Many environmental factors contribute to the development of respiratory diseases. The World Health Organization's 2002 report “Reducing Risks, Promoting Healthy Life” emphasized the importance of environmental factors in lung disease and stated that controlling air pollution and tobacco consumption would be among the most important interventions to promote good health (1). The report noted that the burden of lung disease is unevenly distributed and can be traced to regional environmental challenges, nutrition, and poverty, as well as to a person’s underlying state of health. Because of the difficulty in assessing the prevalence and amount of exposure, the precise risk each environment poses is unknown. Risk assessment is further complicated by socioeconomic and genetic factors that may predispose a person to respiratory disease or alter the prognosis. However, by understanding the mechanisms of disease, defining high-risk populations, and intervening to mitigate or reduce environmental exposures, the burden of disease may be significantly lessened.
Whom does it affect?

**Epidemiology, prevalence, economic burden, vulnerable populations**

The lungs are the main interface between the body and the environment. Consequently, the lungs are a common site of environmentally induced disease. Thousands of environmental toxins and commercial chemicals are now in use, the particles of which may become aerosolized or airborne in the form of fibers, fumes, mists, or dust. Inhabitants of major metropolitan areas may inhale more than 2 milligrams of dust each day, and workers in dusty occupations may inhale up to 100 times that amount.

The lungs are equipped with a complex system to reduce the effect of potentially harmful inhaled toxins and to preserve the sensitive gas exchange mechanism of the alveolar surface, so pulmonary function in most persons is rarely affected despite this exposure. Nevertheless, environmentally related lung disease has increased over the past several decades, probably owing to exposure to respiratory toxins, mainly tobacco smoke and air pollutants.

Understanding and quantifying the contributions of environmental exposures to lung disease is difficult because individuals respond differently to the same factors. The variations in response arise from different susceptibilities,
including genetic predisposition, developmental stages of life, presence of co-existing diseases, other exposures, and lifestyle differences such as varying nutritional status and physical activity levels. Despite the difficulties inherent in teasing apart environmental contributions to human disease, a number of studies have shown that environmental exposures, particularly during fetal development, can profoundly affect subsequent genetic expression.

For example, environmental factors are known to play important roles in the pathogenesis of asthma—both in terms of main effects and those exerted indirectly through complex interactions with gene variants. The increase in the prevalence, incidence, and severity of asthma over the last 20 years, along with epidemiologic studies on the environment, provides strong evidence that exposures, including air pollution, play an important role in the development of this disease. These changes have occurred too rapidly to be accounted for by genetic changes in the population.
Although demographic factors, such as age, race, and socioeconomic status, appear to be risk factors for asthma, the increasing prevalence and severity of asthma suggest that airborne allergens, smoking behavior, agents in the workplace, indoor and outdoor air pollution, viruses, domestic and occupational exposure to toxins contained within bacteria (endotoxins), and immunization against certain infectious diseases play a role as well. Moreover, \textit{in utero} exposures have been identified as important risk factors for the development of asthma.

While prenatal exposure to diesel exhaust particles and environmental tobacco smoke is associated with an increased risk of asthma, maternal ingestion of fruits, vegetables, and oily fish appears to be protective. In addition, it appears that gestational exposure to an environment rich in microbial compounds protects against the development of allergic hypersensitivity (atopy) and may affect the innate immune response to allergens. However, host genetic factors are also important in disease development; people exposed to environmental tobacco smoke are at greater risk of developing asthma if they carry certain genetic factors (for example, those found at chromosome 17q21).

\section*{What are we learning about this disease?}

\textbf{Pathophysiology, causes: genetic, environment, microbes}

The development of environmentally induced lung disease is a function of the toxicity of the inhaled substance, the intensity and duration of exposure, and an individual’s susceptibility. The physical state of the inhaled substance (for example, solid, fume, or mixture), the size, and other characteristics (for example, solubility) principally determine the initial site of disease activity. Smaller particles (0.1 to 1.0 microns) are more likely to reach the lungs’ alveoli, but airborne particles up to 5 microns in size may also do so. In general, larger particles (10 microns or greater) are trapped and removed by the mucus and cilia of the upper respiratory tract.

Although the respiratory tract is quite resilient in the face of the plethora of agents in the environment, disruption of mechanisms to clear inhaled material may occur if an individual is exposed to highly concentrated particles in certain situations or if an exposure occurs during strenuous labor. Depending on the inhaled substance, acute or chronic reactions occur as particles are deposited on the alveolar surface. Acute reactions are characterized by swelling (edema) and inflammation,
CASE STUDY

A 55-year-old woman sought medical attention for progressive breathlessness. She grew up in a household where her father smoked. She herself smoked on average a pack of cigarettes per day for 40 years and worked with rosin solder. Five years earlier, she had developed breathlessness, and two years earlier she had to stop working because of this symptom. Since then, her condition worsened, and she required 2 liters of supplemental oxygen per minute. She remembered that working with solder increased her shortness of breath, as did days with high air pollution. She used a wood stove in winter for heat and had a cat in the home, to which she was allergic. Her father died of emphysema.

A pulmonologist found wheezes with prolonged expiration. Her pulmonary function tests showed severe obstruction (which improved after she inhaled a bronchodilator), trapped air in her lungs, and markedly reduced diffusing capacity—a measure of oxygen transfer through the lungs. She was continued on oxygen and inhalers, and given advice and help to quit smoking. She was advised to remove the cat from her home, stop using the wood stove, and stay indoors on high air pollution days.

Comment

This case depicts the complexity of assessing the impact that various environmental factors may have on the cause or aggravation of lung disease. In what appears to be well-defined respiratory disease of a known cause, such as chronic obstructive pulmonary disease (COPD) due to tobacco use, many other environmental factors may contribute to the onset of disease and worsening of symptoms with disease progression.

