Streptococcus pyogenes, Bordetella pertussis and *Corynebacterium diphtheriae*

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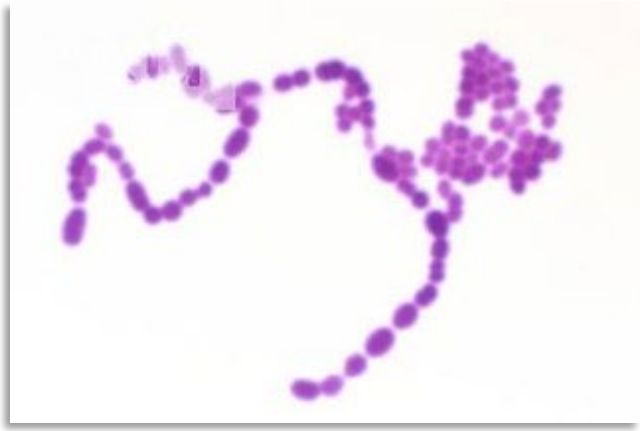
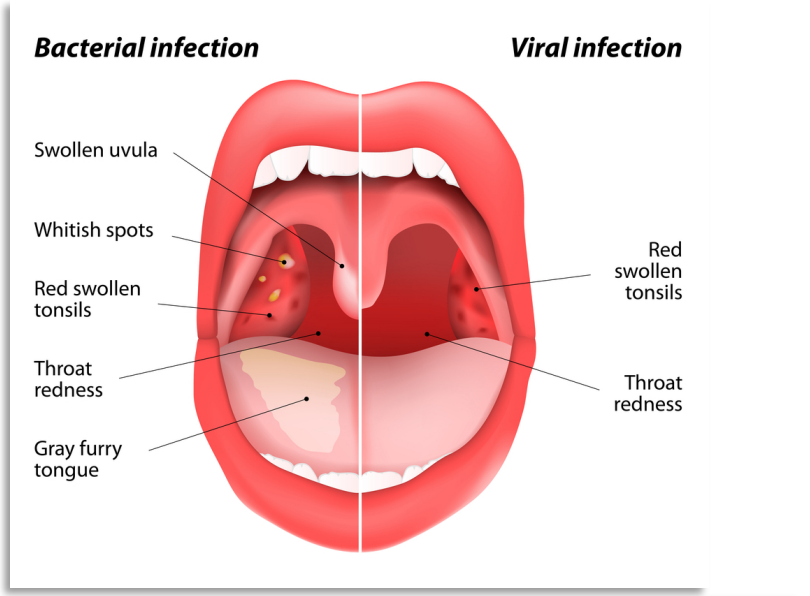
Streptococcus pyogenes (GAS) respiratory infections

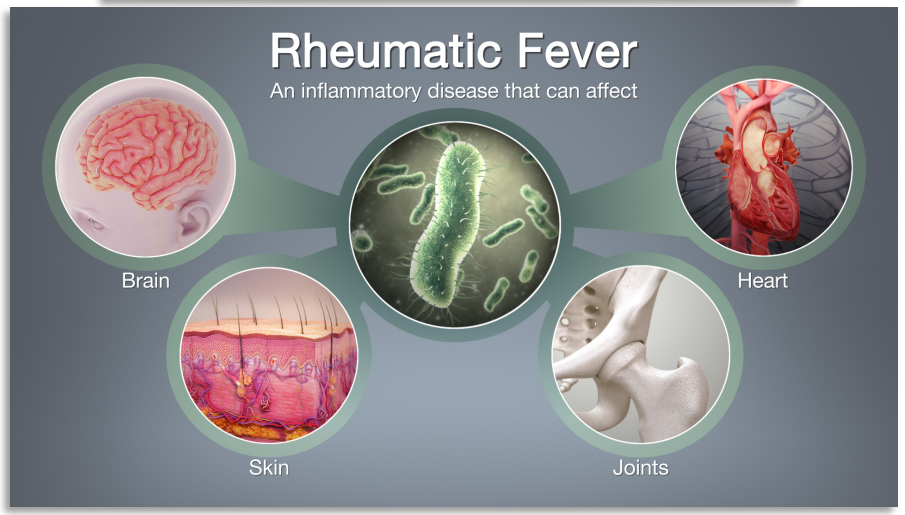
- **Gram-positive cocci** arranged in chains and beta-hemolytic on blood agar and **bacitracin sensitive**
- Hyaluronic acid capsule inhibits phagocytosis. M protein is a major virulence factor being anti-phagocytic determinant and responsible for molecular mimicry implicated in rheumatic fever
- Pili (fimbriae) extend through the capsule and mediate adherence to epithelial cells which is critical for colonization of the oropharynx. Protein F binds fibronectin on host cells facilitating mucosal adherence, especially in the oropharynx
- In GAS, immune evasion explains acute pharyngitis and host mimicry explains delayed immune sequelae.



Streptococcus pyogenes Upper Respiratory Tract Infection Clinical Syndrome

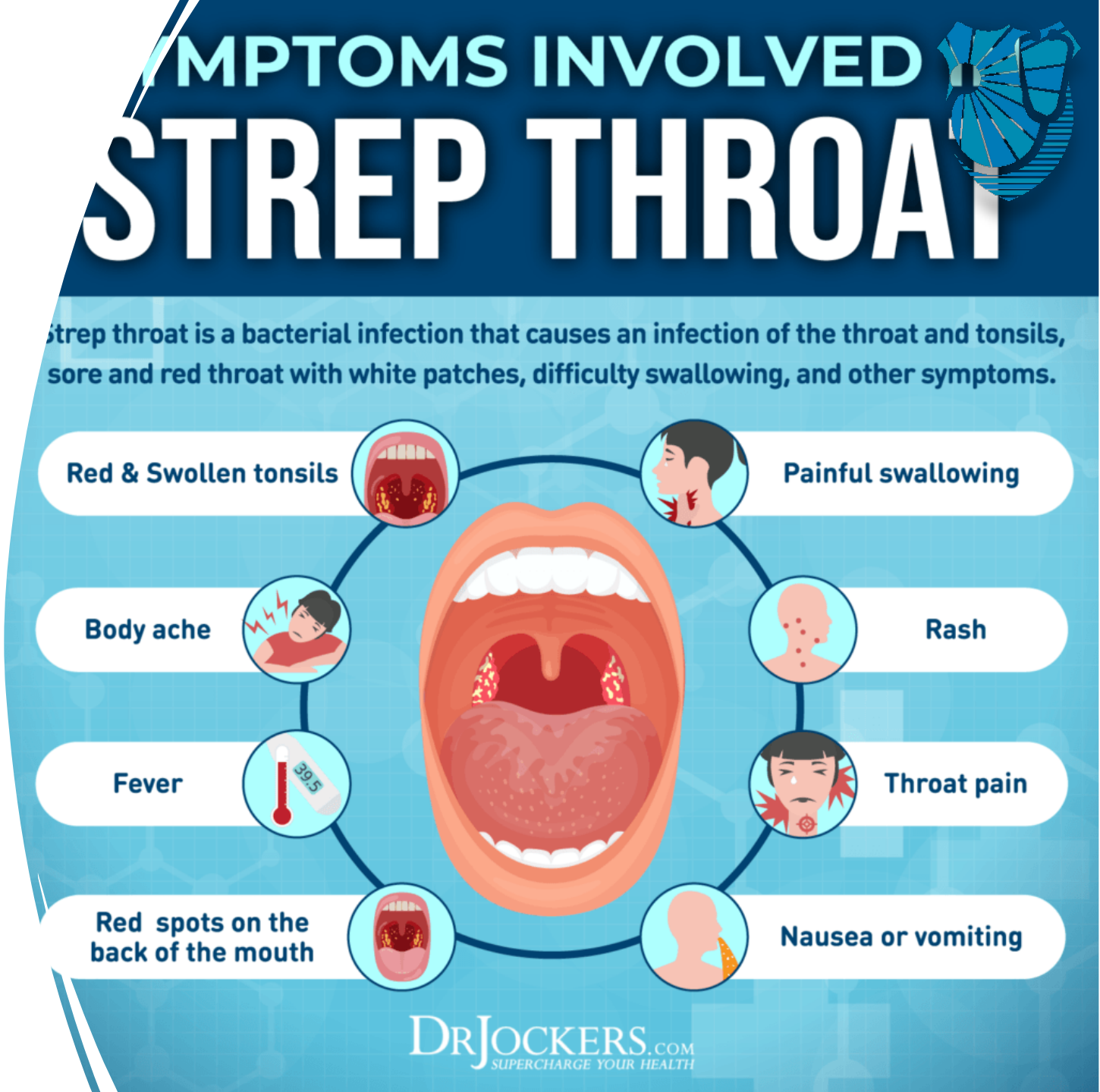
- Acute pharyngitis/tonsilitis is a common inflammatory condition of the posterior pharynx and tonsils
- It is caused by multiple viruses and bacteria.
- **Only one pathogen requires etiologic diagnosis and specific therapy: *Streptococcus pyogenes* (Lancefield group A β-hemolytic streptococcus (GAS))**
- GAS pharyngitis can trigger post-infectious immune complications (acute rheumatic fever and post-streptococcal glomerulonephritis)





