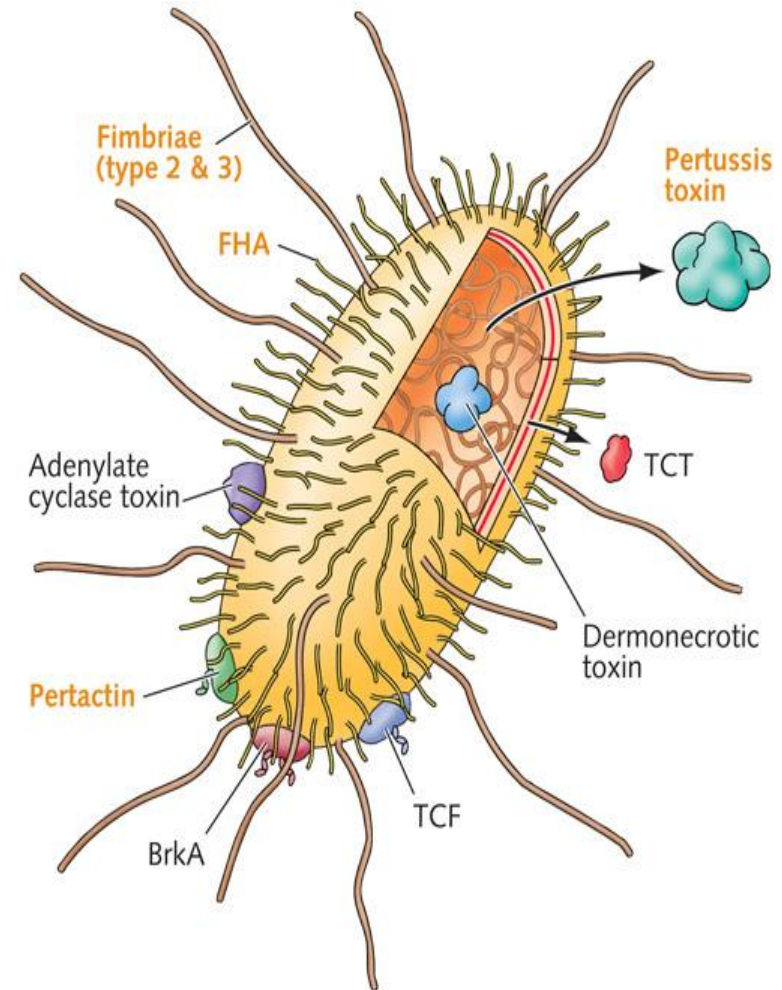
Pathogenesis, Pathology and Virulence factors

- **Filamentous hemagglutinin**, a large surface protein, and fimbriae (surface appendages) mediate adhesion to ciliated epithelial cells and are essential for tracheal colonization.
- **Pertussis toxin** (a classic A/B structure toxin) promotes lymphocytosis, sensitization to histamine, and enhanced insulin secretion that disrupts function of signal transduction in many cell types.
- The filamentous hemagglutinin and pertussis toxin are secreted proteins and are found outside of the *B pertussis* cells.

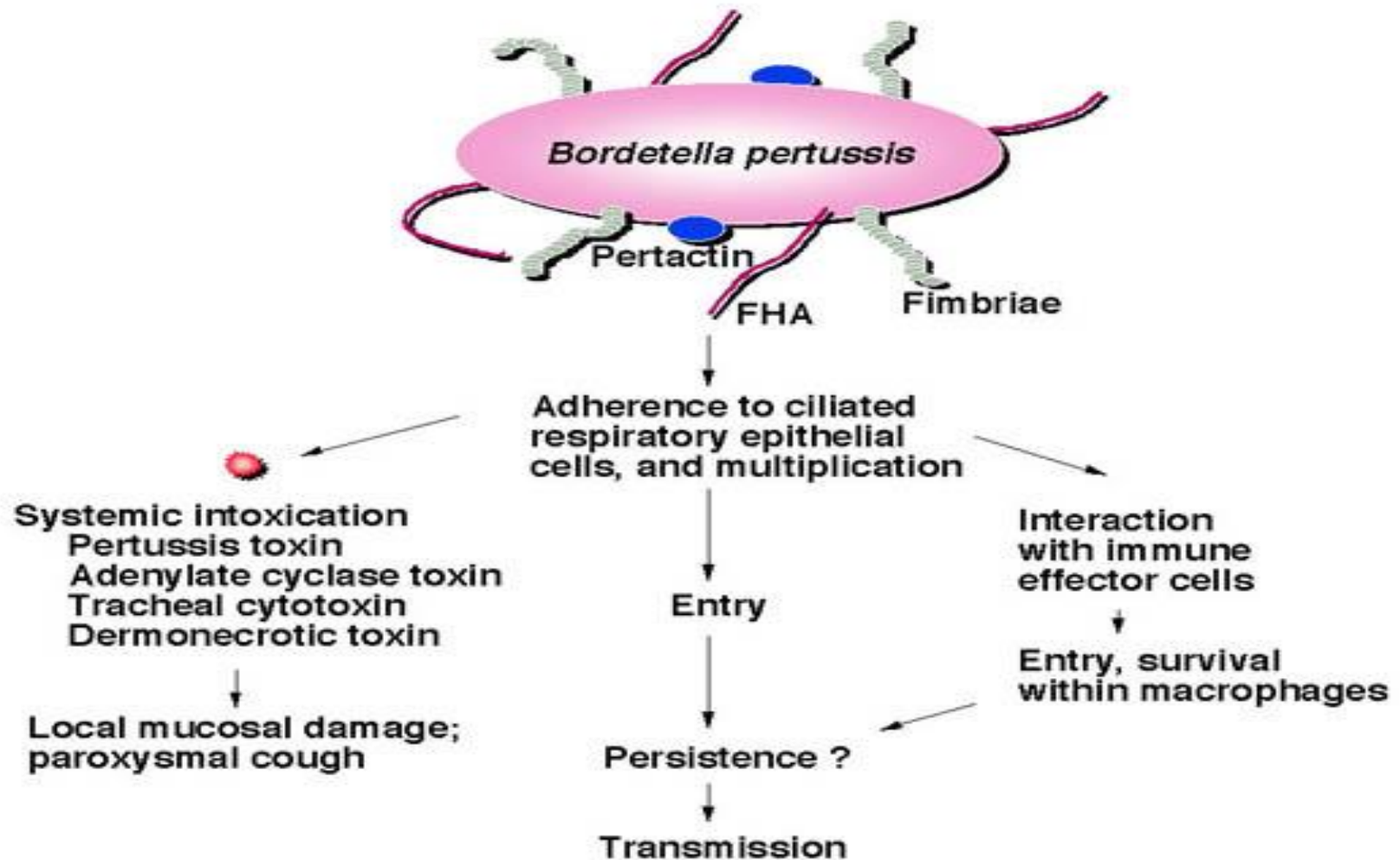


Pathogenesis, Pathology and Virulence factors






- Adenylate cyclase toxin (ACT), dermonecrotic toxin (DNT), and hemolysin. ACT is an important virulence factor that inhibits phagocyte function but the role of DNT in pertussis is unknown.
- The tracheal cytotoxin kills respiratory epithelial cells in vitro.
- The lipooligosaccharide in the cell wall may also be important in causing damage to the epithelial cells of the upper respiratory tract.



