

*Current Concepts***OCCUPATIONAL RESPIRATORY  
DISEASES**

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**M**ATERIALS inhaled in the workplace can lead to all the major chronic lung diseases except those due to vascular disease. The physician should consider the possibility of occupational exposure when a working or retired adult presents with unexplained respiratory illness. Even exposure in office buildings<sup>1</sup> and hospitals<sup>2</sup> occasionally causes illness. Identifying a workplace-related cause of disease is important because it can lead to cure and to prevention for others. Because of differences in the metabolism and susceptibility of hosts, one occupational agent may cause many diseases, just as cigarette smoke causes several distinct disorders. Conversely, one respiratory disease may have several occupational causes.<sup>3</sup> The recognition of occupational causes can be made difficult by delayed responses that occur at home after work and by years of latency between exposure in the workplace and the occurrence of disease.

The incidence of diseases caused by mineral dust has declined recently in postindustrial countries, and asthma has emerged as the principal occupational lung disease.<sup>4,5</sup> Each year, new substances are introduced into the workplace, and some are found to cause lung disease.<sup>6,7</sup>

The airways, from nares to alveoli, come into contact with 14,000 liters of air in the workplace during a 40-hour workweek. Physical activity can increase ventilation, and thus exposure to contaminants, up to 12 times the levels at rest. As ventilation increases, breathing shifts from nasal to a combination of oral and nasal, allowing a greater volume of air to bypass the cleansing nasopharynx and further increasing the exposure of the lower airways to inhaled materials (Fig. 1). Strong irritants (such as ammonia) produce an aversive response, whereas materials with little sen-

sory effect (such as asbestos) can be inhaled for prolonged periods and result in serious injury.

**PATHOPHYSIOLOGY AND PATHOGENESIS****Rhinitis and Laryngitis**

Nasal hairs and turbinates filter particles and gases (Fig. 1). The initial nasal mucosal response is vascular dilation and increased permeability, rhinorrhea, and congestion.<sup>8,9</sup> Allergens cause sneezing, itching, rhinorrhea, and congestion, whereas irritants cause burning or irritation and congestion.<sup>10</sup> Numerous substances in the workplace, from latex-coated cornstarch particles to common cleaning solutions, cause allergic and irritant upper-airway disease (Table 1).