Clinical presentation of GAS pharyngitis

- Abrupt onset
- Intense sore throat
- Fever, chills
- Malaise, headache
- Tender anterior cervical lymphadenopathy
- Pharyngeal or tonsillar exudates



Streptococcus pyogenes URTI Diagnosis

- A Strep Throat **Rapid Antigen Detection Test** (RADT): High specificity, positive test is sufficient to treat
- **Throat culture: The gold standard**; recommended if RADT negative in children
- **Clinical scoring systems?** The Centor Score and McIsaac Guide are clinical tools to estimate the probability of group A Strep in patients with sore throats, to guide whether strep testing and antibiotics are needed. The Centor Score uses four symptoms (fever, tonsillar exudate, tender anterior cervical nodes, no cough), each worth 1 point (0-4 total). The McIsaac Guide (or modified Centor) adds age, giving +1 for ages 3-14, 0 for 15-44, and -1 for 45+, resulting in a score from -1 to 5.
  Controversial value?
- ASO confirms past streptococcal exposure not acute pharyngitis.

Streptococcus pyogenes URTI Treatment and Prevention

Antibiotic treatment

First-line therapy: Penicillin V or Amoxicillin. GAS remains universally susceptible to penicillin

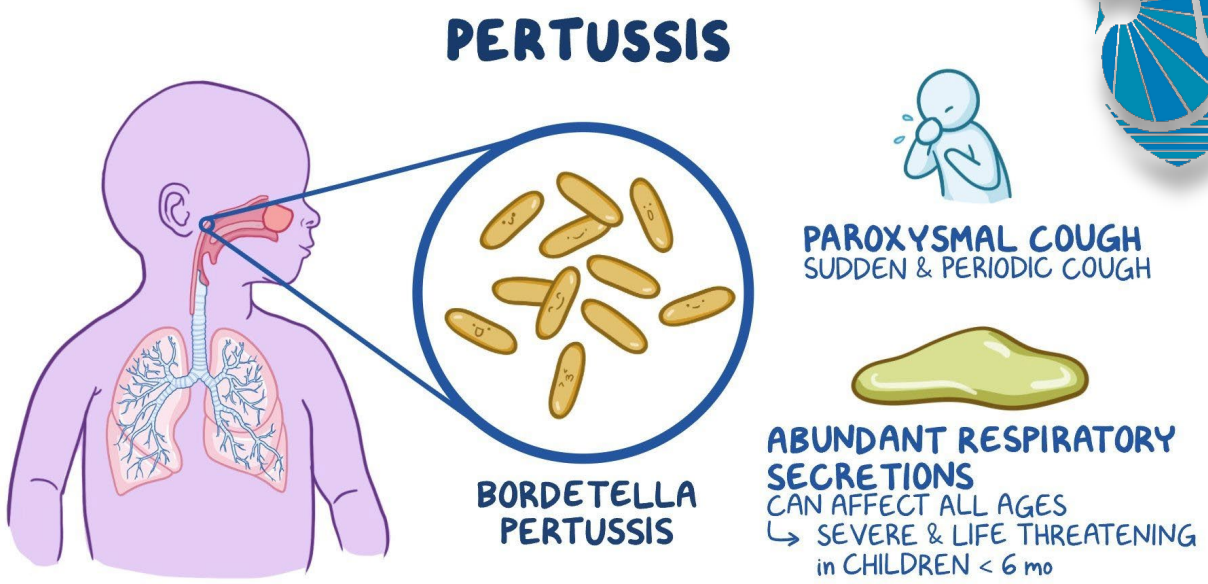
Penicillin allergy: Macrolide (e.g., azithromycin) Duration 10 days for β-lactams. Shorter course acceptable for azithromycin

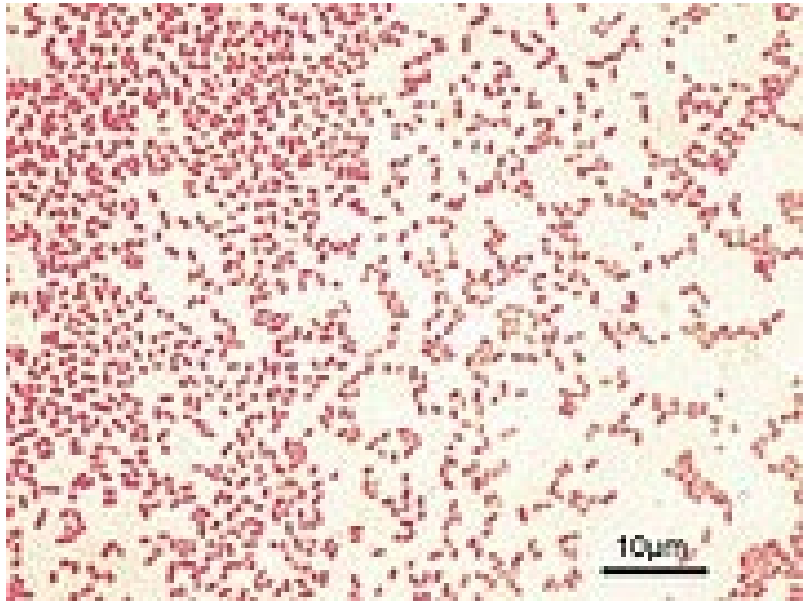
Goals of therapy: Prevent acute rheumatic fever, reduce symptom duration, and decrease transmission