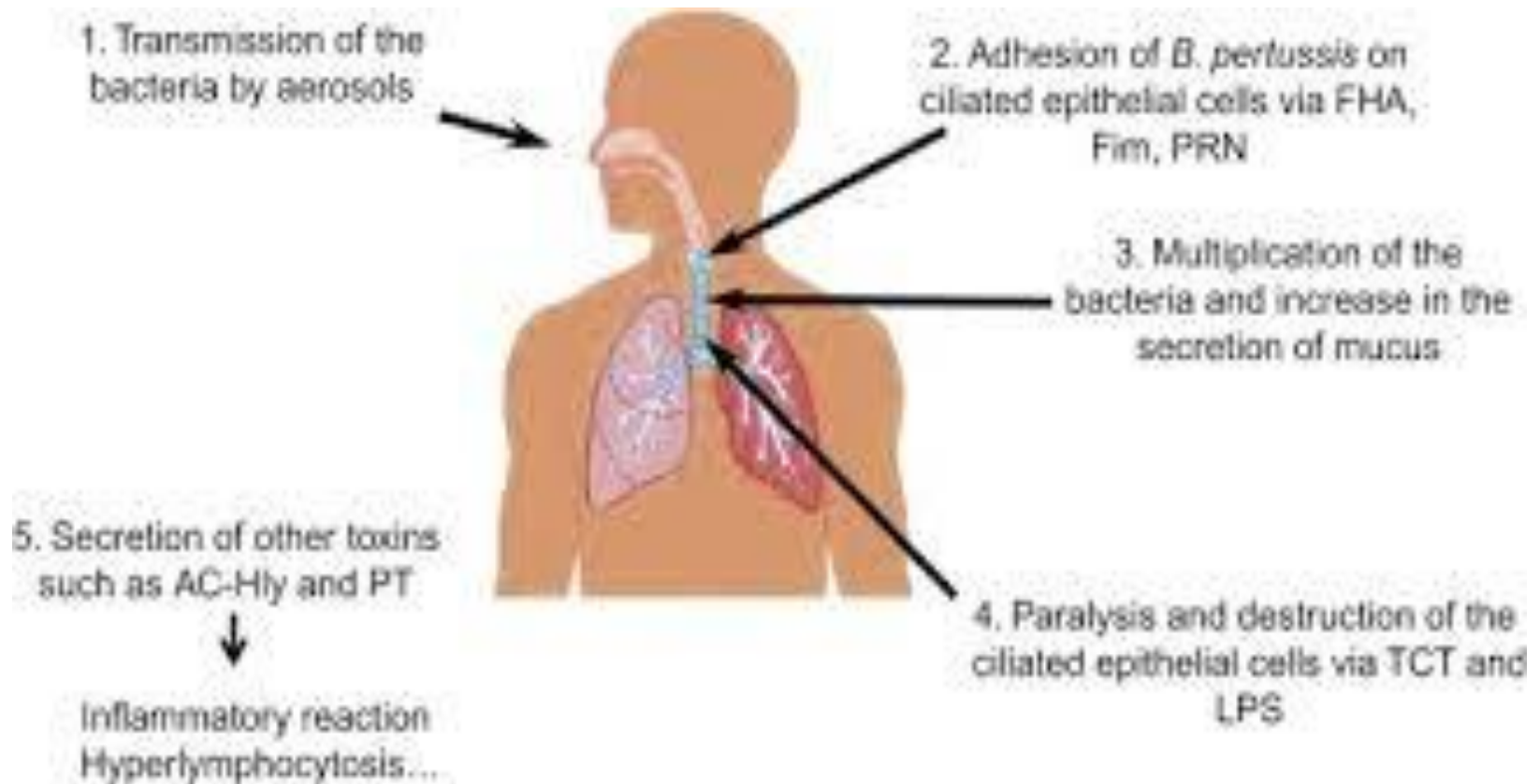
Pathogenesis of *Bordetella pertussis*



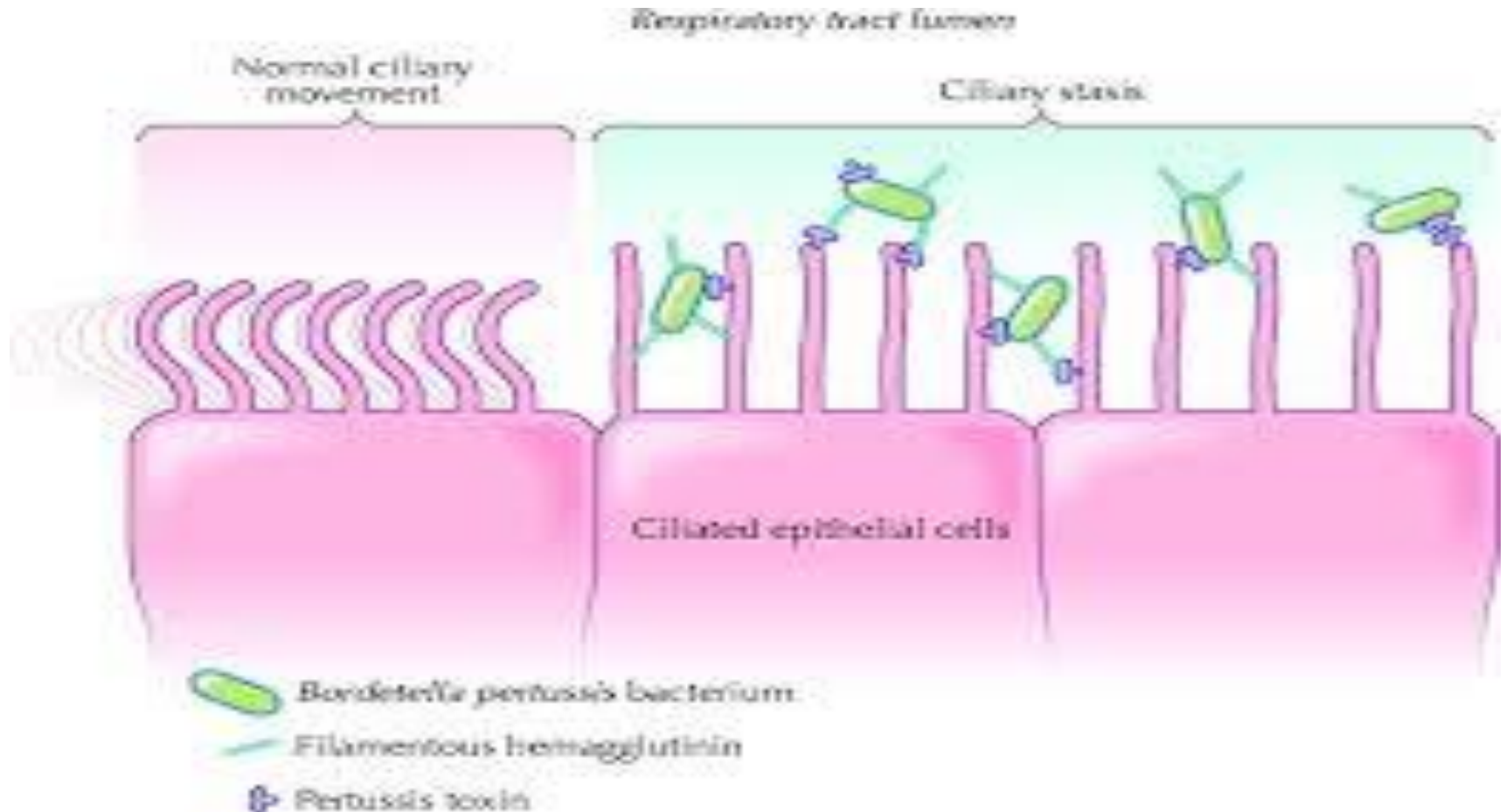
Pathogenesis, Pathology and Virulence factors

- The organism **adheres** to and  **multiplies** rapidly on the epithelial surface of the trachea and bronchi and  **interferes** with ciliary action. The bacteria  **liberate** the toxins and substances that  **irritate** surface cells, **causing** coughing and marked lymphocytosis. Later,  there may be **necrosis** of parts of the epithelium and polymorphonuclear infiltration, with peribronchial inflammation and interstitial pneumonia.

Pathogenesis, Pathology and Virulence factors

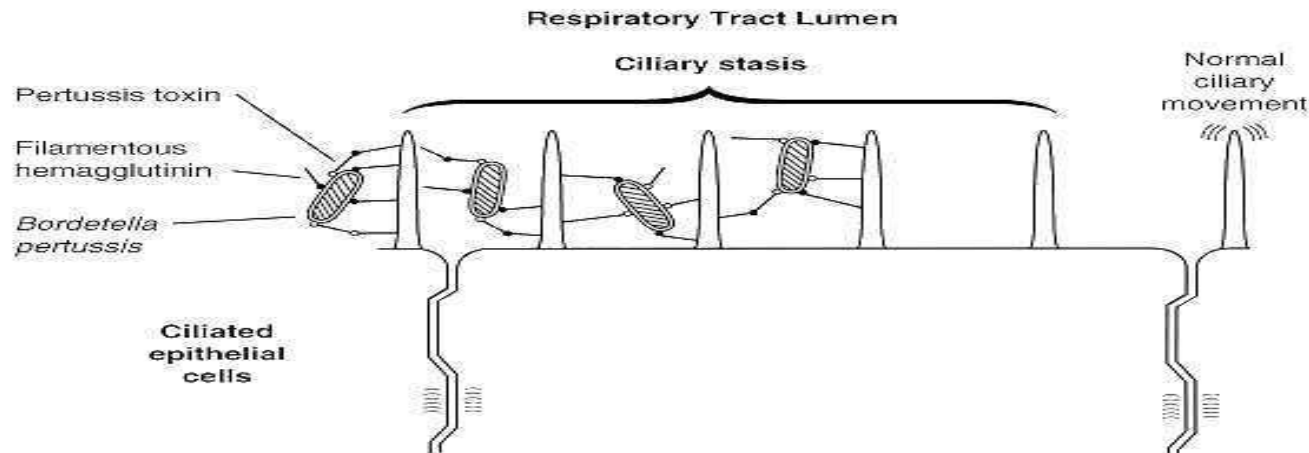


Pathogenesis, Pathology and Virulence factors



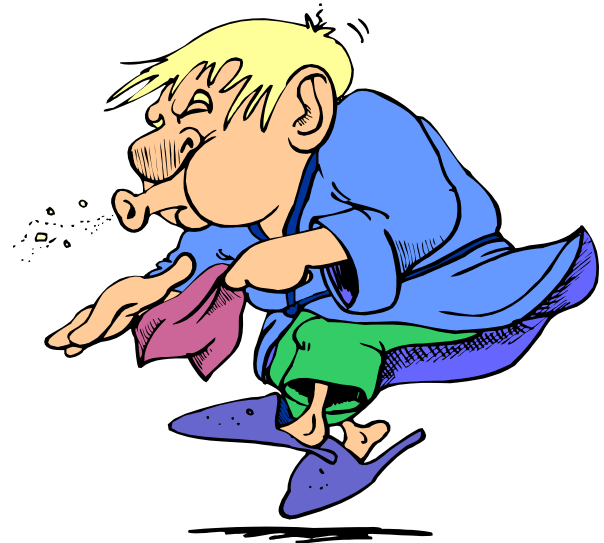
Pathogenesis, Pathology and Virulence factors

- **Secondary invaders** such as staphylococci or *H influenzae* may give rise to bacterial pneumonia.
- **Obstruction of the smaller bronchioles** by mucous plugs results in diminished oxygenation of the blood. This probably contributes to the frequency of convulsions in infants with whooping cough.



Clinical Symptoms

- After an incubation period of about 2 weeks, the “**catarrhal stage**” develops, with mild coughing and sneezing.
- During this stage, large numbers of organisms are sprayed in droplets, and the patient is highly infectious but not very ill.



Clinical Symptoms

- During the “**paroxysmal**” stage, the cough develops its explosive character and the characteristic “whoop” upon inhalation. This leads to rapid exhaustion and may be associated with vomiting, cyanosis, and convulsions. The “whoop” and major complications occur predominantly in infants. Paroxysmal coughing predominates in older children and adults.



Clinical Symptoms

- The white blood count is high (16,000-30,000/ μ L), with an absolute lymphocytosis.
- Convalescence is slow. *B pertussis* is a common cause of prolonged cough in adults.

ends with the **convalescence stage** is characterized by fewer paroxysmal coughing episodes and usually disappears in 2-3 weeks, but may continue for months.

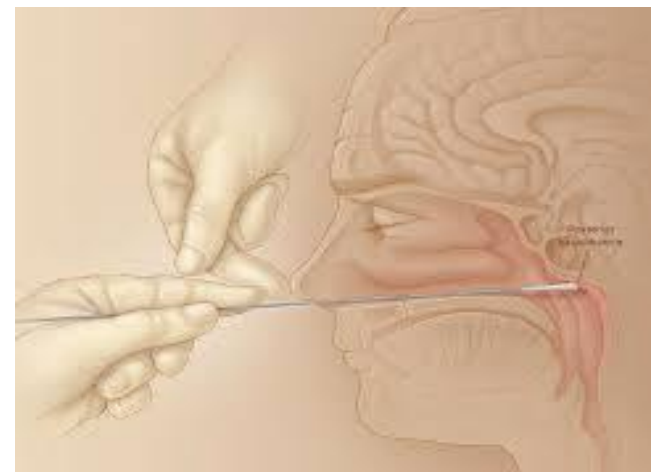
Fever minimal to absent. Symptoms subside gradually over months (convalescent stage 1-2 wks)

Lab. Diagnosis



□ A. Specimens

- Nasopharyngeal (NP) swabs or NP aspirates.
- Nasal swabs are not acceptable
- For adults, cough droplets expelled directly onto a “cough plate” held in front of the patient’s mouth, during a paroxysm is a less desirable method of specimen collection.



Lab. Diagnosis

- **B. Direct Fluorescent Antibody Test**
- The fluorescent antibody (FA) reagent can be used to examine nasopharyngeal swab specimens. However, false-positive and false-negative results may occur; the sensitivity is about 50%.
- The FA test is most useful in identifying *B pertussis* after culture on solid media.



Fluorescein-labeled antibody attached to *Legionella* bacilli

Lab. Diagnosis

□ C. Culture

- NP aspirates or swabs are cultured on solid media (Bordet-Gengou medium) with high percentage of blood (20%-30%) to inactivate inhibitors in the agar, and also contain potato and glycerol.
- The antibiotics in the media tend to inhibit other respiratory microbiota but permit growth of *B pertussis*.



Figure 37-1 Growth of *Bordetella pertussis* on Regan-Lowe agar.

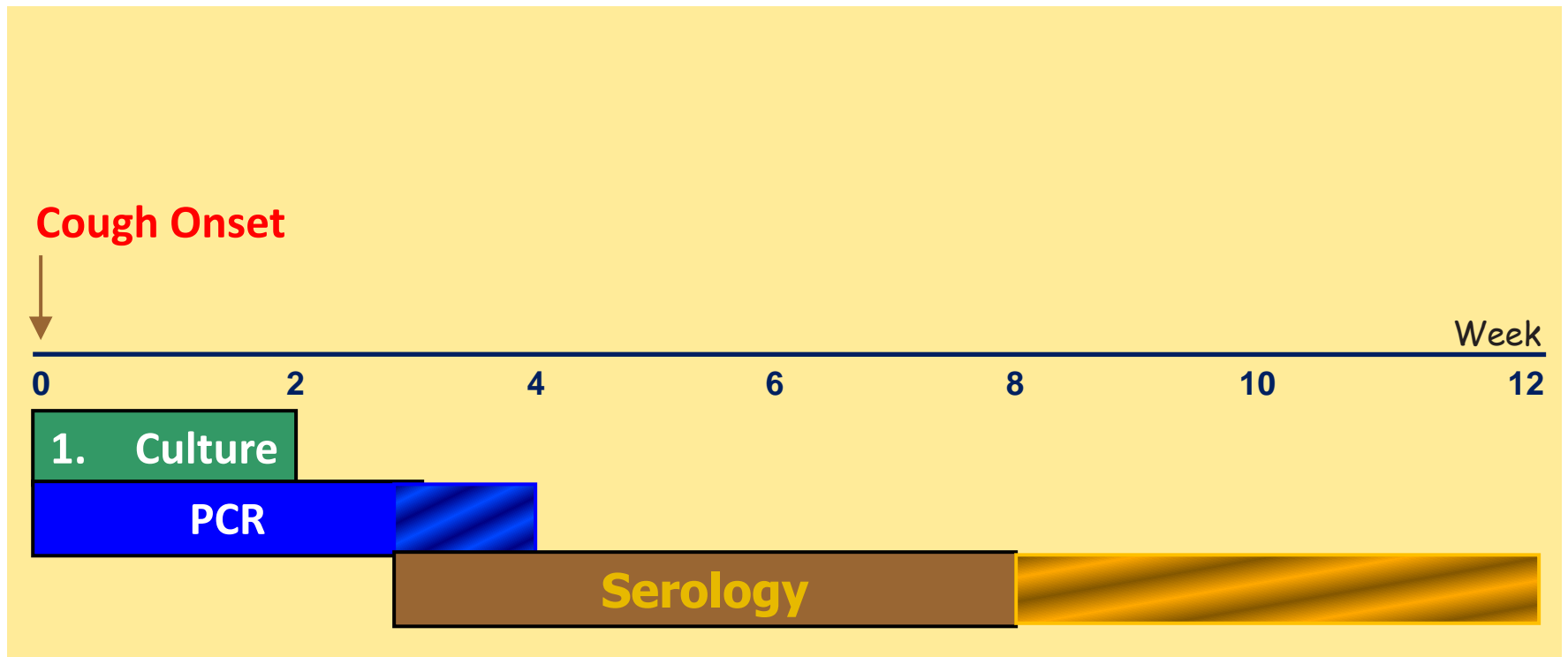
Selective media for *B. pertussis* includes Regan-Lowe, Bordet-Gengou, or charcoal agar. Successful isolation declines with previous exposure to antibiotic therapy effective against pertussis or if specimens are collected beyond the first two weeks of illness. Isolation is also difficult for vaccinated patients.

Lab. Diagnosis

- **D. immunofluorescence staining** or by **slide agglutination** with specific antiserum.
- **E. Polymerase Chain Reaction**
- **F. Serology**
 - Production of IgA, IgG, and IgM antibodies occurs after exposure to *B pertussis* and these antibodies can be detected by enzyme immunoassays.
 - Serologic tests on patients are of little diagnostic help acutely because a rise in agglutinating or precipitating antibodies does not occur until the third week of illness.



