Miscellaneous respiratory tract infections

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Atypical Pneumonia

- Atypical pneumonia caused by *Mycoplasma* and *Chlamydia*, *Legionella*.. These related to Gram-ve bacteria.. Attached to respiratory mucosa..Not common part of Respiratory flora..Opportunistic pathogens
- 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.
- ***M. pneumoniae*** **:** The smallest size Bacteria ..Lack Cell Wall.. Lipid bi-layer Membrane.. Aerobic Growth, Respiratory /Urinary Mucosa.. Various *Mycoplasma* spp. Associated with disease.. Human, Animals, Birds

-"walking pneumonia" because patients are still functional
-called atypical because they don't present as classical pneumonia (confined to 1 lobe, high fever, etc.), and their treatments differ from classical pneumonia
-mild fever, dry cough, shortness of breath
-extra pulmonary symptoms (sore throat, headache)
-all of the atypical pneumonias are gram –ve bacteria, that can be part of the normal flora
-mycoplasma is unique because it **doesn't** have a cell wall, so antibiotics like penicillins won't work on them

Mycoplasma

- *M. pneumoniae* ..spread by droplet infection.. often develop Low fever & dry cough symptoms ..few days-weeks.. anemia, rashes, neurological syndromes..meningitis, encephalitis.
- Acute/ Subacute Pharyngitis.. Bronchitis.. Common Infection in Fall-Winter.. Mostly Old children & young Adults.
- Severe forms of M pneumonia have been described in all age groups.
- Lab Diagnosis: Special culture medium.. PCR.., Pleural fluid, Blood. Serological Cold-Agglutination Test.. Increased antibody titers.
- Treatment: levofloxacin, moxifloxacin, Macrolides/ Azithromycin.. No Vaccine

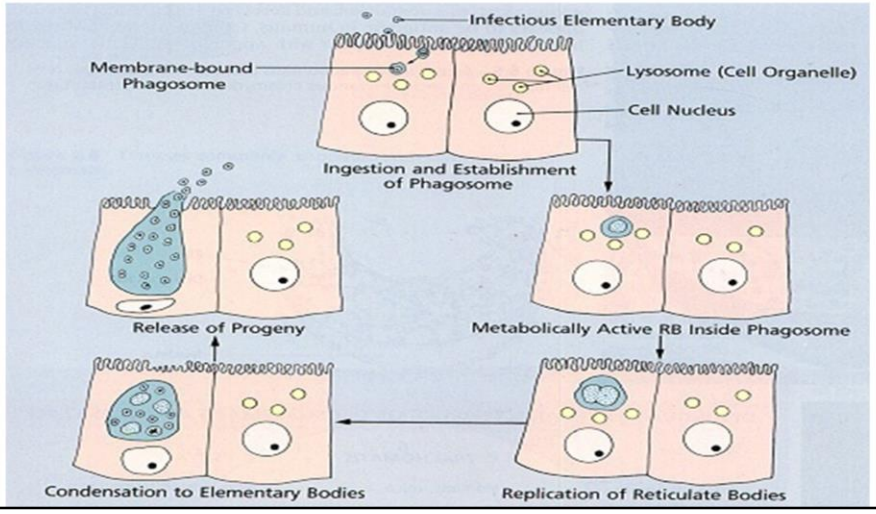
-mode of transmission is via droplets
-focus on mode of transmission, prevention, and vaccines
-mycoplasma are part of the normal flora on the respiratory mucosa, as well as the genitourinary tract
-M. pneumoniae tend to affect school age children, as well as teens (>5 and <20 yrs. Old)
-we don't use culture for diagnosis (takes about a month)
-almost the size of large viruses
-pleomorphic, often are contaminants in other cultures
-PCR and cold agglutination test (positive in 70% of patients) are faster
-most specific test is microimmunofluorescence (MIF)
    -done by comparing diluted antibody titres from a sick patient and a healthy patient
-Most patients resolve spontaneously, but they remain infectious to others (household contact results in a 50-90% transmission rate)
-Treatment with macrolides and fluoroquinolones
-Mycoplasma is an extracellular infection (attachment using a protein called PI)

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.

-chlamydial pneumonia accounts for 15% of all pneumonia cases
-**obligate intracellular infection**
-C. trachmoatis is the causative agent of STDs (not important for RS)

Chlamydia Life Cycle



-**obligate intracellular**
-biphasic morphology:
-elementary bodies: **extracellular** and **infectious** form
-reticulate body (RB): **intracellular** and **reproductive** form and metabolically active (unable to survive extracellularly), they also form intracellular granules (inclusions) that can be stained

Chlamydophila 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

-mode of transmission is droplets
-called chlamydophila to distinguish from chlamydia trachomatis, which causes STDs
-tend to infect children
-you can culture these, but PCR, MIF, and ELISA are better
-**MIF is gold standard of diagnosis**
-again, penicillins don't work, so we use macrolides, fluoroquinolones and tetracyclines

Chlamydophila 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.

-causes disease calls psittacosis (previously called ornithosis
-mode of transmission is via inhalation of the bacteria from birds, **not droplets** (usually from people who work with them or work in slaughterhouses)
-gold standard of diagnosis is **MIF**
-treatment like C. pneumoniae
-person to person transmission has never been documented

Legionella pneumonphila

- **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, 0ld 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.

