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A Review On Respiratory Tract Infections

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Abstract

Bacteria, fungi and viruses are the major microbes which can enter both nasal and lung region. The present article gives an outline of different bacteria, viruses and fungi which causes respiratory tract infection (RTI). Streptococcus pyogenes, Bacterial rhinosinusitis, Diphtheria, Bacterial pneumonia, Pneumococcal pneumonia, Haemophilic pneumonia and Mycoplasma pneumonia, Tuberculosis, Pertussis (Whooping Cough) Legionnaires Disease and Q disease are the RTI caused by the bacteria. Infections like Histoplasmosis, Blastomycosis, Coccidioidomycosis, Aspergillosis, Candidiasis, and Mucormycosis are some of the examples of respiratory tract caused by fungi. RTI caused by viruses included influenza, common cold, measles, mumps, rubella, chickenpox, and syndromes like SARS and MERS. The present article discusses about the various organisms that causes respiratory tract infection.

Keywords: Upper respiratory tract infection, lower respiratory tract infection, bacteria, Streptococcus pneumonia, Staphylococcus, Influenza, opportunistic infection, Aspergillosis, Histoplasmosis, Mucoromycosis

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Introduction

Respiratory tract infections are caused by bacteria (Gram positive (G +Ve) and Gram negative (G-ve)), fungi, fungal spores, and viruses. They lodge in the upper and lower respiratory tract causing common cold and pneumonia. Some of these are opportunistic in nature. In some cases the major symptoms will be associated with skin but they also infect the upper respiratory and lower respiratory tract as their route of entry to human body is through nasal region. Some of these infections can spread to other parts of the body leading to fatality.

Bacterial infection of respiratory tract

Gram +ve and Gram –ve bacteria causes RTI and in some cases it can affect other parts of the body.

Streptococcus pyogenes

Streptococcus pyogenes transmitted through air droplets enters the respiratory tract and forms a condition called Streptococcal pharyngitis. They are G+ve cocci in chain. Connective tissues are degraded by using hyaluronidase, collagenase and streptokinase. Streptokinase causes cleavage of blood clots, which assists in the spread of the pathogen.

The classic symptoms of streptococcal pharyngitis include fever, pain redness, swelling of palatine tonsils and affect the soft and hard palatine regions. The mode of transmission is by droplet and direct contact.

Serological diagnosis with group A antigen and culture methods are used for diagnosis of S.pyogens[1]

Bacterial rhinosinusitis

Nasopharynx contains diverse microbes and most of them are opportunistic in nature. Bacterial rhino sinusitis is often seen as secondary infection after the onset of a viral infection. As the bacteria affect the nose and paranasal sinuses it is also called rhinosinusitits. Bacterial rhinosinusitis are caused by Streptococcus pneumonia, Haemophilus influenza, and Moraxella catarrhalis.

Diphtheria

The causative agent of diphtheria, Corynebacterium

diphtheria, is a G+ve rod that belongs to the phylum Actinobacteria. Diphtheroids are commensals but, some strains of C. diphtheriae has a temperate bacteriophage-encoded protein—the diphtheria toxin giving them pathogenic nature. It can also cause impetigo-like lesions on the skin. Children are more affected than adults older than fourty and is transmitted through droplets and aerosols produced by coughing. After colonizing the throat, the bacterium remains in the oral cavity and begins producing the diphtheria toxin. Toxin has two subunit A(effector) and B(binding unit) and blocks host-cell protein synthesis by inactivating elongation factor (EF) and leads to death of cell. Dead cells accumulate and form psuedomembrane (classical sign of diphtheria). The pseudo membrane enlarges to obstruct the fauces of the pharynx or trachea and can lead to suffocation and death. Toxin spreads throughout the body; it can damage other tissues as well damaging the heart and nerve cells. The disease is diagnosed by bacterial culture using throat swabs, toxin detected by amplifying tox gene using polymerase chain reaction and antigen detection like radial immunodiffusion or Elek'simmunodiffusion test.