No approved commercial vaccine for GAS

Bordetella pertussis

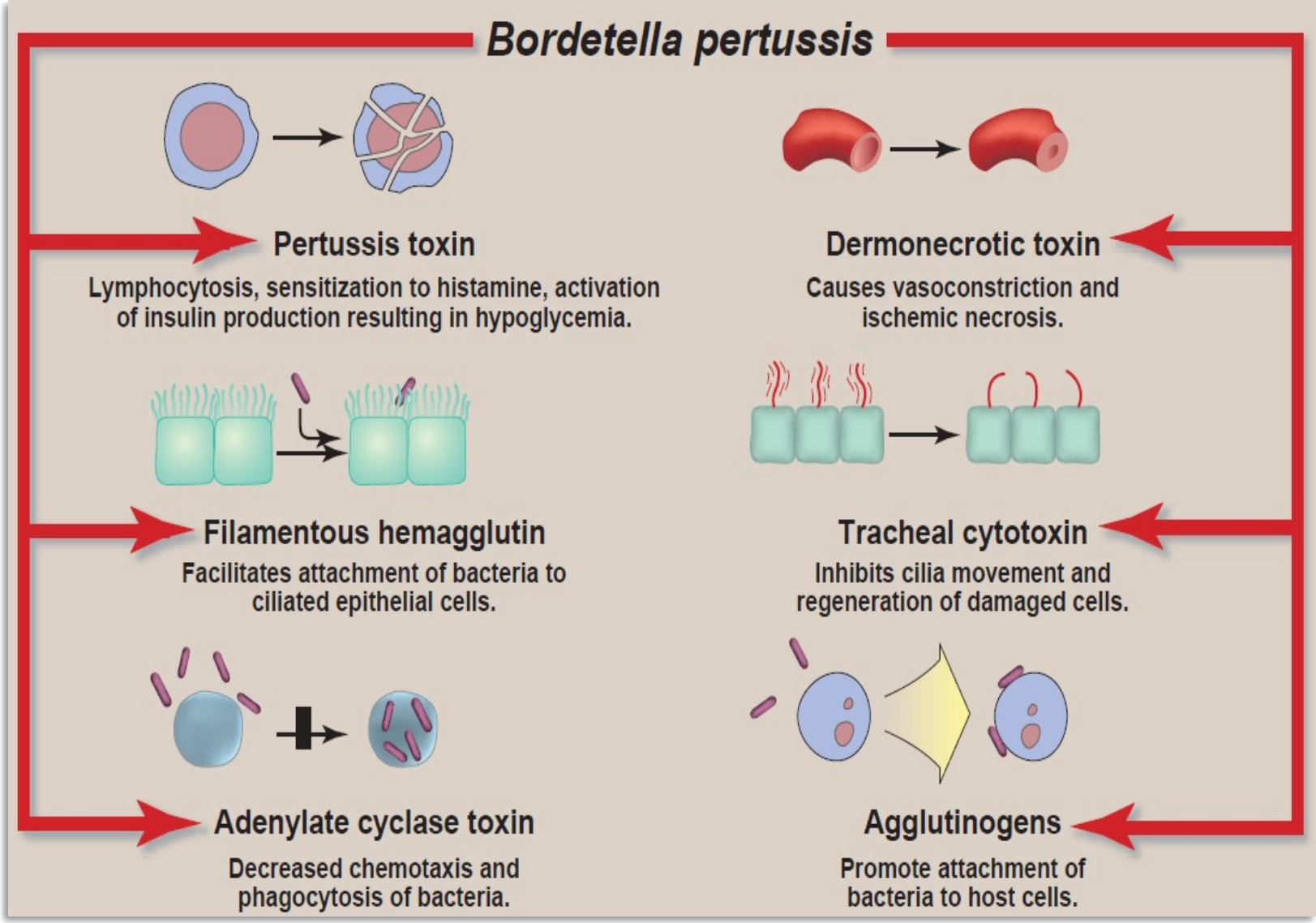
- Small **Gram-negative coccobacillus**
- Strict aerobe, highly fastidious
- Adheres to ciliated respiratory epithelium (**does not invade**)
- Transmission: respiratory droplets
- Reservoir: humans only (no environmental reservoir)
- Highly contagious, especially in unvaccinated populations

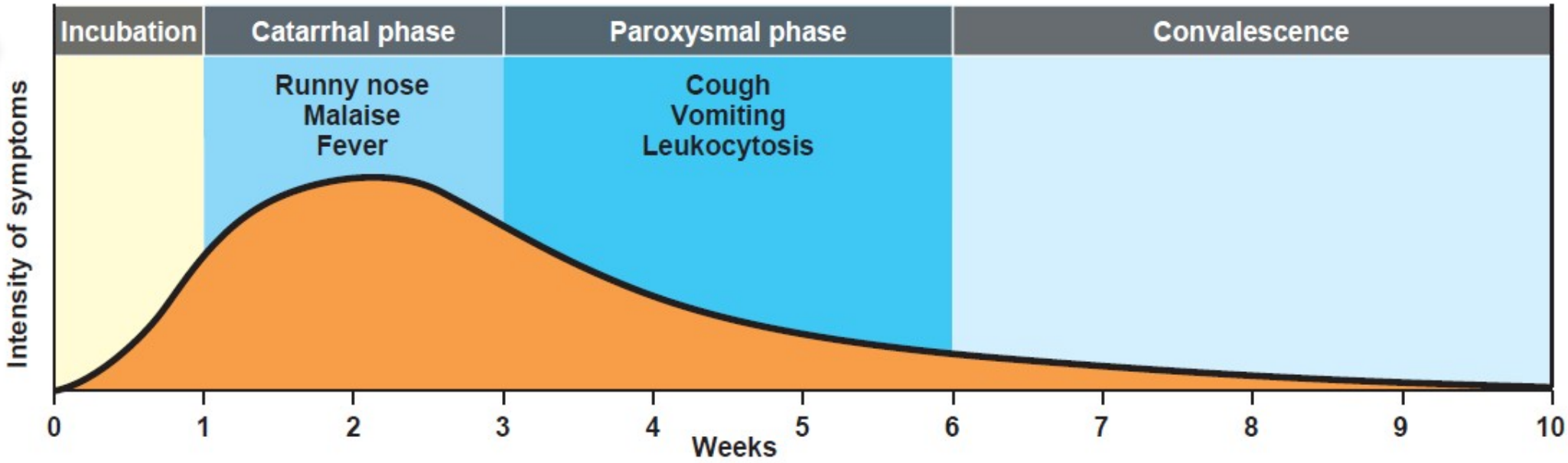




Bordetella pertussis virulence factors

- **Adhesins** that aid in colonization via attachment to ciliated respiratory epithelial cells: Filamentous hemagglutinin (**FHA**), pertactin (**PRN**), and **fimbriae**
- **Pertussis toxin (PT)**
- Adenylate cyclase toxin (ACT)
- Tracheal cytotoxin (TCT)
- Dermonecrotic toxin (DNT)



