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November 2012

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Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (**COPD**) refers to chronic bronchitis and emphysema, a pair of two commonly co-existing diseases of the lungs in which the airways become narrowed. [1] This leads to a limitation of the flow of air to and from the lungs causing shortness of breath. In contrast to asthma, the limitation of airflow is poorly reversible and usually gets progressively worse over time.

COPD is caused by noxious particles or gas, most commonly from tobacco smoking, which triggers an abnormal inflammatory response in the lung. [2][3] The inflammatory response in the larger airways is known as chronic bronchitis, which is diagnosed clinically when people regularly cough up sputum. In the alveoli, the inflammatory response causes destruction of the tissues of the lung, a process known as emphysema. The natural course of COPD is characterized by occasional sudden worsenings of symptoms called acute exacerbations, most of which are caused by infections or air pollution.

The diagnosis of COPD requires lung function tests. Important management strategies are smoking cessation, vaccinations, rehabilitation, and drug therapy (often using inhalers). Some patients go on to requiring long-term oxygen therapy or lung transplantation. [2]

Worldwide, COPD ranked as the sixth leading cause of death in 1990. It is projected to be the fourth leading cause of death worldwide by 2030 due to an increase in smoking rates and demographic changes in many countries. [4] COPD is the 4th leading cause of death in the U.S., and the economic burden of COPD in the U.S. in 2007 was $42.6 billion in health care costs and lost productivity. [5][6]

COPD is also known as **chronic obstructive lung disease** (COLD), **chronic obstructive airway disease** (COAD), **chronic airflow limitation** (CAL) and **chronic obstructive respiratory disease** (CORD).

Signs and symptoms

One of the most common symptoms of COPD is shortness of breath (dyspnea). People with COPD commonly describe this as: "My breathing requires effort," "I feel out of breath," or "I can't get enough air in". [7] People with COPD typically first notice dyspnea during vigorous exercise when the demands on the lungs are greatest. Over the years, dyspnea tends to get gradually worse so that it can occur during milder, everyday activities such as housework. In the advanced stages of COPD, dyspnea can become so bad that it occurs during rest and is constantly present.

Other symptoms of COPD are a persistent cough, sputum or mucus production, wheezing, chest tightness, and tiredness. [8][9]

People with advanced (very severe) COPD sometimes develop respiratory failure. When this happens, cyanosis, a bluish discoloration of the lips caused by a lack of oxygen in the blood, can occur. An excess of carbon dioxide in the blood can cause headaches, drowsiness or twitching (asterixis). A complication of advanced COPD is cor pulmonale, a strain on the heart due to the extra work required by the heart to pump blood through the affected lungs. [10] Symptoms of cor pulmonale are peripheral edema, seen as swelling of the ankles, and dyspnea.

There are a few signs of COPD that a healthcare worker may detect although they can be seen in other diseases. Some people have COPD and have none of these signs. Common signs are:

tachypnea, a rapid breathing rate

wheezing sounds or crackles in the lungs heard through a stethoscope

breathing out taking a longer time than breathing in

enlargement of the chest, particularly the front-to-back distance (hyperinflation)

active use of muscles in the neck to help with breathing

breathing through pursed lips

increased anteroposterior to lateral ratio of the chest (i.e. barrel chest).

Cause

Smoking

The primary risk factor for COPD is chronic tobacco smoking. In the United States, 80 to 90% of cases of COPD are due to smoking.[11] [12] Exposure to cigarette smoke is measured in pack-years[13], the average number of packages of cigarettes smoked daily multiplied by the number of years of smoking. The likelihood of developing COPD increases with age and cumulative smoke exposure, and almost all life-long smokers will develop COPD, provided that smoking-related, extrapulmonary diseases (cardiovascular, diabetes, cancer) do not claim their lives beforehand.[14]

Occupational exposures

Intense and prolonged exposure to workplace dusts found in coal mining, gold mining, and the cotton textile industry and chemicals such as cadmium, isocyanates, and fumes from welding have been implicated in the development of airflow obstruction, even in nonsmokers.[15] Workers who smoke and are exposed to these particles and gases are even more likely to develop COPD. Intense silica dust exposure causes silicosis, a restrictive lung disease distinct from COPD; however, less intense silica dust exposures have been linked to a COPD-like condition.[16] The effect of occupational pollutants on the lungs appears to be substantially less important than the effect of cigarette smoking.[17]