Optimal Timing in Weeks for Diagnostic Testing



Immunity



- Recovery from whooping cough or immunization is followed by immunity that is not lifelong.
- Second infections may occur but are usually milder; reinfections occurring years later in adults may be severe. It is probable that the first defense against *B pertussis* infection is the antibody that prevents attachment of the bacteria to the cilia of the respiratory epithelium.
- Antibodies to PT are highly immunogenic

Treatment



- Administration of erythromycin during the catarrhal stage of disease promotes elimination of the organisms and may have prophylactic value.
- Treatment after onset of the paroxysmal phase rarely alters the clinical course.
- Oxygen inhalation and sedation may prevent anoxic damage to the brain.

Treatment



- Azithromycin is the drug of choice. Note that azithromycin reduces the number of organisms in the throat and decreases the risk of secondary complications but has little effect on the course of the disease at the “prolonged cough” stage because the toxins have already damaged the respiratory mucosa.
- Supportive care (e.g., oxygen therapy and suction of mucus during the paroxysmal stage is important, especially in infants).

Prevention

□ There are two types of vaccines:

1 . **an acellular vaccine** containing purified proteins from the organism.

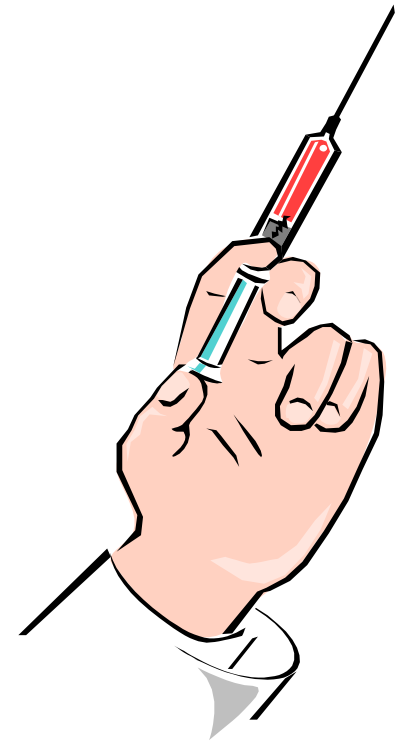
2. **a killed vaccine** containing inactivated *B. pertussis* organisms.

□ The acellular vaccine has fewer side effects than the killed vaccine but has a shorter duration of immunity.



Prevention

- The pertussis vaccine is usually given combined with diphtheria and tetanus toxoids (DTaP) in three doses beginning at 2 months of age. A booster at 12 to 15 months of age and another at the time of entering school are recommended.
- Because outbreaks of pertussis have occurred among teenagers, a booster for those between 10 and 18 years old is recommended. This vaccine, called Boostrix, contains diphtheria and tetanus toxoids also.



Prevention



- To protect newborns, pregnant women should receive pertussis vaccine. Antipertussis IgG will pass the placenta and protect the newborn.
- The **killed vaccine** is no longer used in the United States because it is suspected of causing various side effects, including postvaccine encephalopathy at a rate of about one case per million doses administered.
- Azithromycin is useful in prevention of disease in exposed, unimmunized individuals. It should also be given to immunized children younger than 4 years who have been exposed because vaccine-induced immunity is not completely protective.

BORDETELLA PARAPERTUSSIS



- This organism may produce a disease similar to whooping cough, but it is generally less severe.
- The infection is often subclinical.
- *B parapertussis* grows more rapidly than typical *B pertussis* and produces larger colonies.
- It also grows on blood agar.
- *B parapertussis* has a silent copy of the pertussis toxin gene.

Questions?



Cutaneous viral diseases

Cutaneous viral diseases cause lesions or papules to form on the skin. In many cases, these lesions can stick around for a long time or come back after disappearing for a while.

Herpes Simplex Virus (HSV): Herpes simplex virus (HSV) type-1 and 2, of the *Herpesviridae* family, are enveloped double-stranded DNA viruses.

- The herpes virus family contains several of the most important human pathogens. Clinically the virus exhibit human pathogens with spectrum of diseases. Some have a wide host range, where are others have a narrow host range
- The outstanding property of herpes viruses is their ability to establish lifelong persistent infections in their hosts and to undergo periodic reactivation.
- Herpes viruses that are commonly infect humans include:
 - 1) Herpes simplex viruses type 1&2.
 - 2) Varicella- Zoster virus.
 - 3) Cytomegalovirus(CMV).
 - 4) Human herpes viruses 6,7
 - 5) Epstein- Barr viruses.
 - 6) Kaposi sarcoma associated herpes virus.

Properties of Herpes viruses:

1. **Virion:** Spherical
2. **Genome:** dsDNA, Linear.
3. **Protein:** more than 35 proteins in virion.
4. **Envelope:** contain viral glycoprotein and Fc receptor.
5. **Replication:** in the nucleus and bud from the nuclear membrane.

❖ Pathogenesis

a) primary infection

Herpes simplex is one of the most common viral infections in humans. Primary infection is usually acquired in early childhood, between two and five years of age. Humans are the only natural hosts. Asymptomatic carriers form the more important source of infection.

The virus enters through defects or broken in the skin or mucous membranes and multiplies locally with cell-to-cell spread. The virus enters cutaneous nerve fibres and is transported intra-axonally to the dorsal root ganglia where it replicates. migration of the virus can take place from the ganglia to the skin and mucosa to cause cutaneous and mucosal lesions. The virus remains latent in the ganglia to be

reactivated periodically in some individuals causing recurrent oral and genital lesions. **HSV-1** it is limited to the oropharynx but **HSV-2** occurs in the genital tract.

b) latent infection

HSV have ability to stay as latent virus in infected cells for life time. The stimuli or trigger which is lead for the reactivation of the latent virus are:

- 1) Axonal injury
 - 2) Fever
 - 3) Physical or emotion al stress.
 - 4) Exposure to ultraviolet, sunlight
- Infection especially pneumococcal and meningococcal.

Mode of Transmission:

HSV-1 transmitted by direct contact with infected saliva, skin lesions or respiratory secretions.

HSV-2 is transmitted sexually (Venereal disease) and also from maternal genital to newborn (Perinatal).

• **Laboratory diagnosis:**

1- Direct Detection

- Take a scraping from the base of the vesicles and stain it with Giemsa stain and examine under light microscope or Electron microscope to see the multinucleated giant.

- Electron microscopy of vesicle fluid - rapid result but cannot distinguish between HSV and VZV, Immunofluorescence of skin scrapping - can distinguish between HSV and VZV.

2- PCR - Now used routinely for the diagnosis of herpes simplex encephalitis

3- Virus Isolation

HSV-1 and HSV-2 are among the easiest viruses to cultivate. It usually takes only 1 - 5 days

3- Serology use to detect (IgM&IgG) after 4-7 days by ELISA test.

Varicella-Zoster Virus (VZV)/ Human Herpes virus 3

Transmission: Direct contact, Respiratory droplet.

Disease: Two disease caused by Varicella-Zoster Virus :

1. **Varicella (Chicken pox):** It is the acute disease that occurred by the primary contact with the virus which include Erythematous ulcerating

encrusting vesicles beginning on the face and trunk and then progressing towards the extremities, as well as mucous membranes and Presents fever, lymphadenopathy. Spontaneously resolves in < 1 week.

2- **Zoster (shingles)** it is disease occur in response to the reactivation of latent VZV in neurons in sensory ganglia.

Pathogenesis and clinical features:-

a)Varicella

The infection is occur through the mucosa of the conjunctiva and upper respiratory tract followed by initial replication in the regional lymph node then after primary and secondary viremia the virus transported by the mononuclear cells to the skin this associated with typical vesicles of chicken pox.

b) Zoster

The lesions of Zoster are histopathologically identical to those of varicella. the lesion is closely to the areas of innervation of dorsal root ganglia. the reactivation is occurred as a result of lowering of immunity which allows for replication of the virus and then it travel down with the nerve to the skin and induce vesicle formation.

Laboratory diagnosis:

1-Direct detection

staining of the smear which has been taken from the base of the vesicle and examine under the microscope to see a multinucleate giant cell.

2- Virus Isolation:

culture of the vesicle fluid in human cell.

3- serology

Elisa or IF test by detect antibodies. the presence of VZV IgG is indicative of past infection and immunity. The presence of IgM is indicative of recent primary infection.

Viral gastroenteritis is an inflammation of the inside lining of your gastrointestinal tract. It can be caused by rotavirus, norovirus, adenovirus, and other viruses. Babies can be vaccinated against rotavirus. Symptoms of viral gastroenteritis are nausea, vomiting, and watery diarrhea

Rotavirus is a genus of double-stranded RNA viruses in the family *Reoviridae*. Rotaviruses are the most common cause of diarrhoeal disease among infants and young children. Nearly every child in the world is infected with a rotavirus at least once by the age of five.

Structure

The genome of rotaviruses consists of 11 unique double helix molecules of RNA (dsRNA) which are 18,555 nucleotides in total. Each helix, or segment, is a gene, numbered 1 to 11 by decreasing size. Each gene codes for one protein, except genes 9, which codes for two. The RNA is surrounded by a three-layered icosahedral protein capsid. Viral particles are up to 76.5 nm in diameter and are not enveloped.

Transmission

Rotaviruses are transmitted by the fecal-oral route, via contact with contaminated hands, surfaces and objects, and possibly by the respiratory route. Viral diarrhoea is highly contagious. The feces of an infected person can contain more than 10 trillion infectious particles per gram; fewer than 100 of these are required to transmit infection to another person.

Diagnosis of infection with a rotavirus normally follows diagnosis of gastroenteritis as the cause of severe diarrhea. Most children admitted to hospital with gastroenteritis are tested for rotavirus A.

Specific diagnosis of infection with rotavirus A is made by finding the virus in the child's stool by enzyme immunoassay. There are several licensed test kits on the market which are sensitive, specific and detect all serotypes of rotavirus A. Other methods, such as electron microscopy and PCR (polymerase chain reaction), are used in research laboratories. Reverse transcription-polymerase chain reaction (RT-PCR) can detect and identify all species and serotypes of human rotaviruses.

Treatment

Treatment of acute rotavirus infection is nonspecific and involves management of symptoms and, most importantly, management of dehydration. If untreated, children can die from the resulting severe dehydration. Depending on the severity of diarrhoea, treatment consists of oral rehydration therapy, during which the child is given extra water to drink that contains specific amounts of salt and sugar.

Viral hepatitis is an infection that causes liver inflammation and damage.. Researchers have discovered several different viruses that cause hepatitis, including hepatitis A, B, C, D, and E.

Hepatitis A virus

Hepatitis A virus (HAV), classified as hepatovirus, is a small, unenveloped symmetrical RNA virus which shares many of the characteristics of the picornavirus family, and is the cause of infectious or epidemic hepatitis transmitted by the fecal-oral route.

Hepatitis B virus

Hepatitis B virus (HBV), a member of the hepadnavirus group, double-stranded DNA viruses which replicate, unusually, by reverse transcription. Hepatitis B virus is endemic in the human population and hyperendemic in many parts of the world. A number of variants of this virus have been described. Natural hepadna virus infections also occur in other mammals including woodchucks, beechy ground squirrels and ducks.

Hepatitis C virus

Hepatitis C virus (HCV), is an enveloped single-stranded RNA virus which appears to be distantly related (possibly in its evolution) to flaviviruses, although hepatitis C is not transmitted by arthropod vectors. Hepatitis C virus is associated with chronic liver disease and also with primary liver cancer in some countries.

Hepatitis D virus

Hepatitis D virus (HDV) is an unusual, single-stranded, circular RNA virus with a number of similarities to certain plant viral satellites and viroids. This virus important cause of acute and severe chronic liver damage in many regions of the world.

Hepatitis E virus

Hepatitis E virus (HEV), the cause of enterically-transmitted non-A, non-B hepatitis, is another non-enveloped, single-stranded RNA virus, This virus is responsible for high mortality (15–20%), during pregnancy particularly during the third trimester.

Diagnosis of hepatitis is made on the basis of some or all of the following: a person's signs and symptoms, medical history including sexual and substance use history, blood tests, imaging, and liver biopsy. In general, for viral hepatitis and other acute causes of hepatitis, the person's blood tests and clinical picture are

sufficient for diagnosis. For other causes of hepatitis, especially chronic causes, blood tests may not be useful. In this case, liver biopsy is the gold standard for establishing the diagnosis.

The treatment of hepatitis varies according to the type, whether it is acute or chronic, and the severity of the disease.

- **Activity:** Many people with hepatitis prefer bed rest, though it is not necessary to avoid all physical activity while recovering.
- **Diet:** A high-calorie diet is recommended.
- **Drugs:** People with hepatitis should avoid taking drugs metabolized by the liver.

Viral hemorrhagic fevers (VHFs) are a group of diseases that are caused by several distinct families of viruses. The term “viral hemorrhagic fever” refers to a condition that affects many organ systems of the body, damages the overall cardiovascular system, and reduces the body’s ability to function on its own. Symptoms of this type of condition can vary but often include bleeding, or hemorrhaging. Some VHFs cause relatively mild illness, while others can cause severe, life threatening disease. Most VHFs have no known cure or vaccine.

