**ACUTE BRONCHITIS**

Acute bronchitis refers simply to inflammation of the tracheobronchial tree. The cause is usually infectious, but allergens and irritants can produce a similar clinical picture. Bronchitis typically occurs in the setting of an upper respiratory illness and is therefore observed more frequently in the winter months.

Acute bronchitis is common throughout the world and is one of the top 5 reasons for physician visits in countries that track such data.

Bronchitis is nearly always self-limited in the otherwise healthy individual, although it frequently results in absenteeism from work and school. Severe cases occasionally produce deterioration in those with significant underlying cardiopulmonary disease or other comorbid conditions.

**Causes**

Influenza, parainfluenza, adenovirus, rhinovirus, and a number of other viruses have been implicated.

M pneumoniae and Chlamydia pneumoniae have also been implicated, but the role of other bacterial pathogens remains difficult to validate given the difficulties associated with collecting adequate sputum samples and the problem of asymptomatic carriage of putative pathogens such as Streptococcus pneumoniae and Haemophilus influenzae.

Bordetella pertussis should be considered in the incompletely vaccinated child; however, studies increasingly report this bacterium as the causative agent in adults as well.

**Pathophysiology**

Although bronchitis refers to inflammation of the trachea and bronchi, other segments of the respiratory tract may also be involved because acute bronchitis usually occurs in relation to the common cold or other respiratory illness.

**CLINICAL**

**History**

A purulent cough generally is the defining presentation for acute bronchitis.

The following symptoms may also be present:

* Fever
* Malaise
* Rhinorrhea or nasal congestion
* Sore throat
* Wheezing
* Dyspnea
* Chest pain
* Myalgias or arthralgias
* Occupational history may be important in determining whether irritants play a role.

**Physical**

No uniform definition describes acute bronchitis. The physical examination findings may include rhonchi or wheezes, but in most cases the examination is unremarkable.

Occasionally, findings may suggest a particular etiology.

Bullous myringitis suggests Mycoplasma pneumoniae infection, although it is not specific.

Conjunctivitis and adenopathy suggest adenovirus, although these also are not specific.

**Imaging Studies**

* Chest radiography

Chest radiography may be necessary to exclude pneumonia, particularly when abnormalities exist in either the vital signs or pulse oximetry readings.

Lungs appear normal in uncomplicated cases.

 **TREATMENT**

Care for acute bronchitis is primarily supportive and should ensure that the patient is oxygenating adequately.

Therapy is generally symptomatic and includes use of analgesics, antipyretics, antitussives, and expectorants.

Among otherwise healthy individuals, antibiotics have not demonstrated consistent benefit in the symptomatology or natural history of acute bronchitis. Nonetheless, surveys from Europe, Australia, and the United States show that 80% of patients with acute bronchitis receive antibiotics. Antibiotic overuse contributes to the emergence of drug-resistant organisms. Cognizant of this, the Centers for Disease Control and Prevention (CDC) recently collaborated with a number of medical societies to publish a series of articles on the judicious use of antibiotics for several common conditions, including bronchitis, and have recommended against routine antibiotic use in uncomplicated bronchitis.

Several studies have shown conflicting results on the use of zinc as an adjunct treatment against influenza A. Most recent studies have shown favorable results; however, participants complained of a bad taste and significant nausea.

**Antibiotics**

Studies have focused on healthy individuals (excluding people with asthma) or patients with chronic obstructive pulmonary disease (COPD). Antibiotics may offer a small beneficial effect in the patient with COPD. Therefore, extending antibiotic therapy to people with asthma and other patients with limited cardiopulmonary reserve may be reasonable. If an antibiotic is to be used, a macrolide is a reasonable first choice because the macrolides are active against mycoplasmal and chlamydial organisms and B pertussis.

1. Erythromycin (EES, E-Mycin, Ery-Tab) - Used for prophylaxis in penicillin-allergic patients undergoing dental, oral, or respiratory tract procedures. Inhibits RNA-dependent protein synthesis, possibly by stimulating dissociation of peptidyl tRNA from ribosomes, resulting in arrest of bacterial replication.

Adult Dose 250-500 mg PO qid or 333 mg PO tid

2. Clarithromycin (Biaxin) - Reversibly binds to P site of 50S ribosomal subunit of susceptible organisms and may inhibit RNA-dependent protein synthesis by stimulating dissociation of peptidyl tRNA from ribosomes, inhibiting bacterial growth.

Adult Dose 250-500 mg PO bid

2. Azithromycin (Zithromax) - Used to treat mild-to-moderate infections caused by susceptible strains of microorganisms; indicated for chlamydial and gonorrheal infections of genital tract.

Adult Dose Day 1: 500 mg PO Days 2-5: 250 mg PO

3. Tetracycline (Sumycin) - For susceptible bacterial infections of both gram-positive and gram-negative organisms as well as infections caused by mycoplasmal, chlamydial, or rickettsial organisms. Inhibits bacterial protein synthesis by binding with 30S and possibly 50S ribosomal subunit(s). Provides coverage for mycoplasmal, chlamydial, and B pertussis organisms, but less effective than erythromycin.