Air pollution

Studies in many countries have found that people who live in large cities have a higher rate of COPD compared to people who live in rural areas.[18] Urban air pollution may be a contributing factor for COPD as it is thought to slow the normal growth of the lungs although the long-term research needed to confirm the link has not been done. In many developing countries indoor air pollution from cooking fire smoke (often using biomass fuels such as wood and animal dung) is a common cause of COPD, especially in women.[19]

Genetics

Some factor in addition to heavy smoke exposure is required for a person to develop COPD. This factor is probably a genetic susceptibility. COPD is more common among relatives of COPD patients who smoke than unrelated smokers.[20] The genetic differences that make some peoples' lungs susceptible to the effects of tobacco smoke are mostly unknown. Alpha 1-antitrypsin deficiency is a genetic condition that is responsible for about 2% of cases of COPD. In this condition, the body does not make enough of a protein, alpha 1-antitrypsin. Alpha 1-antitrypsin protects the lungs from damage caused by protease enzymes, such as elastase and trypsin, that can be released as a result of an inflammatory response to tobacco smoke.[21]

Other risk factors

A tendency to sudden airway constriction in response to inhaled irritants, bronchial hyperresponsiveness, is a characteristic of asthma. Many people with COPD also have this tendency. In COPD, the presence of bronchial hyperresponsiveness predicts a worse course of the disease.[17] It is not known if bronchial hyperresponsiveness is a cause or a consequence of COPD. Other risk factors such as repeated lung infection and possibly a diet high in cured meats may be related to the development of COPD.

COPD as an autoimmune disease

Main article: Autoimmunity

There is mounting evidence that there may be an autoimmune component to COPD.[22] Many individuals with COPD who have stopped smoking have active inflammation in the lungs.[23] The disease may continue to get worse for many years after stopping smoking due to this ongoing inflammation.[23] This sustained inflammation is thought to be mediated by autoantibodies and autoreactive T cells.[24][25][23]

Disease process

It is not fully understood how tobacco smoke and other inhaled particles damage the lungs to cause COPD. The most important processes causing lung damage are:

- Oxidative stress produced by the high concentrations of free radicals in tobacco smoke.
- Cytokine release due to inflammation as the body responds to irritant particles such as tobacco smoke in the airway.
- Tobacco smoke and free radicals impair the activity of antiprotease enzymes such as alpha 1-antitrypsin, allowing protease enzymes to damage the lung.

Pathology

Chronic bronchitis

Main article: chronic bronchitis

Lung damage and inflammation in the large airways results in chronic bronchitis. Chronic bronchitis is defined in clinical terms as a cough with sputum production on most days for 3 months of a year, for 2 consecutive years.[26] In the airways of the lung, the hallmark of chronic bronchitis is an increased number (hyperplasia) and increased size (hypertrophy) of the goblet cells and mucous glands of the airway. As a result, there is more mucus than usual in the airways, contributing to narrowing of the airways and causing a cough with sputum. Microscopically there is infiltration of the airway walls with inflammatory cells. Inflammation is followed by scarring and remodeling that thickens the walls and also results in narrowing of the airways. As chronic bronchitis progresses, there is squamous metaplasia (an abnormal change in the tissue lining the inside of the airway) and fibrosis (further thickening and scarring of the airway wall). The consequence of these changes is a limitation of airflow.[27]

Patients with advanced COPD that have primarily chronic bronchitis rather than emphysema were commonly referred to as "blue bloaters" because of the bluish color of the skin and lips (cyanosis) seen in them.[28] The hypoxia and fluid retention leads to them being called "Blue Bloaters."