Although VHFs are caused by several families of viruses, these viruses share some common characteristics:

They are RNA viruses. These viruses are the most common cause of emerging disease in people because RNA viruses change over time at a high rate.

They are covered, or enveloped, in a lipoprotein outer layer, making it easier to destroy these viruses with physical (heat, sunlight, gamma rays) and chemical (bleach, detergents, solvents) methods.

They naturally exist in animal or insect populations, referred to as host populations, and are generally restricted to the geographical areas where the host species live.

They spread to people when a person encounters an infected animal or insect host. After the initial spread into the human population, some VHF viruses can continue to spread from person-to-person.

Outbreaks of VHFs in people can be difficult to prevent since they can occur sporadically and cannot be easily predicted.

NISSERIAE

Msc safaa abdul ameer

The Neisseria are Gram-negative cocci that usually occur in pairs. They are aerobic, nonsporulating, nonmotile, oxidase-positive cocci typically arranged in pairs. *N. meningitidis* and *N. gonorrhoeae* are medically important pathogens, and are found associated with or inside polymorphonuclear cells. Some Neisseriae sp are normal inhabitants of the human respiratory tract.

Cultural characteristics

Meningococci have exacting growth requirements and do not grow on ordinary media. Growth occurs on media enriched with blood, serum or ascetic fluid, which promote growth by neutralizing certain inhibiting substances in culture media rather than by providing additional nutritional needs

They are strict aerobes, no growth occurs anaerobically. The optimum temperature for growth is 35-36°C. no growth takes place below 30°C. Optimum pH is 7.4-7.6. Growth is facilitated by 5-10 percent CO₂ and high humidity. On solid media after incubation for 24 hrs, the colonies are small translucent, round, convex, bluish grey, with a smooth glistening surface and with entire edges. Blood agar, chocolate agar and Mueller-Hinton starch casein hydrolysate agar are the media commonly used for culturing meningococci.

Pathogenicity

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

Diagnosis • Gram stain of CSF (gram-negative diplococci) is sensitive and specific but is of limited value for blood specimens (too few organisms are generally present, except in overwhelming sepsis)

- Culture is definitive, but organism is fastidious and dies rapidly when exposed to

cold or dry conditions

- Tests to detect meningococcal antigens are insensitive and nonspecific
- NAATs are not yet widely used

Treatment, Control, Prevention

- Empiric 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
- Chemoprophylaxis for contact with persons with the disease is with rifampin, ciprofloxacin, or ceftriaxone
- Breast-feeding infants have passive immunity (first 6 months). 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, which is important.

NEISSERIA GONORRHOEAE (GONOCOCCUS)

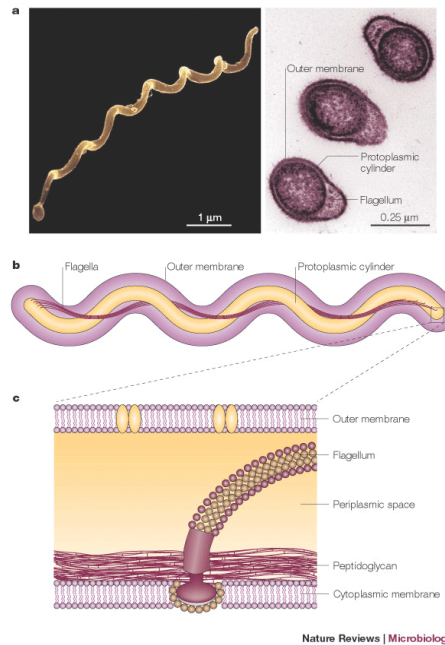
The organism appears as a diplococcus with the adjacent sides concave, being typically kidney shaped. It is predominantly within the polymorphs. Gonococci possess pili on their surface. Pili facilitate adhesion of the cocci to the mucosal surfaces and promote virulence by inhibiting phagocytosis.

Pathogenicity Gonorrhea is a venereal disease which has been known since ancient times. The name gonorrhea, meaning flow of seed. The disease is acquired by sexual contact. Infection of the lower genital tract can result in a purulent or pus like discharge from the genitals which may be foul smelling. *N.gonorrhoeae* can also cause conjunctivitis, pharyngitis, proctitis or urethritis, prostatitis and orchitis. Conjunctivitis is common in neonates and silver nitrate or antibiotics are often applied to their eyes as a preventive measure against gonorrhea. Infection of the genitals in females with *N.gonorrhoeae* can result in pelvic inflammatory disease if left untreated, which can result in infertility

Treatment, Control, Prevention

- Ceftriaxone with either azithromycin or doxycycline is currently the treatment of choice, although high-level resistance to cephalosporins, as well as to penicillins and fluoroquinolones, has been observed
- For neonates, prophylaxis with 1% silver nitrate; ophthalmia neonatorum is

treated with ceftriaxone • Prevention consists of patient education, • Effective vaccines are not available



Spirochetes

The spiral morphology of spirochetes is produced by a flexible, peptidoglycan cell wall around which several axial fibrils are wound. *T. pallidum*

Pathogenesis and Clinical Diseases

1- **Primary syphilis:** painless skin ulcer named ((primary chancre)) occurs at site of skin penetration.

a- A chancre contains numerous spirochetes, and is infectious.

b-histologically endarteritis and periarteritis, and infiltrated by PMLs, and macrophages.

c-slow growth, and the bacteria disseminated to all tissues mainly skin, mucus membrane and lymph nodes.

2-**Secondary syphilis:** fever, flue-like illnesses, generalized lymphadenopathy, and mucocutaneous lesions, it is highly infectious. Lasted for few weeks ended with latency.

3-**Tertiary syphilis:** some cases progress to third stage, where granulomata or ((Gumma)) are formed in any tissue lead to severe destruction of skin, bone, cartilage...

Other will progress to either neurosyphilis or cardiovascular syphilis.

4-Congenital syphilis: in utero infection either lead to latent infection, malformation, or death of fetus, survival with manifestation of rhinitis, then maculopapular rash, and organ tissue destructions will follow if infants are not dead.

Clinical Disease • Gonorrhea: characterized by purulent discharge from 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

Diagnosis • Gram stain of urethral specimens (presence of gram-negative diplococci) is

accurate only for symptomatic males

- Gram stain of synovial fluid is diagnostic for septic arthritis

- Culture of genital specimens is sensitive and specific but has been replaced with nucleic acid amplification tests (NAATs) in most laboratories

- Culture is the test of choice for all other specimens

Treatment, Control,

Prevention

- **Ceftriaxone with either azithromycin or doxycycline is currently the treatment of choice**, although high-level resistance to cephalosporins, as well as to penicillins

and fluoroquinolones, has been observed

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

- Prevention consists of patient education,

- Effective vaccines are not available

Enteric group of bacteria

Different microorganism are present in the intestinal tract of man.
Enteric group includes following bacteria

1- *Escherichia coli* :

- 1 – gram negative
- 2 – motile
- 3 – lactose fermented
- 4 – non capsulated

Some types of *E. coli*, particularly *E. coli* O157:H7, can cause intestinal infection and produce Shiga toxin.

Pathogenicity: gastroenteritis (children under 2 year), urinary tract infection

2- *klebsiella*

General characters

1. gram negative
2. non motile
3. lactose fermented
4. capsulated

Pathogenicity: Respiratory tract infection, Urinary tract infection

3- *pseudomonas*

1. Gram negative
2. Motile
3. Non lactose fermented

Pathogenicity: Urinary tract infection, Otitis media, Secondary infection of wounds and burns.

4- *Salmonella*

General character

1. Gram negative
2. Motile
3. Non lactose fermented

Pathogenicity: Salmonellae are often pathogenic for humans or animals when acquired by the oral route. They are transmitted from animals and animal products to humans, where they cause enteritis, systemic infection, Septicemia, Food poisoning and enteric fever

5 – *shigella*

1. Gram negative
2. non Motile
3. Non lactose fermented

Pathogenicity: Bacillary dysentery

Clinical Findings: After a short incubation period (1–2 days), there is a sudden onset of abdominal pain, fever, and watery diarrhea. The diarrhea has been attributed to an exotoxin acting in the small intestine.

A day or so later, as the infection involves the ileum and colon, the number of stools increases; they are less liquid but often contain mucus and blood. Each bowel movement is accompanied by straining and tenesmus (rectal spasms), with resulting lower abdominal pain. In more than half of adult cases, fever and diarrhea subside spontaneously in 2–5 days. However, in children and the elderly, loss of water and electrolytes may lead to dehydration, acidosis, and even death.

6 – *Vibrio cholera*

General character

1. Gram negative
2. Thin
3. Curved (comma) shape
4. Motile
5. Non lactose ferment
6. Grow at alkaline pH

Most *Vibrio* species are halotolerant, and NaCl often stimulates their growth. Some vibrios are halophilic, requiring the presence of NaCl to grow.

Pathogenicity: it cause cholera , disease transmitted by contaminated water milk fruit About 60% of infections with classic *V cholerae* are asymptomatic. The incubation period is 1–4 days for persons who develop symptoms, depending largely upon the size of the inoculum ingested. There is a sudden onset of nausea and vomiting and profuse diarrhea with abdominal cramps. Stools, which resemble "rice water", contain mucus, epithelial cells, and large numbers of vibrios.

There is rapid loss of fluid and electrolytes, which leads to profound dehydration, circulatory collapse, and anuria. The mortality rate without treatment is between 25% and 50%.

The diagnosis of a full-blown case of cholera presents no problem in the presence of an epidemic. However, sporadic or mild cases are not readily differentiated from other

diarrheal diseases.

Prevention

1. Health education
2. Food safety
3. Water purification

Treatment

1. The primary treatment is oral rehydration therapy (Rehydration by mouth)
2. Antibiotics: tetracycline, Erythromycin, chloramphenicol ...

Immunity

Immunity: the resistance offered by the host to the harmful effect of pathogenic microbial infection.

Types of immunity:

- 1- **natural immunity or innate immunity:** Basic immunity which may be genetically passed on from One generation to other generation.
- 2- **acquired immunity:** Acquired during life time , and divided to

a- active acquired immunity

it is the resistance developed as a result of antigenic stimulus it may be

natural: this acquired after infection.

artificial: this acquired artificially by inoculation .

b-passive acquired immunity it may be

natural : transmission of antibodies from the mother to the fetus can occur through placenta and breast feed.

Artificial :produce by injection of serum of animals that been immunized Actively.

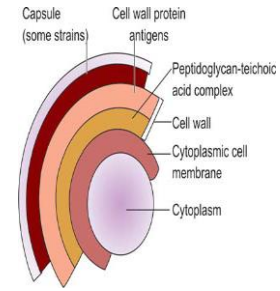
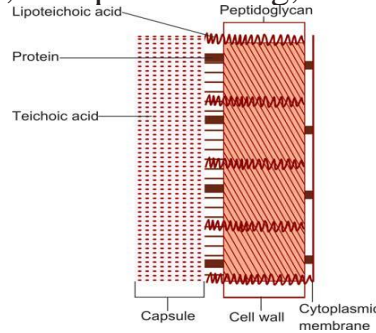
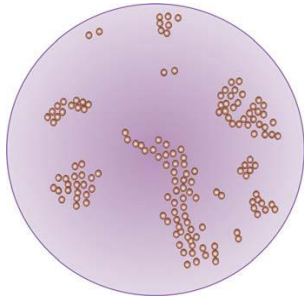
Antigen

Protein, polysaccharide or polypeptide when introduced into the body stimulates the production of antibody and react specifically with such antibody .

Antibody

Is hormonal substance produce in response to an antigenic stimulus, it serve as protective agent against organism

Staphylococci These are nonmotile, nonspore forming, Gram positive



staphylococci

Cell wall of staphylococci

Antigenic structure of Staph. aureus

cocci which measure around 0.7 to 1.2 μm in diameter, production of coagulase aerobic and facultative an aerobic growth at 37C°.manitol salt agar is selective media

SPECIES OF STAPHYLOCOCCUS

- *Staphylococcus aureus* golden yellow colonies
- *Staphylococcus epidermidis* gray to white colonies
- *Staphylococcus saprophyticus*. lymon yellow colonies

Table 1 Determinants of pathogenicity of Staph. aureus

<i>Surface antigens</i>	<i>Enzymes</i>	<i>Toxins</i>
Capsule	Coagulase	Haemolytic toxins lysisRBC
Polysaccharide A	Staphylokinase digest blood clot	• Alpha-lysin
Protein A	Hyaluronidase digest c.t	• Beta-lysin
	Nuclease	• Gamma-lysin
	Lipase	• Delta-lysin
	Phosphatase	Leucocidin lysisneutrophi,macrophage
	Penicillinase in activite pencillin	
Enterotoxins	Proteases	Epidermolytic toxins
		Toxic shock syndrome toxin (TSST)organ failir

Pathogenesis and Clinical Features

The pathogenesis of staphylococcal diseases relates to resistance to phagocytosis, to the action of several staphylococcal enzymes, to the development of delayed hypersensitivity and to the activities of toxins Two types of diseases are produced by *Staph. aureus*: invasive and toxigenic The invasive lesions are suppurative whereas toxinoses are nonsuppurative.

