Respiratory Infections

Respiratory infections are a common cause of acute illnesses, especially in pediatrics. Infections are frequently divided into infections that cause problems in the upper respiratory tract (above the epiglottis; for example pharyngitis, croup, otitis media and sinusitis) or infections of the lower respiratory tract (below the epiglottis) such as bronchitis, bronchiolitis, bronchopneumonia (including community acquired, aspiration, hospital acquired (nosocomial) pneumonias).

Pneumonia occurs because of inflammation in the lung parenchyma caused by bacteria, viruses or fungi that evade our normal host defenses. Particles in the upper airway can be aspirated or inhaled bypassing the normal mechanical protective mechanisms e.g. closure of the vocal cords, beating mucociliary cells-the “escalator”, and/or immune mechanisms such as alveolar macrophages, neutrophils (IL-8 produced by respiratory epithelium which stimulates migration of PMNs), antibody and complement. All of these cause inflammation but help also with the clearance of bacteria from the airway.

There are many pathogens that can cause community acquired pneumonia (CAP) and these will be detailed in this lecture. In general, in over 50% of the cases of pneumonia, the physician caring for the patient cannot identify the exact cause. This is because many of the organisms that cause CAP are “atypical pathogens” including bacteria such as mycoplasma, chlamydia, and legionella species. These organisms are “atypical” not because they are not the most common cause, but because the symptoms are different from the classic pneumococcal pneumonia which presents with fever, cough and is acute in onset with a focal, lobular infiltrate on chest xray. The atypical pneumonias often present with an atypical CXR (chest xray) such as bilateral infiltrates. Atypical pathogens do not usually respond to cell wall antibiotics like penicillin.

Other pathogens that cause CAP include: non-typeable H. influenzae, Mycoplasma pneumoniae, Chlamydia pneumoniae, S. aureus, Streptococcus pyogenes, N. meningitidis, Moraxella catarrhalis, Klebsiella pneumoniae (and other gram negative rods), Legionella species, influenza virus, respiratory syneytial virus, adenovirus, parainfluenza virus, etc. Organisms that cause pneumonia and have specific epidemiological risk factors include Chlamydia psittaci (psittacosis), Coxiella burnetti (Q fever), Francisella tularensis (tularemia), and endemic fungi (Histoplasmosis, blastomycosis, and coccidioidomycosis).
An incomplete list of microbial organisms causing atypical pneumonia.

<table>
<thead>
<tr>
<th>Category</th>
<th>Organism</th>
<th>Main diseases</th>
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<tr>
<td>Bacteria</td>
<td><em>Bacillus anthracis</em></td>
<td>Anthrax</td>
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<td><em>Bordetella species</em>, including <em>B pertussis</em>,</td>
<td>Whooping cough and others</td>
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<td><em>B parapertussis</em>, and <em>B holmesii</em></td>
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<td><em>Brucella species</em></td>
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<td><em>Burkholderia pseudomallei</em></td>
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<td><em>Francisella tularensis</em></td>
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<td><em>Corynebacterium cluster</em></td>
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<td></td>
<td><em>Legionella pneumophila</em></td>
<td>Atypical (necococcal) pneumonia</td>
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<td><em>Leptospira interrogans</em></td>
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<td><em>Pasteurella multocida</em></td>
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<td>Plague</td>
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<td>Bacteria-like</td>
<td><em>Chlamydia pneumonia</em> (TWAR)</td>
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<td><em>Chlamydia trachomatis</em></td>
<td>Atypical pneumonia</td>
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<td><em>Chlamydia psittaci</em></td>
<td>Atypical pneumonia and others</td>
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<td><em>Mycoplasma pneumoniae</em></td>
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<td>Rickettsia</td>
<td><em>Coxiella burnetii</em></td>
<td>Atypical (walking) pneumonia</td>
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<td><em>Rickettsia rickettsiae</em></td>
<td>Acute Q fever</td>
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<td>Rickettsiosis</td>
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<td>Viruses</td>
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<td><em>Hantavirus</em></td>
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<td><em>Herpesvirus</em>, including <em>HSV, CMV, VZV, EBV, HHV-6, HHV-7, and HHV-8</em></td>
<td>Hantavirus pulmonary syndrome</td>
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<td><em>Influenza virus A, B, and C</em></td>
<td>Atypical pneumonia and others</td>
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<td><em>Measles virus</em></td>
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<td><em>Metapneumoviruses</em></td>
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<td><em>Non-SARS coronavirus</em></td>
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<td><em>Parainfluenza virus 1, 2, and 3</em></td>
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<td><em>Respiratory syncytial virus</em></td>
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<td><em>Rhinoviruses</em></td>
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<td><em>SARS virus</em></td>
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<td>Fungi</td>
<td><em>Aspergillus species</em></td>
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<td><em>Candida species</em></td>
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<td><em>Coccidioides immitis</em></td>
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<td><em>Cryptococcus neoformans</em></td>
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<td><em>Histoplasma capsulatum</em></td>
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<td>Protozoa</td>
<td><em>Pneumocystis carinii</em></td>
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<td><em>Toxoplasma gondii</em></td>
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Clinical Scenario #1 (Mycoplasma Pneumoniae)