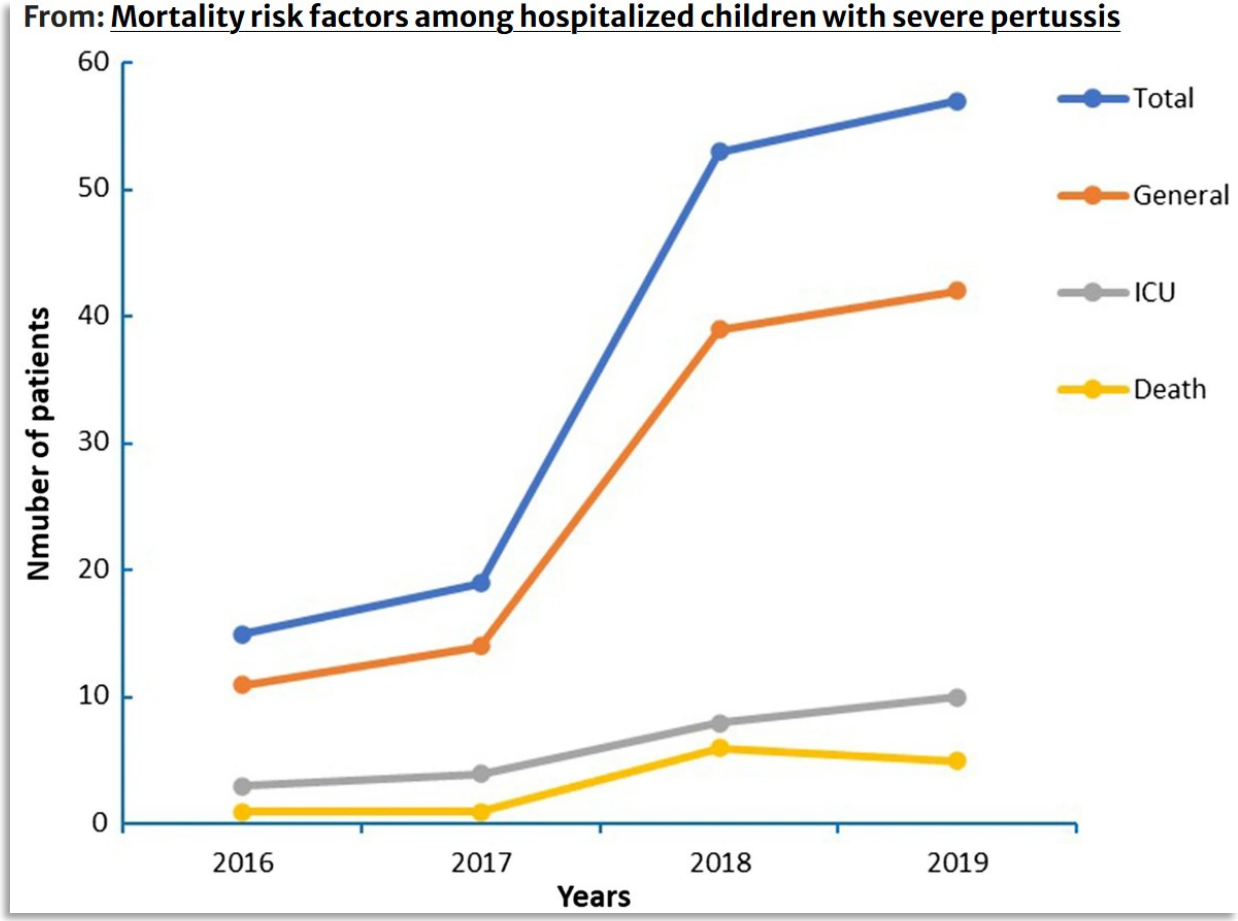


Pertussis: Stages and clinical manifestations

1. **Catarrhal phase (about 1-2 weeks):** Non-specific URI symptoms such as rhinorrhea, sneezing, mild cough, low-grade fever. The highest bacterial load and most contagious stage. This is when antibiotics are most effective in reducing transmission
2. **Paroxysmal phase (about 2-6 weeks):** Paroxysms of severe coughing. Inspiratory "whoop" (more obvious in children). Post-tussive vomiting. Apnea in infants. Marked lymphocytosis due to pertussis toxin (increased cAMP, impaired lymphocyte trafficking).
3. **Convalescent phase (weeks-months "*100-day cough*"):** Gradual decrease in cough frequency and severity. Cough may recur with subsequent URIs. Bacteria largely cleared, toxins no longer produced.

Pertussis “whooping cough” complications

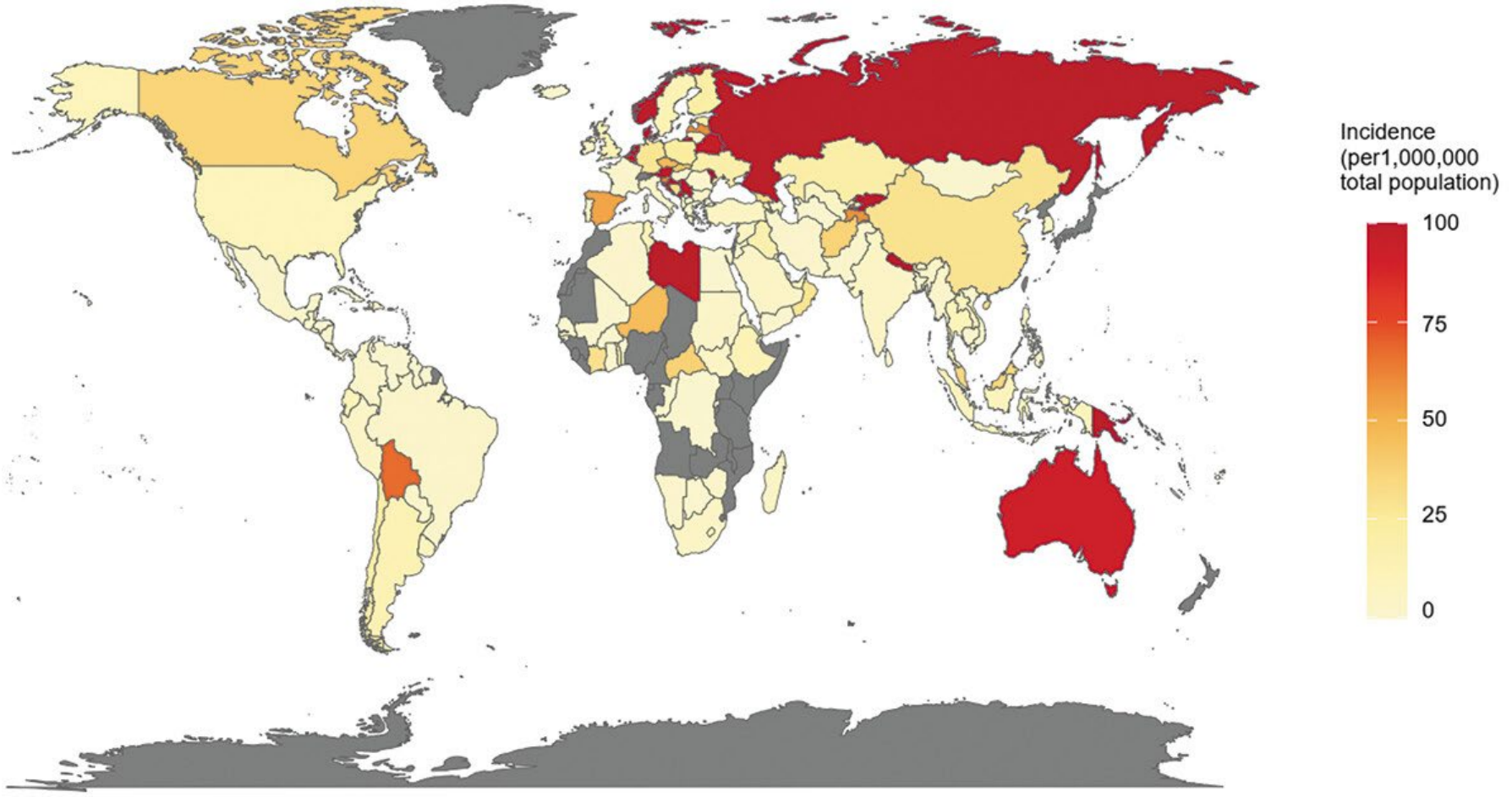
- Pneumonia (most common cause of death). Usually secondary bacterial pneumonia.
- Apnea leading to hypoxia. Vagal reflexes triggered by airway irritation
- Encephalopathy / seizures. From hypoxia, hypoglycemia.
- Weight loss, dehydration. Post-tussive vomiting, poor feeding and increased metabolic demand
- Mortality especially in young infants.



Source: Shi, T., Wang, L., Du, S. et al. Mortality risk factors among hospitalized children with severe pertussis. BMC Infect Dis 21, 1057 (2021).