Clinical entities caused by Staph. aureus

Invasive (suppurative

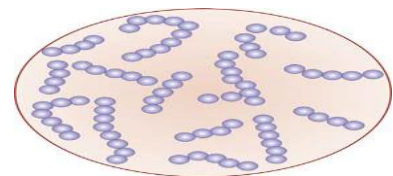
Carbuncle/furuncle
Microabscesses
Abscesses in deep organs
Osteomyelitis
Pneumonia
Septicaemia
Endocarditis
Pyoarthritis
Meningitis
Urinary tract infection
Pharyngitis
Endodontitis
Styes and conjunctivitis
Wound infection
Impetigo

Toxinoses Nonsuppurative)

Food poisoning
Toxic shock syndrome
Scalded skin syndrome
Enterocolitis

Treatment

When penicillin was introduced almost all the strains of *Staph. aureus* were sensitive to this drug. Now more than 50% isolates show resistance to it. The resistance is due to the production of penicillinase (beta lactamase) by the organism which inactivates penicillin. Penicillinase resistant penicillins such as methicillin, oxacillin and cloxacillin can be used in treating patients having infection with penicillinase producing strains. Cephalosporins are the drugs of choice in those who are hypersensitive to penicillin.



Lac -6 STREPTOCOCCI

Streptococci are Gram-positive, nonmotile, nonsporeforming, catalase-negative cocci that occur in pairs or chains. Most streptococci are facultative anaerobes, and some are obligate (strict) anaerobes. Most require enriched media (blood agar). . *Streptococcus pneumoniae* (a major cause of human pneumonia) and *Streptococcus mutans* (causes of dental caries). *Streptococcus pneumoniae* has a polysaccharide capsule that acts as a virulence factor for the organism

Group A streptococci *Strep. pyogenes* causes:

- Strep throat - a sore, red throat, sometimes with white spots on the tonsils
- Scarlet fever - an illness that follows strep throat. It causes a red rash on the body.

- Impetigo - (superficial) infection of epidermal layers of skin.
- Toxic shock syndrome
- Cellulitis and necrotizing fasciitis (flesh-eating disease)

Rheumatic fever is a nonsuppurative complication of *S. pyogenes* pharyngitis. Rheumatic fever is an inflammatory disease affecting primarily the heart and joints. Although severe, it can take an extended period of time to develop. The mechanism of chronic immunopathology of rheumatic fever is not resolved. M protein cross-reacts with heart myosin leading to autoimmunity. Also the group A streptococcal cell wall is highly resistant to degradation in the host. These antigens persist for months *in vivo* and experimentally elicit diseases that resemble rheumatic arthritis and carditis. Rheumatic arthritis should not be confused with the most common rheumatic disease - rheumatoid arthritis. Early termination of throat infections with penicillin therapy decreases the incidence of the subsequent development of rheumatic carditis. **Acute glomerulonephritis** is an immune complex disease of the kidney. **Group B streptococci** *S. agalactiae* can cause blood infections, pneumonia and meningitis in newborns. Adults can also get group B strep infections, especially if they are elderly or already have health problems. Strep B can cause urinary tract infections, blood infections, skin infections and pneumonia in adults. (*S. faecalis* can cause nosocomial infections, urinary tract infections, bacteremia, endocarditis, meningitis, and can be found in wound infections along with many other bacteria

Streptococcus pneumoniae causes pneumonia, acute sinusitis, otitis media, meningitis, bacteremia, sepsis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis,

Hemolysis reactions on blood agar

- Alpha hemolysis ,partial :*S.pneumonia*
- Beta hemolysis ,complet ,*S.pyogenes*
- Gamma hemolysis ,non *S.faecalis*
- **Treatment**

All groups of streptococci are sensitive to **penicillin G** and most are sensitive to **erythromycin**. Penicillin is effective in more than 90% of cases and should be the drug of choice. In patients who are allergic to penicillin, erythromycin is recommended. Tetracyclines and sulfa drugs are generally not recommended because streptococci are quick to develop resistance to these agents..

Lac -7 NEISSERIA

The Neisseria are Gram-negative cocci that usually occur in pairs. They are aerobic, nonsporulating, nonmotile, oxidase-positive cocci typically arranged in pairs. *N.meningitidis* and *N. gonorrhoeae* are medically important pathogens, and are found associated with or inside polymorphonuclear cells. Some Neisseriae sp are normal inhabitants of the human respiratory tract.

- 1- **Neisseria gonorrhoeae** or Gonococcus (GC) is a gram negative, kidney shaped diplococcus, It cause gonorrhea which is a sexually transmitted disease (STD). Man is the only natural host of *N. gonorrhoeae*. Gonorrhoea has been identified as co-factor of HIV transmission. Further untreated gonococcal infection can cause pelvic inflammatory disease (PID) which may lead to chronic pelvic pain, ectopic pregnancy and infertility.

Clinical Disease • Gonorrhoea: characterized by **purulent discharge** from 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.

2- **Neisseria** is simply known as **meningococcus**, is aerobic, gram negative diplococcus. It exists as normal flora in the throat or nasopharynx of up to 40% of individuals. It may be seen in genital tract area where its presence is of no pathological significance. *Neisseria meningitidis* is non motile and non spore forming. *N. meningitidis* has a polysaccharide capsule that surrounds the outer membrane of the bacterium and protects against immune mechanism of human. It is considered to be an essential virulence factor for the bacteria. Based on the capsular polysaccharide

- Meningococemia: 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

Treatment,

- Empiric 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

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

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

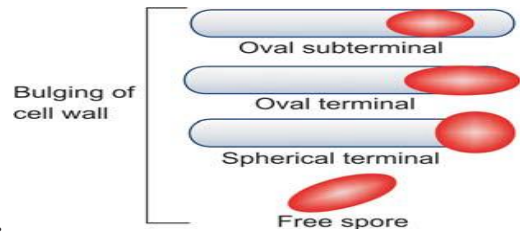
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Genus *Mycobacterium*

Lact 8- *Clostridium*

The anaerobic bacteria are easily separated into two groups, those with and without spores. The spore forming anaerobes constitute the genus *Clostridium*.

These are gram-positive bacilli, produce powerful exotoxins and occur across a wide variety of habitats. The important member of the non-spore bearing anaerobes is *Bacteroides*. Anaerobic infections are generally polymicrobial. These bacteria are found in mixed infections with other anaerobes, facultative anaerobes and aerobes



1. Location of spores of Clostridium

Spore	Species
Central or equatorial	<i>C.bifermentans</i>
Subterminal	<i>C.perfringens</i>
Oval or terminal	<i>C.tertium</i>
Spherical and terminal	<i>C.tetani</i>

Classification of clostridia according to pathogenicity

Group	Species
Tetanus	<i>C.tetani</i>
Acute colitis	<i>C.difficile</i>
Food poisoning	
• Gastroenteritis	<i>C.perfringens</i> type A
• Botulism	<i>C.botulinum</i>
Gas gangrene	<i>C.perfringens</i>

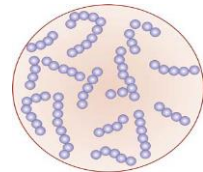
Treatment

Removal of dead tissue from the wound is the first step in treatment. Penicillin or other antibiotics alongwith antitoxin should be given and are helpful if all dead tissue is removed.

STREPTOCOCCI Streptococci are Gram-positive, nonmotile, nonsporeforming, catalase-negative cocci that occur in pairs or chains. Most streptococci are facultative anaerobes, and some are obligate (strict) anaerobes. Most require enriched media (blood agar). Serologic grouping is based on antigenic differences in cell wall carbohydrates (groups A to V), in cell wall pili-associated protein, and in the polysaccharide capsule in group B streptococci. Rebecca Lancefield developed the serologic classification scheme in 1933. β -hemolytic strains possess group-specific cell wall antigens, most of which are carbohydrates. These antigens can be detected by immunologic assays and have been useful for the rapid identification of some important streptococcal pathogens. The most important groupable streptococci are A, B and D. Among the groupable streptococci, infectious disease (particularly pharyngitis) is caused by group A. Group A streptococci have a hyaluronic acid capsule. *Streptococcus pneumoniae* (a major cause of human pneumonia) and *Streptococcus mutans* (among the causes of dental caries) and other so-called viridans streptococci do not possess group antigen. *Streptococcus pneumoniae* has a polysaccharide capsule that acts as a virulence factor for the organism

Streptococci - classification. Group A streptococci causes.

- Strep throat - a sore, red throat, sometimes with white spots on the tonsils
- Scarlet fever - an illness that follows strep throat. It causes a red rash on the body.
- Impetigo - a skin infection
- Toxic shock syndrome
- Cellulitis and necrotizing fasciitis (flesh-eating disease) Rheumatic fever is a nonsuppurative complication of *S. pyogenes* pharyngitis.



Rheumatic fever is an inflammatory disease affecting primarily the heart and joints. Although severe, it can take an extended period of time to develop. The mechanism of chronic immunopathology of rheumatic fever is not resolved. M protein cross-reacts with heart myosin leading to autoimmunity. Also the group A streptococcal cell wall is highly resistant to degradation in the host. These antigens persist for months in vivo and experimentally elicit diseases that resemble rheumatic arthritis and carditis.

Rheumatic arthritis should not be confused with the most common rheumatic disease - rheumatoid arthritis. Early termination of throat infections with penicillin therapy decreases the incidence of the subsequent development of rheumatic carditis.

Acute glomerulonephritis is an immune complex disease of the kidney. Group B streptococci can cause blood infections, pneumonia and meningitis in newborns. Adults can also get group B strep infections, especially if they are elderly or already have health problems. Strep B can cause urinary tract infections, blood infections, skin infections and pneumonia in adults. Group D streptococci is now classified as an Enterococcus. Enterococci are distantly related to other streptococci and have been moved into the genus Enterococcus; the most commonly isolated are *E. (S1) faecalis* can cause nosocomial infections, urinary

tract infections, bacteremia, endocarditis, meningitis, and can be found in wound infections along with many other bacteria. *Streptococcus pneumoniae* causes pneumonia, acute sinusitis, otitis media, meningitis, bacteremia, sepsis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, and brain abscess. *S. pneumoniae* is the most common cause of bacterial meningitis in adults and children, and is one of the top two isolates found in ear infection, otitis media.

STREPTOCOCCI - GRAM STAIN The genus *Streptococcus* is a diverse collection of Gram-positive cocci typically arranged in pairs or chains (in contrast to the clusters formed by *Staphylococcus*

STREPTOCOCCI - BLOOD AGAR CULTURE Most species of streptococci are facultative anaerobes, and some grow only in an atmosphere enhanced with carbon dioxide (capnophilic growth). The classification of species are used: - hemolytic patterns: complete (β) hemolysis, incomplete (α) hemolysis, and no (γ) hemolysis; - serologic properties: Lancefield groupings (originally A to W); - biochemical (physiologic) properties.. Alpha-hemolysis *Streptococcus pneumoniae*, *Streptococcus salivarius*, *viridans* are referred to collectively as viridans streptococci, a name derived from *viridis* (Latin for "green"), referring to the green pigment formed by the partial, α -hemolysis of blood agar. Encapsulated, virulent strains of *S. pneumoniae* often forming highly mucoid, glistening colonies (production of capsular polysaccharide) surrounded by a zone of α -hemolysis. When α -hemolysis is present, the agar under the colony is dark and greenish. *Streptococcus pneumoniae* and a group of oral streptococci (*Streptococcus viridans* or viridans streptococci) display alpha hemolysis. This is sometimes called green hemolysis because of the color change in the agar. Other synonymous terms are incomplete hemolysis and partial hemolysis.. *Streptococcus pyogenes* - beta hemolysis. Streptolysin, an exotoxin, is produced by the bacteria which causes the complete lysis of red blood cells. Streptolysin O is oxygen-sensitive cytotoxin, secreted by most GAS, and interacts with cholesterol in the membrane of eukaryotic cells (mainly red and white blood cells, macrophages, and platelets

SEROLOGIC PROPERTIES TESTING Bacitracin sensitivity test is useful in helping identify *Streptococci* and other Gram-positive bacteria. This test determines whether the bacterium is either sensitive (susceptible) to bacitracin or resistant to the drug. *Streptococcus pyogenes* (GAS) is inhibited by the small amount of bacitracin in the disk (visible zone of inhibition of growth).

CAMP test (β -hemolytic streptococci Group B, GBS) *S. agalactiae* is the only species that has the group B antigen.give positive result.