• Myra is a 21 year old medical student living in the dorm room studying for exams
• She goes to student health complaining of low grade fever, headache, non-productive cough, sore throat and general malaise
• Her exam reveals mild fine inspiratory rales
• The doctor sends her for an x-ray that reveals bilateral infiltrates

This is the classic scenario for *Mycoplasma pneumoniae*, the so-called walking pneumonia. The x-ray appears worse than the patient looks clinically. *M. pneumoniae* symptoms (atypical pneumonia or tracheobronchitis) were first described in 1938 by Ryeman but the organism was not identified at the time. Infections with Mycoplasma usually occur in children 5-9 years of age and young adults.

**Mycoplasma pneumoniae**

**Physiology and structure**

Mycoplama is the smallest free-living bacteria. It does not have a cell wall, and the cell membrane contains sterols not present in other bacteria. Because it does not have a cell wall, this organism is resistant to “cell wall” antibiotics such as penicillins, cephalosporins, vancomycin, and others. *M. pneumoniae* is a strict aerobe and grows only on special enriched media. Mycoplasma grows slowly e.g. 1-6 hours generation time and most labs do not culture for this organism. Laboratory confirmation is usually by serology or PCR-research based. Bedside tests that suggest the diagnosis of mycoplasma include cold agglutinins (IgM antibodies that bind to the I antigen of the red cells). When the blood is put on ice, the I antigens appear on RBCs and the antibodies cause a snowflaky precipitate to form.

**Pathogenesis and immunity**

Mycoplasma has a unique protein, the P1 protein, that acts as an attachment factor and facilitates the attachment to the sialic receptors of the respiratory epithelium and to red cells. Mycoplasma is interesting because it remains extracellular and interacts with the cilia in the respiratory tract causing both the cilia and the epithelia cells to be destroyed which leads to loss of these cells and then interference of normal airway clearance which leads to contamination of the airway with microbes which cause mechanical irritation and then chronic cough. *M pneumoniae* also acts as a super antigen stimulating PMNs and macrophages to the site with subsequent release of cytokines including TNF α, IL-1 and IL-6.

Immunity to Mycoplasma is local and systemic. IgA appears early and disappears by 4 weeks, IgG appears at 3-4 weeks. Testing using complement fixation techniques is difficult and lacks specificity. Antibody-directed tests such as enzyme-linked immunosorbent assays and immunofluorescence, are used more often. The production of cold-agglutinins, a non-specific reaction to the outer membrane of the glycolipids of the *M. pneumoniae* (e.g. IgM antibodies that bind to the I antigen on the surface of RBC’s when cold) are a useful but nonspecific test. Cold agglutinins are positive in ~65% of symptomatic cases.
Epidemiology and clinical presentation
Unlike other respiratory infections, illness due to *M. pneumoniae* does not follow a seasonal pattern. Infections more commonly occur in children, young adults (e.g. it is the cause of 50% of the pneumonias for college age students). Infection is spread by droplets (hence outbreaks occur in close quarters e.g. college, military) and the incubation period is 2-3 weeks with infectious droplets being shed 2-8 days prior to developing symptoms.

Typically, *M. pneumoniae* produces a mild upper respiratory tract illness- a cold- especially in young children. Patients develop low-grade temperatures (100-102), malaise, headache, dry, non-productive cough that is worse at night and persists for weeks. Lower tract disease may occur in the form of tracheobronchitis and “atypical pneumonia” or walking pneumonia (since the xray (a diffuse interstitial infiltrate) appears worse than the clinical or laboratory exam of the patient e.g. normal WBC). These lower tract infections occur more often in adolescents suggesting a cellular immune response to this infection rather than antibody mediated. Some of the complications that have been noted with Mycoplasma infections and pneumonia include otitis media, erythema multiforme (red and white patchy rash often on hands), hemolytic anemia, myocarditis, pericarditis, neurologic abnormalities.