Penicillin and erythromycin effectively control C. diphtheria infections and toxins are nullified using antitoxins (preformed antibodies against the toxin).

Pneumococcal Pneumonia

The most common cause of community-acquired bacterial pneumonia is Streptococcus pneumonia. This Gram-positive, lancet shaped, alpha haemolytic Streptococcus is commonly found a normal microbiota of the human respiratory tract and appears as pairs[2]. The pneumococcal initially colonize the bronchioles of the lungs and spread to all part of lungs. The polysaccharide capsule prevents the phagocytic clearance. Pneumolysin O is a protein helps in the attachment of bacteria to the host cells and induces cytokine production. The cytokine induces inflammation and accumulation of neutrophils and red blood cells inside the alveoli. Bloody sputum is the main symptom of this disease. The infection is identified by microscopic observation and blood culture. Alpha haemolysis is observed on blood agar medium. All clinical pneumococcal isolates are stereotyped using the quelling reaction with typing antisera produced by the CDC. S. pneumonia is extremely sensitive to optochin and colonies are rapidly destroyed by the addition of 10% solution of sodium deoxycholate.

Haemophilus Pneumonia

They are Gram negative and cocobacillus in nature, Aerosols containing H. influenza are the main agents for transmitting disease. These are fastidious in nature as they grow well on media containing factor X (hemin) and factor V (NAD), like chocolate agar. The organisms are confirmed by antigen antibody interaction and isolation methods.

Mycoplasma Pneumonia (Walking pneumonia)

Mycoplasma pneumonia a wall less slow growing pleomorphic bacteria causes Pneumonia also called Walking pneumonia is spreaded through aerosols. Fever and cough are the main symptom of walking pneumonia. The pathogenesis is by using specialized attachment organelle which bind to ciliated cells and damaging the epidermal cells. Mycoplasma grows very slowly when cultured. To prevent the growth of other fast growing organism penicillin and thallium acetate are added to agar. The recovery from M. pneumonia infections are faster and can be cured by macrolide antibiotic therapy.

Chlamydial Pneumonias and Psittacosis

Chlamydial pneumonia and Psittacosis are caused by obligate intracellular pathogens. Chlamydophila pneumoniae (formerly known as Chlamydia pneumoniae), Chlamydophila psittaci (formerly known as Chlamydia psittaci), and Chlamydia trachomatis. Of the three, Chlamydophila pneumoniae is the most common and is transmitted via respiratory droplets or aerosols. Chlamydia trachomatis, the causative agent of the sexually transmitted chlamydia, can also cause congenital chlamydia

Diagnosis of chlamydia by culturing tends to be difficult and slow. Because they are intracellular pathogens, they require multiple passages through tissue culture. PCR and serologically based tests are used for easier identification of these pathogens. Tetracycline and macrolide antibiotics are typically prescribed for treatment.

Pseudomonas Pneumonia

Pseudomonas aeruginosa is a nosocomial infection leading to bacterial pneumonia in patients with cystic fibrosis (CF). P aeruginosa secretes exotoxins and acts as virulence factor. Defective Cystic fibrosis transmembrane receptor (CFTR) results in accumulation of mucus in the alveoli. Mucocilary escalator is inhibited and defensins produced by the host will not be effective. Exopolysaccharide secreted by the organism helps them to escape the phagocytosis process and enable them to multiply inside the lungs. The major cause of death in

patients with CF is due to lung damage[3].