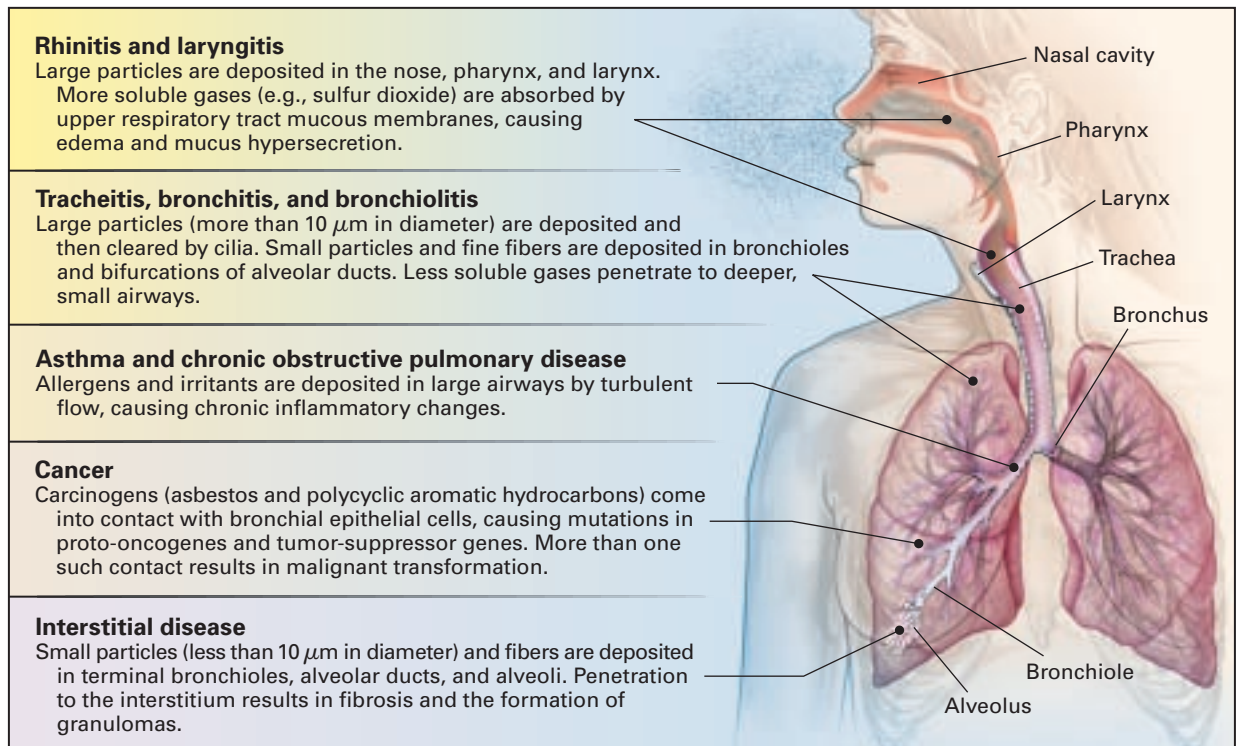
The presence of several risk factors, both occupational and nonoccupational, can contribute to the development of disease. In the general population, an increased risk of rhinosinusitis is associated with a family history and previous allergic disease. Occupational rhinitis is distinguished from perennial and seasonal rhinitis by an improvement in symptoms when the person is away from work. Some people have enhanced responses to environmental tobacco smoke and other substances.<sup>12</sup> Nonirritant rhinorrhea occurs with cold air, exposure to cholinergic substances, or exposure to cholinesterase-inhibiting substances. Allergic occupational rhinitis often precedes occupational asthma. Chromic acid and other substances produce nasal ulceration and perforation of the septum (Table 1), whereas nickel and certain wood dusts cause nasal carcinoma.<sup>13,14</sup>

The larynx, which has the smallest cross-sectional area in the respiratory tract, forms a narrow in the airstream where air velocity increases, eddies form, and particulate matter is deposited. Inflammation and edema of the vocal cords result from irritants and allergens or from the drainage of inflammatory mediators from nasal passages. The inadvertent mixing of bleach (hypochlorous acid) with common institutional detergent solutions that contain phosphoric acid generates chlorine gas, a potent irritant. The mixing of detergents with ammonia generates monochloramine and dichloramine, which are also potent irritants.<sup>11,15</sup> Such exposures have also been associated with vocal-cord dysfunction, which is a narrowing of the vocal-cord aperture during inspiration that produces asthma-like symptoms.<sup>16</sup>

**Tracheitis, Bronchitis, and Bronchiolitis**

Soluble gases are absorbed by the upper-airway mucosa, whereas less soluble gases penetrate to the alveoli. The location of particle deposition in the airways is determined by the concentration and size of

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**Figure 1.** Occupational Respiratory Diseases.

Shown are categories of occupational respiratory disease, their anatomical locations within the respiratory system, examples of common causative substances, and their pathophysiologic effects.

the particles. Particles that are 10  $\mu\text{m}$  or more in diameter are deposited in the nose and pharynx, whereas particles that are 5  $\mu\text{m}$  in diameter or smaller may penetrate to the alveoli. Particles of intermediate size are deposited in differing proportions at intervening levels (Fig. 1).

Acute bronchitis results from mucosal inflammation after exposure. The condition is treated with inhaled corticosteroids (e.g., taken as two puffs of beclomethasone four times a day, with each puff delivering 50  $\mu\text{g}$ ) until it subsides. Asthma may be a sequela after bronchitis has resolved.<sup>17</sup> Chronic irritation can lead to hyperplasia and hypersecretion of the mucous glands. A cough with mucus production on most days for three months per year over two consecutive years is diagnostic of chronic bronchitis and correlates with histologically confirmed mucous hyperplasia.<sup>18</sup> Many occupational substances produce industrial bronchitis, just as cigarette smoke causes smoker's bronchitis.<sup>19</sup> Bronchitis is found in persons whose occupation involves exposure to dust or who work in chemical and food processing, mining, storage and processing of grains and feeds, cotton-textile milling, and welding.<sup>20-22</sup> The degree of exposure can be reduced by the substitution of materials, wetting of the dust, better ventilation of the workstation, or the use of mask

respirators that filter particles or chemicals.<sup>23</sup> Bronchitis can often be reversed by reducing the amount of exposure. Chronic bronchitis is treated with inhaled ipratropium bromide taken as two puffs every four to six hours, with each puff delivering 18  $\mu\text{g}$ .

