

# 5



## *Chronic Obstructive Pulmonary Disease (COPD)*

Chronic obstructive pulmonary disease (COPD) is an umbrella term for conditions, including chronic bronchitis and emphysema, that impede the flow of air in the bronchi and trachea. COPD is the fourth-leading cause of death in the United States and is a major cause of sickness. It is currently the fifth-leading cause of death worldwide, but the World Health Organization projects it will become the third-leading cause by 2030 (1). COPD is both preventable and treatable.

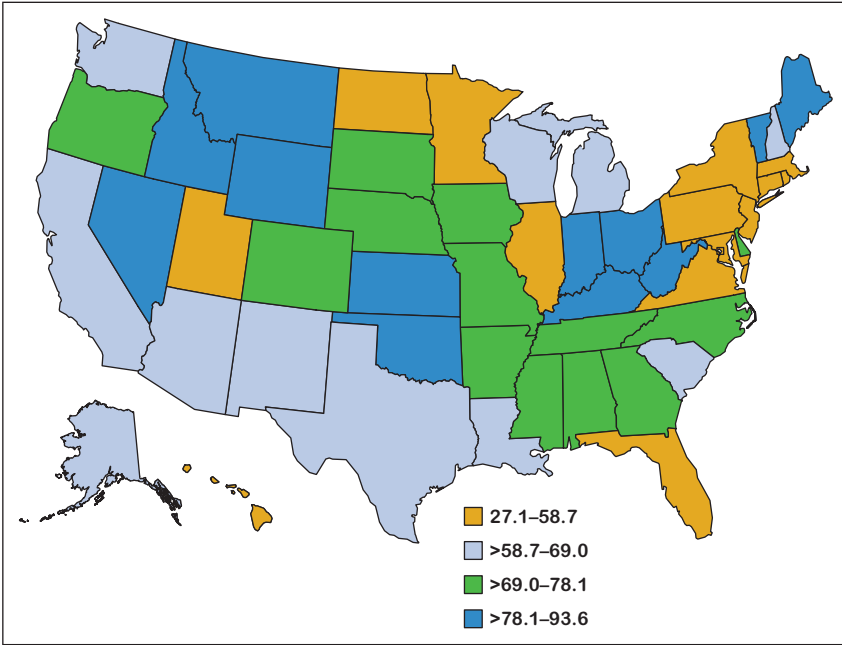
International organizations have more specifically defined COPD as “a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.”

### **Whom does it affect?**

#### ***Definition, epidemiology, prevalence, economic burden, and vulnerable populations***

Chronic obstructive pulmonary disease is diagnosed using a medical device called a spirometer, which measures air volume and flow, the main components of common clinical breathing tests (pulmonary function tests). The measurement

Rate of COPD deaths by state, per 100,000 population



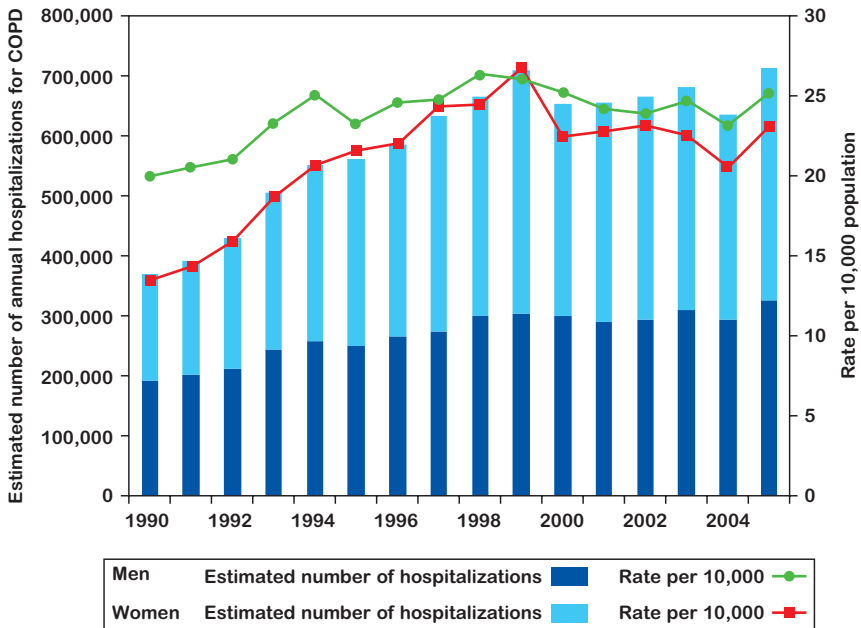
Deaths from COPD vary by state, which may reflect differences in smoking, diagnosis, or treatment. Centers for Disease Control and Prevention. *National Vital Statistics System*. Atlanta: 2005.

of the forced expired volume of air in one second ( $FEV_1$ ) as a percentage of the total amount of air that can be forcefully exhaled (forced vital capacity or FVC) is the main functional way of defining COPD. An  $FEV_1/FVC$  ratio less than 0.70 after a patient is given a bronchodilator usually indicates that he or she has COPD. A progressive disease, COPD is widely recognized as having four stages of severity. At its most severe stage, the  $FEV_1$  is less than 30 percent of normal (2).