Adult Dose 50-500 mg PO qid

4. Doxycycline (Bio-Tab, Doryx, Vibramycin) - Provides coverage for mycoplasmal and chlamydial organisms but not active against B pertussis; inhibits protein synthesis and bacterial growth by binding with 30S and possibly 50S ribosomal subunits of susceptible bacteria.

Adult Dose 100 mg PO bid

**Analgesics/antipyretics**

These agents are used to control fever as well as myalgias and arthralgias.

1. Ibuprofen (Ibuprin, Advil, Motrin) - Usually DOC for treatment of mild to moderate pain if no contraindications exist. Inhibits inflammatory reactions and pain, probably by decreasing activity of enzyme cyclooxygenase, which results in inhibition of prostaglandin synthesis.

Adult Dose 400-800 mg PO q4-6h

2. Acetaminophen (Tylenol, Panadol, Aspirin-free Anacin) - DOC for treatment of pain in those with documented hypersensitivity to aspirin or NSAIDs, with upper GI disease, or taking PO anticoagulants

Adult Dose 625-1000 mg PO q4h; not to exceed 4 g/d

**Antitussives and expectorants**

Little data exist on the efficacy of expectorants outside the test tube. The prototype antitussive, codeine, has been used successfully in some chronic cough and induced cough models, but little clinical data exist on upper respiratory infections. Existing data indicate that codeine is slightly better or equal in efficacy to guaifenesin, dextromethorphan, or even placebo.

1. Guaifenesin and codeine (Robitussin A-C, Guiatuss AC, Mytussin AC) -- Treats minor cough resulting from bronchial and throat irritation.

Adult Dose 5-10 mL q4-8h; not to exceed 60 mL/d

2. Guaifenesin with dextromethorphan (Humibid DM, Mytussin, Robitussin DM) -- Treats minor cough resulting from bronchial and throat irritation.

Adult Dose 10 mL PO q4h

**Bronchodilators**

Studies have shown an advantage to using bronchodilators, which may even be superior to antibiotics, for bronchitis symptoms. Patient numbers in trials, however, are disappointingly few given how commonly acute bronchitis is diagnosed.

1. Albuterol sulfate (Proventil, Ventolin) - Beta-agonist used in treatment of bronchospasm refractory to epinephrine. Relaxes bronchial smooth muscle by action on beta2-receptors and shows little effect on cardiac muscle contractility.

Adult Dose 2 puffs q4-6h or 2-4 mg PO tid/qid

**Antiviral agents**

Influenza vaccinations offer greater protection for the appropriate populations because they offer coverage for influenza A and B. However, amantadine and rimantadine can be useful during epidemics of influenza A. Zaminivir, the newest agent, is undergoing clinical trials and may be effective for influenza A and B.

1. Rimantadine (Flumadine) -- Inhibits viral replication of influenza A virus subtypes H1N1, H2N2, and H3N2. Prevents viral penetration into host by inhibiting uncoating of influenza A.

Adult Dose 200 mg PO qd or 100 mg PO bid

2. Amantadine (Symmetrel) -- Antiviral that prevents penetration of virus into host by inhibiting uncoating of influenza A; rimantadine appears to have a better adverse effect profile and can be taken once a day.

Adult Dose 100 mg PO bid for 5 d

**Prevention**

Patients with underlying cardiopulmonary disease should receive influenza vaccinations annually.

In certain situations such as nursing homes, amantadine or rimantadine should also be administered when an index case is found until the vaccine has had a chance to take effect.

A benefit may exist to influenza vaccination of healthy patients to reduce absenteeism.

**Complications**

Fewer than 5% of patients with bronchitis develop pneumonia. Incidence of subsequent pneumonia, however, remains unaffected by the use of antibiotics.

Prognosis

For the vast majority of patients, the prognosis is excellent.

**CHRONIC BRONCHITIS**

Bronchitis is an inflammation of the bronchial tubes, or bronchi. Bronchi are the air passages that extend from the trachea into the small airways and the alveoli. Viruses, bacteria, parasites, smoking, or inhalation of chemical pollutants or dust may cause inflammation.

**Definition**

Chronic bronchitis is a condition associated with excessive tracheobronchial mucus production sufficient to cause cough with expectoration for at least 3 months during a period of 2 consecutive years.

Chronic bronchitis is associated with hypertrophy of the mucus-producing glands found in the mucosa of large cartilaginous airways.

**Frequency**

In the US: Approximately 8 million people have chronic bronchitis, and 2 million have emphysema.

Bronchitis affects males more than females.

**Causes**

1. Infections, such as Mycoplasma species, Chlamydia pneumoniae, Streptococcus pneumoniae, Moraxella catarrhalis, and Haemophilus influenzae. Viral infection, such as influenza, parainfluenza, adenovirus, rhinovirus, and respiratory syncytial virus.

