ABCs of Vaccines

Part 1: DTaP, Hib, PCV, & IPV

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PUBLIC HEALTH DIVISION
IMMUNIZATION UNIT

Overview

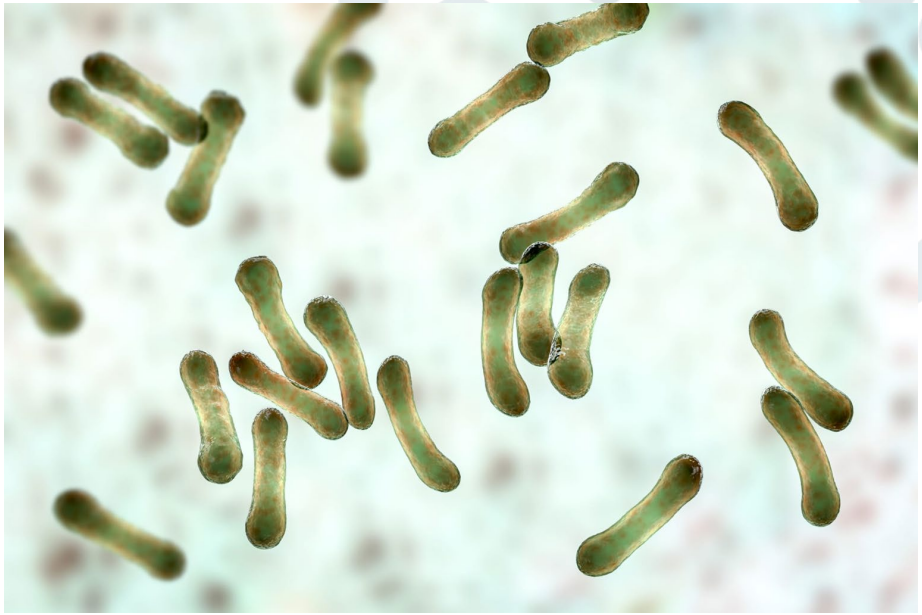
Disease causative agent, pathogenesis, and vaccination for:

- Diphtheria
- Tetanus
- Pertussis
- *Haemophilus influenzae* type B
- Pneumococcal
- Polio

Diphtheria

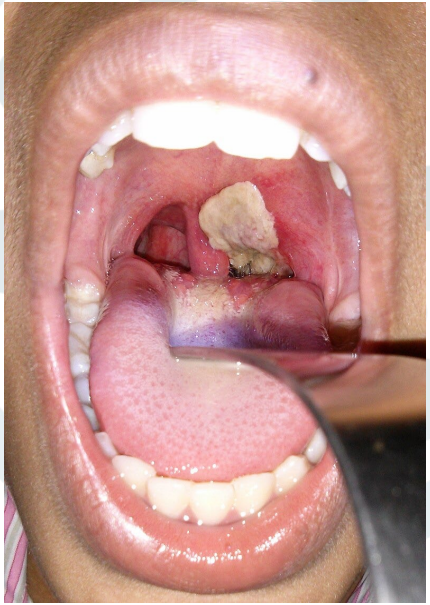
Corynebacterium diphtheriae

- Aerobic gram-positive bacillus
- Toxin production (toxigenicity) occurs only when the bacillus itself is infected by corynebacteriophages (a type of virus) carrying the genetic information for the toxin
    - Diphtheria toxin causes the local and systemic manifestations of diphtheria



Diphtheria pathogenesis

- Toxigenic diphtheria bacilli acquired in the nasopharynx
  - Toxin inhibits cellular protein synthesis, destroys local tissue, and forms a pseudomembrane
- Toxin produced in the pseudomembrane is absorbed into the bloodstream and then distributed to the tissues of the body
  - This causes major complications such as myocarditis, polyneuropathies, and nephritis
- Non-toxin producing strains can cause mild to severe exudative pharyngitis, cutaneous lesions, endocarditis, bacteremia, and septic arthritis



Diphtheria epidemiology

- Humans are the reservoir
- Occurs worldwide, particularly in countries with suboptimal vaccination coverage
  - Most frequently occurs during winter and spring in temperate areas
- Person-to-person transmission through respiratory droplets
  - May also occur from exposure to infected skin lesions or articles soiled with discharges from these lesions
- Transmission occurs as long as virulent bacilli are present in discharges and lesions