Treatment and prevention
Treatment is with erythromycin or tetracycline (or doxycycline- children over 9 years old). Prevention is difficult since disease is spread by droplets and close contact and organisms are shed for weeks. Isolation is not feasible. No vaccines are available.

Chlamydial pneumonias: *trachomatis, pneumonia, and psittaci*

Clinical scenario 2 (Chlamydial pneumonia)
- JM 10 week old infant born to a 16 year old mom
- Pregnancy history limited due to lack of prenatal care but baby born full term, no complications, left hospital 2 days
- Seen by pediatrician at 2 weeks old with eye discharge was given eye drops
- Returned to ER (2-4 weeks later): RR 60, cough but no fever
- CXR done and bloods drawn and child was admitted

This is an example of *Chlamydia trachomatis* pneumonia in an infant. You typically see diffuse infiltrates bilaterally with some perivascular cuffing. The baby’s risk factor for acquiring this infection was his mother’s history of a lack of prenatal care and the possibility that she carried the chlamydia due to an untreated genital infection. The baby received eyedrops which clear the infection locally without eradicating the organism systemically so the baby went on to develop pneumonia. There will be more information on Chlamydia to follow in the STD lecture.
Microbiology
Chlamydia is an intracellular parasite because it uses the host energy, ATP, unlike other organisms. It resembles a gram negative bacteria in that Chlamydia has a trilaminar outer membrane that contains LPS even though it is not Gram(-).

Chlamydia species are unique for their two phase life cycle. The elementary body (EB) is the infectious yet metabolically inactive spore-like particle that enters the cell through various mechanisms including endocytosis via clathrin-coated pits. It is converted to the reticulate body (RB) that divides by binary fission in the host cell and is then converted back into elementary bodies for extrusion from the cell and infection of new cells.

Two genera in this family cause respiratory tract diseases, chlamydia (trachomatis) and chlamydophila (consisting of pneumoniae and psittaci). A single strain of C. pneumonia is responsible for the clinical disease with this organism. The strain is called TWAR, named for the first two laboratory isolates of this chlamydial species (TW-183 and AR-39).

Pathogenesis and immunity
Chlamydial species infect non-ciliated columnar, cuboidal, or transitional epithelial cells found in the respiratory tract. Organisms multiply in alveolar macrophages and perivascular and peribronchiolar infiltrates develop. Clinical manifestations are due to destruction of cells during replication and host inflammatory responses. Immunity is not long lasting. Organisms are not readily cultured and thus detection relies on serology or antigen tests (DFA, ELISA) or the more sensitive amplification tests now available (PCR).

Epidemiology, clinical syndromes, prevention and treatment
C. trachomatis
Neonatal pneumonia due to C. trachomatis usually presents between 1-3 months of life (usually 6 weeks). Infants present with a staccato-like cough, rapid respiratory rate, and often do not have fever. On physical examination, wheezing is rarely heard. Diagnostic evaluation reveals hyperinflation and diffuse infiltrates on chest radiograph and a peripheral eosinophilia.

Diagnosis may be made by culture or non-culture tests of the nasopharynx. Non-culture tests of the nasopharynx have a lower sensitivity rate and may yield negative results. An IgM antibody test for C. trachomatis with a titer of > 1:32 is strongly suggestive of disease. Children with disease consistent with C. trachomatis pneumonia should be started on therapy (erythromycin) while waiting for diagnostic test results. Infection in newborns may be prevented by screening and treating pregnant women.

C. pneumoniae
Risk for infection increases with age such that by young adulthood, 50% of the population is seropositive for infection with C. pneumonia. TWAR may cause pneumonia (up to 28% of school age pneumonias and <10% of adult cases of outpatient pneumonias), bronchitis and sinusitis (5% of cases) and infrequently pharyngitis (<1%). Asymptomatic carriage of C. pneumonia has been documented. Disease may result after a prolonged incubation period of up to 21 days.
Respiratory disease due to *C. pneumonia* often has an indolent course beginning with non-specific upper respiratory symptoms such as rhinorrhea or sore throat and progressing to chronic cough that may persist for weeks despite appropriate antibiotic therapy. Patients are usually afebrile. Chest radiographs often show a lobar consolidation but disease may also present as a diffuse interstitial pattern, or with bilateral involvement with pleural effusions and lymphadenopathy. Patients usually have a normal peripheral white blood cell count.