Tuberculosis

M. tuberculosis is an acid-fast, high G + C, Gram-positive, nonspore-forming rod and slow growing. Mycolic acid present on the cell wall of bacteria determines the permeability. M. tuberculosis can enter any part of the body and form tubercles. The mode of transmission of the bacteria is by inhalation of respiratory droplets or aerosols containing mycobacteria[4]. The bacterium enters the lungs through inhalation and inside the lungs the alveolar macrophages engulf the bacteria. The bacterium has the ability to prevent the fusion of the phagosome with the lysosome. The presence of the bacteria inside the alveoli leads to activation of neutrophils and macrophages and migration of cells to that area. Activated immune cells damage the infected and normal cells causing liquefaction. The cells during this stage will soft and caseous. Due to calcium deposition inside the alveoli cells and accumulation of dead immune cells, the area become thick and form a complex called Ghon complex[5]. Initial stages of infection it is called as primary tuberculosis and later on the reactivation of infection is called secondary tuberculosis. The bacteria can enter the blood and enter different parts of the body and this condition is called disseminated tuberculosis. The formation of tubercle and Ghon complex can be identified by X-ray diagnosis of the infected lung. The disease can also be diagnosed by Acid fast staining of the patient's sputum. As this is a slow growing organism the culturing the organism is difficult. The identification of organism is done by PCR methods.

The treatment modality for TB is using antibiotics. Due to misuse of antibiotics more organisms become resistant to these drugs and based on drug resistance M. tuberculosis are named as multidrug resistance tuberculosis (MDR-TB) and extensively drug-resistant (XDR-TB) tuberculosis strains. So for treatment combination of different antibiotics like isoniazid, rifampin, ethambutol, and pyrazinamide are given for one month. The prevention of the disease can be done by vaccination using Bacillus Calmette-Guérin (BCG) strain of M. bovis commonly found in cattle.

Pertussis (Whooping Cough)

Whoophing cough is caused by Bordetella pertussis, a Gram-negative Coccobacillus. Due to the accumulation of mucus in the respiratory tract, the blockage of air passage will occur and the patient produce a whoop sound during coughing. The cough lasts for more than two weeks. Infants and children are more affected with the disease. Following inhalation, B. pertussis specifically attaches to epithelial cells using an adhesin, filamentous hemagglutinin. The organism produces A-B exotoxin also called the pertussis toxin (PT). The mechanism of action of PT is by increasing the expression of the cyclic adenosine monophosphate (cAMP) levels and disrupts cellular signaling. The exotoxin increases the level of inflammatory mediators like histamine and serotonin. Tracheal toxin damages the ciliated epithelial cells and accumulation of mucus in the lungs. The CDC reported 20 pertussis-related deaths in 2012, but that number had declined to five by 2015[5].

Specimen collected directly from a nasopharyngeal (NP) is streaked onto Bordet-Gengou medium within twenty four hours of collection of sample. B. pertussis infection is diagnosed using PCR techniques and ELISA methods.

Legionnaires Disease

An aerobic Gram-negative bacillus, Legionella pneumophila is commonly seen in cooler region like air-conditioning cooling towers, humidifiers, misting systems, and fountains. The mechanism of pathogenesis is by preventing the fusion of phagosome with the lysosome by the protein secreted by the microbes which can bind to endosomal membrane. The disease can range from mild to severe pneumonia, depending on the status of the host's immune defences. Although this disease primarily affects the lungs, it can also cause fever, nausea, vomiting, confusion, and other neurological effects.

Culturing of L. pneumophila is difficult and is fastidious bacterium. Warthin-Starry silver-precipitate is used to visualize this pathogen. Detection of Legionella antigen in a patient's urine is specific and selective and takes less than one hour.

Legionnaire disease can be effectively treated with fluoroquinolone and macrolide antibiotics. However, the disease is sometimes fatal; about 10% of patient's die of complications [6].

Q Fever

The zoonotic disease Q fever is caused by a rickettsia, Coxiella burnetii. The primary reservoirs for this bacterium are domesticated livestock such as cattle, sheep, and goats. The bacterium may be transmitted by ticks or through exposure to the urine, feces, milk, or amniotic fluid of an infected animal. In humans, the primary route of infection

is through inhalation of contaminated farmyard aerosols. It is, therefore, largely an occupational disease of farmers. Humans are acutely sensitive to C. burnetii—the infective dose is estimated to be just a few cells[7]. Symptoms associated with acute Q fever include high fever, headache, coughing, pneumonia, and general malaise. In a small number of patients (less than 5%)[8]. The condition may become chronic, often leading to endocarditis, which may be fatal. Diagnosing rickettsial infection by cultivation in the laboratory is both difficult and hazardous because of the easy aerosolization of the bacteria, so PCR and ELISA are commonly used.

