Miscellaneous respiratory tract infections

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CORYNEBACTERIUM DIPHTHERIAE

• *C. diphtheriae* causes diphtheria

• Other Corynebacterium species (diphtheroids) are implicated in opportunistic infections.
CORYNEBACTERIUM DIPHTHERIAE

• Corynebacteria, club shaped Gram positive rods (wider at one end) and are arranged in palisades or in V- or L-shaped formations (or chinse letters)

• The rods have a beaded appearance. The beads consist of granules of highly polymerized polyphosphate—a storage mechanism for high-energy phosphate bonds.

• The granules stain metachromatically (i.e., a dye that stains the rest of the cell blue will stain the granules red).

https://www.microbiologyinpictures.com/bacteria%20photos/corynebacterium%20diphtheriae%20photos/corynebacterium%20diphtheriae%20020.jpg
Transmission

• Humans are the only natural host of *C. diphtheriae*

• Both toxigenic and nontoxigenic organisms reside in the upper respiratory tract and are transmitted by airborne droplets (similar to other respiratory pathogens).

• The organism can also infect the skin at the site of a preexisting skin lesion.

• This occurs primarily in the tropics but can occur worldwide in indigent persons with poor skin hygiene.
Pathogenesis

• Mainly exotoxin mediated (similar to other G+ve rods), however, the bug must establish itself in the throat first (invasiveness) prior to exotoxin production.

• Diphtheria toxin inhibits protein synthesis by ADP-ribosylation of elongation factor-2 (EF-2) used to maintain elongation of the peptide chain = no protein synthesis in eukaryotic cell.

• Similar to other toxins it is formed in an A- B fashion (active/binding)

• As mentioned, the toxin is encoded on a gene trasmitted by transduction on a temperate phage
Diphtheria is rare now thanks to vaccines, however we should be aware of the thick throat pseudomembrane. The other aspects are nonspecific: fever, sore throat, and cervical adenopathy. There are three prominent complications:

1. Extension of the membrane into the larynx and trachea, causing airway obstruction.
2. Myocarditis accompanied by arrhythmias and circulatory collapse.
3. Nerve weakness or paralysis, especially of the cranial nerves.
FIGURE 17–7  Diphtheria. Note whitish-gray pseudomembrane covering posterior pharynx and marked inflammation of palate and pharynx. Caused by diphtheria toxin, an exotoxin that inhibits protein synthesis by inhibiting elongation factor-2. (Courtesy of Dr. Peter Strebel.)
• Paralysis of the muscles of the soft palate and pharynx can lead to regurgitation of fluids through the nose.
• Peripheral neuritis affecting the muscles of the extremities also occurs.
• Cutaneous diphtheria causes ulcerating skin lesions covered by a gray membrane.
• These lesions are often indolent and often do not invade surrounding tissue. Systemic symptoms rarely occur.
Laboratory Diagnosis

• For diphtheria we need to show the presence of the organism and production of the toxin (due to presence of atoxigenic strains).

• Due to the quick nature of toxin mediated disease, the decision to treat with an antitoxin should be clinical and not wait for lab confirmation.

• A throat swab should be cultured on Loeffler’s medium (cream colored colonies are shown in the slant), a tellurite plate (black colonies seen a tellurium salt that is reduced to elemental tellurium within the organism thus black colored colonies), and a blood agar plate.

• The typical gray-black color of tellurium in the colony is a telltale diagnostic criterion.

• If *C. diphtheriae* is recovered from the cultures then we can confirm toxin (either animal inoculation, antibody-based gel diffusion precipitin test or PCR test for the presence of the gene).
• Smears of the throat swab should be stained with both Gram stain and methylene blue.

• Although the diagnosis of diphtheria cannot be made by examination of the smear, the finding of many tapered, pleomorphic Gram-positive rods can be suggestive.

• The methylene blue stain is excellent for revealing the typical metachromatic granules (the club shape is due to these granules).
Treatment

• 1) ANTITOXIN) The treatment of choice is antitoxin, which should be given **immediately** on the basis of **clinical impression** (not on lab confirmation, this takes while to get both isolation of organism and detection of toxin)

• The need for immediate treatment with antitoxin is due to the toxin’s RAPID and IRREVERSIBLE action on cells, thus antitoxin will work on unbound toxin in the blood only

• 2) ANTIBIOTICS) Treatment with penicillin G or erythromycin is **also recommended** with antitoxin but not as a substitute.