(BIOCHEMICAL) PROPERTIES TESTING *Streptococcus pneumoniae*, *Streptococcus viridans* are referred to collectively as viridans streptococci, a name derived from *viridis* (Latin for "green"), referring to the green pigment formed by the partial hemolysis of blood agar. The α -hemolytic (viridans) streptococci are classified by biochemical testing. is a chemical used in cell culture techniques for the of *Streptococcus pneumoniae*, which is optochin-sensitive (positive result), from other alphahemolytic streptococci such as *Streptococcus viridans* which are resistant

Bile solubility test distinguishes *Streptococcus pneumoniae* from all other alpha-hemolytic (viridans) streptococci. *Streptococcus pneumoniae* is bile soluble whereas all other alpha-hemolytic streptococci are bile resistant. A clearing of the turbidity in the bile tube indicates a positive test.

ANTISTREPTOLYSIN O (ASO) is the antibody made against streptolysin O the first bacterial markers used for diagnosis and follow up of rheumatic fever or scarlet fever as many people are exposed to these bacteria and remain asymptomatic, the presence of ASO does not indicate disease. Acceptable values, where there is no clinical suspicion of rheumatism are as follows: • Adults: less than 200 units • Children: less than 400 units This titre has a significance only if it is greatly elevated (>200), or if a rise in titre can be demonstrated in paired blood samples taken days apart

C-REACTIVE PROTEIN (CRP) is found in the blood and is a response to inflammation in the body. It can also be an indicator of the presence of infection, trauma or serious illness. Chronic inflammation can keep CRP levels elevated, which can increase the risk of cardiovascular conditions such as heart attacks or stroke. C-reactive protein is produced by the liver.

- **Treatment**

All groups of streptococci are sensitive to **penicillin** Penicillin is effective in more than 90% of cases and should be the drug of choice. In patients who are allergic to penicillin, erythromycin is recommended. Tetracyclines and sulfa drugs are generally not recommended because streptococci are quick to develop resistance to these agents.

Bacteriology, branch of microbiology dealing with the study of bacteria.

The beginnings of bacteriology paralleled the development of the microscope. The first person to see microorganisms was probably the Dutch naturalist Antonie van Leeuwenhoek, who in 1683 described some animalcules, as they were then called, in water, saliva, and other substances. These had been seen with a simple lens magnifying about 100–150 diameters. The organisms seem to correspond with some of the very large forms of bacteria as now recognized.

Bacterial cell structure

Cell Wall

The cell wall is the outermost component common to all bacteria (except *Mycoplasma* species, which are bounded by a cell membrane, not a cell wall). Some bacteria have surface features external to the cell wall, such as a capsule, flagella, and pili, which are less common components.

Function of the cell wall:

1. Give shape and rigidity of the cell and supports the weak cytoplasmic membrane.
2. Osmotic protection
3. It plays an important role in cell division.
4. It is the site of major antigenic determinants of the cell surface.
5. It is a good target for antibiotic treatment.
6. In G negative, it is responsible for the nonspecific endotoxin.

Special components of G +ve cell wall:

1. teichoic & teichuronic acids:

These are water-soluble polymers found within the cell wall of Gram-positive bacteria.

Functions of teichoic acids are:

- 1- Provide rigidity to the cell-wall by attracting cations such as magnesium and sodium.

2- Assist in regulation of cell growth by limiting the ability of autolysin to break the bond between the N-acetyl glucosamine and the N-acetylmuramic acid.

2. polysaccharides:

These include certain neutral sugars e.g. mannose, arabinose & galactose which exists as subunits of polysaccharide in the cell wall.

Special components of G -ve cell wall:

1. **Outer membrane:** it is bilayered structure; its inner leaflet resemble cell membrane and the outer leaflet composed of a lipopolysaccharide (**LPS**).
2. **Lipopolysacharride:** it is extremely toxic to animals called the endotoxin. It composed of three distinct units:
 - a- **A phospholipid called lipid A:** responsible for the toxic effect.
 - b- **A core polysacharride** of five sugars linked to lipid A,
 - c- An outer polysaccharide repeating units represent the major surface antigen called **O antigen**.
3. **lipoprotein:** Molecules of lipoprotein, its function is to stabilize the outer membrane & anchor it to the peptidoglycan layer.
4. **The periplasmic space :** The space between the inner and outer membranes, contains peptidoglycan layers and gel like solution of proteins. It constitute approximately 10-20% of the cell volume.

Differences between cell wall of Gram positive and Gram negative bacteria

Character	Gram positive	Gram negative
Thickness	Thicker	Thinner
Periplasmic space	Absent	Present
Lipids	Absent or small	Present
Teichoic acid	Present	Absent
Peptidoglycan	16- 80nm	2nm

➤ **The cytoplasmic membrane:**

It is composed of a phospholipid bilayer similar to that in eukaryotic cells, lies just inside the peptidoglycan layer of the cell wall. The membranes of prokaryotes are distinguished from those of eukaryote cells by the absence of sterols (except Mycoplasma).

Functions of cytoplasmic membrane:

1. Permeability and active transport of molecules into the cells.
2. Energy generation by phosphorylation.
3. Secretion of enzymes and toxins.

➤ **Cytoplasm and cytoplasmic structure:**

It is a viscous watery solution which has many organic and inorganic solutes. It contains certain structures such as ribosomes, mesosomes, inclusion granules and vacuoles.

It has two distinct areas when seen in electron microscope:

1- an amorphous matrix: contains ribosomes, nutrient granules, metabolites, and plasmids.

2- an inner area: nucleoid region composed of DNA.

A- Granules: storage areas for nutrients .

B- Ribosomes: the site of protein synthesis, and they differ from eukaryotic ribosomes in size and chemical composition.

Nucleoid

The nucleoid is the area of the cytoplasm in which DNA is located. The DNA of prokaryotes is a single, circular molecule that has a molecular weight (MW) of approximately 2×10^9 and contains about 2000 genes. (By contrast, human DNA has approximately 100,000 genes.).

➤ **Additional components outside**

the cell wall:

1- Capsule is a gelatinous layer surrounding the bacterial cell. This layer usually composed of polysaccharide with one exception, the capsule of *B. anthracis* is poly D-glutamic acid. The importance of capsule:


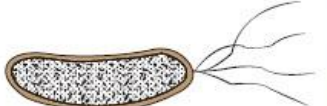

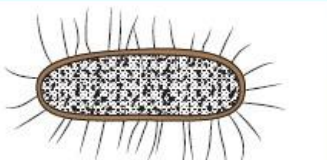
- 1 -Virulence factor since it resist phagocytosis.
- 2 - Specific identification of microorganism made by using antiserum against the capsular polysaccharide (quelling reaction).
- 3- Capsular polysaccharides are used as antigens in certain vaccines.
- 4- May play an important role of adherence of bacteria to host tissues.

Additional components outside the cell wall:

3- Flagella (flagellum):

Bacterial flagella are long, thread-like extensions composed entirely of protein, that moves the bacteria toward nutrients and other attractants in a process called chemotaxis.

Table 7.1: Arrangement of bacterial flagella

Structure	Flagella type	Example
	Monotrichous(single flagella on one side)	<i>Vibrio cholera</i>
	Lophotrichous(tuft of flagella on one end)	<i>Pseudomonas fluorescens</i>
	Amphitrichous(single or tuft on both ends)	<i>Aquaspirillum serpens</i>
	Peritrichous(flagella throughout the cells)	<i>Salmonella typhi</i>

Factor affecting bacterial growth

- Growth of bacteria is affected by many factors such as nutrition concentration and other environmental factors.

Some of the important factors affecting bacterial growth are:

1. Nutrition concentration
2. Temperature
3. Gaseous concentration
4. pH
5. Ions and salt concentration
6. Available water

1. Nutrient concentration:

- If culture media is rich in growth promoting substance, growth of bacteria occurs faster. Decrease in nutrient concentration decreases the growth rate.
- Different bacteria have different nutritional requirement.
- With increase in concentration nutrition, growth rate of bacteria increases up to certain level and then growth rate remains constant irrespective of nutrition addition.

2. Temperature:

- Temperature affects the growth of bacteria by various ways.
- The lowest temperature that allows the growth is called minimum temperature and the highest temperature that allows growth is called maximum temperature.
- There is no growth below minimum and above maximum temperature.
- Below minimum temperature cell membrane solidifies and become stiff to transport nutrients in to the cell, hence no growth occurs.
- Above maximum temperature, cellular proteins and enzymes denatures, so the bacterial growth ceases.
- When temperature is increases continuously from its minimum, growth rate of bacteria increases because the rate of metabolic reaction increases with increase in temperature.
- At certain temperature the growth rate become maximum, this temperature is known as optimal temperature.

- On further increasing the temperature above optimal, growth rate decreases abruptly and completely ceases with reaching maximum temperature.

3. pH:

- pH affects the ionic properties of bacterial cell so it affects the growth of bacteria.
- Most of the bacteria grow at neutral pH (6.5-7.5). However there are certain bacteria that grow best at acidic or basic pH.

4. Ions and salt:

- All bacteria requires metal ions such as K^+ , Ca^{++} , Mg^{++} , Fe^{++} , Zn^{++} , Cu^{++} , Mn^{++} etc to synthesize enzymes and proteins.
- Most bacteria do not require NaCl in media however they can tolerate very low concentration of salt.
- There is some halophilic bacteria such as *Archeobacteria* that require high concentration of salt in media.

5. Gaseous requirement:

- Oxygen and carbon-dioxide are important gases that affects the growth of bacteria.
- Oxygen is required for aerobic respiration and obligate aerobic bacteria must require O_2 for growth. Eg. *Mycobacterium*, *Bacillus*
- For obligate anaerobes Oxygen is harmful or sometime lethal. However facultative anaerobes can tolerate low concentration of O_2 .
- Carbon-dioxide is needed for capnophilic bacteria. Such as *Campylobacter*, *Helicobacter pylori*

6. Available water:

- Water is the most essential factor for bacterial growth.
- Available water in the culture media determines the rate of metabolic and physiological activities of bacteria.
- Sugar, salts and other substances are dissolved in water and are made available for bacteria.

Growth of bacteria

Growth: means an increase in size, number weigh and mass.

Doubling time (generation time): Mean the time required for cells in a microbial population to grow, divide and produce two new cells.

Generation time depend on

- 1- species of microorganism
- 2- nutrients
- 3- Environmental condition (pH, Temp. etc)
- 4- Growth phase.

There are four main phases of growth :

- 1- lag phase.
- 2- exponential phase (log phase).
- 3- Stationary phase
- 4- decline (death) phase

When a small number of cells from a pure cultures are inoculated into a liquid medium (broth), the cells exhibit a characteristic growth curve that can be thought of in four phases.

1- During the lag phase cells are shifting their metabolism to grow on the new medium.

There are two important characteristics of a lag phase:

A- cells are rapidly making new DNA and RNA.

B- inducing the synthesis of new enzymes needed for cell division, and thus there is a great deal of metabolic activity (including synthesis) taking place, but there is no increase in cell numbers.

The length of lag phase depend on:

1. The condition of M.O.
2. The nature of media, that mean the phase may long if the inoculum is from an old culture or if the culture is refrigerated.

2- during the log growth phase :

Cell division occurs at a maximum rate the growth conditions provided by the medium and those environmental conditions. This is called the exponential phase (log phase), because cell numbers are increasing (doubling) at exponential rate.

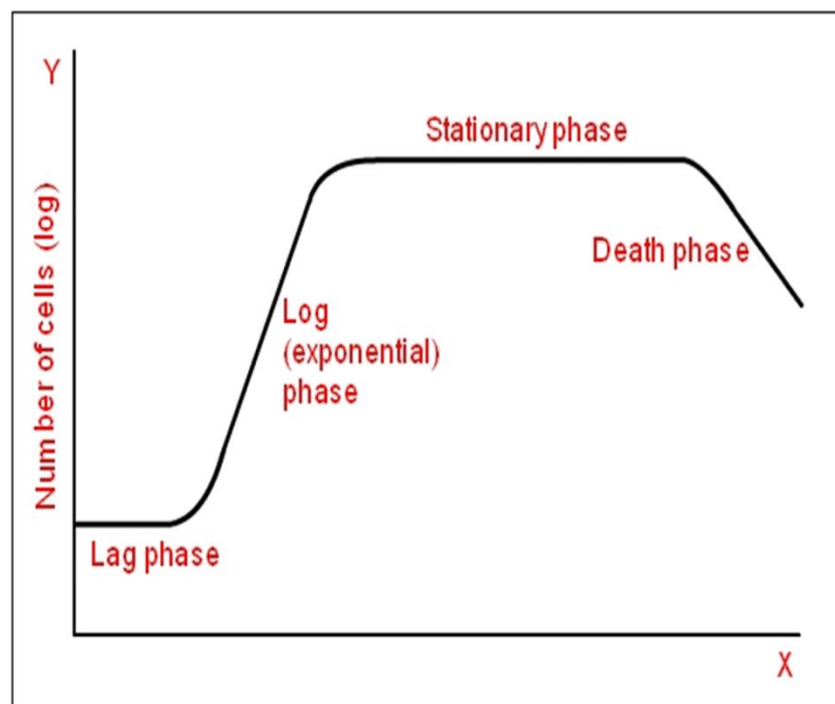
3- stationary phase :

There is no net increase or decrease in cells numbers depends on the bacterial type.