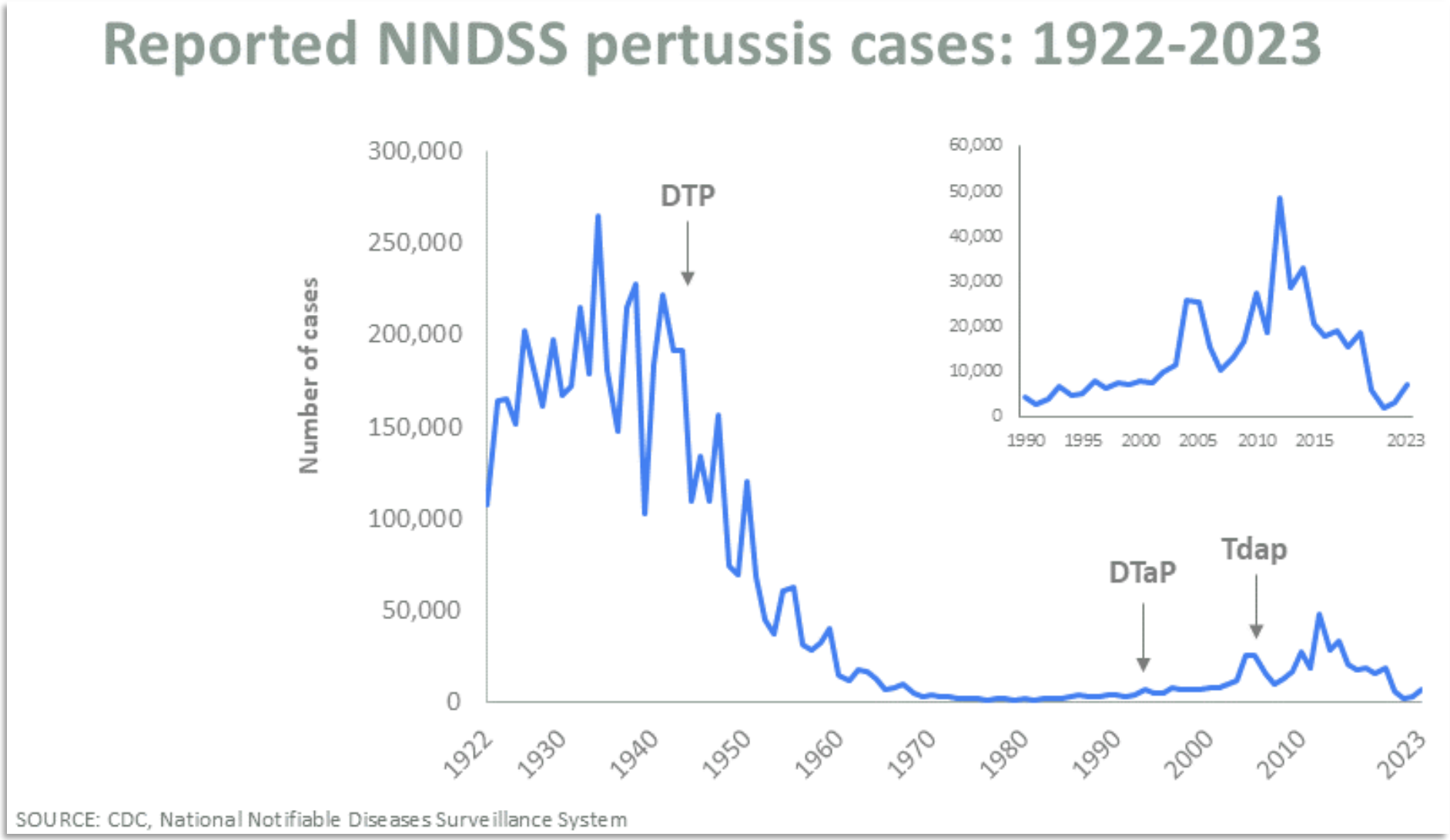
Pertussis epidemiology

Before vaccination, 3 million child deaths annually worldwide (pre-1970). Introduction of whole-cell pertussis vaccines in the 1950s and expansion of global immunization programs in the 1970s resulted in a dramatic decline in incidence and mortality. E.g., USA decrease from 157/100,000 (1940s) to <1/100,000 (1970s). Concerns over reactogenicity of wP vaccines resulted in transition to aP vaccines with lower and shorter duration of efficacy.



Source: Wang, S., Zhang, S., & Liu, J. (2025). Resurgence of pertussis: Epidemiological trends, contributing factors, challenges, and recommendations for vaccination and surveillance. Human Vaccines & Immunotherapeutics, 21(1).

Pertussis epidemiology



NNDSS: National Notifiable Diseases Surveillance System

Pertussis diagnosis

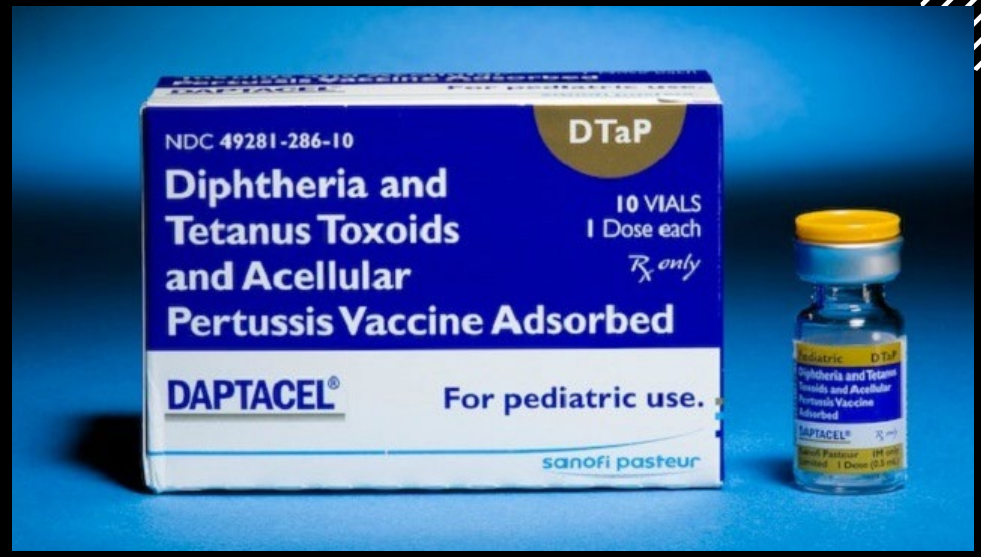
- PCR (nasopharyngeal swab): most sensitive early in disease
- Culture on Regan-Lowe or Bordet-Gengou agar
- Serology useful later in illness anti-PT (antibody to pertussis toxin) ELISA
- Leukocytosis with absolute lymphocytosis is classic
- Diagnostic timing matters: PCR is the best in catarrhal and early paroxysmal stages. Culture value declines after 3 weeks

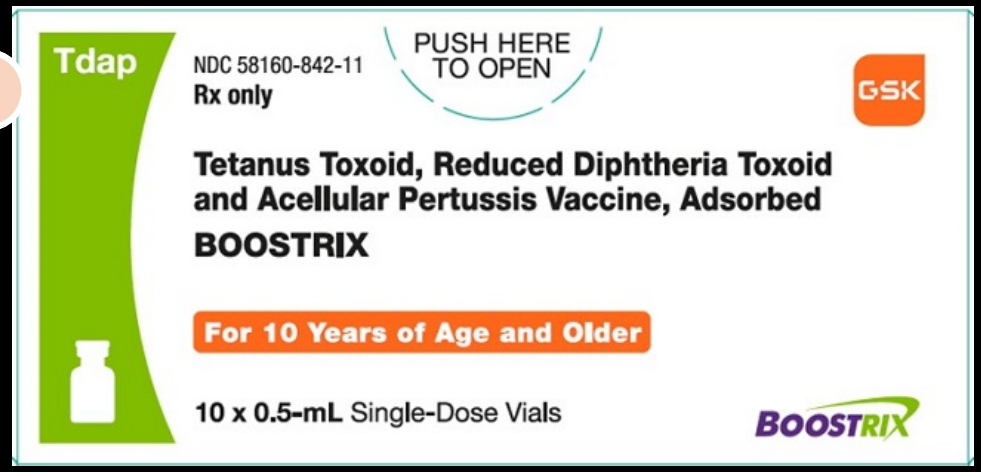
Pertussis management

- Antibiotic treatment does not alter the clinical course once paroxysmal cough is established. The goals are to reduce transmission and protect vulnerable contacts. First-line antibiotics are macrolides (azithromycin, clarithromycin). Alternative is trimethoprim-sulfamethoxazole.
- **Supportive care is the mainstay of management** and includes rest, fluids, avoiding irritants, humidifiers, and small meals to manage severe coughing fits, especially in infants who often need hospitalization for oxygen, suctioning, or monitoring due to risks like apnea and pneumonia.