2. Exposure to irritants, such as pollution, chemicals, and cigarette smoke, may also cause acute bronchial irritation.

Air pollution levels have been associated with increased respiratory health problems among people living in affected areas. The Air Pollution and Respiratory Health Branch of the National Center for Environmental Health directs the fight of the Centers for Disease Control and Prevention (CDC) against respiratory illness associated with air pollution.

3. Cigarette smoking is indisputably the predominant cause of chronic bronchitis. Recent studies indicate that smoking marijuana causes similar damage.

Smoking impairs ciliary movement, inhibits function of alveolar macrophages, and leads to hypertrophy and hyperplasia of mucus-secreting glands.

Smoking can also increase airway resistance via vagally mediated smooth muscle constriction.

Unless some other factor can be isolated as the irritant that produces the symptoms, the first step in dealing with chronic bronchitis is to stop smoking.

**Pathophysiology**

During an episode of acute bronchitis, the cells of the bronchial-lining tissue are irritated and the mucous membrane is hyperemic and edematous, diminishing bronchial mucociliary function. Consequently, the air passages become clogged by debris and irritation increases. In response, copious secretion of mucus develops, which causes the characteristic cough of bronchitis. For instance, with Mycoplasma pneumonia, bronchial irritation results from the attachment of the organism (Mycoplasma pneumoniae) to the respiratory mucosa, with eventual sloughing of affected cells. Acute bronchitis usually lasts about 10 days. If the inflammation extends downward to the ends of the bronchial tree, into the small bronchi (bronchioles), and then into the air sacs, bronchopneumonia results.

Chronic bronchitis is a condition associated with excessive tracheobronchial mucus production sufficient to cause cough with expectoration for at least 3 months during more than 2 consecutive years. The alveolar epithelium is both the target and the initiator of inflammation in chronic bronchitis.

Predominance of neutrophils and peribronchial distribution of fibrotic changes result from the action of interleukin 8 (IL-8), colony-stimulating factors, and other chemotactic and proinflammatory cytokines. Airway epithelial cells release these inflammatory mediators in response to toxic, infectious, and inflammatory stimuli, in addition to decreased release of regulatory products such as ACE or neutral endopeptidase.

**Histologic Findings**

Goblet cell hyperplasia, mucosal and submucosal inflammatory cells, edema, peribronchial fibrosis, intraluminal mucus plugs, and increased smooth muscle are characteristic findings in small airways in chronic obstructive lung disease.

**CLASSIFICATION**

Chronic bronchitis can be categorized as

* simple chronic bronchitis
* chronic bronchitis with obstruction (or chronic mucopurulent bronchitis).

Mucoid sputum production characterizes simple chronic bronchitis. Persistent or recurrent purulent sputum production in the absence of localized suppurative disease, such as bronchiectasis, characterizes chronic mucopurulent bronchitis.

Chronic bronchitis with obstruction must be distinguished from chronic infective asthma. The differentiation is based mainly on the history of the clinical illness. Patients who have chronic bronchitis with obstruction present with a long history of productive cough and late onset of wheezing, whereas patients who have asthma with chronic obstruction have a long history of wheezing with late onset of productive cough.

Chronic bronchitis may result from a series of attacks of acute bronchitis, or it may gradually evolve because of heavy smoking or inhalation of air contaminated with other pollutants in the environment. When so-called smoker's cough is continual rather than occasional, the mucus-producing layer of the bronchial lining has probably thickened, narrowing the airways to the point where breathing becomes increasingly difficult. With immobilization of the cilia that sweep the air clean of foreign irritants, the bronchial passages become more vulnerable to further infection and the spread of tissue damage.

 **CLINICAL**

**History**

Obtain a complete history, including information on exposure to toxic substances and smoking. Patients with chronic bronchitis are often overweight and cyanotic. Initially, cough is present in the winter months. Over the years, the cough progresses from hibernal to perennial, and mucopurulent relapses increase in frequency, the duration and severity of which increase to the point of exertional dyspnea. Symptoms of acute bronchitis include the following:

* Fever
* Cough and sputum production

Cough begins early in the course of many acute respiratory infections and tends to become more prominent as the disease progresses.

In one prospective study of acute respiratory disease, 45% of patients were coughing 2 weeks after presentation, and 25% were coughing after 3 weeks. Sputum production was reported in approximately half of the patients in whom cough occurred.

An initially dry cough may later induce production of mucoid sputum, which characteristically develops a more purulent character in the later stages of illness.

* Sore throat
* Runny or stuffy nose
* Headache
* Muscle aches
* Extreme fatigue
* Nausea, vomiting, and diarrhea are rare.
* Severe cases may cause general malaise and chest pain. With severe tracheal involvement, burning, substernal chest pain associated with respiration, and coughing may occur.
* Dyspnea and cyanosis are not observed in adults unless the patient has underlying COPD or another condition that impairs lung function.