Diphtheria clinical features

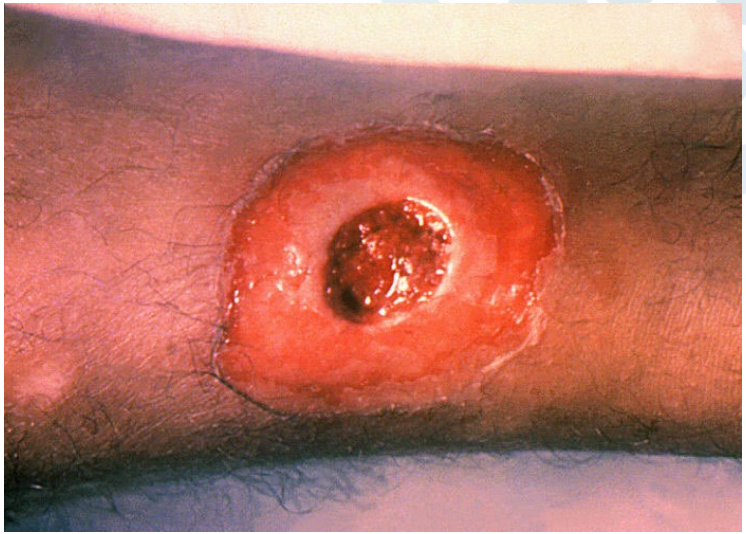
- Incubation period 2 to 5 days
- May involve any mucous membrane
- In untreated people, the organism can be present in discharges and lesions 2 to 6 weeks after infection
- Classified based on the site of disease
  - Respiratory (pharyngeal, tonsillar, laryngeal, nasal)
  - Non-respiratory (cutaneous and other mucus membranes)
- Most common sites of infection are the pharynx and tonsils

Pharyngeal and tonsillar diphtheria

- Infection at these sites is associated with substantial systemic absorption of toxin
- Early symptoms include malaise, sore throat, anorexia, and low-grade fever
- Within 2 to 3 days, a bluish-white membrane forms and extends
  - Varies in size from a small patch on the tonsils to covering most of the soft palate
  - Membrane is firmly adherent to the tissue, and forcible attempts to remove it can cause bleeding
  - Can lead to respiratory obstruction
- Some may develop severe disease
  - Marked edema of the submandibular areas and anterior neck - “bull neck”
  - Severe prostration, pallor, rapid pulse, stupor and coma
  - Death can occur within 6 to 10 days

Cutaneous diphtheria

- Scaling rash or ulcers with clearly demarcated edges and an overlying membrane
- Quite common in the tropics



Medical management

- Diphtheria antitoxin
  - Produced in horses
  - Used for the treatment of respiratory diphtheria since the 1890s
  - Only available from the CDC, through an Investigational New Drug (IND) protocol
  - Neutralizes circulating toxin and prevents progression of disease
- Antibiotics
  - Administered along with antitoxin to those with respiratory diphtheria

Diphtheria secular trends

- Nationally notifiable disease
  - Required to be immediately reported to WDH in Wyoming
- Up to 200,000 cases and 15,000 deaths annually before the vaccine was introduced
- From 1996-2018, 14 U.S. cases reported

Prevention

- Diphtheria disease might not confer immunity
  - Unvaccinated or incompletely vaccinated persons recovering from diphtheria should begin or complete immunization

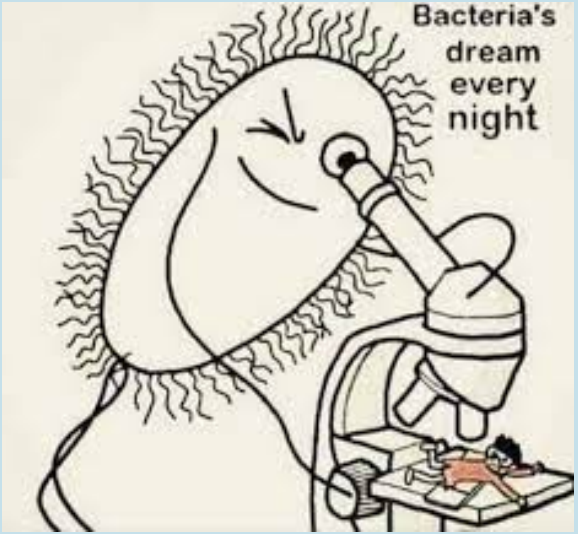
Diphtheria vaccines

- First developed in the early 1920s, and incorporated with tetanus and pertussis vaccine for routine use in the 1940s
- Inactivated, toxoid-based vaccines
  - Always in a vaccine along with tetanus, and sometimes pertussis
- Intramuscular (IM) injection
- Primary series at 2, 4, and 6 months of age, with boosters at 15-18 months and 4-6 years with a DTaP-containing vaccine
- 1 dose at 11-12 years of Tdap, and every 10 years thereafter with Tdap or Td
- Vaccine efficacy estimated to be 97%