Pertussis prevention

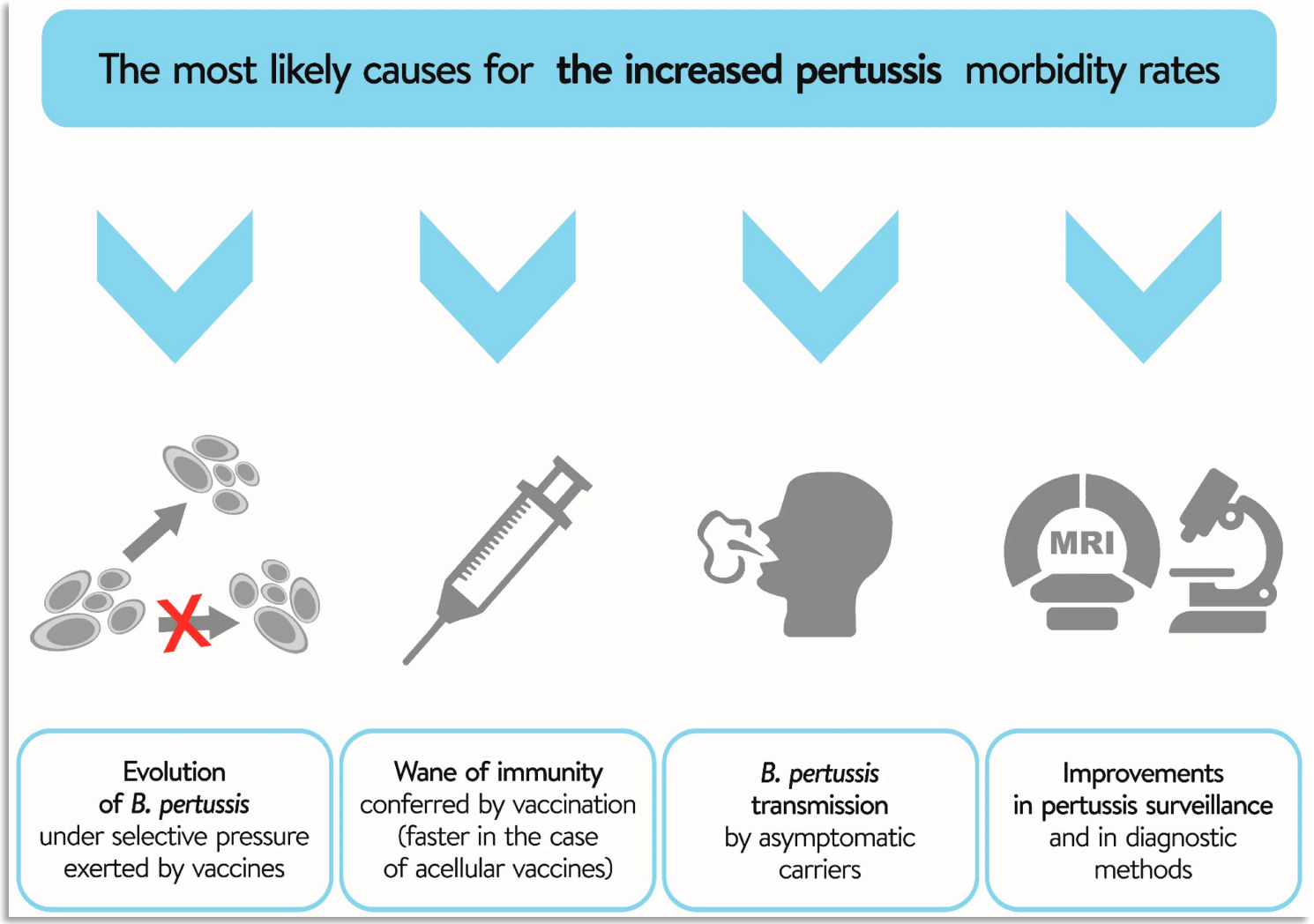
- Acellular pertussis vaccine (aP) contains purified *Bordetella pertussis* antigens (e.g. pertussis toxoid, FHA). Induces antibodies that reduce disease severity but does not fully prevent colonization or transmission.
- Routine immunization is administered as combined vaccines: DTaP in infants and children; Tdap in adolescents and adults.
- Effectiveness vaccination reduced severe disease, mortality, especially in infants but protection wanes over time justifying the need for adolescent and adult boosters





Pertussis prevention

- Herd immunity is essential. Rapid resurgence occurs when vaccination rates decline due to vaccine hesitancy, conflict, disrupted health systems
- Adults with waning immunity are a major source of infant infection
- Contact chemoprophylaxis is indicated for close contacts, regardless of vaccination status. Macrolides are critical when contacts include infants, pregnant women, and immunocompromised individuals



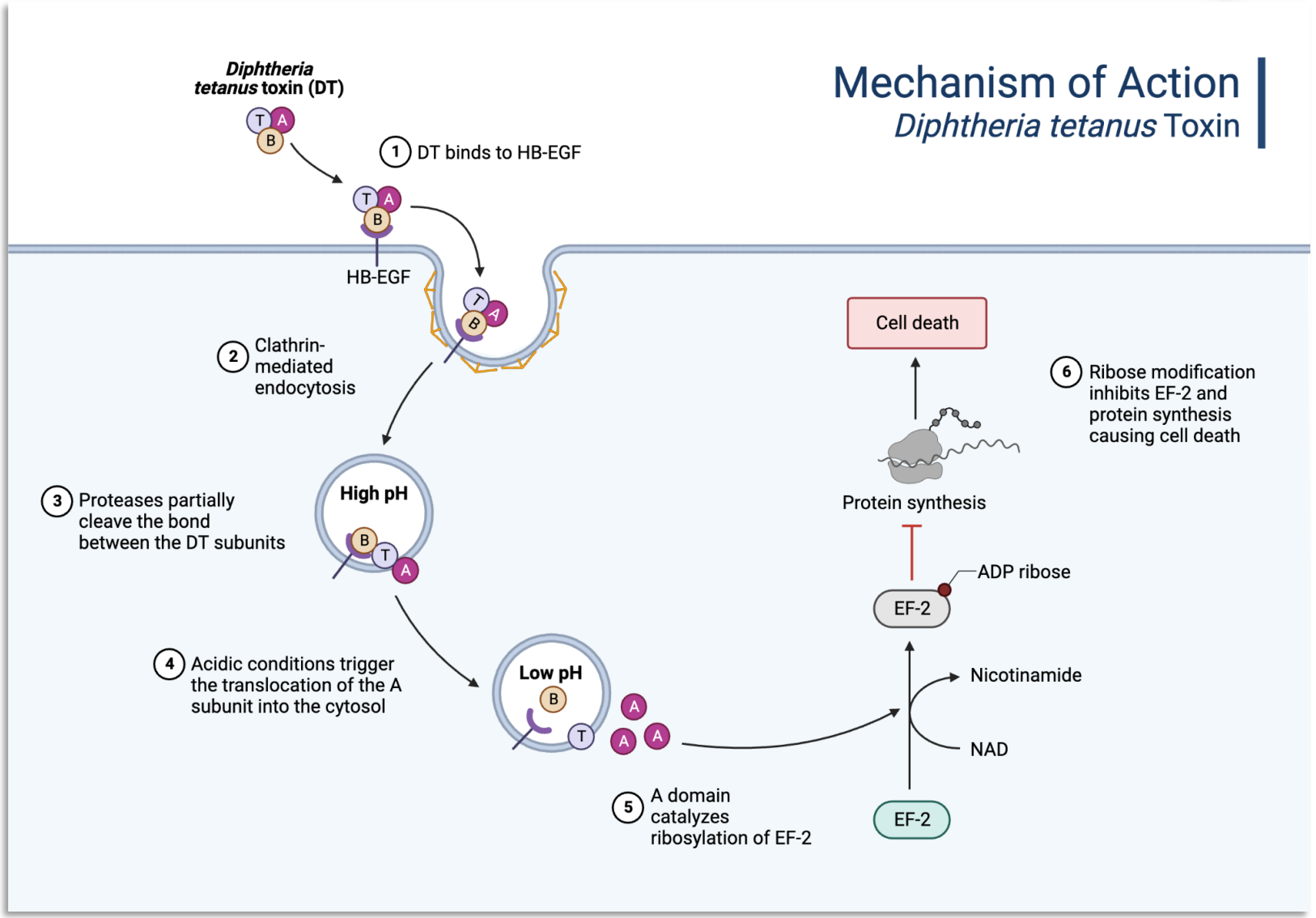
Source: Szwejser-Zawislak E, Wilk MM, Piszczek P, Krawczyk J, Wilczyńska D, Hozbor D. Evaluation of Whole-Cell and Acellular Pertussis Vaccines in the Context of Long-Term Herd Immunity. Vaccines. 2023; 11(1):1.