**Physical**

1. Patients may be afebrile or have a low-grade fever.

2. Diffuse wheezes, high-pitched continuous sounds, and the use of accessory muscles can be observed in severe cases. Occasionally, diffuse diminution of air intake or inspiratory stridor occurs; these findings indicate obstruction of a major bronchi or the trachea, which requires sequentially vigorous coughing, suctioning, and, possibly, intubation or even tracheostomy.

3. Sustained heave along the left sternal border indicates right ventricular hypertrophy secondary to chronic bronchitis.

4. Clubbing on the digits and peripheral cyanosis indicate cystic fibrosis.

5. Bullous myringitis may suggest mycoplasmal pneumonia.

6. Conjunctivitis, adenopathy, and rhinorrhea suggest adenovirus infection.

**Lab Studies**

1. Bronchitis may be suspected in patients with an acute respiratory infection with cough. However, because many more serious diseases of the lower respiratory tract cause cough, bronchitis must be considered a diagnosis of exclusion.

2. Obtain cultures of respiratory secretions for influenza virus, M pneumoniae, and Bordetella pertussis when these organisms are suspected. Culture methods and immunofluorescence tests have been developed for laboratory diagnosis of C pneumoniae.

3. Obtain a throat swab.

4. Obtain a CBC count with differential.

5. Sputum cytology may be helpful if the cough is persistent.

5. Blood culture may sometimes be helpful if bacterial superinfection is suspected.

**Imaging Studies**

1.Order chest radiographs.

2. Perform bronchoscopy to exclude foreign body aspiration, tuberculosis, tumors, and other chronic diseases of the tracheobronchial tree and lungs.

**TREATMENT**

**Diet:**

The value of a diet of fruits, vegetables, and salads is debatable. The value of antioxidants is not proven.

**Medical Care**

Therapy is generally aimed toward alleviation of symptoms.

To alleviate symptoms, a doctor may prescribe a combination of medications that both open up obstructed bronchial airways and thin obstructive mucus so that it can be coughed up more easily.

Antitussive medications and antipyretic medications may be used to treat bronchitis.

A steam vaporizer near the bed can also be helpful in easing chest congestion at night.

Among otherwise healthy individuals, antibiotics have not demonstrated any consistent benefit in the symptomatology or natural history of acute bronchitis. Antibiotics are recommended to patients with bronchiectasis or COPD exacerbation or if purulent sputum production has lasted beyond 7 days without evidence of improvement to other conventional therapy.

Care for acute bronchitis is primarily supportive and should ensure that the patient is oxygenating adequately.

**Antibiotics**

Studies have focused on healthy individuals (asthmatic patients excluded) or patients with COPD. A small beneficial effect of antibiotics in treating patients with COPD appears to exist, and TMP/SMX remains a good and inexpensive choice. Therefore, it may be reasonable to extend antibiotic use to asthmatic patients and others with limited cardiopulmonary reserve. If an antibiotic is to be used, a macrolide is a reasonable first choice because it is active against mycoplasmal and chlamydial organisms and B pertussis.

Erythromycin (E.E.S., E-Mycin, Ery-Tab) - Inhibits bacterial growth, possibly by blocking dissociation of peptidyl t-RNA from ribosomes, causing RNA-dependent protein synthesis to arrest. For treatment of staphylococcal, streptococcal, chlamydial, and mycoplasmal infections.

Adult Dose 250-500 mg PO qid or 333 mg PO tid

Clarithromycin (Biaxin) - Reversibly binds to the P site of the 50S ribosomal subunit of susceptible organisms and may inhibit RNA-dependent protein synthesis by stimulating the dissociation of peptidyl t-RNA from ribosomes. Results in bacterial growth inhibition.

Adult Dose 250-500 mg PO bid

Azithromycin (Zithromax) - Treats mild-to-moderate microbial infections.

Adult Dose Day 1: 500 mg PODays 2-5: 250 mg PO qd

Tetracycline (Sumycin) or Doxycycline (Bio-Tab, Doryx, Vibramycin) - Tetracycline: Treats gram-positive and gram-negative organisms as well as mycoplasmal, chlamydial, and rickettsial infections. Inhibits bacterial protein synthesis by binding with 30S and, possibly, 50S ribosomal subunit(s). Less effective than erythromycin.

Doxycycline: Provides coverage for mycoplasmal and chlamydial organisms but not active against B pertussis. Inhibits protein synthesis and bacterial growth by binding with 30S and, possibly, 50S ribosomal subunits of susceptible bacteria.

Adult Dose Tetracycline: 250-500 mg PO qidDoxycycline: 100 mg PO bid on day 1, then 100 mg PO qd for 7-10 d

Cefditoren (Spectracef) - Semisynthetic cephalosporin administered as prodrug. Hydrolyzed by esterases during absorption and distributed in circulating blood as active cefditoren. Bactericidal activity results from inhibition of cell wall synthesis via affinity for penicillin-binding proteins. No dose adjustment necessary for mild renal impairment (CrCl 50-80 mgL/min/1.73 m2) or mild-to-moderate hepatic impairment. Indicated for the treatment of acute exacerbation of chronic bronchitis caused by susceptible strains of Streptococcus pyogenes. The 400-mg dose is indicated for the treatment of AECB caused by susceptible strains of H influenzae, Haemophilus parainfluenzae, S pneumoniae (penicillin-susceptible strains only), or M catarrhalis.