Emphysema

Main article: emphysema

Lung damage and inflammation of the air sacs (alveoli) results in emphysema. Emphysema is defined as enlargement of the air spaces distal to the terminal bronchioles, with destruction of their walls.[26] The destruction of air space walls reduces the surface

area available for the exchange of oxygen and carbon dioxide during breathing. It also reduces the elasticity of the lung itself, which results in a loss of support for the airways that are embedded in the lung. These airways are more likely to collapse causing further limitation to airflow. The effort made by patients suffering from emphysema during exhalation, causes a pink color in their faces, hence the term commonly used to refer to them, "pink puffers".

Pathophysiology

Narrowing of the airways reduces the rate at which air can flow to and from the air sacs (alveoli) and limits the effectiveness of the lungs. In COPD, the greatest reduction in air flow occurs when breathing out (during expiration) because the pressure in the chest tends to compress rather than expand the airways. In theory, air flow could be increased by breathing more forcefully, increasing the pressure in the chest during expiration. In COPD, there is often a limit to how much this can actually increase air flow, a situation known as expiratory flow limitation. [29]

If the rate of airflow is too low, a person with COPD may not be able to completely finish breathing out (expiration) before he or she needs to take another breath. This is particularly common during exercise when breathing has to be faster. A little of the air of the previous breath remains within the lungs when the next breath is started. When this happens, there is an increase in the volume of air in the lungs, a process called dynamic hyperinflation. [29]

Dynamic hyperinflation is closely linked to shortness of breath (dyspnea) in COPD. [30] It is less comfortable to breathe with hyperinflation because it takes more effort to move the lungs and chest wall when they are already stretched by hyperinflation.

Another factor contributing to shortness of breath in COPD is the loss of the surface area available for the exchange of oxygen and carbon dioxide with emphysema. This reduces the rate of transfer of these gasses between the body and the atmosphere and can lead to low oxygen and high carbon dioxide levels in the body. A person with emphysema may have to breathe faster or more deeply to compensate, which can be difficult to do if there is also flow limitation or hyperinflation.

Some people with advanced COPD do manage to breathe fast to compensate, but usually have dyspnea as a result. Others, who may be less short of breath, tolerate low oxygen and high carbon dioxide levels in their bodies but this can eventually lead to headaches, drowsiness and heart failure.

Advanced COPD can lead to complications beyond the lungs such as weight loss (cachexia), pulmonary hypertension and right-sided heart failure (cor pulmonale). Osteoporosis, heart disease, muscle wasting and depression are all more common in people with COPD. [2]

Acute exacerbations of COPD

Main article: Acute exacerbation of chronic obstructive pulmonary disease

An acute exacerbation of COPD is a sudden worsening of COPD symptoms (shortness of breath, quantity and color of phlegm) that typically lasts for several days. It may be triggered by an infection with bacteria or viruses or by environmental pollutants. Typically, infections cause 75% or more of the exacerbations; bacteria can roughly be found in 25% of cases, viruses in another 25%, and both viruses and bacteria in another 25%. Pulmonary Embolism can also cause exacerbations of COPD. Airway inflammation is increased during the exacerbation resulting in increased hyperinflation, reduced expiratory air flow and worsening of gas transfer. This can also lead to hypo ventilation and eventually hypoxia, thus can lead to insufficient tissue perfusion then cell necrosis. [2]

Diagnosis

The diagnosis of COPD should be considered in anyone who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease such as regular tobacco smoking.[2][31] No single symptom or sign can adequately confirm or exclude the diagnosis of COPD[32] although COPD is uncommon under the age of 40 years.

Spirometry

The diagnosis of COPD is confirmed by spirometry,[2] a test that measures breathing. Spirometry measures the forced expiratory volume in one second (FEV_1) which is the greatest volume of air that can be breathed out in the first second of a large breath. Spirometry also measures the forced vital capacity (FVC) which is the greatest volume of air that can be breathed out in a whole large breath. Normally at least 70% of the FVC comes out in the first second (i.e. the FEV_1/FVC ratio is >70%). In COPD, this ratio is less than normal, (i.e. FEV_1/FVC ratio is <70%) even after a bronchodilator medication has been given.