COPD is a common chronic disease. Most estimates of COPD put its prevalence in the adult population in the 5 to 10 percent range, although these estimates vary by the specific criteria used. The Third National Health and Nutrition Examination Survey (NHANES III) data—the most recent U.S. survey that included spirometry—showed a prevalence of COPD in adults of 6.8 percent (1). Over 50 percent of people with evidence of COPD, though, have never been

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Estimated number of men and women hospitalized for COPD



*COPD hospitalizations increased until about 2000 and then leveled off. COPD rates shadow smoking rates with a delay of several years. DeFrances CJ, Hall MJ, for the Division of Health Care Statistics. 2005 National Hospital Discharge Survey. Hyattsville, MD: 2007.*

diagnosed with disease. This proportion is even higher among people with mild disease, which is most amenable to intervention (3).

COPD is responsible for about 700,000 hospitalizations annually in the United States. In recent years, the hospitalization rate among women has increased and is now similar to the rate among men. In 2005, more than 126,000 adults in the United States died from COPD (4). Age-adjusted mortality rates varied dramatically by state, from a low of 27.1 per 100,000 in Hawaii to a high of 93.6 per 100,000 in Oklahoma.

COPD has an enormous financial burden, with estimated direct medical costs in 1993 of \$14.7 billion. The estimated indirect cost related to morbidity (loss of work time and productivity) and premature mortality is an additional \$9.2 billion, for a total of \$23.9 billion annually. By 2002, this cost was estimated at \$32.1 billion annually (1).

### CASE STUDY

*A 52-year-old woman sought medical attention for increasing shortness of breath on exertion for over two years. She used to walk 9 holes of golf with her women's group every Wednesday, but over the last year she has had to use a golf cart. She has attributed this change to getting old. She was told three years earlier that she had "a touch of asthma" and was given an inhaler to use when she was symptomatic. In the last six months, she had three trips to the emergency department for "acute bronchitis." She had smoked for about 15 years, but stopped 20 years ago. Spirometry showed an FEV<sub>1</sub> of 62 percent of that predicted and an FEV<sub>1</sub>/FVC of 0.58.*

#### **Comment**

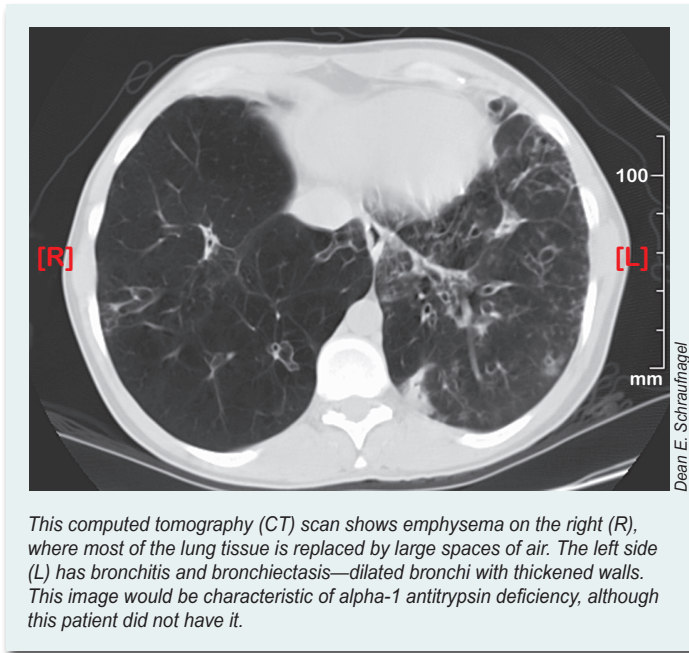
*This case highlights several typical features of COPD. First, it is becoming increasingly common among women, and women are more likely to be misdiagnosed (5). Second, people with COPD are told they have asthma or another respiratory disease. Third, the symptoms can occur long after a person has stopped smoking, and, in some cases, in the absence of a smoking history altogether. People often attribute their breathing problems to other causes, and they may feel that once they have stopped smoking they will no longer suffer its consequences.*

## **What we are learning about the disease**

### ***Pathophysiology, causes: genetic, environment, microbes***

COPD comprises a collection of different processes, including chronic or recurrent bronchitis, emphysema, and airway responsiveness that contribute to the disease. The most important risk factor for COPD in the United States is cigarette smoking. Other factors, including occupational or environmental exposures to dusts, gases, vapors, biomass smoke, malnutrition, early life infections, recurrent respiratory infections, genetic predisposition, increased airways responsiveness, and asthma may be important in many individuals (3).