• Antibiotics will reduce bacterial count and this toxin production, they will also reduce the chance of a carrier state
Prevention

• Diphtheria is now rare in the world due to its inclusion in the scheduled vaccine regiment (DTaP) with diphtheria toxoid.

• In warzones or areas with lapse in immunization, reemergence (and atypical symptoms) are on the rise

• formaldehyde treatment of the toxin, destroys the toxin but leaves intact the antigenicity

• Immunization consists of three doses given at 2, 4, and 6 months of age, with boosters at 1 and 6 years of age.

• Because immunity wanes, a booster every 10 years is recommended.

• Immunization does not prevent nasopharyngeal carriage of the organism.
Atypical Pneumonia


- Causing mostly milder forms of pneumonia. Characterized by slow development of symptoms unlike other forms of pneumonia which can develop more quickly. More severe early symptoms.

Mycoplasma


- Severe forms of M pneumonia have been described in all age groups.

- **Lab Diagnosis**: Special culture medium. PCR. Sputum, pleural fluid. Blood. Serological Cold-Aggutination Test. Increased antibody titers.

- **Treatment**: Levofloxacin, moxifloxacin, Macrolides/Azithromycin. No Vaccine
Chlamydia species

• **Chlamydia. Attached** human mucosal membrane... **obligate intracellular.** intracytoplasmic inclusions. Rapidly killed outside body, dryness & high temperature > 4 C.

• **Life cycle**: Infectious elementary bodies attached to the host mucosa and promoting its entry. Cytoplasm phagosome. producing **reticulate bodies** in inclusion. released **elementary bodies**.

• **Chlamydia trachomatis. Serotypes C, K**: Common cause of sexually transmitted disease (STD) Nonspecific urethritis.. mother to newborn babies..maternal fluid.. Atypical pneumonia..Eye infection.. **Opthalmia neonatorum**

• About half of all newborns with Chlamydial pneumonia develop inclusion conjunctivitis.. 1-2 weeks starts mild - severe eyes redness, swollen eyelids, inflammation & yellow thick discharge eyes.

• **A & C serotypes** of endemic Ch. trachomatis cause **Trachoma**. conjunctival scarring, damage eyelids & Cornea. blindness.
Chlamydia Life Cycle

1. Infectious Elementary Body
2. Membrane-bound Phagosome
3. Lysosome (Cell Organelle)
4. Cell Nucleus
5. Ingestion and Establishment of Phagosome
6. Release of Progeny
7. Metabolically Active RB Inside Phagosome
8. Condensation to Elementary Bodies
9. Replication of Reticulate Bodies
Chlamydial Pneumonia

• *C. pneumoniae*: droplets infection..Infants/children often develops gradually.. several weeks mild respiratory symptoms, dry irritating prolonged cough..nasal congestion.. with/without fever..Few weeks..No blood sepsis.

• *C. pneumoniae* infections in adults.. often asymptomatic, mild, May include sore throat, headache, fever, dry cough.

• Clusters of infection have been reported more common in Children than Adults.

• **Diagnosis & treatment**: Sputum, throat-nasal swab..
  MaCoy Cell Culture, ELSA Specific antibodies, PCR and Microimmunofluorescence MIF.

• Treatment: Tetracyclines, Macrolides, levofloxacin, moxifloxacin .. No Vaccine
Chlamydia Psittaci

- **C. psittaci** causes Zoonotic diseases.. Human infection followed contact with **birds** (parrots, pigeons, turkeys, and ducks).. A rare human disease called **psittacosis** (**ornithosis**).

- Humans respiratory tract can be infected via inhalation bacteria shed from feathers, secretions, and droppings localized inflammation in Bronchi & lung tissues.

- **Signs Symptoms:** Starts mild..flu-like & ended with severe disease including fatal **pneumonia**, associated high fever, dry cough, headache.

- Diagnosis &Treatment similar to other Chlamydia.
Legionella pneumonophila

- **Leginonella** Gram negative, Pathogenic-Nonpahogenic spp. often found in natural aquatic bodies and wet soil. Facultative Anaerobes Growth in Cold/Hot (4- 80C) Water..Transmitted, Inhalation via Air Condition, Wet Soil.. Cause outbreak of disease.