Spirometry can help to determine the severity of COPD.[2] The FEV_1 (measured post-bronchodilator) is expressed as a percent of a predicted "normal" value based on a person's age, gender, height and weight:

The severity of COPD also depends on the severity of dyspnea and exercise limitation. These and other factors can be combined with spirometry results to obtain a COPD severity score that takes multiple dimensions of the disease into account.[33]

Other tests

An x-ray of the chest may show an over-expanded lung (hyperinflation) and can be useful to help exclude other lung diseases. Complete pulmonary function tests with measurements of lung volumes and gas transfer may also show hyperinflation and can discriminate between COPD with emphysema and COPD without emphysema. A high-resolution computed tomography scan of the chest may show the distribution of emphysema throughout the lungs and can also be useful to exclude other lung diseases.

A blood sample taken from an artery can be tested for blood gas levels which may show low oxygen levels (hypoxemia) and/or high carbon dioxide levels (respiratory acidosis). A blood sample taken from a vein may show a high blood count (reactive polycythemia), a reaction to long-term hypoxemia.

Management

There is currently no cure for COPD; however, COPD is both a preventable and treatable disease. Clinical practice guidelines for the management of COPD are available from the Global Initiative for Chronic Obstructive Lung Disease (GOLD),[34] a collaboration that includes the World Health Organization and the U.S. National Heart, Lung, and Blood Institute. The major current directions of COPD management are to assess and monitor the disease, reduce the risk factors, manage stable COPD, prevent and treat acute exacerbations and manage comorbidity.[2]

The only measures that have been shown to reduce mortality is smoking cessation and supplemental oxygen.[35]

Risk factor reduction

Smoking cessation

Main article: Smoking cessation

Smoking cessation is one of the most important factors in slowing down the progression of COPD. Once COPD has been diagnosed, stopping smoking slows down the rate of progression of the disease. Even at a late stage of the disease it can significantly reduce the rate of deterioration in lung function and delay the onset of disability and death.[27] It is the only standard intervention that can improve the rate of progression of COPD.[35]

Smoking cessation starts with an individual decision to stop smoking that leads to an attempt at quitting. Often several attempts are required before long-term smoking cessation is achieved.[36] Some smokers can achieve long-term smoking cessation through "willpower" alone. However smoking is highly addictive[37] and many smokers need further support to quit. The chance of successfully stopping smoking can be greatly improved through social support, engagement in a smoking cessation programme and the use of drugs such as nicotine replacement therapy, bupropion and varenicline.[36]

The policies of governments, public health agencies and anti-smoking organizations can reduce smoking rates by encouraging smoking cessation and discouraging people from starting smoking.[36] These policies are important strategies in the prevention of COPD.

Occupational health

Measures can be taken to reduce the likelihood that workers in at-risk industries such as coal mining will develop COPD. Some examples of these measures are: education of workers and management about the risks, promoting smoking cessation, surveillance of workers for early signs of COPD, the use of personal dust monitors, the use of respirators and dust control.[38] Dust control can be achieved by improving ventilation, using water sprays and by using mining techniques that minimize dust generation. If a worker develops COPD, further lung damage can be reduced by avoiding ongoing dust exposure, for example by changing the work role.

Air pollution

Air quality can be improved by pollution reduction efforts which should lead to health gains for people with COPD. A person who has COPD may experience fewer symptoms if they stay indoors on days when air quality is poor.[2]

Management of stable COPD

Bronchodilators

Bronchodilators are medicines that relax smooth muscle around the airways, increasing the calibre of the airways and improving air flow. They can reduce the symptoms of shortness of breath, wheeze and exercise limitation, resulting in an improved quality of life for people with COPD.[39] They do not slow down the rate of progression of the underlying disease.[2] Bronchodilators are usually administered with an inhaler or via a nebulizer.

There are two major types of bronchodilator, β_2 agonists and anticholinergics. Anticholinergics appear to be superior to β_2 agonists in COPD. Anticholinergeics reduce respiratory deaths while β_2 agonists have no effect on respiratory deaths.[40] Each type may be either long-acting (with an effect lasting 12 hours or more) or short-acting (with a rapid onset of effect that does not last as long).