Corynebacterium diphtheriae: General features

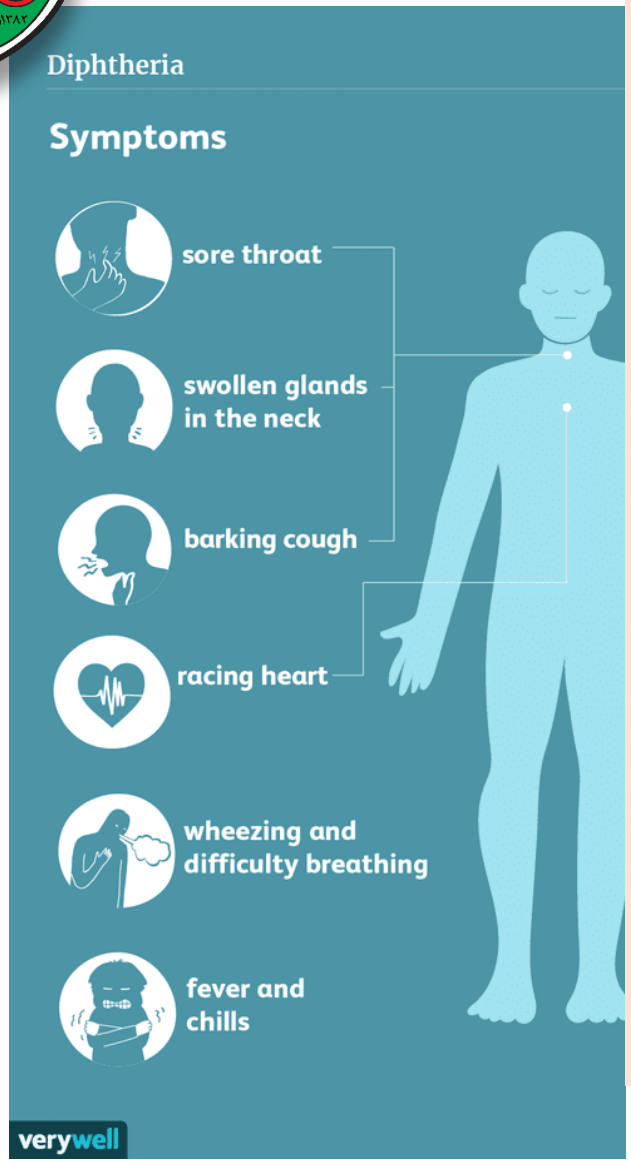
- Gram-positive, pleomorphic, club-shaped bacilli. Often arranged in V/L shapes (“Chinese letters”).
- Non-motile, non-spore-forming, aerobic or facultative anaerobe
- Only toxigenic strains cause disease. Toxin production requires lysogenic conversion by β-phage
- Transmission: Respiratory droplets

Diphtheria toxin

- A-B exotoxin with B subunit binding to heparin-binding epidermal growth factor (HB-EGF) receptor on host cells and mediates endocytosis of the toxin. A (active) subunit cause ADP-ribosylation of elongation factor-2 (EF-2) causing irreversible inhibition of protein synthesis
- Local effects (respiratory tract): Necrosis of pharyngeal epithelium, gray, adherent pseudomembrane (fibrin + necrotic cells + bacteria). Systemic toxicity (toxin dissemination): Myocarditis, Peripheral neuropathy