Diphtheria toxoid -containing vaccines

- DTaP (Daptacel and Infanrix)
- Td (Tenivac)
- Tdap (Adacel and Boostrix)
- DTaP-HepB-IPV (Pediarix)
- DTaP-IPV/Hib (Pentacel)
- DTaP-IPV (Kinrix and Quadracel)
- DTaP-IPV-Hib-HepB (Vaxelis)

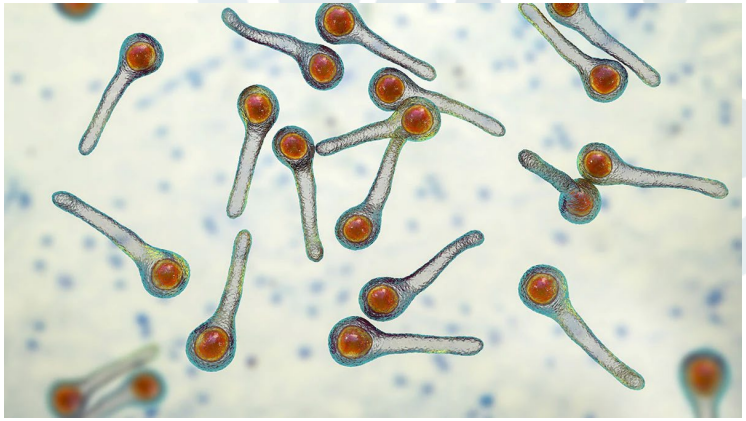
Questions?



Tetanus

Clostridium tetani

- Anaerobic gram-positive, spore-forming bacteria
- The bacterium is sensitive to heat and cannot survive in the presence of oxygen
  - The spores, however, are extremely resistant to heat and usual antiseptics
- Spores are widely distributed in soil and in the intestines and feces of horses, sheep, cattle, dogs, cats, rats, guinea pigs, and chickens
- Two exotoxins are produced
  - Tetanospasmin – a neurotoxin that produces the clinical manifestations of tetanus
    - One of the most potent toxins known



Tetanus pathogenesis

- Usually enters the body through a wound
- Spores germinate in the presence of anaerobic conditions
- Toxins are produced and are disseminated in the blood and lymphatics
  - Tetanospasmin binds to peripheral motor end plates, the spinal cord, the brain, and the sympathetic nervous system
    - Interferes with neurotransmitter release to block inhibitory impulses, leading to unopposed muscle contraction and spasm

Tetanus epidemiology

- Occurs worldwide
- Transmission is primarily by contaminated wounds
  - In recent years, more cases have resulted from minor wounds because severe wounds are more likely to be appropriately treated
  - Elective surgery, burns, deep puncture wounds, crush wounds, otitis media, dental infection, and animal bites
- Peaks in summer months in temperate climates
- Not contagious from person to person
  - The only vaccine-preventable disease that is infectious, but not contagious!

Tetanus clinical features

- Incubation period ranges from 1 to 21 days
  - In general, the further the injury site is from the central nervous system, the longer the incubation period
- Three forms
  - Generalized
    - Most common form
  - Local
    - Uncommon form where patients have persistent contraction of muscles in the same anatomic area as the injury
  - Cephalic
    - Rare form occasionally occurring with otitis media in which *C. tetani* is present in the flora of the middle ear or following injuries to the head

Generalized tetanus

- 80% of reported cases
- Presents with a descending pattern
- Trismus (lockjaw) is usually the first sign
- Stiffness of neck, difficulty swallowing, and rigidity of abdominal muscles follow
- Other symptoms
  - Fever, sweating, hypertension, episodic tachycardia
- Spasms may occur frequently and last for several minutes, and continue for 3-4 weeks
- Complete recovery may take months

Tetanus complications

- Laryngospasms
- Fractures of the spine or long bones
- Hypertension and abnormal heart rhythms
- Nosocomial infections from prolonged hospitalization
- Pulmonary embolism
- Aspiration pneumonia
- Death

Tetanus medical management

- Wound care
- Tetanus immune globulin (TIG)
  - Removes unbound toxin only
- Vaccination

Tetanus secular trends

- Nationally notifiable disease
- 500-600 cases annually before vaccine introduction in the U.S.
- 1 case in Wyoming in 2024

Tetanus vaccines

- Tetanus disease does not result in immunity due to potency of the toxin
- Tetanus toxoid vaccine was developed in 1924
- Inactivated, toxoid-based vaccines
  - Always in a vaccine along with diphtheria, and sometimes pertussis
- IM injection
- Primary series at 2, 4, and 6 months of age, with boosters at 15-18 months and 4-6 years with a DTaP-containing vaccine
- 1 dose at 11-12 years of Tdap, and every 10 years thereafter with Tdap or Td