Doxycycline is the first-line drug to treat acute Q fever. In chronic Q fever, doxycycline is often paired with hydroxychloroquine.

Fungal infections of respiratory tract

Invasive fungal infections occur in both immunocompetent and immunocompromised patients.

Histoplasmosis:

Histoplasmosis is an intracellular infection of the reticuloendothelial system caused by the dimorphic fungus Histoplasma capsulatum. Infection is acquired by inhalation. The large majority infections are asymptomatic and as in tuberculosis, heal, leaving behind an area of miliary calcification. The fungus H capsulatum is endemic to the Ohio and Mississippi River valleys, Central American and Southeast Asian rivers, and the Mediterranean[9]. H capsulatum grows optimally in caves and bird roosting areas with rich nitrogen soil. Itraconazole (mild and chronic pulmonary disease) and combination of Amphotericin B (AmB) with itraconazole (moderate-to-severe) are used for treatment of histoplasmosis[10].

Blastomycosis:

Blastomyces dermatitidis is endemic to the Great Lakes, the Mississippi and Valleys of Ohio River, the South eastern United States, and the African Mediterranean[11, 12]. The fungus grows in dead or decaying wood and acidic soil and near to bodies of water. Blastomycosis occurs with mold inhalation into the alveoli, where further dissemination may ensue[10,11]. Extrapulmonary dissemination involving the skin occurs in up to 40% of cases[13] Treatment includes itraconazole for mild-to-moderate disease and liposomal AmB (L-AmB) followed by itraconazole for life-threatening pulmonary infections[10].

Sporotrichosis

Sporothrix schenckii is globally located and not endemic to certain regions[13]. This fungus may be found in soil, decaying material, moss, hay, and infected animals. Infection results primarily from cutaneous contact with sporotrichosis[11,13]. Pulmonary sporotrichosis and nodular lesions result from inhaling S schenckii. Mild-to-moderate pulmonary disease requires Iitraconazole, whereas AmB followed by itraconazole is used for treating severe disease [10].

Coccidioidomycosis:

Coccidioidomycosis is endemic to South America, Central America, northern Mexico, and the western U.S., fungal growth occurs in nitrogen-enriched soil from rodent and bat droppings[10,14]. Coccidioides immitis and Coccidioide sposadasii are indistinguishable fungi, with C immitis being more common. Inhalation of a few inocula may cause pulmonary disease, with presentation as community-acquired pneumonia in endemic areas. Immunocompromised patients are treated with fluconazole or itraconazole. In serious pulmonary disease, treatment with AmB is initiated, followed by an azole[10.14].

Aspergillosis

Aspergilla fungi isolated from soil, plant debris, and indoor environments—are the most common cause of mortality due to invasive fungal infections[10, 15]. Severely immunocompromised patients the spores entered in to lungs cause pulmonary aspergillosis (IPA) and chronic necrotizing aspergillosis in patients with chronic lung diseases. Aspergilloma and allergic bronchopulmonary aspergillosis (identified in patients with a hypersensitivity to aspergillus antigens) are noninvasive manifestations[16]. The primary treatment for IPA is voriconazole and lipid-based AmB formulations, echinocandins, and posaconazole[10].

Cryptococcosis

Cryptococcosis is an opportunistic infection seen in immunocompromised individuals, including HIV or AIDS patients and organ-transplant recipients. Most of these show no symptoms, which results in a dormant infection[10,17, and 18]. Found in soil contaminated with pigeon droppings, cryptococcosis commonly presents as cryptococcal meningoencephalitis; it also occurs as an isolated primary infection in the lungs after spore inhalation [19] The spores can disseminate in to the central nervous system.