Adult Dose 200 mg PO with meals bid for 10 dModerate renal impairment (CrCl 30-49 mL/min/1.73 m2: No more than 200 mg PO bidSevere renal impairment (CrCl <30 mL/min/1.73 m2): 200 mg PO qd

Trimethoprim and sulfamethoxazole (Bactrim DS, Septra) -- Inhibits bacterial synthesis of dihydrofolic acid by competing with para-aminobenzoic acid, resulting in inhibition of bacterial growth. Antibacterial activity of TMP-SMZ includes common urinary tract pathogens, except Pseudomonas aeruginosa. As with tetracycline, it has in vitro activity against B pertussis. Not useful in mycoplasmal infections.

Adult Dose 160 mg TMP/800 mg SMZ PO q12h for 10-14 d

Amoxicillin (Biomox, Trimox, Amoxil) - Interferes with synthesis of cell wall mucopeptides during active multiplication, resulting in bactericidal activity against susceptible bacteria

Adult Dose 250-500 mg PO q8h; not to exceed 3 g/d

Ciprofloxacin (Cipro) - Has a bacteriocidal property by inhibiting the DNA gyrase and consequently cell growth.

Adult Dose 250-500 mg PO bid for 7-14 d

**Antitussives/expectorants**

Sparse data attest to the efficacy of expectorants outside the test tube.

Guaifenesin with dextromethorphan (Humibid DM, Robitussin DM) -- Treats minor cough resulting from bronchial and throat irritation.

Adult Dose 10 mL PO q4h; not to exceed 40 mL/24h

Guaifenesin and codeine (Robitussin AC) -- The prototype antitussive, codeine, has been used successfully in some chronic cough and induced-cough models, but little clinical data in upper respiratory tract infections exist.

Adult Dose 5-10 mL PO q4-8h; not to exceed 60 mL/d

**Bronchodilators**

Studies (although limited) have shown an advantage to using bronchodilators and possible superiority to antibiotics for relieving bronchitis symptoms.

Albuterol (Proventil, Ventolin) -- Relaxes bronchial smooth muscle by action on beta2 receptors with little effect on cardiac muscle contractility.

Adult Dose 2-4 mg/dose PO divided tid/qid; not to exceed 32 mg/dMDI: 2 puffs q4-6h; not to exceed 12 inhalations/d

**Antivirals**

Influenza vaccinations offer greater protection for the appropriate populations because they offer coverage for influenza A and B. However, amantadine and rimantadine can be useful during epidemics of influenza A. Zaminivir, the newest agent, is undergoing clinical trials and may be effective for influenza A and B.

Rimantadine (Flumadine) - Inhibits viral replication of influenza A virus H1N1, H2N2, and H3N2. Prevents viral penetration into host by inhibiting uncoating of influenza A.

Adult Dose 200 mg PO qd or 100 mg PO bid

Amantadine (Symmetrel) - Prevents penetration of virus into host by inhibiting uncoating of influenza A. Rimantadine appears to have a better adverse effect profile and can be taken qd.

Adult Dose 100 mg PO bid for 5 d

**Analgesics/antipyretics**

Often helpful in relieving the associated lethargy, malaise, and fever associated with illness.

Ibuprofen (Ibuprin, Advil, Motrin) - Usually the DOC for treatment of mild to moderate pain if no contraindications exist.

Adult Dose 400-800 mg PO q4-6h

Acetaminophen (Tylenol, Panadol, Aspirin-Free Anacin) - DOC for treatment of pain in patients with documented hypersensitivity to aspirin or NSAIDs, with upper GI disease, or who are taking oral anticoagulants.

Adult Dose 325-650 mg PO q4-6h or 1000 mg tid/qid; not to exceed 4 g/d

**Complications**

* Lower respiratory tract infection and pneumonia
* Hemoptysis

**CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND EMPHYSEMA**

Chronic obstructive pulmonary disease is estimated to affect 32 million persons in the United States and is the fourth leading cause of death in this country. Patients typically have symptoms of both chronic bronchitis and emphysema, but the classic triad also includes asthma. Most of the time COPD is secondary to tobacco abuse, although cystic fibrosis, alpha-1 antitrypsin deficiency, bronchiectasis, and some rare forms of bullous lung diseases may be causes as well.

Patients with COPD are susceptible to many insults that can lead rapidly to an acute deterioration superimposed on chronic disease. Quick and accurate recognition of these patients along with aggressive and prompt intervention may be the only action that prevents frank respiratory failure.

**Frequency**

Two thirds of men and one fourth of women have emphysema at death. Approximately 8 million people have chronic bronchitis and 2 million have emphysema.

COPD is the fourth leading cause of death in the United States, affecting 32 million adults.

Men are more likely to have COPD than women.