- Lung Mucosa..multiply intracellular within the macrophages.. High Fever .. Incub. period 2-10 days .. Nonproductive /Productive dry cough. .. Shortness of breath, Chest pain, Muscle aches, Joint pain, Diarrhea, Renal Failure, higher mortality rate. Legionnaires' disease is not contagious

- **Risk factors** include heavy cigarette smoking, Old age, underlying diseases such as renal failure, cancer, diabetes, or chronic obstructive pulmonary, suppressed immune systems, corticosteroid.

- **Diagnosis & treatment**: Special Culture Media, blood/urine specimen for detection Specific antibodies or Antigens by PCR, or ELSA .. Macrolides (azithromycin), levofloxacin, moxifloxacin .. No Vaccine.
OPPORTUNISTIC MYCOSES

• Opportunistic mycoses are caused by globally distributed fungi that are either members of the human microbiota, such as Candida species, or environmental yeasts and molds.

• They can produce disease ranging from superficial skin or mucous membrane infections to systemic involvement of multiple organs.

• Patients at risk include those with hematologic dyscrasias (eg, leukemia, neutropenia), patients with HIV/AIDS with CD4 counts less than 100 cells/μL, as well as those treated with immunosuppressive (eg, corticosteroid) or cytotoxic drugs.
Candidiasis

- **Candida albicans** is the most important species of candida (other species C. parapsilosis, C. glabrata, C. tropicalis, C. guilliermondii, and C. dubliniensi).
- **Candida albicans** is oval gram positive budding yeast which produce pseudohyphae.
- It colonises the mucous membranes of the upper respiratory, GIT & female genital tracts.
- It causes superficial infections but can predominate with lowering in immunity causing infection so it is one of the opportunistic fungi.
Predisposing factors to *Candida* infections

1- Diseases as AIDS & diabetes melllitus.
2- Drugs: prolonged treatment with broad spectrum antibiotics & corticosteroids.
3- General debility.
4- Indwelling urinary catheters.
Pathogenesis & Symptomatology

Skin invasion
- They are red & weeping lesions.
- Mainly affect worm moist areas. Such as axilla, intergluteal folds or infra mammmary folds.
- Mostly in obese & diabetics.
- Pseudo diaper rash

Mouth infection
- C. albicans produces white patches in the mouth (oral thrush or moniliasis).
- Sometimes oral leukoplakia, esophagitis, gastritis

Vulvovaginitis
- With itching & thick vaginal discharge.
- Common with diabetic woman & prolonged use of antibiotics, IUCD, Pregnancy.

Nails infection
- Occurs with repeatedly immersing in water (dish washing).
- Painful redness, swelling of nail folds, thickening & loss of nail (paronychia).

Systemic candidiasis
- Occur in diabetics & Immuno suppressed persons.

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Laboratory diagnosis

Direct microscopic examination

- Specimens from skin, vaginal discharge or exudates from mucous surfaces are examined.
- *C. albicans* is oval gram positive budding yeast cell with pseudohyphae.

Culture

On nutrient agar, corn meal agar & SDA. Colonies are creamy in color & identified by:

1. **Morphology:** oval budding gram +ve yeast cells.
2. **Differentiation tests:**
   a. **Germ tube test:** germ tube is formed when colonies incubated with human serum at 37 C for 30 min.
   b. **Chlamydospore formation on corn meal agar.**
   c. **Biochemical reactions:** *C. albicans* ferments glucose & maltose with acid & gas production.
Germ tube

Terminal Chlamydospore & pseudohyphyae

Treatment

Oropharyngeal or oesophageal thrush

Skin lesions

Systemic candidiasis

- Nystatin ointment
- Nystatin
- Fluconazole
- Caspofungin IV
- Ketoconazole (orally)
- Amphotericin B (IV)
Cryptococcus neoformans

- *Cryptococcus neoformans* causes cryptococcosis.
- A widespread **encapsulated yeast** that inhabits soil around pigeon roosts
- Common infection of **AIDS, cancer or diabetes patients**
- Infection of **lungs** leads to cough, fever, and lung nodules
- **Dissemination to meninges** and **brain** can cause severe neurological disturbance and death.
Diagnosis

Microscopic
  • India Ink for capsule stain (50-80% + CSF)