The treatment strategy of severe symptomatic pulmonary cryptococcosis is AmB formulation with or without flucytosine, followed by oral fluconazole, For immunosuppressed or immunocompetent patients exhibiting mild-to-moderate symptoms, fluconazole therapy is recommended[10,17].

Candida pneumonia

Infection is in the pulmonary area is rare and difficult to diagnosis. Primary Candida pneumonia refers to an invasive infection in the lungs, while secondary pneumonia refers to dissemination of invasive candidiasis[10,20]. Colonization of the lung parenchyma with Candida species is common; in critically ill patients, however, and defence mechanisms are rendered ineffective, thus enabling penetration of lung tissue. Triazole antifungals and echinocandins, AmB formulations are effective for treating pulmonary candidiasis [20, 21].

Mucormycosis

Pulmonary mucormycosis is primarily observed in patients with a predisposing condition of neutropenia or corticosteroid use[22]. Fungal attachment and damage of endothelial cells and invasion of vessel thrombosis, and successive tissue necrosis can lead to disseminated mucormycosis infections. These complications make for poor penetration of antifungal agents.

Treatment should include control of the predisposing problem, debridement of necrotic tissue, and antifungal therapy. Current recommendations for efficacious treatment of mucormycosis include AmB formulations, posaconazole, and iron chelation therapy. Although echinocandins as monotherapy do not act against mucormycosis, a few studies have found improved outcomes when AmB and an echinocandin are used[10, 14].

Pneumocystis jirovecii

Pneumocystis pneumonia (PCP)

PCP mostly seen in patients with HIV/ AIDS, hematologic and solid malignancies, organ transplant, and diseases requiring immunosuppressive agents. Infection occurs through the inhalation of airborne spores, with further maturation occurring in the lungs[23].

PCP is extremely resistant to common antifungal therapy, including AmB formulations and triazole antifungal. Trimethoprim / sulfamethoxazole remains the mainstay for PCP treatment and prophylaxis. Drugs like primaquine plus clindamycin, atovaquone, or IV pentamidine. In addition, dapsone is an alternative for prophylactic therapy[10].

Viral infection of respiratory tract

The Common Cold

More than 200 different viruses are known to cause the common cold. Viruses coming in Rhinoviruses, coronaviruses, and adenoviruses group are related to common cold. The aerosols produced during the coughing and sneezing persist on environmental surfaces for up to a week[24]. The route of entry of the viruses is nasal mucosa and eyes. The optimum temperature for replication is below normal body temperature (37 °C [98.6 °F]). The localisation of virus is seen in the cooler part of body such as nasal cavities. The attachment of the virus causes irritation of mucosa and causing inflammation. Running nose, congestion in the air passage, sore throat coughing and sneezing are the common signs and symptoms of the disease. A slight increase in body temperature is seen in common cold. The virus after entering the nasal region, it can also enter in ears, pharynx, and larynx causing inflammation. The symptoms subside within a week or two. Once infected by the virus it activates the cell mediated immunity and develops memory cells leading to lifelong immunity.

Influenza

Influenza viruses are enveloped RNA virus and exist as eight segments, each coated with ribonucleoprotein and encoding one or two specific viral proteins. The envelope contains two spike proteins hemagglutinin (H) and neuraminidase (N). The hemagglutinin spike protein binds to sialic acid receptors on the host receptors. Following inhalation, the influenza virus uses the hemagglutinin protein to bind to sialic acid receptors on host respiratory epithelial cells. The virus fuses with the host cell and the RNA enters the host cell where it will be transcribed and translated by using the host mechanism to produce viral proteins. The influenza viruses A (most virulent/pandemic), B(less virulent), and C (mild virulent) make up three of the five major groups of orthomyxoviruses. Influenza A virus can infect a variety of animals, including pigs, horses, pigs, and even whales and dolphins.