COPD occurs predominantly in individuals older than 40 years.

**Causes**

In general, the vast majority of COPD cases are the direct result of tobacco abuse. While other causes are known, such as alpha-1 antitrypsin deficiency, cystic fibrosis, air pollution, occupational exposure (eg, firefighters), and bronchiectasis, this is a disease process that is somewhat unique in its direct correlation to a human activity.

**Pathophysiology**

COPD is a mixture of 3 separate disease processes that together form the complete clinical and pathophysiological picture. These processes are chronic bronchitis, emphysema and, to a lesser extent, asthma. Each case of COPD is unique in the blend of processes; however, 2 main types of the disease are recognized.

* Chronic bronchitis

In this type, chronic bronchitis plays the major role. Chronic bronchitis is defined by excessive mucus production with airway obstruction and notable hyperplasia of mucus-producing glands.

Damage to the endothelium impairs the mucociliary response that clears bacteria and mucus. Inflammation and secretions provide the obstructive component of chronic bronchitis. In contrast to emphysema, chronic bronchitis is associated with a relatively undamaged pulmonary capillary bed.

Emphysema is present to a variable degree but usually is centrilobular rather than panlobular. The body responds by decreasing ventilation and increasing cardiac output. This V/Q mismatch results in rapid circulation in a poorly ventilated lung, leading to hypoxemia and polycythemia.

Eventually, hypercapnia and respiratory acidosis develop, leading to pulmonary artery vasoconstriction and cor pulmonale. With the ensuing hypoxemia, polycythemia, and increased CO2 retention, these patients have signs of right heart failure and are known as "blue bloaters."

* Emphysema

The second major type is that in which emphysema is the primary underlying process. Emphysema is defined by destruction of airways distal to the terminal bronchiole.

Physiology of emphysema involves gradual destruction of alveolar septae and of the pulmonary capillary bed, leading to decreased ability to oxygenate blood. The body compensates with lowered cardiac output and hyperventilation. This V/Q mismatch results in relatively limited blood flow through a fairly well oxygenated lung with normal blood gases and pressures in the lung, in contrast to the situation in blue bloaters. Because of low cardiac output, however, the rest of the body suffers from tissue hypoxia and pulmonary cachexia. Eventually, these patients develop muscle wasting and weight loss and are identified as "pink puffers."

 **CLINICAL**

**History**

Patients with COPD present with a combination of signs and symptoms of chronic bronchitis, emphysema, and asthma. Symptoms include worsening dyspnea, progressive exercise intolerance, and alteration in mental status. In addition, some important clinical and historical differences can exist between the types of COPD.

**In the chronic bronchitis group, classic symptoms include the following:**

* Productive cough, with progression over time to intermittent dyspnea
* Frequent and recurrent pulmonary infections
* Progressive cardiac/respiratory failure over time, with edema and weight gain.

**In the emphysema group, the history is somewhat different and may include the following set of classic symptoms:**

* A long history of progressive dyspnea with late onset of nonproductive cough
* Occasional mucopurulent relapses
* Eventual cachexia and respiratory failure

**Physical**

 Depending on the type of COPD, physical examination may vary.

**Chronic bronchitis (blue bloaters)**

* Patients may be obese.
* Frequent cough and expectoration are typical.
* Use of accessory muscles of respiration is common.
* Coarse rhonchi and wheezing may be heard on auscultation.
* Patients may have signs of right heart failure (ie, cor pulmonale), such as edema and cyanosis.
* Because they share many of the same physical signs, COPD may be difficult to distinguish from CHF. One crude bedside test for distinguishing COPD from CHF is peak expiratory flow. If patients blow 150-200 mL or less, they are probably having a COPD exacerbation; higher flows indicate a probable CHF exacerbation.

**Emphysema (pink puffers)**

* Patients may be very thin with a barrel chest.
* They typically have little or no cough or expectoration.
* Breathing may be assisted by pursed lips and use of accessory respiratory muscles; they may adopt the tripod sitting position.
* The chest may be hyperresonant, and wheezing may be heard; heart sounds are very distant.
* Overall appearance is more like classic COPD exacerbation.

**Lab Studies:**

* Arterial blood gas

Arterial blood gas (ABG) analysis provides the best clues as to acuteness and severity.

In general, renal compensation occurs even in chronic CO2 retainers (ie, bronchitics); thus, pH usually is near normal.

Generally, consider any pH below 7.3 a sign of acute respiratory compromise.

* Serum chemistry

These patients tend to retain sodium.

Diuretics, beta-adrenergic agonists, and theophylline act to lower potassium levels; thus, serum potassium should be monitored carefully.

Beta-adrenergic agonists also increase renal excretion of serum calcium and magnesium, which may be important in the presence of hypokalemia.

* CBC - Polycythemia

**Imaging Studies:**

* Chest x-ray

Chronic bronchitis is associated with increased bronchovascular markings and cardiomegaly.

Emphysema is associated with a small heart, hyperinflation, flat hemidiaphragms, and possible bullous changes.