Culture
  • Bird seed agar
  • Routine blood culture

PCR
Aspergillosis: Diseases of the Genus *Aspergillus*

- Very common airborne soil fungus
- 600 species, 8 involved in human disease; *A. fumigatus* most commonly
- Serious opportunistic threat to AIDS, leukemia, and transplant patients
- Infection usually occurs in lungs – spores germinate in lungs and form fungal balls; can colonize sinuses, ear canals, eyelids, and conjunctiva
- Bronchopulmonary allergy or Invasive aspergillosis in preformed cavities can produce necrotic pneumonia, and infection of brain, heart, and other organs.
- Surgery, Amphotericin B and nystatin
Zygomycosis

• Zygomycota are extremely abundant saprophytic fungi found in soil, water, organic debris, and food.

• Genera most often involved are *Rhizopus, Absidia, and Mucor.*

• Usually harmless air contaminants invade the membranes of the *nose, eyes, heart,* and *brain* of people (Rhinocerebral mucormycosis) with *diabetes* and malnutrition, with severe consequences.

• **main host defense is phagocytosis**
Diagnosis is made by direct smear and by isolation of molds from respiratory secretions or biopsy specimens.

Treatment: Control Diabetes, surgery & amphotericin B

Prognosis: very poor
PNEUMOCYSTIS

- Pneumocystis jirovecii is the cause of a lethal pneumonia in immunocompromised persons, particularly those with AIDS.

- Definite diagnosis of pneumocystosis depends on finding organisms of typical morphology in appropriate specimens (Sputum, BAL)

- The organism has not been grown in culture

- TMP-SMX is treatment of choice
Endemic mycosis

• Endemic mycosis is caused by a thermally dimorphic fungus, and the infections are initiated in the lungs following inhalation of the respective conidia.

• Each of the four primary systemic mycoses—coccidioidomycosis, histoplasmosis, blastomycosis, and paracoccidioidomycosis—is geographically restricted to specific areas of endemicity.

• Most infections are asymptomatic or mild and resolve without treatment. However, a small but significant number of patients develop pulmonary disease.
Dimorphic Fungus: Histoplasmosis-1


• The primary site of infection is usually pulmonary. Inhalation dust with microconidia. Phagocytosed by macrophages, obligate intracellular parasites. Causing slight inflammatory reaction. Most cases of histoplasmosis are asymptomatic/subclinical, benign. Flu-like syndrome.

• Few may develop chronic progressive lung disease. Granuloma & fibrosis, chronic cutaneous or systemic disease involve any internal organ. Fatal systemic disease.

• All infected persons become positive by histoplasmin skin test.
Histoplasma capsulatum in infected White Blood cells
Coccidioidomycosis & Blastomycosis

• *Coccidioides immitis* & *Blastomyces dermatitidis*. Soil inhabiting Dimorphic Fungus. Endemic in south-western U.S.A., northern Mexico and various parts South America.

• Respiratory infection, resulting from the inhalation of microconidia, often resolves rapidly leaving the patient with a strong specific immunity to re-infection.

• Some individuals the disease may progress to a chronic pulmonary condition or a systemic disease involving the meninges, bones, joints, subcutaneous, cutaneous tissues. Antigen Skin test positive. Not significant in diagnosis.
Laboratory Diagnosis

• **Direct microscopy and culture** should be performed on all specimens (sputum, bronchial washings, CSF, pleural fluid tissue biopsies from various visceral organs).

• **wet mounts in 10% KOH with india ink.** Ovoid-budding yeast cells (b) Gram-stain smear..

• **Cultures on Sabouraud dextrose agar** should be maintained for one month at 25C. fungal growths & Wet Mount. Identification produces hyphae-like conidio-phores & Spores. Color of fungal growth

• **Serological tests are of limited value.** not significant

• Detection of Histoplasma antigen in blood & urine is significant
Paracoccidioidomycosis

• Paracoccidioides brasiliensis is the thermally dimorphic fungal agent of paracoccidioidomycosis (South American blastomycosis), which is confined to endemic regions of Central and South America.

• P. brasiliensis is inhaled, and initial lesions occur in the lung. After a period of dormancy that may last for decades, the pulmonary granulomas may become active, leading to chronic, progressive pulmonary disease or dissemination.
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