Most lung diseases are considered to be of unknown cause (idiopathic) unless there are strong clinical, physiologic, and pathologic associations with an environmental etiology. Of note, environmental factors can result in most types of lung disease, including asthma, COPD, interstitial lung disease, infectious lung disease, pulmonary hypertension, and lung cancer. These and other lung diseases, including genetically determined diseases such as cystic fibrosis and alpha-1 antitrypsin deficiency, may be aggravated by environmental factors. Unless environmental factors are considered, an important opportunity for case finding, treatment, and prevention of future disease will be missed.
while chronic reactions are characterized by connective tissue scarring (fibrosis) and the formation of specific aggregates of immune cells (granulomas).

Several factors may make certain individuals more susceptible to inhaled toxins. These include genetic tendencies, the inability to clear substances from the lower respiratory tract, the presence of coexisting pulmonary diseases, and the effects of concomitant exposures, such as cigarette smoke.

Environmental lung diseases are difficult to diagnose and study epidemiologically because of the extended time from exposure to clinical expression of disease, which often ranges from years to decades. In addition, individuals can be exposed to several substances at one time, and they may work in a number of professions and do a variety of tasks in their lifetime (2–4).

How is it prevented, treated, and managed?

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

The first step in preventing environmentally related lung disease is to recognize the exposure–disease relationship. Then, primary prevention is achieved with
reduction, modification, or elimination of the exposure or environment. These changes may involve behavior modifications at the individual level, such as smoking cessation. Other interventions require societal and global approaches to prioritize and target environmental modifications with public health policy implications. Some of these efforts necessitate legislation and public policy for implementation, such as the use of air quality standards to reduce air pollution or bans on the advertisement of tobacco products or on smoking in public places to reduce tobacco smoke. Education is an important aspect of prevention of environmentally induced lung disease.

The treatment of environmentally induced lung disease usually includes recommendations for exposure reduction or modification to reduce disease

Annual prevalence of smoking

The number of Americans who smoke has declined steadily from 1965 to 1999. The decline is most dramatic among men, but rates have declined among women as well, except among those age 65 or older. National Center for Health Statistics.
impairment. The prognosis of environmentally induced lung diseases is usually dictated by the underlying disease and not always by the environment itself, except in some occupational lung diseases. However, it is important to remember that, as a group, these are preventable diseases.

Are we making a difference?

Research past, present, and future

Significant strides have been made in linking environmental factors and lung disease by using epidemiologic and toxicologic studies combined with an effort to determine the mechanisms by which the disease develops. This approach has resulted in a reduction in occupational lung disease caused by dust, called pneumoconiosis, and asbestos-related lung disease in communities surrounding industrial sources. In addition, the ongoing recognition of new environmental factors in lung disease, such as exposure to smoke from burning wood and other plants commonly used in developing countries for heat, has been an important accomplishment in this area.

What we need to cure or eliminate environmentally induced lung disease

The cornerstone of controlling, reducing, and eliminating environmentally associated respiratory disease is improving indoor, outdoor, and workplace air quality in the United States. In addition, several important advances are necessary (5). First, the ability to assess the environment and the exposure must be improved in order to understand the impact environmental factors have on disease and to determine whether new environmental factors might result in disease. Assessment methods are needed that can monitor a person’s total exposure to environmental factors over a lifetime instead of during a certain time period or in one situation. This assessment could be accomplished at least partially with the development of biomarkers that indicate exposure to precipitating factors from in utero to the end of life. Research efforts that address the complexity of the exposures are most likely to show the effect of environmental factors on lung disease.

Second, more needs to be learned about the interaction between the individual and the environment to better define at-risk populations. These efforts...
should not only identify populations at high risk for disease but should also consider how modifications of environmental factors could reduce disease impact. An integrative approach will be required for these research efforts, including reliance on advancing genetic technologies, along with bioinformatics and complex biostatistical methodologies. In addition to identifying genetic factors associated with risk of exposure, this research could identify biomarkers of disease and define potential pathogenic pathways that may be targeted to reduce or treat disease.

Third, the mechanisms by which environmental toxins affect disease development need to be defined. Although it is well-established that outdoor air pollution increases the risk of cardiovascular disease and indoor air pollution due to biomass smoke increases risk of childhood infection, the molecular pathways by which these toxicants exert their effect are unknown.

Cotinine is a byproduct of nicotine and is measured in the blood or urine (in nanograms per milliliter). Its presence in nonsmokers indicates their level of tobacco smoke exposure and risk for disease caused by secondhand smoke. National Health and Nutrition Examination Survey.
Finally, to control environmental lung disease on a population basis, multidisciplinary research and public health programs are needed to translate what is learned about these toxins and molecular pathways into environmental change to help people who are at risk of respiratory disease. At present, there are too few researchers and clinicians who have an interest and ability to conduct environmental research. Thus, an important first step to move this field forward is to train more researchers. With these approaches and the development of partnerships between researchers and the public at large, the role of environmental factors in lung disease will continue to be defined and methods to prevent disease will be implemented.
CHAPTER 8  Environmentally Induced Lung Disease

References


Web sites of interest

World Health Organization
The World Health Report 2002—Reducing Risks, Promoting Healthy Life
www.who.int/whr/2002/en/

Centers for Disease Control and Prevention
2006 Surgeon General’s Report—The Health Consequences of Involuntary Exposure to Tobacco Smoke
www.cdc.gov/tobacco/data_statistics/sgr/2006/index.htm

United States Environmental Protection Agency
Learn the Issues
www.epa.gov/epahome/learn.htm

National Institute of Environmental Health Science—National Institutes of Health Environmental Health Topics: Conditions & Diseases
www.niehs.nih.gov/health/topics/index.cfm