β_2 agonists

β_2 agonists stimulate β_2 receptors on airway smooth muscles, causing them to relax. There are several β_2 agonists available. Albuterol (common brand name: Ventolin) and terbutaline are widely used short acting β_2 agonists and provide rapid relief of COPD symptoms. Long acting β_2 agonists (LABAs) such as salmeterol and formoterol are used as maintenance therapy and lead to improved airflow, exercise capacity, and quality of life.[41]

Anticholinergics

Anticholinergic drugs cause airway smooth muscles to relax by blocking stimulation from cholinergic nerves. Ipratropium is the most widely prescribed short acting anticholinergic drug. Like short-acting β_2 agonists, short-acting anticholinergics provide rapid relief of COPD symptoms and a combination of the two is commonly used for a greater bronchodilator effect. Tiotropium is the most commonly prescribed long-acting anticholinergic drug in COPD. It is has more specificity for M_3 muscarinic receptors so may have fewer side-effects than other anticholinergic drugs. Regular use is associated with improvements in airflow, exercise capacity, quality

of life and possibly a longer life. [42][43] *In January 2010, a new research has shown that ipratropium used to treat COPD has increased cardiovascular morbidity in treatment of COPD.* [44] *At the same time Tiotropium was shown to be effective in eliminating the risk of all cause mortality, cardiovascular mortality and cardiovascular events.* [45]

Corticosteroids

Corticosteroids act to reduce the inflammation in the airways, in theory reducing lung damage and airway narrowing caused by inflammation. [46] Unlike bronchodilators, they do not act directly on the airway smooth muscle and do not provide immediate relief of symptoms. Some of the more common corticosteroids in use are prednisone, fluticasone, budesonide, mometasone, and beclomethasone. Corticosteroids are used in tablet or inhaled form to treat and prevent acute exacerbations of COPD. Well-inhaled corticosteroids (ICS) have not been shown to be of benefit for people with mild COPD, however, they have been shown to decrease acute exacerbations in those with either moderate or severe COPD. [47] They however have no effect on overall one-year mortality and are associated with increased rates of pneumonia. [48]

Other medication

Theophylline is a bronchodilator and phosphodiesterase inhibitor that in high doses can reduce symptoms for some people who have COPD. More often, side effects such as nausea and stimulation of the heart limit its use. [2] In lower doses, it may slightly reduce the number of COPD exacerbations. [49] The investigative phosphodiesterase-4 antagonists, roflumilast and cilomilast have completed Phase-2 clinical trials. Tumor necrosis factor antagonists such as infliximab suppress the immune system and reduce inflammation. Infliximab has been trialled in COPD but there was no evidence of benefit with the possibility of harm. [50]

Supplemental oxygen

Supplemental oxygen can be given to people with COPD who have low oxygen levels in the body. Oxygen is provided from an oxygen cylinder or an oxygen concentrator and delivered to a person through tubing via a nasal cannula or oxygen mask. Supplemental oxygen does not greatly improve shortness of breath but can allow people with COPD and low oxygen levels to do more exercise and household activity. Long-term oxygen therapy for at least 16 hours a day can improve the quality of life and survival for people with COPD and arterial hypoxemia or with complications of hypoxemia such as pulmonary hypertension, cor pulmonale, or secondary erythrocytosis. [51] High concentrations of supplemental oxygen can lead to the accumulation of carbon dioxide and respiratory acidosis for some people with severe COPD; lower oxygen flow rates are generally safer for these individuals.

Pulmonary rehabilitation

Pulmonary rehabilitation is a program of exercise, disease management and counselling coordinated to benefit the individual. [52] Pulmonary rehabilitation has been shown to improve shortness of breath and exercise capacity. It has also been shown to improve the sense of control a patient has over their disease as well as their emotions. [53]

Nutrition

Being either underweight or overweight can affect the symptoms, degree of disability and prognosis of COPD. People with COPD who are underweight can improve their breathing muscle strength by increasing their calorie intake. [2] When combined with regular exercise or a pulmonary rehabilitation programme, this can lead to improvements in COPD symptoms.

Cold weather protection

One of the major winter hazards for individuals with respiratory problems is breathing cold air. For many people with COPD, breathing cold air causes bronchospasm and increased breathlessness.