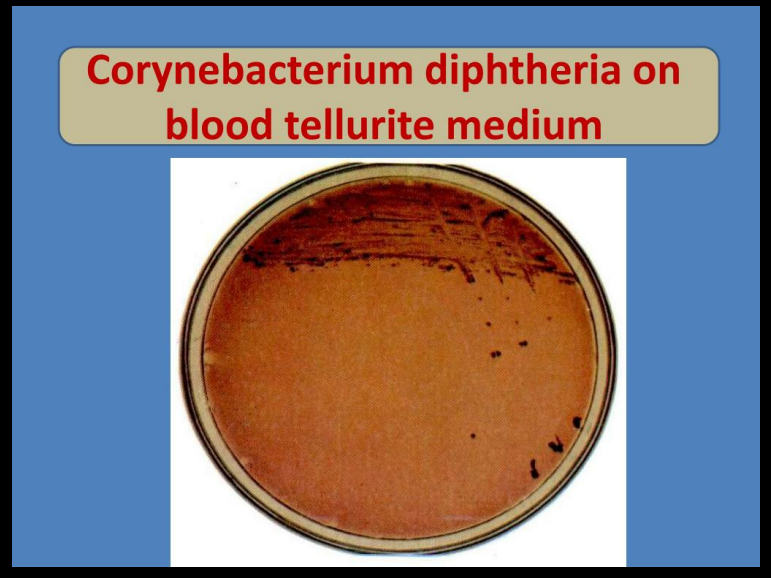
Diphtheria clinical features

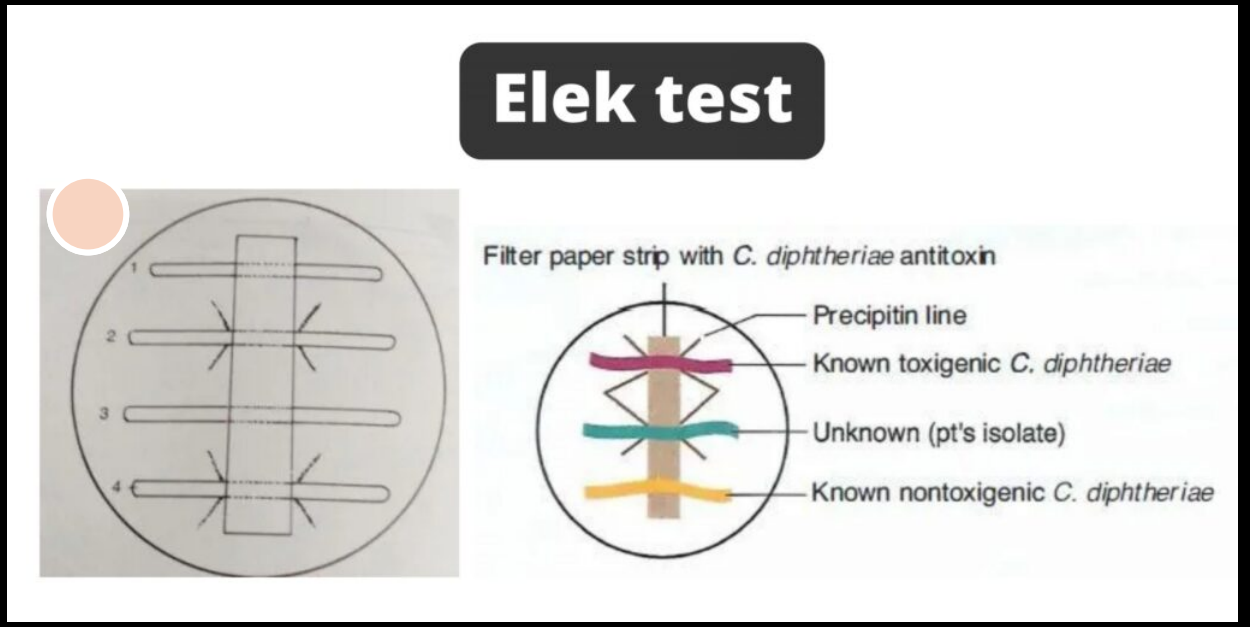


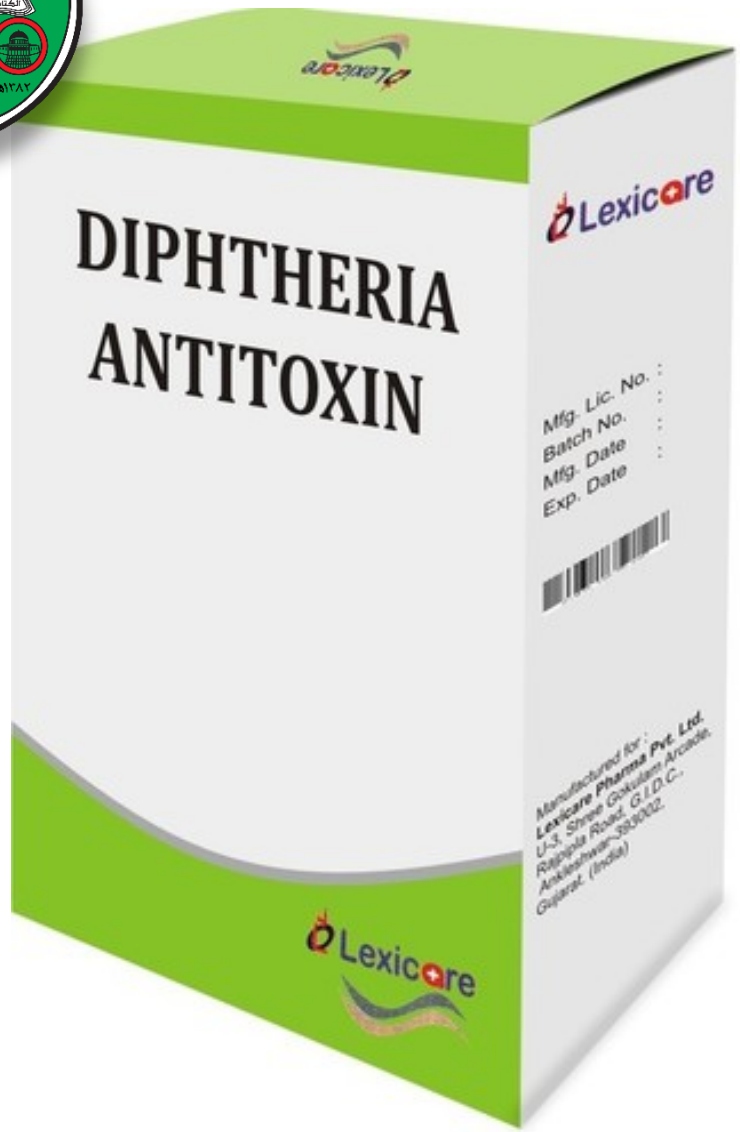
- Respiratory diphtheria (most common): Gradual onset of sore throat, malaise, low-grade fever, and characteristic pseudomembrane (gray, thick, adherent membrane over tonsils and pharynx). It bleeds on attempted removal. Airway involvement with hoarseness, dysphagia, and risk of airway obstruction
- Neck findings include cervical lymphadenitis and soft-tissue edema. Produces the classic “bull neck” appearance
- Systemic (toxin-mediated) complications include myocarditis causing arrhythmias, heart block, heart failure. Neurologic such as peripheral neuropathy (cranial nerve palsies, limb weakness) due to demyelination. Renal: Acute kidney injury (less common)

Diagnosis

- Diagnosis is primarily clinical and we should not wait for laboratory confirmation to start treatment
- Microbiological confirmation
- Culture of throat swab on tellurite agar that produces black colonies
- Toxin detection via Elek test: Immunodiffusion assay that confirms diphtheria toxin production
- Molecular testing by PCR for toxin (*tox*) gene in reference laboratories





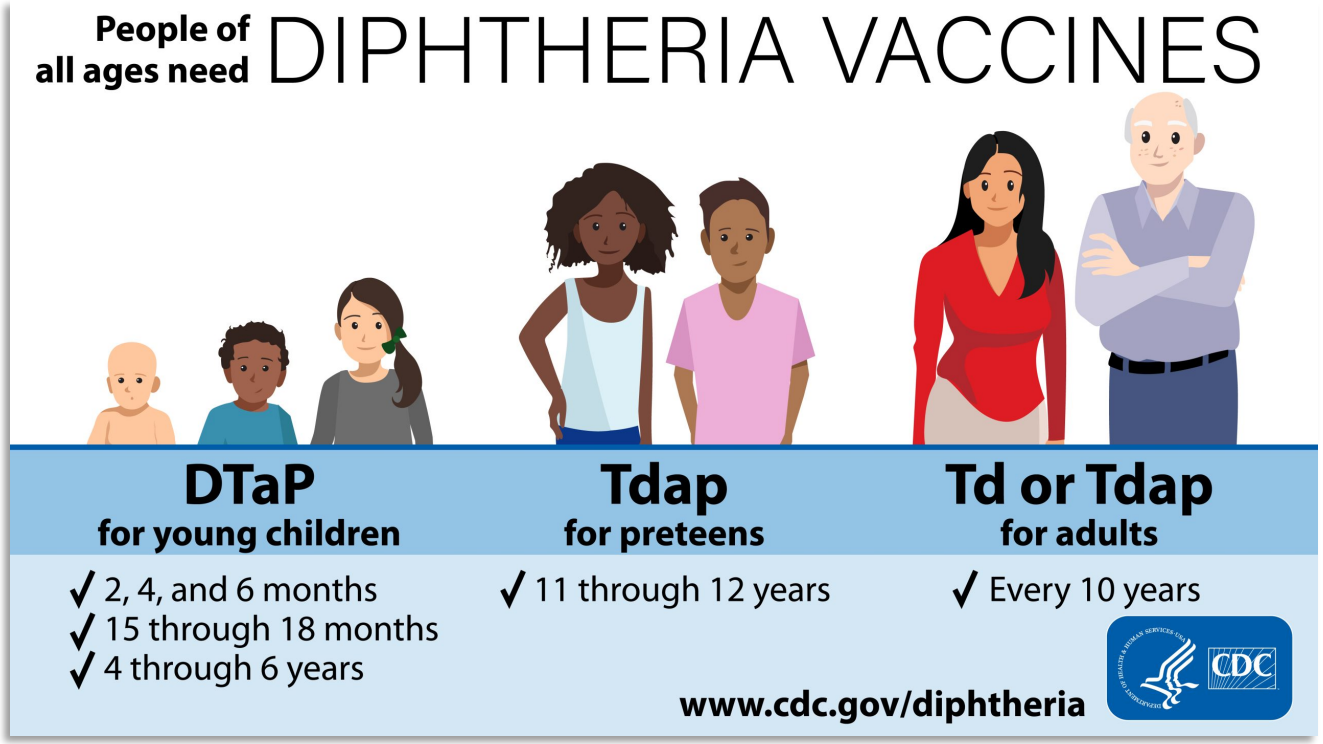


Diphtheria management

- **Diphtheria is a medical emergency**. Do not wait for laboratory confirmation
- **Administer diphtheria antitoxin immediately which neutralizes circulating (unbound) toxin**. Early administration is critical. Hospitalization is needed for continuous airway monitoring due to risk of sudden airway obstruction
- Antibiotic therapy is needed to eradicate organism and stop further toxin production (Erythromycin, Penicillin). Antibiotics do not replace antitoxin
- Strict isolation should be continued until two consecutive negative throat cultures. Avoid scraping pseudomembrane due to risk of bleeding and toxin release

Prevention by Diphtheria Vaccination

- Diphtheria vaccination uses toxoid that induces neutralizing antibodies against diphtheria toxin
- Combined vaccines: DTaP (children) DT / Td / Tdap (adolescents and adults). Routinely administered as part of national immunization programs
- Provides excellent protection when vaccination coverage is high and prevents both disease and toxin-mediated complications
- Booster doses are required every 10 years in adults and necessary due to waning immunity
- Population (herd) immunity is essential for disease control. Diphtheria resurges when vaccination rates decline. Outbreaks often occur in under-immunized communities



Prevention of Pertussis and Diphtheria: Public Health Considerations

- Pertussis and Diphtheria remain public health threats where: vaccine uptake is low; booster schedules are incomplete; public health surveillance is weak.
- Waning immunity in adolescents and adults contributes to pertussis resurgence. Adults often act as reservoirs for infant infection.
- Asymptomatic carriers of *Corynebacterium diphtheriae* can silently trigger outbreaks. This is particularly dangerous in under-immunized populations.
- Global travel and migration increase risk of importation of cases and require sustained border and community surveillance

Thank You!
Wishing You All the Best!