1. Some bacteria stop growing but full maintain their viability.
2. Others reach a state in which the rate of new cell formation is equal to the rate cell death.
3. Food begins turn out, toxic waste products accumulate, pH changes, the rate of fission begins to decline and the organisms die in increasing number.

4- Death (decline) phase :

1. The number of viable bacterial cells begins to decline.
2. In some cases death is accompanied by cell lysis, leading a decrease in the direct microscopic count.



Microbiology Lac(10+11)
Gram Positive Bacilli (Spore Forming)

safaa abdul ameer

A- Strict anaerobic – Genus Clostridium. B- Strict aerobic – Genus Bacillus

Clostridium Species

Large anaerobic gram positive, spore-forming rods, Oval or spherical spores, motile rods Catalase negative. Many decompose protein or form toxins and some do both, Synthesize organic acids, alcohols, exotoxins

•Cause wound infections, tissue infections, food intoxications
. Their natural habitat is the soil or the intestinal tract of human and animals, where they live as saprophytes. Among the pathogens are the organisms causing:

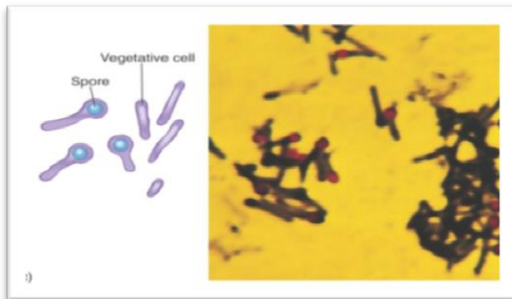
1- Botulism

2- Tetanus

3- Gas gangrene

4- Pseudomembranous colitis

Clostridium tetani: Tetanus



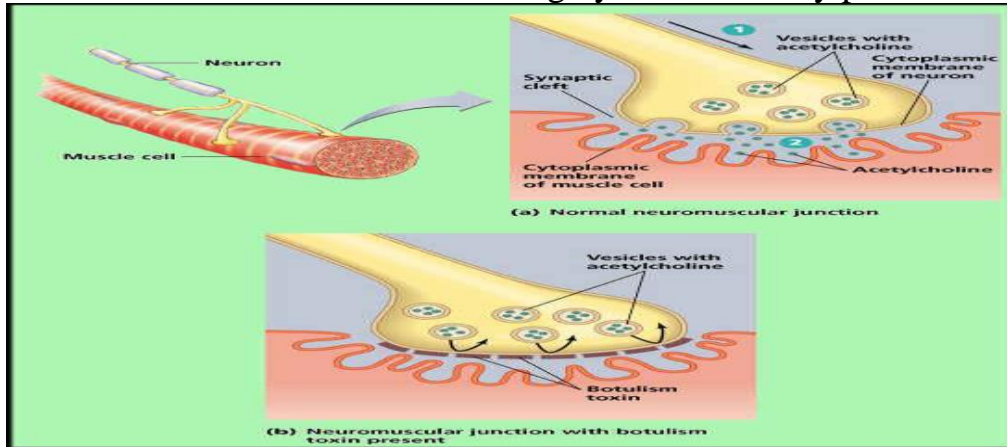
Common resident :of soil and GI tracts of animals

- Causes tetanus or lockjaw, a neuromuscular disease
- Most commonly among geriatric patients and IV drug abusers; neonates in developing countries
Spores:enter accidental puncture wounds, burns, umbilical stumps, frostbite, crushed body parts.
- Anaerobic environ: ideal for vegetative cells growth/release toxin.
- Tetanospasmin**: neurotoxin: paralysis: bind to motor nerve endings; block release of neurotransmitter for muscular contraction inhibition
- Muscles contract uncontrollably
- Death**most often due to paralysis of respiratory muscles

Treatment and prevention

It is important to control spasm and maintain airway and nutrition. ATS (antitetanus serum) may be administrated to neutralize the toxin.

Neonatal tetanus can be prevented by immunizing the pregnant mother with two doses of tetanus toxoid and following by clean delivery practices.



Clostridium perfringens

- *C. perfringens* produces a huge array of invasins & exotoxins
- causes **wound** and **surgical infections** that lead to **gas gangrene**, in addition to severe **uterine** infections. Clostridial hemolysins and extracellular enzymes such as proteases, lipases, collagenase & hyaluronidase, contribute to the invasive process.
- *C. perfringens* also produces an enterotoxin as an important cause of **food poisoning** (Usually in improperly sterilized (canned) foods in which endospores have germinated).
- **Food poisoning:** *C. perfringens* is classified into 5 types on the basis of its ability to produce one or more of the major lethal toxins. Enterotoxin (CPE)- type A is the most common food poisoning agents worldwide.
- **Gas gangrene:** occurs at the site of a recent surgical wound. Patients who develop this disease often have underlying blood vessel disease, diabetes.
- *C. perfringens* produces many different toxins, 4 of which (alpha, beta, epsilon, iota) can cause potentially deadly syndromes. The toxins cause damage to tissues, blood cells, and blood vessels.
- Gas gangrene is marked by a high fever, brownish pus, gas bubbles under the skin, skin discoloration, and a foul odor.

Virulence factors

toxins –

alpha toxin –causes RBC rupture, edema and tissue destruction
collagenase

hyaluronidase
Dnase

Treatment and prevention

Penicillin G is the drug of choice, although metronidazole can be used effectively. Antibiotics are accompanied by aggressive surgical debridement and drainage along with the administration of hyperbaric oxygen.

Bacillus species

Spore forming gram positive strict aerobic capsulated bacilli, arranged in long chains; spores may central, subterminal or terminal, depending on the species. Most members are saprophytic prevalent in soil, water, air.

Bacillus anthracis

The anthrax bacilli, (*B. anthracis*), was the first bacterium shown to be the cause of a disease. In 1877, Robert Koch grew the organism in pure culture, demonstrated its ability to form endospores, and produced experimental anthrax by injecting it into animals.

B. anthracis cause the disease Anthrax in animals in which the organism is transmitted through eating vegetations containing the spores. Human is infected through contact with animals or their products.

Type of clinical infection

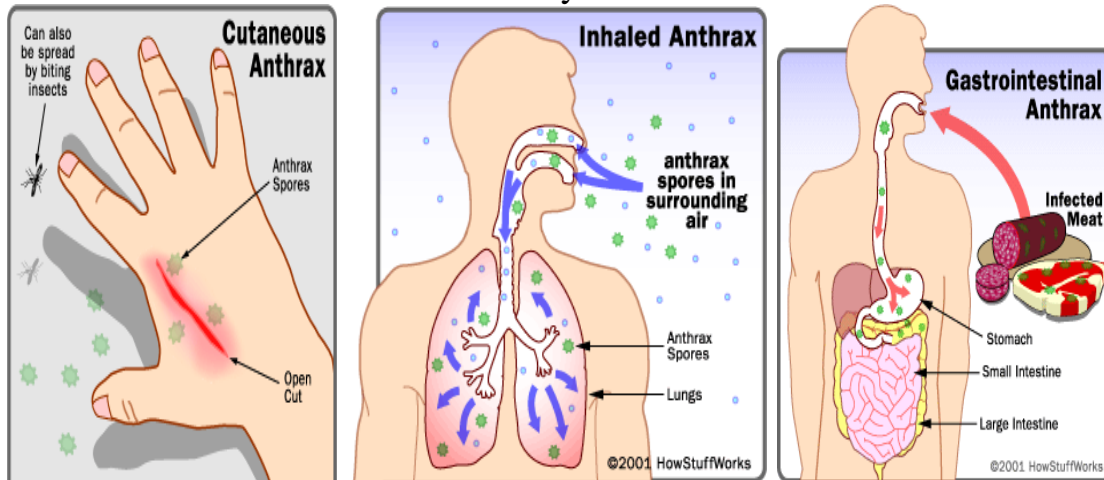
A- Cutaneous Anthrax (malignant pustule)

Generally occurs on exposed surfaces of the arms, face and neck through wound contamination by the spores of the organism. About 95% of the cases with a mortality rate 20%.

B-Inhalation Anthrax (wool sorter disease)

About 5% of the cases with 85-90% mortality.

C- Gastrointestinal Anthrax: Is very rare.



Laboratory Diagnoses

Specimen: Aspirate or swab from cutaneous lesion, Fluid, pus, blood, sputum.
Gram stain. Culture on blood agar and chocolate agar, animal inoculation and by detecting of antigen in the infected tissues.

Treatment

Penicillin and ciprofloxacin are the drug of choice. In case of penicillin allergy, erythromycin, doxycyclin, Tetracycline, chloramphenicol, Erythromycine, Clindamicine may be used.

Prevention

- Vaccination of animal herds
- Proper disposal of carcasses

LAC :1 INTRODUCTION

Microbiology is the study of Microorganisms (or microbes), microscopic or so small that they cannot be seen with the naked eye, inhabit every corner of the globe, some of them are harmful and responsible for many deadly human diseases and others are useful which form the basis of many industrial processes and degraded dead bodies help in recycling of essential elements.

Classification of Microorganisms:

1. Viruses and prions.
2. Bacteria and Archaeobacteria.
3. Fungi, molds and yeasts.
4. Protozoa and helminthes.

Introduction to Virology

Viruses are extremely small agents, can't be seen under light microscope. Their particle sizes between 20-300 nm. They can pass through filters, which prevent the most of bacteria. **Viruses Are Obligate Cellular Parasites**

- Viruses multiply (replicate) inside host cells
- Viruses utilize cellular machineries for replication
- synthesis of proteins
- synthesis of membranes
- synthesis of amino acid, carbohydrates and lipids generation of energy

VIROIDS

. These are RNA molecules which are resistant to heat but destroyed by nuclease. Till date, no viroid has been shown to cause human disease.

PRIONS

The name prion has been derived from proteinaceous infectious particles. These are sensitive to proteases but resistant to nucleases and UV rays. Strong evidence is now available to incriminate these in causing transmissible spongiform encephalopathies (TSE)

CLASSIFICATION

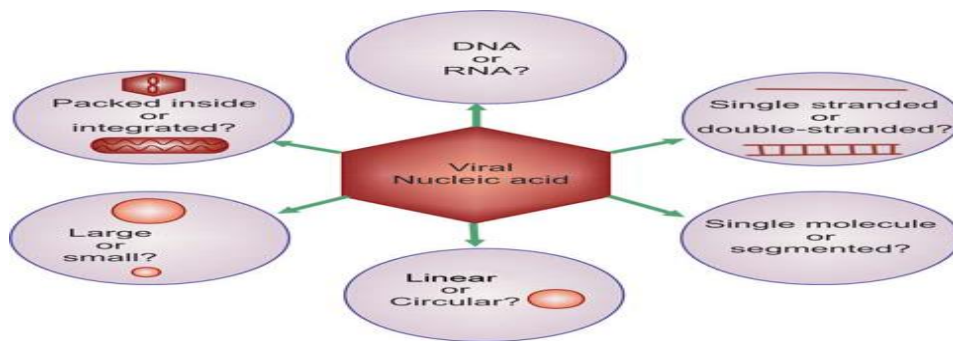
The classification of viruses has traditionally been done based on their structural properties:

1 Presence of DNA or RNA

2 Presence of nucleic acids in a single strand or double Strand

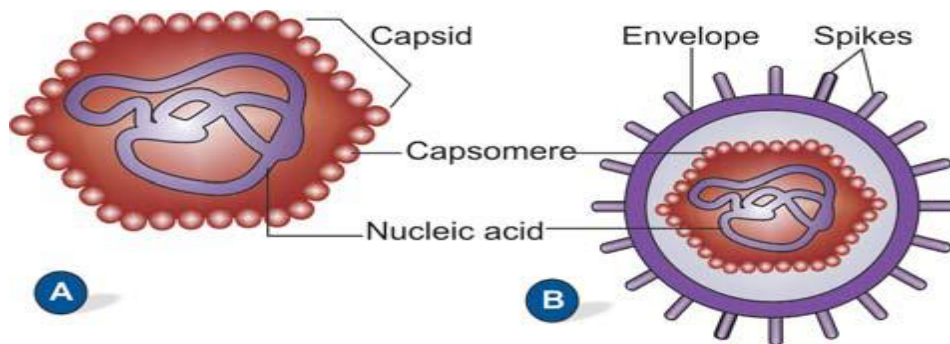
3 - Shape of the protein shell (icosahedral, spherical, other)

