Ministery of Higher education and scientific research

University of Tikrit

College of science

Department of Biology

Lectures of Pathogenic Bacteria

For Diploma students – Pathological analyses - 2024-2025

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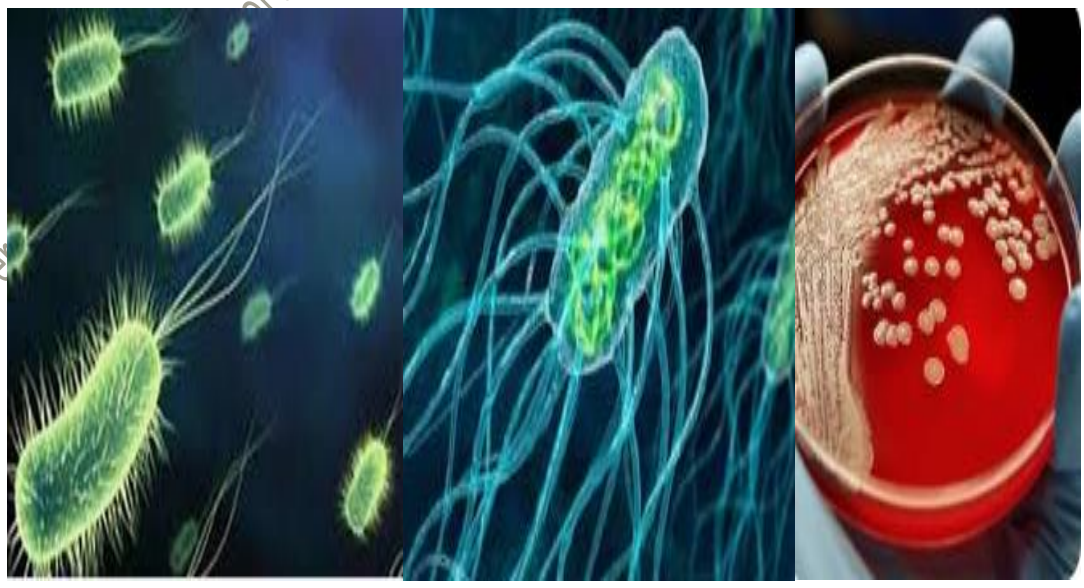

Corynebacteria

Corynebacteria (from the Greek koryne, club) are small and pleomorphic. The genus Corynebacterium includes many species of aerobic and facultative Gram-positive rods. The cells tend to have clubbed ends and often remain attached after division, forming "Chinese letter" or palisade arrangements. Spores are not formed. Growth is generally best under aerobic conditions on media enriched with blood or other animal products, but many strains grow anaerobically. Colonies on blood agar are typically small (1-2 mm), and most are non hemolytic. Catalase is produced, and many strains form acid (usually lactic acid) through carbohydrate fermentation. Surface and cell wall structure is similar to other Gram-positive bacteria.

Corynebacterium diphtheriae

Corynebacterium diphtheriae produces a powerful exotoxin that is responsible for diphtheria. Other corynebacteria are nonpathogenic commensal inhabitants of the pharynx, nasopharynx, distal urethra, and skin; they are collectively referred to as "diphtheroids."

EPIDEMIOLOGY

Corynebacterium diphtheriae is transmitted by droplet spread, by direct contact with cuta neous infections, and, to a lesser extent, by fomites . Some subjects become convalescent pharyngeal or nasal carriers and continue to harbor the organism for weeks, months, or longer. Diphtheria is rare where immunization is widely practiced. In the United States, for example, fewer than 10 cases are now reported each year. These usually occur as small outbreaks in populations that have not received adequate immunization, such as migrant workers, transients, and those who refuse immunization on religious grounds.