Correctly managing symptoms and protecting against breathing cold air in the winter can help prevent breathing problems like exacerbations. Exacerbations are common in the winter months and cause a significant rise in COPD hospital admissions.

The common cold or other forms of respiratory tract infections may also be potentially serious for the COPD patient. Many respiratory tract infections are contagious. During the winter, the incidence of the common cold and upper respiratory tract infections is much higher than during other times of the year.

For people with COPD, it is important to maintain a healthy lifestyle and keep active during fall and winter. They should dress appropriately for cold temperatures by wearing insulated winter clothing and keeping the head and face warm. During short exposures the body can lose a lot of heat and energy if not properly protected.

People with COPD should have annual flu and pneumonia vaccinations and avoid exposure to contaminates to avoid catching a cold. They should also wash their hands regularly and drink large amounts of fluids. Avoiding contact with people who are suffering from a cold will also reduce the risk.

To improve comfort during cold exposure, a facemask that is designed to warm breathed air can be worn. A facemask can protect against cold weather hazards.

Surgery

Surgery is sometimes helpful for COPD in selected cases. A bullectomy is the surgical removal of a bulla, a large air-filled space that can squash the surrounding, more normal lung. Lung volume reduction surgery is similar; parts of the lung that are particularly damaged by emphysema are removed allowing the remaining, relatively good lung to expand and work better. Lung transplantation is sometimes performed for severe COPD, particularly in younger individuals.

Prognosis

COPD usually gradually gets worse over time and can lead to death. The rate at which it gets worse varies between individuals. The factors that predict a poorer prognosis are: [2]

- Severe airflow obstruction (low FEV_1)
- Poor exercise capacity
- Shortness of breath
- Significantly underweight or overweight
- Complications like respiratory failure or cor pulmonale
- Continued smoking
- Frequent acute exacerbations

Epidemiology

In the United States, the prevalence of COPD is approximately 1 in 20 or 5%, totalling approximately 13.5 million people in USA, [55] or possibly approximately 25 million people if undiagnosed cases are included. [56]

History

COPD has probably always existed but has been called by different names in the past. Bonet described a condition of “voluminous lungs” in 1679. In 1769, Giovanni Morgagni described 19 cases where the lungs were “turgid” particularly from air.[57] The first description and illustration of the enlarged airspaces in emphysema was provided by Ruysh in 1721."History of pathologic descriptions of COPD" (PDF). http://www.mhprofessional.com/downloads/products/0071457399/0071457399_chap40.pdf. Matthew Baillie illustrated an emphysematous lung in 1789 and described the destructive character of the condition.[57] Badham used the word "catarrh" to describe the cough and mucus hypersecretion of chronic bronchitis in 1814. He recognised that chronic bronchitis was a disabling disorder.

René Laennec, the physician who invented the stethoscope, used the term "emphysema" in his book *A Treatise on the Diseases of the Chest and of Mediate Auscultation* (1837) to describe lungs that did not collapse when he opened the chest during an autopsy. He noted that they did not collapse as usual because they were full of air and the airways were filled with mucus.[57]

In 1842, John Hutchinson invented the spirometer, which allowed the measurement of vital capacity of the lungs. However, his spirometer could only measure volume, not airflow.[58] Tiffeneau in 1947 and Gaensler in 1950 and 1951 described the principles of measuring airflow.

The terms chronic bronchitis and emphysema were formally defined at the CIBA guest symposium of physicians in 1959. The term COPD was first used by William Briscoe in 1965 and has gradually overtaken other terms to become established today as the preferred name for this disease.

See also

- COPD Awareness Month
- Restrictive lung disease
- Obstructive lung disease

Footnotes

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External links

COPD-BOLD International Research Platform

National Heart, Lung and Blood Institute - COPD U.S. NHLBI Information for Patients and the Public page.

Global Initiative for Chronic Obstructive Lung Disease (GOLD)

"Economic Impact of COPD and Cost Effective Solutions". *Access Economics*. The Australian Lung Foundation. October 2008. http://www.accesseconomics.com.au/publicationsreports/showreport.php?id=178.