4 -Presence or absence of an envelope

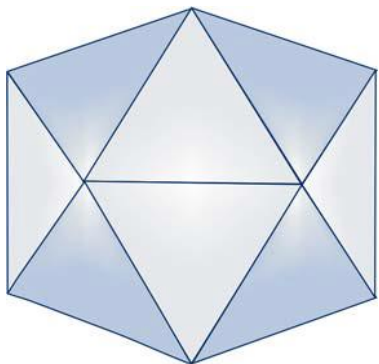


The Nature of Viruses

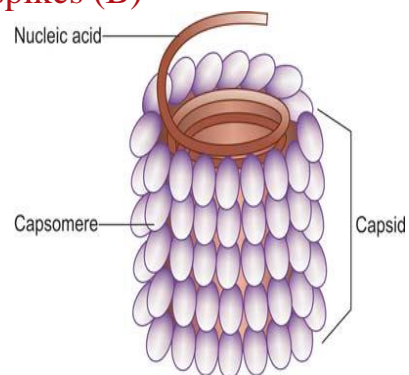
□ Viruses contain one kind of nucleic acid (**DNA or RNA genome**) inside a protein shell (**capsid**), which may be surrounded by a lipid bilayer membrane (**envelope**). The resulting complete virus particle is called a **virion**



Naked virus (A) and enveloped virus with spikes (B)



An icosahedron



Morphology of helical virus

The life cycle of virus (**Replication**) The replication of the viruses is happened in the host cells that can be represented in the following processes:

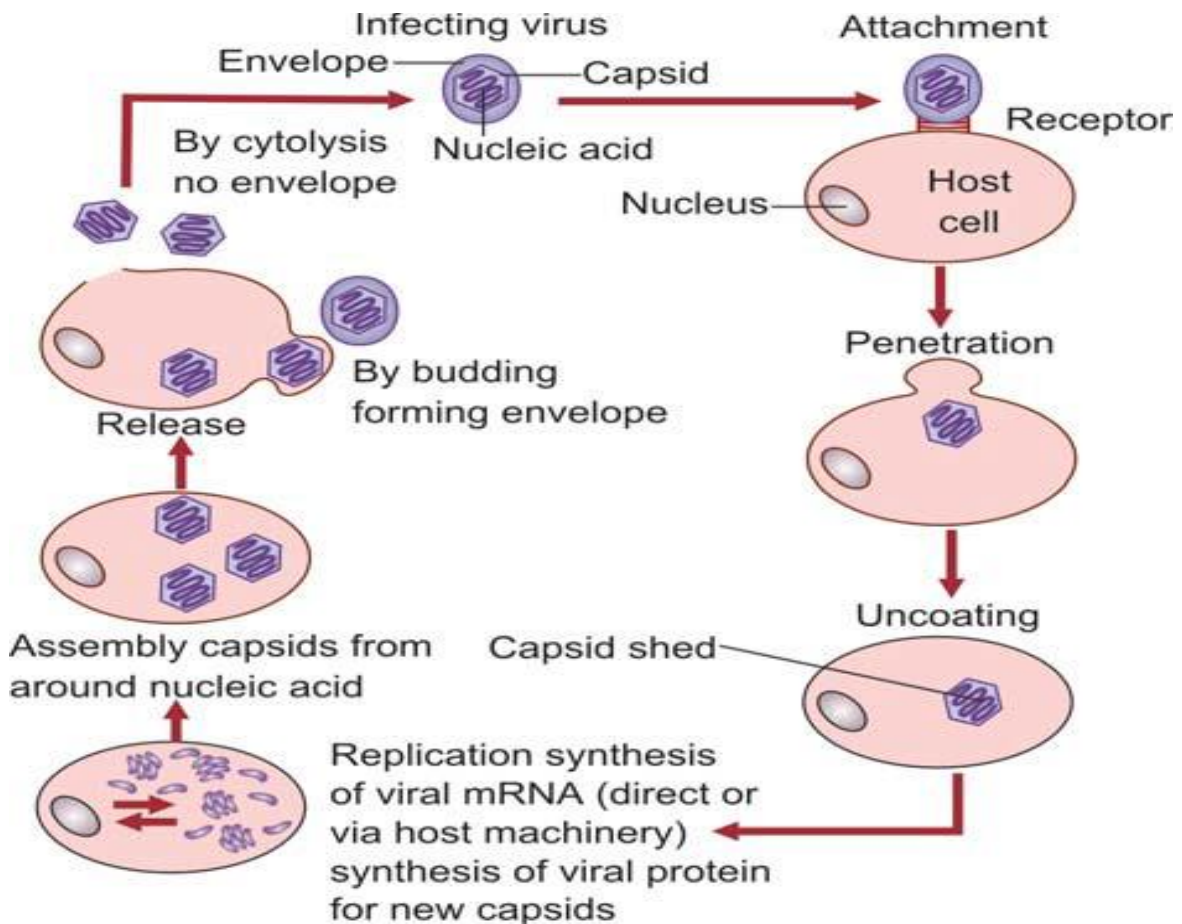
1-Attachment and Absorption The virus attaches itself to the host cell surface by means of the specific receptors on its capsid or envelope that are complementary to those on the host cells. The host cells lacking the appropriate receptors can not be infected with virus.

2-Penetration After the absorption the virus particle (virion) is carried into the cell by process called pinocytosis or phagocytosis.

3-Uncoating The virus particle release nucleic acid in the cytoplasm of the host cell by uncoating of the virion, this uncoating of by means of the lysozymal enzymes, which produced by the host cell in the case of infection with envelope virion, that have DNA, this nucleic acid combined DNA of the host cell, which are be induced to multiplication the results of this replication is high amounts production of viral DNA. This process is induced by coded and translated of mRNA of the host cell. The same process when the host cell is infected with naked virion that have RNA, but the replication The result of these metabolic processes is then turned to the replication of new viral particles.

4-Maturation Protein capsid are condensed around molecule of viral nucleic acid to form new virion particles.

5-Release Virion particles or mature viruses are released from the host cell by two ways: a)-The naked viruses that are replicated in cytoplasm of the host cell are released from the cell by lyses of the host cell membrane. b)-The envelope viruses are released by extrusion through the cell membrane of the host.



Infection and replication of viruses

Viruses that infect the respiratory tract:

Rhinoviruses, Coronaviruses, Coxsackieviruses, Adenoviruses, Influenza virus Parainfluenza viruses, Respiratory syncytial virus, Epstein–Barr virus

Respiratory tract infections (RTIs) are [infectious diseases](#) involving the [respiratory tract](#).^[1] An infection of this type usually is further classified as an [upper respiratory tract infection](#) (URI or URTI) or a [lower respiratory tract infection](#) (LRI or LRTI). Lower respiratory infections, such as [pneumonia](#), tend to be far more severe than upper respiratory infections, such as the [common cold](#)

Upper respiratory tract infection

The [upper respiratory tract](#) is considered the airway above the [glottis](#) or vocal cords;. This part of the tract includes the [nose](#), [sinuses](#), [pharynx](#), and [larynx](#).^[2]

Typical infections of the upper respiratory tract include [tonsillitis](#), [pharyngitis](#), [laryngitis](#), [sinusitis](#), [otitis media](#), certain [influenza](#) types, and the [common cold](#).^[3] Symptoms of URIs can include [cough](#), [sore throat](#), [runny nose](#), [nasal congestion](#), [headache](#), low-grade [fever](#), facial pressure, and [sneezing](#).^{[4][5]}

Lower respiratory tract infection[edit]

The **lower respiratory tract** consists of the **trachea** (windpipe), **bronchial tubes**, **bronchioles**, and the **lungs**.^[*citation needed*]

Lower respiratory tract infections are generally more severe than upper respiratory infections. LRIs are the leading cause of death among all **infectious diseases**.^[6] The two most common LRIs are **bronchitis** and **pneumonia**.^[7] **Influenza** affects both the upper and lower respiratory tracts, but more dangerous strains such as the highly pernicious **H5N1** tend to bind to receptors deep in the lungs

RHINOVIRUS

Properties • Non enveloped RNA viruses;

- Symptoms caused by infection of respiratory ciliated epithelial cells stimulates cellular inflammatory response with expression of cytokines and chemokines

Clinical Disease • Primarily an upper respiratory tract infection • Initiated with sore, “scratchy” throat followed closely with rhinorrhea and nasal obstruction; cough, sneezing, headache, and low-grade fever (particularly in children) also develop • Symptoms can persist for 1 week or more

Diagnosis • Definitive diagnosis cannot be made based on clinical parameters

- Virus can be grown in culture but this is rarely performed
- Antigen tests have been replaced in recent years by nucleic acid amplification tests (NAATs)

Treatment, Control, Prevention • No specific antiviral therapy is available • Vaccines are not available

CORONAVIRUSES

Properties • Enveloped RNA virus

- Replicate in ciliated and nonciliated epithelial cells of the nasopharynx
- Stimulate production of cytokines and chemokines resulting in cold symptoms; hyperproduction of this inflammatory response is responsible for the pathology with SARS-CoV and MERS-CoV

Clinical Disease • Infections with the common cold coronaviruses have a 2-day incubation period, with peak symptoms 3 to 4 days after exposure; symptoms similar to rhinovirus infections (sore throat, rhinorrhea, cough, headache)

- SARS-CoV infections not typically associated with coldlike symptoms; typically present with fever, headache, myalgia, followed by a nonproductive cough; progression to severe pulmonary disease most likely in older adults and patients with underlying disease (e.g., diabetes, cardiac disease, hepatitis, chronic pulmonary disease)
- MERS-CoV infections can be restricted to mild upper respiratory tract symptoms, but more likely progresses to respiratory and multiorgan failure

Diagnosis • Although the viruses can be grown with some difficulty in culture, this is rarely done except in public health laboratories • Diagnosis most commonly by

NAATs Treatment, Control, Prevention • No specific antiviral therapy is available • Vaccines are not available

INFLUENZA VIRUSES

Properties • Enveloped RNA viruses with genome divided into 8 segments

- Three types of influenza viruses: A, B, C; A and B associated with epidemics; A is the most virulent
- Strains identified by their surface proteins: hemagglutinin (H), neuraminidase (N)
- Virus infects ciliated columnar epithelial cells of the trachea and bronchials

Clinical Disease • After a 1- to 2-day incubation period, onset is acute with fever, chills, myalgias, and headache, as well as cough, chest pain, and nasal discharge; symptoms may last 1 week or longer • Complications include primary viral pneumonia or secondary bacterial pneumonia (most commonly with *Staphylococcus aureus* and *Streptococcus pneumoniae*)

Diagnosis • Viral culture has generally been replaced with immunoassays or NAATs

- Specific diagnosis is important for guiding antiviral therapy

Treatment,

Control,

Prevention • Treatment and prophylaxis of influenza A and B infections with neuraminidase inhibitors zanamivir or oseltamivir; must be initiated early in infection • Previously influenza A but not B was treated with amantadine or rimantadine, but resistance is now widespread • Multiplex vaccines widely used to control disease

PARAINFLUENZA VIRUSES

Properties • Enveloped RNA virus with four major human serotypes: parainfluenza virus-1 (PIV-1), PIV-2, PIV-3, PIV-4 • Preferentially infect ciliated epithelial cells of the upper and lower respiratory tract Clinical Disease • Most pediatric infections limited to upper respiratory tract with cold symptoms developing about 1 day after exposure to the virus and persisting for a week or more; involvement of the sinuses and middle ear occurs in up to half of children

- PIV-1 and PIV-2 associated with laryngotracheobronchitis (croup) with initial development of fever, rhinorrhea, and pharyngitis, and then progressing to a barking cough associated with stridor and difficulty breathing; PIV-1 disease is generally more severe than PIV-2 disease • PIV-3 disease is more commonly associated with pneumonia and bronchiolitis in children, and PIV-4 primarily causes mild upper respiratory infections

- PIV infections in adults are generally asymptomatic or mild upper respiratory infections, except in immunocompromised patients where severe lower respiratory tract disease can develop and is associated with high mortality

RESPIRATORY SYNCYTIAL VIRUS

Properties • Enveloped RNA virus; two major antigenic groups (A and B) with multiple subgroups; both groups circulate in populations simultaneously

- RSV infects the ciliated columnar epithelial cells of the lower airways as well as pneumocytes
- Clinical Disease • Infection in infants primarily involves the lower respiratory tract, presenting after a 2- to 5-day incubation period as bronchiolitis; pneumonia can develop but croup occurs less commonly

- RSV infections in children and adults present initially as an upper respiratory tract infection with nasal congestion and cough
- Otitis media is associated with pediatric disease and co-infections with bacterial pathogens are responsible for more severe otitis
- Adult disease is primarily mild, although severe lower respiratory disease is well-recognized in elderly, immunocompromised adults and those with underlying cardiopulmonary disease (chronic obstructive pulmonary disease, congestive heart failure)

Diagnosis • Although RSV can be grown in culture, most clinical diagnoses are by NAATs

- Virus shedding in adult patients, even with severe disease, is quantitatively lower than in infants which makes diagnosis more challenging
- Treatment, Control, Prevention
- Mild infections are treated symptomatically
 - Bronchiolitis is generally managed with bronchodilators and corticosteroids
 - Ribavirin is approved for treatment of hospitalized infants with lower respiratory tract disease, although benefits have not been consistently demonstrated for this population or for older children or adults with RSV infections

ADENOVIRUS

Although most respiratory infections are caused by RNA viruses, the nonenveloped DNA virus, adenovirus, has been associated with outbreaks of severe respiratory infections