Viral Pneumonia

Viral pneumonia is caused by adenoviruses, influenza viruses, parainfluenza viruses, and

respiratory syncytial viruses (RSV). RSV is highly contagious and can be spread through respiratory droplets from coughing and sneezing. The symptoms include mild cold-like and in persons with weak first line defence system virus can enter the lungs and cause Pnuemonia. In persons with co morbid condition the disease will be life threatening.

Coronovirus

Corona viruses are enveloped RNA viruses with high rate of transmission. Pandemic diseases like Severe Acute Syndrome (SARS) and Middle East respiratory syndrome (MERS) are two acute respiratory infections caused by corona viruses. The main reservoirs of these viruses are animals like cats, bats, camel etc. Covid-19 diseases are caused by newly modified varients of coronavirus and have high pandemicity. There are no specific treatments for either MERS or SARS. Several recombinant vaccines, however, are being developed.

Measles, rubella (German measles), and chickenpox

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Measles (Rubeola)

The main reason for the death of children is due to infection by rubeola virus[25]. They belong to minus stranded RNA virus possesses an envelope containing hemaglutinin protein. Release of minute particles during coughing, sneezing, breathing are the main agents for the transmission of viruses. Once it enters the body it can cause increase in temperature, inflammation in the conjunctiva, and sore throat. Rashes on the skin surface appear due to viremia and these rashes last for several days. Kopliks spot are the characteristic symptoms of measles disease. The virus can enter the lungs and cause pneumonia; it can cause inflammation of encephalus region of brain and can be a reason for fatality[26].

The appearance of rashes and kopliks spots is used for the diagnosis of disease. Hemagglutination inhibition tests and serological tests may be used to confirm measles infections in low-prevalence settings. MMR (measles, mumps, and rubella) is the vaccine administered for prevention of disease.

Rubella (German measles)

Measles and Germen measles have the common symptoms like fever and rashes on the skin. German measles is caused by Rubella virus. Rubella viruses are belonging to enveloped RNA viruses. Virus enters through respiratory tract and in most of the individuals they are in apparent in nature. Apparent symptoms includes less intense facial rashes which will remain only for two to three days and doesn't have Kopliks spot(2–3 days), not associated with Koplik's spots, and the resulting fever is lower (101 °F [38.3 °C]). Vertical transmission occurs leading to congenital rubella syndrome and can also cause malformation of the foetus or still birth[27]. The disease diagnosis is done by observing the rashes on the faces and can be confirmed by serological methods. Disease subsides within two to three days and can be prevented by MMR.

Chickenpox and Shingles

Varicella zoster belonging to herpes virus family is the causative agent of chicken pox and is also transmitted by direct contact or inhalation of material from the skin lesions. Pregnant ladies will transmitting the virus to the foetus leading to some abnormality or birth defects in the baby called Reye syndrome. The viral infection initially produces pustules on the upper part of the body and the spreads to other part of the body. Varicella zoster, when reaches the lungs can lead to pneumonia in adults. The presence of virus in the blood results in chills and fever. The virus infected individual produces lifelong immunity.

The presence of pustular rashes indicates the presence of Varicella virus and is used for disease diagnosis. Other detection system include antigen antibody testing and isolation viral RNA and its amplification. The disease will subside without any treatment and in severe cases acyclovir is the drug of choice.

Conclusion

The respiratory tract infections are caused by all groups of microbes. In all infections the mode of entry is through respiratory tract and causing cough and later on pneumonia. Even though the organisms mainly cause rashes and pustules but the route of entry of these organisms is also through nasal route causing pneumonia and they are considered as respiratory tract infections. As they are transmitted through air droplets these

infection are rapidly spreading. Diagnosis is by isolation, serological and PCR methods. Most of the respiratory infections are self limiting and others are controlled by antibacterial ,antifungal and antiviral drugs. Prevention of RTI is mainly through vaccines. Vaccines are available for most of the RTI and in the case of viruses the vaccine development is facing problems as variation in structure occurs due to mutation

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