**Other Tests:**

* Pulse oximetry

Pulse oximetry does not offer as much information as ABG.

When combined with clinical observation, this test can be a powerful tool for instant feedback on the patient's status.

* Electrocardiogram

The presence of underlying cardiac disease is highly likely.

Establish that hypoxia is not resulting in ischemia.

Establish that the underlying cause of respiratory difficulty is not cardiac in nature.

* Pulmonary function tests

Decreased forced expiratory volume in 1 second (FEV1) with concomitant reduction in FEV1/forced vital capacity (FVC) ratio

Poor/absent reversibility with bronchodilators

FVC normal or reduced

Normal or increased total lung capacity (TLC)

Increased residual volume (RV)

Normal or reduced diffusing capacity

**TREATMENT**

**Prehospital Care**

The mainstays of therapy for acute exacerbations of COPD are oxygen, bronchodilators, and definitive airway management.

* Oxygen

Adequate oxygen should be given to relieve hypoxia.

The need for intubation can be established quickly at the bedside by asking the patient hold the nebulizer in his or her hand. If the patient becomes so sleepy that the nebulizer starts to fall away, the patient should be intubated regardless of PCO2 level. The cause of increased CO2 production is not decreased respiratory drive but probably reversal of hypoxic arterial vasoconstriction in areas of less-ventilated lung tissue, which increases the extent of ventilation/perfusion defects and thus CO2.

Supply the patient with enough oxygen to maintain a near normal saturation (above 90%) and do not be concerned about oxygen supplementation leading to clinical deterioration. If the patient's condition is that tenuous, intubation most likely is needed anyway.

* Bronchodilator

In the prehospital setting, administer only beta-agonist nebulizer therapy, which should be given as needed.

If necessary and available, continuous positive airway pressure (CPAP) may be used.

Of course, in times of respiratory failure, patients may need intubation in the field.

**Emergency Department Care:**

In addition to oxygen, proper ED care may comprise

* bronchodilators,
* antibiotics,
* magnesium,
* CPAP or biphasic positive airway pressure (BiPAP),
* Heliox (ie, mixture of helium and oxygen),
* definitive airway management via intubation.

All of these should be considered in the context of the individual patient's condition.

**MEDICATION**

Medicines available for ED treatment of COPD include bronchodilators, oxygen, theophylline, corticosteroids and, possibly, magnesium.

Terbutaline can be considered for patients with such significant exacerbations that they are not moving enough air to take full advantage of nebulizer therapy.

The greatest single problem that persists in this area is the underdosing of beta agonists and the nonutilization of anticholinergics. Although only a small subset of patients respond to beta agonists, a reasonable dose approaches continuous nebulization, as is seen in current asthma treatment.

The use of antibiotics is still controversial. These patients are almost uniformly heavily colonized with Haemophilus influenzae, streptococcal pneumonia, and others; however, researchers have not proven these organisms to be the cause of the exacerbation. In fact, viruses are thought to be the instigating factor in as many as half of the cases. In addition, the particular antibiotic chosen seems to have much less effect on outcome than the particular host factors of the patient. Although some meta-analyses have suggested statistically significant improvement in outcome in those patients who receive empiric antibiotic coverage, the lack of quality studies and power leaves the subject open for debate. If antibiotics are given, the choice should provide coverage against pneumococcus, H influenzae, Legionella species, and gram-negative enterics.

* Bronchodilators

These agents act to decrease muscle tone in both small and large airways in the lungs, thus increasing ventilation. Category includes subcutaneous medications, beta-adrenergic agonists, methylxanthines, and anticholinergics. Note that only 10-15% of all patients with COPD have a true reversible (ie, bronchospastic) component; however, because predicting response is impossible on presentation, all patients should be treated with aggressive bronchodilator therapy.

Terbutaline (Brethaire, Bricanyl) - Acts directly on beta2-receptors to relax bronchial smooth muscle, relieving bronchospasm and reducing airway resistance.

Adult Dose 0.25 mg (0.25 mL of 1 mg/mL concentration) SC; not to exceed 0.5 mg SC q4h

Albuterol (Proventil) - Beta-agonist useful in treatment of bronchospasm. Drug selectively stimulates beta2-adrenergic receptors of lungs. Bronchodilation results from relaxation of bronchial smooth muscle, which relieves bronchospasm and reduces airway resistance. Note that prior use of long-acting agents such as salmeterol does not seem to compromise response to albuterol during acute attacks.Use 5 mg/mL solution for nebulization; usually underdosed in acute settings. Many studies have demonstrated that high-dose therapy is most efficacious. Goal is continuous therapy in initial treatment phase. Note that properly used MDI with spacer is equal in effectiveness to nebulized therapy.