*C. pneumonia* has been associated with “atypical pneumonias” as well as atherosclerotic disease. It is interesting to note the association of this pathogen with atherosclerotic heart disease. This was first discovered in 1993 by a pathologist (Dr. Store) in South Africa who was looking at atheromas of patients who had coronary artery disease and he discovered some structures that were later confirmed as elementary bodies of the TWAR strain. Other studies have linked *C.pneumoniae* to atherosclerotic heart disease in that they have shown chlamydia PCR tests positive from the atheromatous plaques. These same studies were not able to grow chlamydia in culture, the gold standard for making a Chlamydia diagnosis. The other problem with the association is that studies have tried to use antibiotics to treat atherosclerotic heart disease to see whether it has any effect on cardiac outcome and, thus far, no significant change in cardiac events while on antibiotics has been shown. Future studies are planned as atherosclerotic heart disease is a major cause of death in the U.S.

Diagnosis of *C. pneumoniae* is usually made with serologic testing using microimmunofluorescence tests to detect *C. pneumonia* specific antibody. IgM antibody develops within 4 weeks and IgG by 6 weeks. PCR testing of sputum, the pharynx or a pathologic specimen is very sensitive and provides a more prompt result. Treatment with standard courses of azithromycin or clarithromycin is often preferred to erythromycin (500 mg four times per day for up to 21 days) or doxycycline (100 mg twice a day for up to 21 days) due to ease of administration and fewer side effects. Either treatment has a clinical efficacy of > 90%. In clinical trials, the efficacy rate of levofloxacin was 98%. Failures do occur and re-treatment may be necessary after a 10-14 day course.

*C. psittaci* Psittacosis, a Greek term meaning parrot, is the disease state associated with this species of chlamydia. It is so named because the initial cases of this type of pneumonia were first associated with sick parrots. Many types of birds may carry and transmit this disease through respiratory droplets. Clinical presentation is usually that of an atypical pneumonia in that the patient has mild clinical symptoms such as cough, fever, malaise and the chest radiograph appears worse than expected. Non-specific central nervous system findings may also be present such as headache, confusion, cranial nerve palsy (including sensorineural hearing loss), meningitis, and seizures. Hepatitis and pericarditis may be complications of this infection. On physical examination, many patients will have fever, pharyngeal erythema and rales on examination of the lungs. Horder’s spots may appear on the skin. These spots are pink blanching maculopapular lesions. Chest
radiographs may show consolidation, a reticular nodular pattern, and/or hilar lymphadenopathy.

Diagnosis of *C. psittaci* may be made by blood culture (within the first 4 days) or sputum culture within the first 2 weeks. However as this is hazardous to laboratory personnel, serologic testing is preferred. Titers of > 1:64 are diagnostic of infection. Treatment strategies include tetracycline 500 mg four times a day or doxycycline 100 mg twice a day for 10-21 days. Erythromycin is an alternative but is less efficacious. Most patients respond to therapy within 24 hours of starting medications.

**Clinical scenario 3 (Legionnaire’s disease)**

- Charlie is a 68 year old retired plumber who recently underwent a renal transplantation
- Felt great and was tinkering around his house updating his bathroom fixtures
- Came for follow up visit complaining of high fever, cough, chills and his wife said that he was acting confused at times
- Laboratory studies reveal WBC 35,000 with left shift, LDH >1000(Lactic dehydrogenase, very high here, indicates that there is probably some pulmonary process going on).
- Chest x-ray reveals multilobar process

**Legionella**

*Legionella* is the cause of 2-6% of community acquired pneumonias. *Legionella* is uncommon among the pediatric population but is an important consideration in immunocompromised, hospitalized patients, and outbreak situations. Historically it was first recognized as an important pathogen during the 1976 outbreak of severe pneumonias and deaths among members of the American Legion convention in Philadelphia.

**Microbiology**

There are 39 species and 60 serogroups however the bulk of the human disease is caused by *L. pneumophila* and *L. micdadei*. Legionella are pleomorphic gram negative bacilli and don’t stain with common reagents and thus need Dieterle’s silver stain. They are fastidious organisms and grow in supplemented media (iron salts, L-cysteine).