Chronic or recurrent bronchitis is a major component of COPD. It consists of bouts of increased cough and sputum production that can occur frequently. The attacks may be related to an acute bacterial or viral infection or a chronic



process that has permanently damaged the airways, known as bronchiectasis. While most people have had an episode of bronchitis at some point in their life, recurrent episodes (typically two to three per year) are frequently observed in COPD.

Emphysema, another component of COPD, entails the destruction of alveoli (air sacs) in the lungs, impairing their ability to bring oxygen into the body and eliminate carbon dioxide.

The best known genetic risk factor for COPD is alpha-1 antitrypsin deficiency. Alpha-1 antitrypsin is a special protein that protects the lungs from enzymes known as proteases. The body's white blood cells seek out and destroy bacteria and viruses trying to invade the lungs. They kill the microbes by releasing enzymes and other toxic products that, in addition to killing the organisms, can damage the lungs. Alpha-1 antitrypsin quickly inactivates the enzymes produced by these white cells, protecting the lung from damage. In individuals

with alpha-1 antitrypsin deficiency, the low level of antitrypsin fails to protect the lungs from enzymatic tissue damage. This is a major cause of COPD in patients with alpha-1 antitrypsin deficiency. There are approximately 100,000 people in the United States who are deficient in alpha-1 antitrypsin because of a genetic defect. These patients can develop lung disease even in the absence of cigarette smoking, although smoking increases their chances of developing it.

COPD is also increasingly associated with other diseases, such as pneumonia, hypertension, heart failure, forms of heart disease, lung vascular disease, cancer, osteoporosis, and depression.

Although the role of environmental factors like cigarette smoke in the causation of COPD is well established, the mechanisms linking the exposure to the disease at the cellular level are still poorly understood. For instance, it is known that a characteristic form of inflammation involving a type of white blood cell (neutrophilic leukocytes) is associated with the structural changes of the lung that are found in chronic bronchitis and emphysema. However, the critical biological pathways remain elusive. This gap in knowledge has been an obstacle to new drug development.

The susceptibility to environmental irritants is likely to be determined by genetic factors. Knowing the genes associated with COPD susceptibility and development would be a significant step forward in better understanding the biology of COPD and identifying new drug targets. One such COPD-associated gene mutation has already been discovered; it is responsible for the COPD seen in patients with alpha-1 antitrypsin deficiency. Although this genetic defect is present in only a small number of patients with COPD, it has already paved the way for new therapeutic interventions and has served as a model for COPD in general.

## **How is it prevented, treated, and managed?**

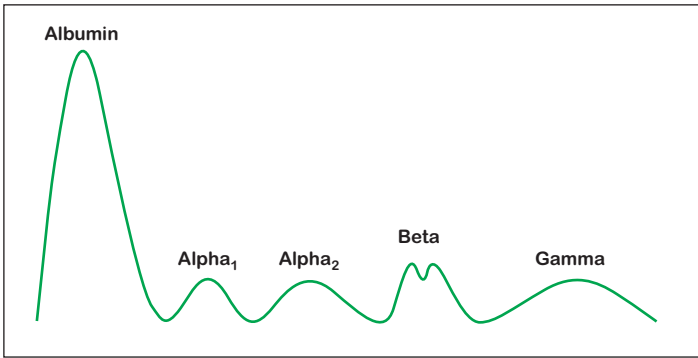
### ***Prevention, treatment, staying healthy, prognosis***

In the United States, the risk factor most strongly associated with COPD is cigarette smoking. Preventing teenagers from starting to smoke and getting established smokers to stop is clearly the most important way to prevent COPD. There are now many strategies to accomplish this, including public campaigns and personal counseling, higher costs for cigarettes, and new medications.