Tetanus toxoid -containing vaccines

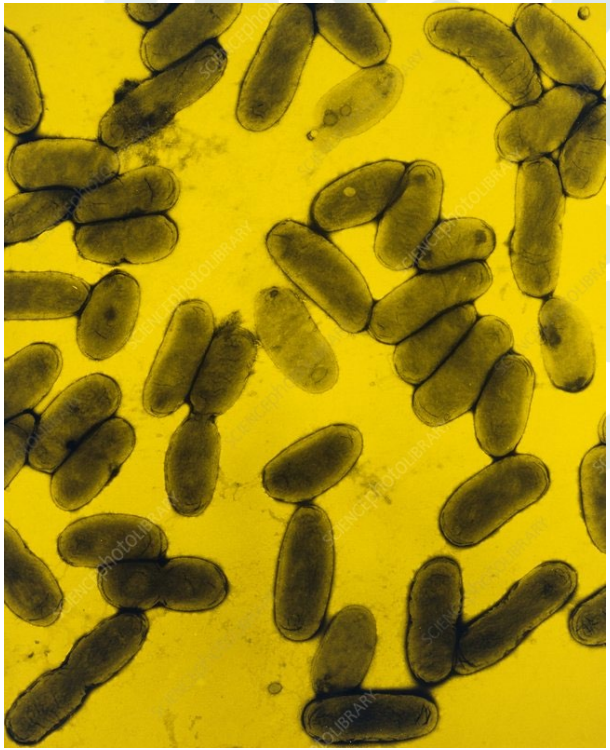
- DTaP (Daptacel and Infanrix)
- Td (Tenivac)
- Tdap (Adacel and Boostrix)
- DTaP-HepB-IPV (Pediarix)
- DTaP-IPV/Hib (Pentacel)
- DTaP-IPV (Kinrix and Quadracel)
- DTaP-IPV-Hib-HepB (Vaxelis)

Questions?

Pertussis

Bordetella pertussis

- Aerobic gram-negative bacteria
- Requires special media for isolation
- Produces antigenic and biologically active components responsible for the clinical features of pertussis disease
  - Pertussis toxin (PT)
  - Filamentous hemagglutinin (FHA)
  - Agglutinogens
  - Adenylate cyclase
  - Pertactin
  - Tracheal cytotoxin



Pertussis pathogenesis

- Primarily a toxin-mediated disease
- Bacteria attach to the cilia of respiratory cells
- Toxins paralyze the cilia and cause inflammation of the respiratory tract
  - Interferes with the clearance of respiratory secretions
- Pertussis antigens allow the organism to evade the immune system

Pertussis epidemiology

- Human disease
- Occurs worldwide
  - Adolescents, adults, and older school-aged children are an important reservoir
- Person-to-person spread through respiratory droplets
- No seasonal pattern, but may increase in summer and fall
- Highly communicable with secondary attack rates of 80% among susceptible household contacts
- Persons are infectious from the beginning of the catarrhal stage through the third week after the onset of paroxysms, or until 5 days after the start of effective antibiotic treatment

Pertussis clinical features

- Incubation period ranges from 4 to 21 days
- The clinical course of illness is divided into 3 stages
  - Catarrhal
    - Insidious onset with cold-like symptoms
    - 1-2 weeks
  - Paroxysmal
    - Bursts of numerous, rapid coughs characterized by a high-pitched whoop
    - The patient may become cyanotic
    - Vomiting and exhaustion may follow coughing episodes
    - 1-6 weeks
  - Convalescence
    - Gradual recovery
    - Weeks to months

Pertussis complications

- Young infants are at the highest risk of developing complications
- Secondary bacterial pneumonia is the most common complication and cause of death
- Neurologic complications such as seizures and encephalopathy may result from hypoxia due to coughing
- Other complications
  - Insomnia
  - Rib fractures
  - Urinary incontinence
  - Syncope
  - Weight loss
  - Dehydration
  - Hernias
  - Rectal prolapse
  - Pneumothorax

Pertussis medical management

- Primarily supportive
- Antibiotics are of some value if administered early
  - Eradicates the organism from secretions, reducing communicability
  - May modify the course of illness if administered early
- Immunity following an infection is not permanent