-causes two diseases: Pontiac fever, and Legionnaires disease (Pontiac fever is very mild and has flu-like symptoms, no treatment needed)
-Legionnaires present with severe pneumonia as well as GI symptoms
-another characteristic of Legionnaires is **hyponatremia** due to fluid and electrolyte imbalance
-aquatic bacteria that is transmitted via water droplets from **air conditioning** (person to person is very rare)
-tend to affect children and elderly with risk factors
-most common used test used for diagnosis is **urine sample** and we look for antigens
-treatment with macrolides and fluoroquinolones
-we can culture legionella easily using a selective media; **charcoal yeast extract** (CYE)

OPPORTUNISTIC MYCOSES

- Opportunistic mycoses are caused by globally distributed fungi that are either members of the human microbiota, such a 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

-**opportunistic:** causes significant disease in immunocompromised patients
-can cause disease in healthy people, but it is not significant
-most common respiratory mycotic infection is candida, but the doctor didn't put it in

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.

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-**encapsulated yeast**
-capsule is antiphagocytic
-reservoir is birds, whose droppings infect soil, and are inhaled
-C. neoformans are neurotropic, after infecting lungs they try to get to CNS and cause meningitis
-pregnant women are also at risk

Diagnosis

Microscopic

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

Culture

- Bird seed agar
- Routine blood culture

PCR

-diagnosis via staining of CSF using India Ink, which shows the capsule (diagnostic of C. neoformans)
-**bird seed agar** is selective for C. neoformans

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 cavitis** can produce **necrotic pneumonia, and infection of brain, hear**t, and other organs.
- Surgery , Amphotericin B and nystatin

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-only need to know A. fumigatus
-can cause **bronchopulmonary allergy** due to inhalation, and **invasive aspergillosis**
-start in the lung, but can migrate to sinuses, ear canal, or conjunctiva
-in diseased lungs, it can cause something called a **fungal ball** (**aspergilloma**), can be confused with cancer
-antifungal medications are not effective against fungal balls, surgery is required

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**

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-also called mucormycosis
-called rhinocerebral mucormycosis because it can spread to the nose and brain and cause destruction of these tissues
-we see this in diabetes patients

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

-mucormycosis patients have poor prognosis because they are immunocompromised to begin with, so any simple infection on top of the mucormycosis can be fatal

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

-mainly in **AIDS** patients
-initially thought to be parasites
-cant be cultured in the lab
-needs to be diagnosed with specimens taken from patients

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.

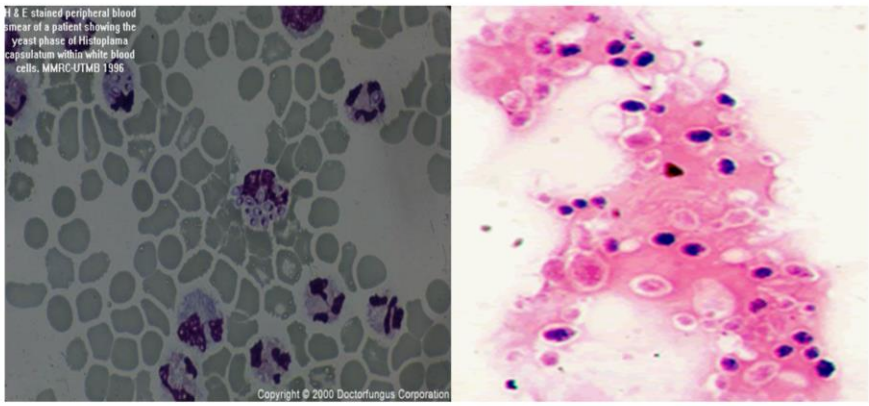
-these are **endemic** diseases; can be seen in healthy people as well as immunocompromised people (more severe)
-not usually seen in Jordan, mainly in south USA and South/Central America
-common trait among all 4 is that they're **dimorphic:**
-exist as a mold/filamentous **fungi at room temperature** (25C), and they transform into a **yeast at body temperature** (37C)
-initially, all of them infect the lung
-in healthy people it presents as an acute infection, in immunocompromised people it presents as a chronic illness and may disseminate all over the body

Dimorphic Fungus: Histoplasmosis-1

- ***Histoplasma capsulatum*..** Dimorphic fungus with conidia and yeast forms at body temperature and hyphae & marcoconidia in vitro culture.. Common in soil enriched with excreta of birds. Endemic in southern U.S.A, Australia.. Less other countries.
- 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.

-H. capsulatum is **not encapsulated** – don't make this mistake!
-the histoplasmin skin test is significant in diagnosis (unique to H. capsulatum)
-**intracellular infection**

Histoplasma capsulatum in infected White Blood cells



-infection is **intracellular**

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.

-mainly found in desert environments
-acute infection in healthy (not very significant for C. immitis, but can be fatal for B. dermatitidis)
-**antigen skin tests are not significant** for 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 Histoplasm antigen in blood & urine is significant

-C. immitis, when viewed microscopically have an appearance of conidia in a bag, which is unique to it
-SDA are used to differentiate based on morphology
-serology is not significant in diagnosis
-**histoplasma antigen found in blood and 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.

-P. brasiliensis is mainly found in South America, can be found in immigrants/tourists in southern USA
-typical presentation is similar to coccidioidomycosis immitis

The End