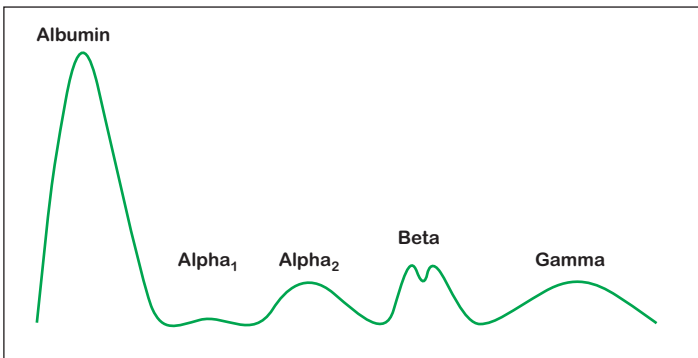
Another primary prevention strategy is to decrease occupational exposures to dusts, vapors, gases, and fumes. Treatment of asthma with disease modifying

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### Normal



### alpha-1 antitrypsin deficiency



Dean E. Schraufnager

*In 1963, a Swedish researcher and a medical resident discovered that the alpha-1 “clump” was missing in patients who developed emphysema at a young age. When they used electrophoresis, a method of purifying blood proteins, the absence of the alpha-1 protein became readily apparent.*

anti-inflammatory agents to prevent airway remodeling may be another primary prevention strategy for COPD.

Secondary prevention aims to detect disease when it is still relatively mild and treatable. While there is evidence that this strategy works in cardiovascular disease and diabetes, evidence that the early detection and treatment of COPD improves outcomes is, at the moment, lacking, but it is an area of active investigation. The hope is that earlier intervention will improve the quality of life in these patients.

Tertiary prevention aims to lessen the complications of established disease. Treatment with bronchodilators, anti-inflammatory agents, and antibiotics according to guidelines can reduce exacerbations of the disease and prevent the accelerated decline in lung function (2). Reducing exposure to air pollution and getting influenza and pneumonia vaccines may also lessen the chance of exacerbations. Alpha-1 antitrypsin replacement is available for those with this deficiency. In advanced disease, oxygen therapy and pulmonary rehabilitation have been shown to be beneficial. In a small number of selected cases, lung surgery, including lung volume reduction surgery and lung transplantation, may be helpful.

At any stage of disease, avoidance of risk factors, such as tobacco smoke or occupational dusts, is important.

## **Are we making a difference?**

### ***Research past, present, and future***

Important work by researchers in the 1950s and 1960s established that cigarette smoking was the major risk factor for disease in the developed world (6). The key intervention of decreasing smoking prevalence, which began with campaigns in the 1960s, has probably resulted in a lower prevalence of COPD compared to what might have been seen otherwise. However, over 20 percent of the U.S. adult population continues to smoke, and more people are exposed to second-hand smoke.

Recent investigations have demonstrated that asthma, ongoing inflammation in the lung, or the presence of other diseases may hasten the progression of COPD. Clinical trials suggest that medications may alter the natural history of disease.

Learning more about the basic biology of inflammation and how airways function is helping to develop new medications. A large National Institutes of Health research program called COPDgene ([www.copdgene.org](http://www.copdgene.org)) is investigating the relationship between genetic and other risk factors and the development and progression of COPD. This project hopes to identify the genes involved in different aspects of COPD. This knowledge will then lead to a better understanding of how and why COPD develops. (For example, it appears that only about half of smokers will develop COPD.) These and other studies may help explain how COPD relates to other diseases of aging and frailty.

**What we need to cure or eliminate COPD**

Decreasing smoking prevalence in the population would, ultimately, reduce the prevalence of COPD. Current therapy is focused on improving the quality of life for patients, but more research on current tools, such as how to best intervene in early disease and when to use antibiotics, could make major differences. Combining epidemiology and basic biology to understand how and why exacerbations occur and what contributes to inflammation will be critically important. The genetic studies could lead to major breakthroughs. Of course, basic discoveries must be tested in clinical trials before their real benefit is known.

## References

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2. Celli BR, MacNee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J* 2004;23:932–946.
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5. Chapman KR, Tashkin DP, Pye DJ. Gender bias in the diagnosis of COPD. *Chest* 2001;119:1691–1695.
6. Fletcher C, Peto R, Tinker CM, Speizer FE. *The Natural History of Chronic Bronchitis and Emphysema*. Oxford, UK: Oxford University Press; 1976.
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## Web sites of interest

American Lung Association

[www.lungusa.org](http://www.lungusa.org)

National Heart, Lung, and Blood Institute

[www.nhlbi.nih.gov/health/public/lung/copd/index.htm](http://www.nhlbi.nih.gov/health/public/lung/copd/index.htm)

Alpha-1 Foundation

[www.alpha-1foundation.org](http://www.alpha-1foundation.org)

American Thoracic Society

<http://patients.thoracic.org>