PATHOGENESIS

Corynebacterium diphtheriae has little invasive capacity, and diphtheria is due to the local and systemic effects of DT, a protein exotoxin with potent cytotoxic features It inhibits protein synthesis in cell-free extracts of virtually all eukaryotic cells, from proto zoa and yeasts to higher plants and humans. Its toxicity for intact cells varies among mam mals and organs, primarily due to differences in toxin

binding and uptake. In humans, the B subunit binds to one of a common family of eukaryotic receptors that regulate cell growth and differentiation, thus exploiting a normal cell function. The production of DT has both local and systemic effects. Locally, its action on epi thelial cells leads to necrosis and inflammation, forming a pseudomembrane composed of a coagulum of fibrin, leukocytes, and cellular debris. The extent of the pseudomembranevaries from a local plaque to an extensive covering of much of the tracheobronchial tree. Absorption and circulation of DT allow binding throughout the body. Myocardial cells are most affected; eventually, acute myocarditis develops.

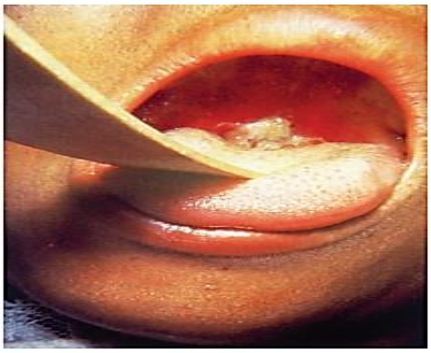

FIGURE 26–3. Diphtheria. Typical appearance of a diphtheritic pseudomembrane adherent to the oropharynx of this child. (Reproduced with permission from Connor DH, Chandler FW, Schwartz DQ, et al: *Pathology of Infectious Diseases*. Stamford CT: Appleton & Lange, 1997.)

DIAGNOSIS

The initial diagnosis of diphtheria is entirely clinical. There are presently no rapid labora tory tests of sufficient value to influence the decision regarding antitoxin administration. Direct smears of infected areas of the throat are not reliable diagnostic tools. Definitive diagnosis is accomplished by isolating and identifying C diphtheriae from the infected site and demonstrating its toxigenicity. Isolation is usually achieved with a selective medium containing potassium tellurite (eg, Tinsdale medium). It should be recognized that although the diagnosis of diphtheria could once be made and confirmed with great confidence, it is now more difficult because experience with the disease is rare. Most physicians have never seen a case of diphtheria, and most laboratories have never isolated the organism and do not even stock the required medium. Because routine throat culture procedures do not detect C diphtheriae, the physician must advise the laboratory of the suspicion of diphtheria in advance. Generally, 2 days are required to exclude C diphtheriae (ie, no colonies isolated on Tinsdale agar); however, more

time is needed to complete identification and toxigenicity testing of a positive culture.

TREATMENT

Treatment of diphtheria is directed at neutralization of the toxin with concurrent elimination of the organism. The former is most critical and is accomplished by promptly administering a diphtheria antitoxin, an antiserum produced in horses. It must be administered early because it only neutralizes circulating toxin and has no effect on toxin already fixed to or within cells. Corynebacterium diphtheriae is susceptible to a variety of antimicrobials, including penicil lins, cephalosporins, erythromycin, and tetracycline. Of these, erythromycin has been the most effective. The complications of diphtheria are managed primarily by supportive measures.

PREVENTION

The mainstay of diphtheria prevention is immunization. The vaccine is highly effective. Three to four doses of diphtheria toxoid produce immunity by stimulating antitoxin pro duction. The initial series is begun in the first year of life. Booster immunizations at 10-yearintervals maintain immunity. Fully immunized individuals may become infected with C diphtheriae because the antibodies are directed only against the toxin, but the disease is mild. Serious infection and death occur only in unimmunized or incompletely immunized individuals. Immunization with DT toxoid prevents serious toxin-medicated disease.

Bacillus

The genus Bacillus includes many species of aerobic or facultative, spore-forming, Gram positive rods. With the exception of one species, B anthracis, they are low-virulence saprophytes widespread in air, soil, water, dust, and animal products. Bacillus anthracis causes the zoonosis anthrax, a disease of animals that is occasionally transmitted to humans. The genus is made up of rod-shaped organisms that can vary from coccobacillary to rather long-chained filaments. Motile strains have peritrichous flagella. Formation of round or oval spores, which may be cen tral, subterminal, or terminal depending on the species, is characteristic of the genus. With Bacillus, growth is obtained with ordinary media

incubated in air and is reduced or absent under anaerobic conditions. The bacteria are catalase-positive and metabolically active. The spores survive boiling for varying periods and are sufficiently resistant to heat that those of one species are used as a biologic indicator of autoclave efficiency. Spores of B anthracis survive in soil for decades.