Adult Dose 5 mg/mL solution: 1 mL (5 mg) in 2-3 mL of saline solution minimum; give multiple nebs in succession; goal is continuous therapy in initial treatment phaseProperly used MDI with spacer equal in effectiveness to nebulized therapy

Theophylline (Theo-Dur, Slo-bid, Theo-24) - Acts to increase collateral ventilation, respiratory muscle function, mucociliary clearance, and central respiratory drive. Acts partly by inhibiting phosphodiesterase, elevating cellular cyclic AMP levels, or antagonizing adenosine receptors in bronchi, resulting in relaxation of smooth muscle.However, clinical efficacy is controversial, especially in acute setting. Author advocates this medicine only if patient was taking medicine already and had subtherapeutic level. Do not give IV form (aminophylline) because it can precipitate arrhythmias, especially in patients such as these who are already in an excess catecholamine state. Measure serum level to adjust dose.Note that most recent meta-analyses and other literature have failed to show a benefit from the use of methylxanthines in acute exacerbations.

Adult Dose Target concentration: 10 mcg/mLDosing = (target concentration - current level) x 0.5 (ideal body weight)Alternatively, 1 mg/kg results in approximately 2 mcg/mL increase in serum levels

Ipratropium bromide (Atrovent) - Anticholinergic medication that appears to inhibit vagally mediated reflexes by antagonizing action of acetylcholine specifically with muscarinic receptor on bronchial smooth muscle. Vagal tone can be increased by as much as 50% in patients with COPD, so this can have a profound effect.Dose can (and should) be mixed with first beta-agonist nebulizer because it can take up to 20 min to begin having effect. Admitted controversy exists regarding efficacy of ipratropium, but it still should be part of total treatment picture.

Adult Dose 0.5 mg/nebulizer treatment; can be mixed with albuterol and used as part of first nebulized treatment on presentation to hospital

* Corticosteroids

These agents have been shown to be effective in accelerating recovery from acute COPD exacerbations. Although they may not make a clinical difference in the ED, they have some effect by 6-8 h into therapy; therefore, early dosing is critical.

Some newer studies are suggesting that inhaled corticosteroids (eg, nebulized budesonide) may be equally effective as IV or PO steroids in the mild-to-moderate exacerbation; however, further studies are needed.

Methylprednisolone (Solu-Medrol, Depo-Medrol, Adlone) - Usually given in IV form in ED for initiation of corticosteroid therapy, although PO form theoretically equally efficacious. Two forms equal in potency, time of onset, and adverse effects. Inhaled corticosteroids probably equally efficacious and have fewer adverse effects for patients discharged from ED.

Adult Dose 125 mg IV q6h recommended dose, but true optimal dose not knownAlternative: 1-2 mg/kg IV q6h; not to exceed 125 mg; this dose often used in children

* Electrolyte supplements

Magnesium is used to replenish stores that become depleted in periods of adrenergic excess such as asthma attacks, COPD exacerbations, and diuretic use.

* Magnesium sulfate

Thought to produce bronchodilation through counteraction of calcium-mediated smooth muscle constriction. Again, for every study showing positive finding, probably another shows no benefit, but given properly, magnesium is safe and may have some benefit.

Adult Dose 1.2-2 g IV over 15 min; not to exceed 150 mg/min

**Further Outpatient Care**

Disposition from the ED depends on the clinical picture for each patient more than any single laboratory value or test. In general, the longer the exacerbation, the more airway edema and debris are present, making resolution in the ED increasingly more difficult. Patients who state that they "feel back to normal" and have no overt reason for admission can reasonably be discharged home with follow-up arrangements. The corollary to this is that patients who state they "do not feel comfortable," regardless of the numbers, are the best predictors of outcome and probably should be admitted. Data on risk factors for relapse and need for admission are limited at present.

For patients who are sent home, nearly all should receive a short steroid burst and an increase in the frequency of inhaler therapy. Close follow-up should be arranged with the patient's regular care provider. Other therapies should be considered on a case by case basis.

Patients with severe or unstable disease should be seen monthly.

When their condition is stable, patients may be seen biannually.

Check theophylline level with each dose adjustment, then every 6-12 months.

For patients on home oxygen, check ABGs yearly or with any change in condition. Monitor oxygen saturation more frequently than ABGs.

**Complications**

Some complications that must be anticipated in COPD treatment include the following:

* Incidence of pneumothorax due to bleb formation is relatively high; consider pneumothorax in all patients with COPD who have increased shortness of breath.
* In patients who require long-term steroid use, the possibility of adrenal crisis is very real; at a minimum, patients with steroid-dependent COPD should receive stress dosing in the event of an exacerbation or any other stressor.
* Infection (common)
* Cor pulmonale
* Secondary polycythemia
* Bullous lung disease
* Acute or chronic respiratory failure
* Pulmonary hypertension
* Malnutrition

**Prognosis**

Patient's age and postbronchodilator FEV1 are the most important predictors of prognosis. Young age and FEV1 greater than 50% of predicted are associated with a good prognosis. Older patients and those with more severe lung disease do worse.

Supplemental oxygen (when indicated) has been shown to increase survival rates.

Smoking cessation improves prognosis.

Cor pulmonale, hypercapnia, tachycardia, and malnutrition indicate a poor prognosis.