Pertussis secular trends

- Notifiable disease
- Average of 175,000 cases annually before vaccine introduction
- Incidence gradually increasing in U.S. since late 1980s with large epidemic peaks since mid-2000s
  - Contributing causes:
    - Waning vaccine-induced immunity
      - Transition to acellular vaccines in the 1990s
    - Increase in diagnostic testing
    - Heightened recognition and reporting
- 85 cases in Wyoming in 2025 as of May 30

Pertussis vaccines

- Whole-cell pertussis vaccines first licensed in 1914, and available as DTP in 1948
- Inactivated, acellular vaccines
  - Always in a vaccine along with tetanus and diphtheria
- IM injection
- Primary series at 2, 4, and 6 months of age, with boosters at 15-18 months and 4-6 years with a DTaP-containing vaccine
- 1 dose at 11-12 years of age
- Adults may receive Tdap every 10 years
- 1 dose of Tdap during each pregnancy between 27 and 36 weeks of gestation
- Vaccine efficacy is 80-85%

Pertussis containing vaccines

- DTaP (Daptacel and Infanrix)
- Tdap (Adacel and Boostrix)
- DTaP-HepB-IPV (Pediarix)
- DTaP-IPV/Hib (Pentacel)
- DTaP-IPV (Kinrix and Quadracel)
- DTaP-IPV-Hib-HepB (Vaxelis)

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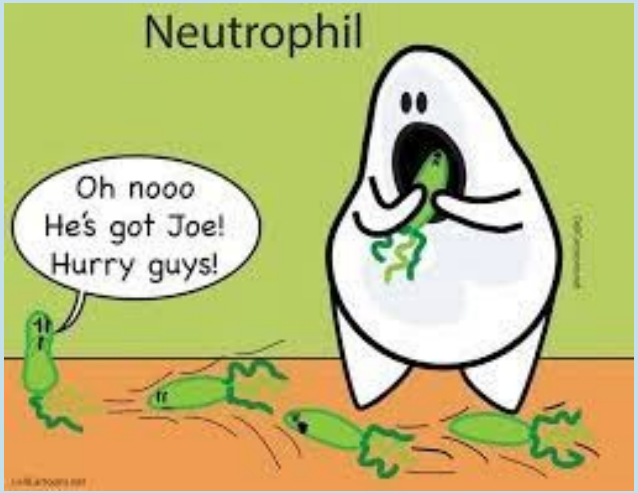
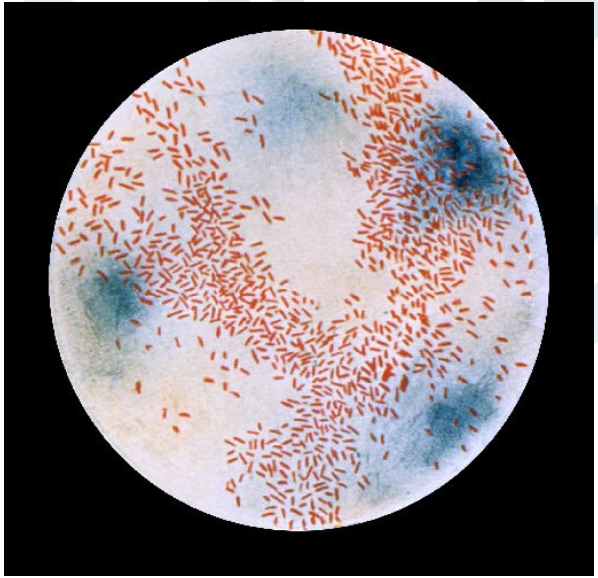


Haemophilus influenzae type b

Haemophilus influenzae type b (Hib)

- Aerobic gram-negative bacteria
- Polysaccharide capsule
  - Key virulence factor
  - 6 different serotypes (a-f) of the capsule
    - Type b caused 95% of invasive disease during the pre-vaccine era
- Does not survive in the environment on inanimate surfaces



Hib pathogenesis

- Enters and colonizes the nasopharynx
- In some persons, Hib causes an invasive infection
  - The exact mode of invasion of the bloodstream is unknown
  - Preceding viral or mycoplasma infection of the upper respiratory tract may be a contributing factor
  - Bacteria spread in the bloodstream to distant sites, with the meninges especially likely to be affected
- Pre-vaccine era, up to 60% of invasive disease occurred before 12 months of age
- Most children acquire immunity by age 6 years through asymptomatic nasopharyngeal carriage