***Bacillus* chains of large gram-positive**

Bacillus anthracis

has a tendency to form very long chains of rods and in culture is nonmo tile and nonhemolytic; colonies are characterized by a rough, uneven surface with multiple curled extensions at the edge resembling a “Medusa head.” Bacillus anthracis has a polypeptide (poly-d-γ-glutamic acid) capsule of a single antigenic type that has antiphagocytic properties similar to those of bacterial polysaccharide capsules. Bacillus anthracis endo spores are extremely hardy and have been shown to survive in the environment for decades. The organism also produces a potent exotoxin complex, which consists of two enzymes, edema factor (EF) and lethal factor (LF) together with a receptor-binding protein called protective antigen (PA). When PA binds to either EF or LF it then acts as a translocase forming a pore-like site on the host cell surface. This allows the complexes to enter the cell. Once in the cytosol multiple toxin actions are expressed including adenyl ate cyclase activity and host protein inactivation. Bacillus anthracis also produces multiple other proteases that digest tissue components.

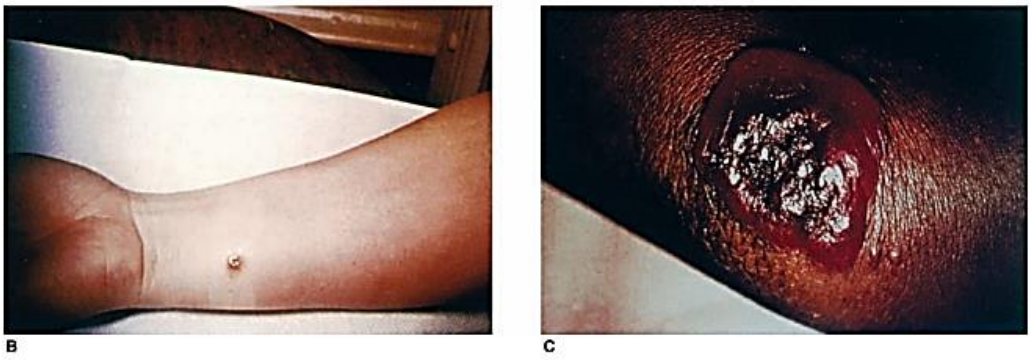

FIGURE 26–9. Anthrax.A. A protein called protective antigen (PA) delivers two other proteins, edema factor (EF) and lethal factor (LF), to the capillary morphogenesis protein-2 (CMP-2) receptor on the cell membrane of a target macrophage, where PA, EF, and LF are transported to an endosome. PA then delivers EF and LF from the endosome into the cytoplasm of the macrophage where they exert their toxic effects. **B.** Early anthrax papule that evolves into **C.** the necrotic eschar called the malignant pustule. (Reproduced with permission from Willey JM: *Prescott, Harley, & Klein's Microbiology*, 7th edition. McGraw-Hill, 2008.)

DIAGNOSIS

Culture of skin lesions, sputum, blood, and CSF are the primary means of anthrax diag nosis. Given some suspicion on epidemiologic grounds, Gram stains of sputum or other biologic fluids showing large numbers of long Gram-positive bacilli can suggest the diag nosis. In September 2001, diagnosis of the first case in Florida was speeded by an infectious disease specialist who knew such rods were extremely rare in the spinal fluid. Large Gram positive bacilli are also unusual in sputum. Bacillus anthracis and other Bacillus species are not difficult to grow. In fact, clinical laboratories frequently isolate the nonanthrax spe cies as environmental contaminants. The saprophytic species are usually β-hemolytic and motile, features not found in B anthracis, but most clinical laboratories are not skilled at separating Bacillus species. Blood cultures are positive in most cases of pulmonary anthrax.

TREATMENT

Antimicrobial treatment has little effect on the course of cutaneous anthrax but does pro tect against dissemination. Almost all strains of B anthracis are susceptible to penicillin, doxycycline, and ciprofloxacin. Although penicillin has long been the treatment of choice .