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Please read this section first

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will not issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: MT-11/00142.

Each attendee should claim THREE CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

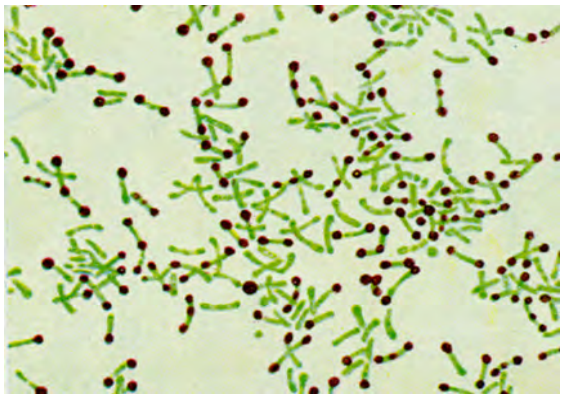
MICROBIOLOGY LEGEND

CYCLE 31 ORGANISM 3

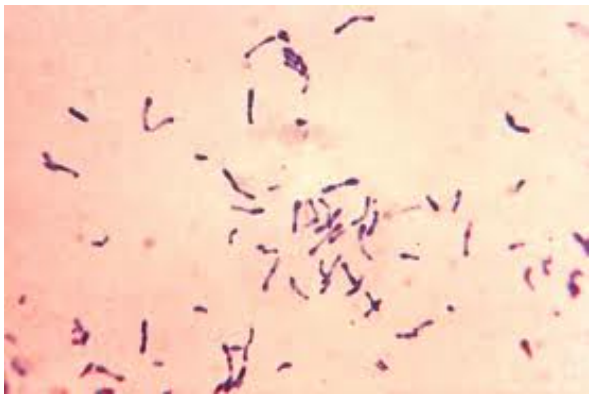
CORYNEBACTERIUM DIPHTHERIAE

Corynebacteria are Gram-positive, aerobic, nonmotile, rod-shaped bacteria classified as Actinobacteria. Corynebacteria are related phylogenetically to Mycobacteria and Actinomycetes. They do not form spores or branches as do the Actinomycetes, but they have the characteristic of forming irregular, club-shaped or V-shaped arrangements in normal growth. They undergo snapping movements just after cell division, which brings them into characteristic forms resembling Chinese letters or palisades.

The genus Corynebacterium consists of a diverse group of bacteria including animal and plant pathogens, as well as saprophytes. Some Corynebacteria are part of the normal flora of humans, finding a suitable niche in virtually every anatomic site, especially the skin and nares. The best known and most widely studied species is Corynebacterium diphtheriae, the causal agent of the disease diphtheria.



Stained Corynebacterium cells. The "barred" appearance. is due to the presence of polyphosphate inclusions called metachromatic granules. Note also the characteristic "Chinese-letter" arrangement of cells.



Gram Stain

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Corynebacterium diphtheriae is a pathogenic bacterium that causes diphtheria. It is also known as the Klebs-Löffler bacillus, because it was discovered in 1884 by German bacteriologists Edwin Klebs (1834 – 1912) and Friedrich Löffler (1852 – 1915).

Classification

Four subspecies are recognized: C. diphtheriae mitis, C. diphtheriae intermedius, C. diphtheriae gravis, and C. diphtheriae belfanti. The four subspecies differ slightly in their colonial morphology and biochemical properties, such as the ability to metabolize certain nutrients, but all may be toxigenic (and therefore cause diphtheria) or non-toxigenic. The diphtheria toxin gene is encoded by a bacteriophage found in toxigenic strains, integrated into the bacterial chromosome.

Diagnosis

In order to accurately identify C. diphtheriae, a Gram stain is performed to show gram-positive, highly pleomorphic organisms with no particular arrangement. An enrichment medium, such as Löeffler's serum, is used to preferentially grow C. diphtheriae. After that, a selective plate known as tellurite agar can be used, which allows all Corynebacteria (including C. diphtheriae) to reduce tellurite to metallic tellurium. The tellurite reduction is colormetrically indicated by brown colonies for most Corynebacteria species or by a black halo around the C. diphtheriae colonies.

Sensitivity

The bacterium is sensitive to the majority of antibiotics, such as the penicillin's, ampicillin, cephalosporin's, quinolone, chloramphenicol, tetracycline's, cefuroxime and trimethoprim.

Clinical Manifestations

Corynebacterium diphtheriae infects the nasopharynx or skin. Toxigenic strains secrete a potent exotoxin which may cause diphtheria. The symptoms of diphtheria include pharyngitis, fever, swelling of the neck or area surrounding the skin lesion. Diphtheritic lesions are covered by a pseudomembrane. The toxin is distributed to distant organs by the circulatory system and may cause paralysis and congestive heart failure.

Pathogenesis

Asymptomatic nasopharyngeal carriage is common in regions where diphtheria is endemic. In susceptible individuals, toxigenic strains cause disease by multiplying and secreting diphtheria toxin in either nasopharyngeal or skin lesions. The diphtheritic lesion is often covered by a pseudomembrane composed of fibrin, bacteria, and inflammatory cells. Diphtheria toxin can be proteolytically cleaved into two fragments: an N-terminal fragment A (catalytic domain), and fragment B (transmembrane and receptor binding domains). Fragment A catalyzes the NAD^+-dependent ADP-ribosylation of elongation factor 2, thereby inhibiting protein synthesis in eukaryotic cells. Fragment B binds to the cell surface receptor and facilitates the delivery of fragment A to the cytosol.

Host Defences

Protective immunity involves an antibody response to diphtheria toxin following clinical disease or to diphtheria toxoid (formaldehyde-inactivated toxin) following immunization.

Epidemiology

Corynebacterium diphtheriae is spread by droplets, secretions, or direct contact. In situ lysogenic conversion of nontoxigenic strains to a toxigenic phenotype has been documented. Infection is spread solely among humans, although toxigenic strains have been isolated from horses. In regions where immunization programs are maintained, isolated outbreaks of disease are often associated with a carrier who has recently visited a subtropical region where diphtheria is endemic. Large-scale outbreaks of disease may occur in populations where active immunization programs are not maintained.

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Diagnosis

Clinical diagnosis depends upon culture-proven toxigenic C diphtheriae infection of the skin, nose, or throat combined with clinical signs of nasopharyngeal diphtheria (e.g. sore throat, dysphagia, bloody nasal discharge, pseudomembrane). Toxigenicity is identified by a variety of in vitro (e.g. gel immunodiffusion, tissue culture) or in vivo (e.g. rabbit skin test, guinea pig challenge) methods.

Control

Immunization with diphtheria toxoid is extraordinarily effective. Diphtheria patients must be promptly treated with antitoxin to neutralize circulating diphtheria toxin.

References

1. http://www.ncbi.nlm.nih.gov/books/NBK7971/
2. http://en.wikipedia.org/wiki/Corynebacterium_diphtheriae

Questions

1. Discuss the morphological characteristics of Corynebacterium.
2. Discuss the classification of Corynebacterium diphtheriae.
3. Discuss the pathogenesis of Corynebacterium diphtheria.