Hib epidemiology

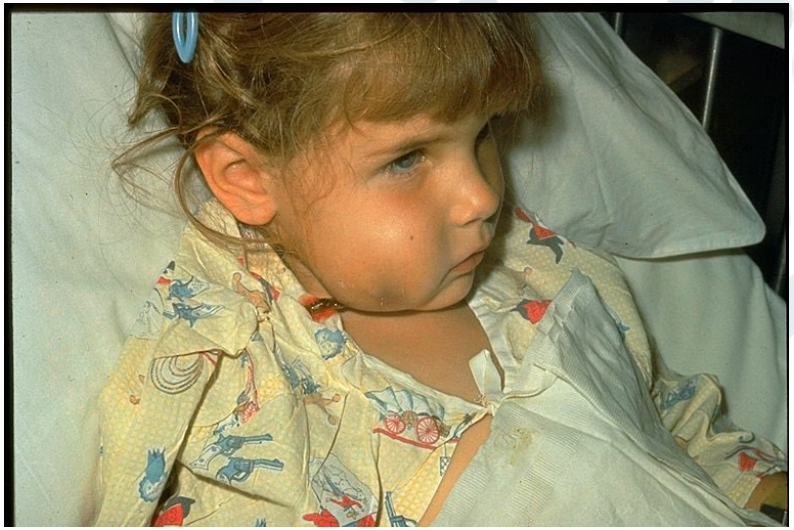
- Occurs worldwide
- Humans are the only known reservoir
- Transmitted person-to-person by respiratory droplets or by direct contact with respiratory tract secretions
- Neonates can acquire infection by aspiration of amniotic fluid or contact with genital tract secretions during delivery
- Bimodal seasonal pattern in the U.S., peaking in September-December and March-May
- Contagious potential is considered limited

Hib clinical features

- The most common diseases resulting from Hib infection are
  - Meningitis
  - Bacteremia
  - Epiglottitis
  - Pneumonia
  - Arthritis
  - Cellulitis

Hib medical management

- Invasive Hib disease generally requires hospitalization
- Prompt antimicrobial therapy with a third-generation cephalosporin
    - Chloramphenicol and ampicillin are an alternative



Hib secular trends

- Notifiable disease
  - All serotypes
  - Isolated from a sterile site
- ~20,000 cases annually in pre-vaccine era
- Incidence has declined 99% since vaccine introduction
- In U.S., 2009-2018, only 36 cases of Hib were reported in patients younger than 5 years

Hib vaccines

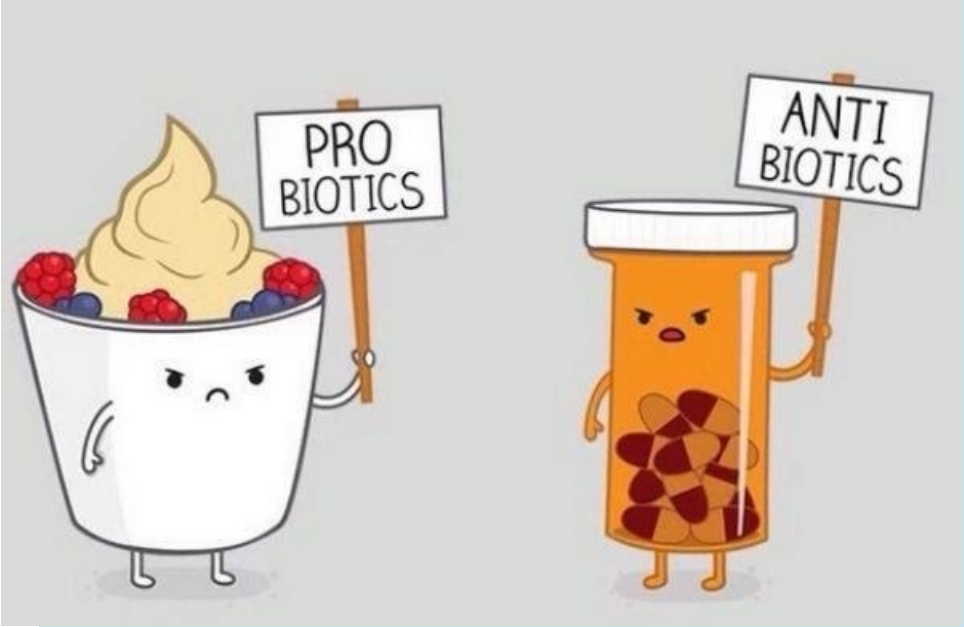
- First Hib conjugate vaccine licensed in 1987
- Inactivated vaccine
- IM injection
- Primary series depends on the brand used
  - ActHIB, Pentacel, Hiberix: 2, 4, 6 months primary series and booster at 12-15 months
  - PedvaxHIB: 2, 4 months primary series, booster at 12-15 months
  - Vaxelis: 2, 4, 6 months primary series, not licensed for the 12-15 months booster dose
- Routine use of the Hib vaccine is not recommended for healthy children aged 5 years or older
- Vaccine efficacy 95-100%