*Legionella* is a facultative intracellular ubiquitous aquatic saprophyte (live inside amoeba). Thus it is found contaminating sources of water e.g. air conditioning systems and water tanks.

**Pathogenesis and Immunity**

Legionella is inhaled and multiplies within macrophages and monocytes in the alveoli (intracellular). It binds to the complement receptor on alveolar macrophages and gets into the cell by endocytosis. Phagolysosome fusion is prevented and thus the organisms survive within the cells. The bacilli proliferate in the lungs and produce proteolytic enzymes, phosphatase, lipase, and nuclease which kill the cell when the vacuole is lysed. This causes multifocal microabscess
formation. Activated/sensitized T cells are needed to kill these organisms (cell mediated immunity). Humoral immunity also plays a limited role.

**Epidemiology**

Disease due to legionella occurs sporadically and epidemically. Incidence peaks late summer to fall. People with greatest risk for disease are those with impaired cellular immunity and/or those with compromised pulmonary function e.g. elderly, transplants, neutropenic patients, smokers, alcoholics, etc and those at risk due to occupational exposure e.g. construction- working with moist environments and water systems (cooling towers, hot tubs, showers etc).

**Clinical Syndromes**

**Legionnaires’disease** - Symptomatic infection due to *legionella* may present as two different syndromes -- pneumonia or influenza like illness. Legionnaires’s disease is severe pneumonia due to *legionella*. Incubation period is up to 10 days and then symptoms manifest themselves abruptly with high fevers (105), rigors, cough (non-productive), headache etc. The pneumonia is usually multilobar with areas of microabscesses. As the disease progresses it spreads from lobe to lobe. Extrapulmonary manifestations include diarrhea, abdominal pain, nausea, mental confusion or delirium. Laboratory evaluation reveals high white cell counts (10-20,000) with a left shift in the majority of cases. Liver and renal functions may also be affected. The overall mortality is 15-20% depending on the immune function of the host. Death is usually due to respiratory or renal failure and/or shock.

**Pontiac Fever** - due to *L. pneumophila* causes a self-limited febrile illness like the flu (fevers, chills, myalgia, headaches etc.). Symptoms last 2-5 days and resolve spontaneously. It is called Pontiac fever after the town, Pontiac, Michigan, in which workers developed these symptoms in 1968 and the Department of Health did a large investigation into the cause.

**Diagnosis**

The rapid and moderately sensitive (70%) method of diagnosing *Legionella* is by using a direct fluorescent antibody test (DFA), in which fluorescein-labeled monoclonal or polyclonal antibodies are directed against *Legionella* species. *Legionella* can be cultured on special media, buffered charcoal-yeast extract agar. Commercially available antigen detection assays (urine test) using EIA or radioimmunoassays are available for detection of *L. pneumophila* serogroup 1 only.

However, Legionellosis is usually diagnosed by serology with a fourfold or greater increase in antibody titer (1: 128 or greater) considered positive. However, as with other illnesses, antibody titers usually are not seen until 3 weeks into the illness. Titers may persist over prolong periods (>1 year).
Prevention and Treatment
Treatment of legionellosis is usually with a macrolide antibiotic (azithromycin, erythromycin) or levofloxacin (a quinolone). β-lactam antibiotics usually are not effective due to the production of β-lactamases.

Hyperchlorination and super-heating have been used to eliminate legionella bacilli from water supplies. Low levels of organisms can persist and usually don’t cause disease. However, if complete elimination is necessary, continuous copper-silver ionization can be used.

Clinical scenario 4 (Bordetella pertussis)
• Jerry, a 7 month old child, comes to clinic with a runny nose, sneezing and slightly irritable
• Diagnosed with URI
• Returns 2 weeks later because he is turning blue with coughing spells. Spells are worse at night, seems to have spasms and then he “whoops” for air.
• Examination reveals mildly dehydrated, not distressed, clear lung exam
• WBC reveals leukocytosis with lymphocytosis

Bordetella pertussis - Whooping cough
Introduction
Bordetella pertussis is the organism responsible for pertussis or whooping cough -- an acute respiratory infection marked by episodic spasmodic coughing in the paroxysmal phase. It causes significant clinical disease such as bronchopneumonia especially in young children (<6 months). A milder form of the disease is caused by B. parapertussis.