Hib containing vaccines

- PRP-T (ActHIB)
- PRP-T (Hiberix)
- PRP-OMP (PedvaxHIB)
- DTaP-IPV/Hib (Pentacel)
- DTaP-IPV-Hib-HepB (Vaxelis)

- PedvaxHIB and Vaxelis are preferentially recommended for American Indian and Alaska Native infants

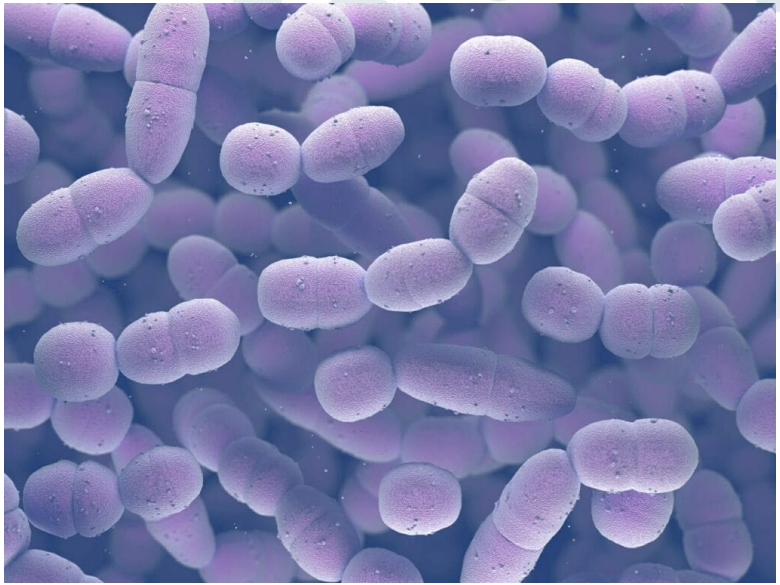
Questions?



Pneumococcal

Streptococcus pneumoniae

- Facultative anaerobic gram-positive bacteria
- Polysaccharide capsule
  - 100 serotypes documented as of 2020
    - Serotype prevalence differs by age and geographic area
    - Most serotypes known to cause serious disease



Pneumococcal pathogenesis

- Pneumococci commonly inhabit the respiratory tract
  - Asymptomatic carriage varies
    - School-age children 20-60%
    - Adults 5-10%
  - The relationship between carriage and the development of natural immunity is poorly understood

Pneumococcal epidemiology

- Occurs worldwide
- Human pathogen
- Transmission via respiratory droplets or autoinoculation
- Infections are more common during the winter and early spring
- Presumably communicable as long as the organism is in the respiratory secretions

Pneumococcal clinical features

- Non-invasive infections
  - Otitis media
  - Sinusitis
- Invasive disease
  - Pneumonia
  - Bacteremia
  - Meningitis

Pneumococcal disease in children

- *S. pneumoniae* is the leading cause of bacterial meningitis among children younger than 5 years old
- Bacteremia without a known site of infection is the most common invasive clinical presentation in children <2 years
- Common cause of otitis media
- Invasive disease risk is highest in:
  - Functional or anatomic asplenia, chronic heart disease, lung disease (including asthma if treated with high-dose corticosteroids), liver disease, CSF leak, cochlear implant
  - Alaska Natives, African Americans, and Navajo and White Mountain Apache populations
  - Attendance at a childcare center

Pneumococcal secular trends

- Not a notifiable disease
- In pre-vaccine era in children <5 years:
  - 17,000 cases of invasive disease
  - 200 deaths
  - 5 million cases of otitis media
- Since vaccine introduction, invasive disease has declined 99% in children

Pneumococcal vaccines

- First polysaccharide vaccine (PPSV) licensed in 1977
  - In 1983 PPSV23 was licensed
- First conjugate vaccine (PCV) licensed in 2000
- Inactivated vaccines
- IM injection
- Primary series at 2, 4, 6 months of age, with booster at 12-15 months
- Routine use of PCV is not recommended for healthy children age 5 years or older
- See immunization schedule for recommendations for children with certain medical conditions
- Vaccine efficacy of PCV against invasive disease in children is 97%

Pneumococcal vaccines for children

- Pneumococcal conjugate
  - PCV15 (Vaxneuvance)
  - PCV20 (Prevnar20)
- Pneumococcal polysaccharide
  - PPSV23 (Pneumovax23)

Questions?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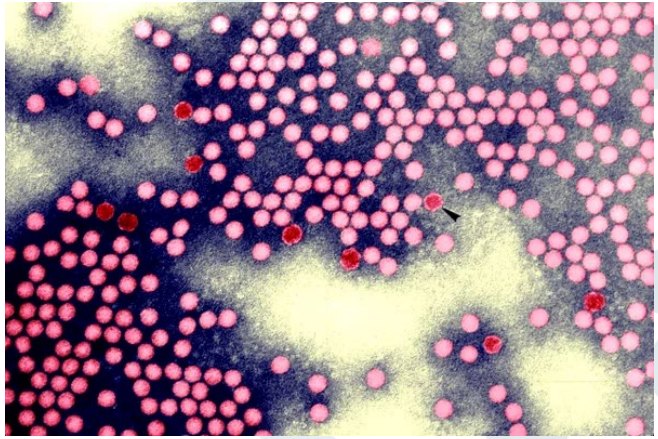
Poliomyelitis

Poliovirus



- Virus
- Enterovirus subgroup of Picornaviridae
- RNA genome
- Three serotypes
  - Type 1, type 2, and type 3
  - Immunity to one serotype does not produce significant immunity to other serotypes
- Rapidly inactivated by heat, formaldehyde, chlorine, and ultraviolet light

Polio pathogenesis

- Virus enters through the mouth and multiplies in the oropharynx and gastrointestinal tract
- During intestinal replication, the virus invades local lymphoid tissue and may enter the bloodstream
  - Infects cells of the central nervous system
  - Destruction of motor neurons of the anterior horn of the spinal cord and brain stem cells results in paralysis
- Virus present in nasopharyngeal secretions for 1-2 weeks and can be shed in stools for several weeks after infection

Polio epidemiology

- Endemic type 1 wild poliovirus persists in Pakistan and Afghanistan
  - Types 2 and 3 have been eradicated
- Humans are the only known reservoir
- Fecal-oral and oral-oral transmission
- Infections typically peak in summer months in temperate climates
- Highly infectious, with seroconversion rates among susceptible household contacts of children nearly 100%

Polio clinical features

- Incubation period
  - Nonparalytic polio 3 to 6 days
  - Paralytic polio 7 to 21 days
- Risk of severe disease and death increases with age
- Types
  - Asymptomatic
    - 70% of all infections in children are asymptomatic
  - Abortive
    - 24% of all infections in children
    - Minor, nonspecific illness without evidence of CNS invasion
  - Nonparalytic aseptic meningitis
    - 1-5% of infections in children
    - Complete recovery occurs
  - Paralytic
    - <1% of all infections in children

Paralytic polio

- Adolescents and adults often suffer from more severe paralysis
- Paralysis is typically asymmetrical, more proximally severe, and associated with absent or reduced deep tendon reflexes and intact sensation
- Often permanent
- Three types
  - Spinal
    - Most common type
    - Often involves the legs
  - Bulbar
    - Involves the facial, oropharyngeal, and respiratory muscles innervated by cranial nerves
  - Bulbospinal
    - Combination of spinal and bulbar
- Post-polio syndrome
  - 25-40% of persons who contracted paralytic polio in childhood experience new or worsening muscle pain and weakness
  - Not an infectious process

Polio secular trends

- Nationally notifiable disease
- 21,000 paralytic cases reported in 1952
- Incidence dramatically decreased following vaccine introduction in 1955
  - Only 61 cases of paralytic polio were reported in 1965
- Last U.S. paralytic cases caused by wild poliovirus:
  - 1979 for locally-acquired
  - 1993 for imported
- In 2022, 1 U.S. case with a vaccine-derived poliovirus strain
- In 2024, 99 confirmed wild polio cases
- Targeted for eradication by the World Health Organization in 1988

Polio vaccines

- Inactivated (IPV) licensed in 1955
  - IM injection
- Live, attenuated trivalent oral (tOPV) licensed in 1963
  - Discontinued in the U.S. in 1999
  - Bivalent OPV is still used internationally and replaced tOPV in April 2016
- Primary series at age 2, 4, 6-18 months, and 4-6 years
- After 3 doses, 99% of recipients are immune
  - Duration of immunity is not known, although probably lifelong

Polio vaccines

- IPV (IPOL)
- DTaP-HepB-IPV (Pediarix)
- DTaP-IPV/Hib (Pentacel)
- DTaP-IPV (Kinrix)
- DTaP-IPV (Quadracel)
- DTaP-IPV-Hib-HepB (Vaxelis)

Questions?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YOU MIGHT CALL THEM SCIENTISTS, BUT FOR ME THEY ARE "PAPARAZZI"!
KOMARNITSKI

Thank you!!

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