Microbiology
Bordetella organisms are small, aerobic, fastidious, gram negative cocobacilli. Of the 7 species identified, 3 cause disease in man: pertussis, parapertussis and bronchiseptica (which usually causes disease in animals but can occasionally infect man). It requires special media (including blood, charcoal and starch- also called Bordet-Gengou agar after the investigators who first isolated the organism in culture in 1906) to grow and prolonged incubation periods. Culture can be used for diagnosis but care must be taken in obtaining a specimen (nasopharyngeal culture preferred), and immediately plating it on appropriate media. Serologic tests can be used following acute and convalescent titers.
Pathogenesis and Immunity

Pertussis is spread primarily by respiratory droplets. The organism colonizes and rapidly multiplies in the mucus membrane of the respiratory tract. Bacteremia does not occur. Disease is caused by the toxins that cause local tissue damage.

1. **Binding and uptake by phagocytic cells**

*B. Pertussis* attaches to the ciliated epithelial cells in the respiratory tract. This is facilitated by the action of the *pertussis toxin* and *filamentous hemagglutinin*. *(See graphic)* Pertussis toxin functions in the adhesion process with its classic A-B subunit. The A unit has the toxic subunit (S1) and the B unit has 5 binding subunits (S2-5) which help with binding. S2 binds to the respiratory epithelium and S3 binds to phagocyte cells. The filamentous hemagglutinin binds to the respiratory epithelial cells and polymophonuclear cells and facilitates uptake into those cells. Other adhesins (*pili and pertactin*) help bind the organism to cells.
2. Toxin production and disease manifestations

Pertussis contains many toxins: pertussis toxin, adenylate cyclase toxin, heat labile toxin. These will be described below.

a. Pertussis toxin
   The S1 portion of the pertussis toxin has adenosine diphosphate (ADP)-riboyslating activity for the surface G protein (whose function is to regulate adenylate cyclase activity). This causes the cyclic adenosine monophosphate (CAMP) levels to be unregulated resulting in increased respiratory secretions and mucus production characteristic of the paroxysmal state of pertussis.

b. Adenylate cyclase/hemolysin toxin and others
   This toxin is activated by intracellular calmodulin and catalyzes the conversion of ATP to CAMP. Adenylate cyclase toxin also inhibits leukocyte chemotaxis, phagocytosis and killing.

c. Heat-labile toxin (dermonecrotic toxin)- causes local tissue destruction.

d. Tracheal cytotoxin destroys ciliated epithelial cells by inhibition of cilia movement and by causing extrusion of the cells. It also stimulates the release of IL-1 which causes fever and the release of nitric oxide from the respiratory cells which in turn kills the epithelial cells.

e. Lipid A and Lipid X are two lipopolysaccharides produced by pertussis. They can activate the alternative complement pathway and stimulate cytokine release.
Epidemiology
The incidence of pertussis has declined significantly since the introduction of an effective vaccine in 1949. Pertussis is still endemic around the world and although it primarily affects children under 1 year of age, there have been an increasing number of cases in older children and adults due to waning immunity.

Clinical Syndromes
Unvaccinated persons and young children are at highest risk for disease. Aerosolized droplets infect the host and after a 7-10 day incubation period, the patient develops symptomatic disease in three stages.

First Stage: Catarrhal stage
This stage resembles the common cold with rhinorrhea (runny nose), sneezing, malaise, anorexia, and low-grade fever.

Second Stage: Paroxysmal Stage
This stage occurs 1-2 weeks after symptoms have begun. During this stage, the patient characteristically coughs and “whoops” – that is a series of coughs followed by an inspiratory whoop. Vomiting after these coughing spasms is a common occurrence. Lymphocytosis is noted at this time. These symptoms are thought to be due to the intense inflammatory response (discussed above) in the airway which causes local obstruction and mucous plugging.
**Third Stage: Convalescent Stage**
After 2-4 weeks, the cough is subsiding however other complications occur such as pneumonia (often due to other organisms that colonize the airway e.g. streptococcus pneumoniae), seizures, and encephalopathy.

**Prevention and treatment**
Although *B. pertussis* is susceptible to erythromycin, antibiotics do not alter the course of the infection but may decrease the communicability. Thus treatment is usually supportive. Chemoprophylaxis is recommended for household contacts without regard to immune status or age.

Whole-cell inactivated vaccines and multivalent acellular vaccines combining diphtheria, pertussis, and tetanus (DPT) are commonly administered to most children in the U.S. and are considered between 80-85% effective. Acellular vaccines are preferred due to a lower incidence of side effects such as pain, erythema at the site, and fever.