Bronchiolitis obliterans — the narrowing and filling of bronchioles — was first described in soldiers who had been exposed to chlorine and phosgene gases, and it was later described in survivors of accidental workplace gassings with chlorine and in workers exposed to nitrogen dioxide generated by freshly stored hay (silo filler's disease). It is manifested by dyspnea, chest tightness, and irreversible airflow obstruction, with onset several hours to days after a heavy exposure to irritant gas (Table 2).<sup>24</sup> Bronchiolitis obliterans may present with radiographic infiltrates or may be clinically confused with asthma, which presents similarly with wheezing and a clear chest x-ray film but which responds to bronchodilators. High-resolution computed tomography may show a patchy interstitial pattern. Early therapy with systemic corticosteroids may reduce long-term morbidity.

#### Asthma

More than 250 substances found in the workplace cause occupational asthma (Table 2). Work-related

**TABLE 1. SELECTED COMMON CAUSES OF OCCUPATIONAL UPPER RESPIRATORY TRACT DISEASE.\***

**Rhinitis and laryngitis†**

- Allergic sensitizers<sup>8</sup>
  - Dust from flour used in baking (wheat, rye, soy, and buck-wheat flour and gluten and amylase), which can also contain mites and fungi
  - Dusts from animal feeds and grains
  - Ethylenediamine in adhesives
  - Latex on cornstarch granules from latex gloves
  - Pollens and mold spores (found in plants and on moist, dark surfaces)
  - Proteins from laboratory animals (such as guinea pigs and rats)
  - Acid anhydrides (used in adhesives and coatings with epoxy resin, circuit boards, and plasticizers)
  - Psyllium (a pharmaceutical stool-bulking agent)
- Irritants
  - Acidic or alkaline cleaning solutions and powders<sup>11</sup>
  - Ammonia
  - Environmental tobacco smoke<sup>12</sup>
  - Hypochlorous acid (bleach)<sup>11</sup>
  - Metalworking fluids (cutting oils)
  - Ozone (in aluminum welding)
  - Sulfur dioxide
  - Volatile organic compounds (in paints, thinners, solvents, and industrial cleaning solutions)

**Rhinorrhea**

- Cold air
- Certain pesticides (carbaryl, malathion, parathion, mevinphos, pyrethrum)

**Nasal ulceration and perforation of the septum**

- Arsenic
- Chromic acid and chromates
- Copper dusts and mists

\*Causes of upper respiratory tract disease are discussed in Bascom and Shusterman.<sup>10</sup>

†Many substances that cause allergic rhinitis may also cause asthma.

asthma can be an exacerbation of asthma that was previously subclinical or in remission (work-aggravated asthma), a new onset of asthma caused by a sensitizing exposure (asthma with latency), or asthma that results from a single heavy exposure to a potent respiratory irritant (asthma without latency, irritant asthma, or the reactive airways dysfunction syndrome).<sup>29</sup> Five to 15 percent of new cases of asthma in working adults are caused by occupational exposure.

Work-aggravated asthma is caused by mechanical irritation of the airways from nonallergenic dust and by chemical irritation. In asthma with latency, high-molecular-weight biologic proteins (e.g., particles from wood products, textiles, grains, crustaceans, or latex that are of 5000 daltons or more) stimulate the production of specific IgE. A later reexposure triggers the release of cytokines, whose effector cells participate in an inflammatory response. Persons who have a history of atopy or who smoke are at greater risk than others for asthma that develops in response to high-molecular-weight antigens. Low-molecular-

**TABLE 2. SELECTED COMMON CAUSES OF OCCUPATIONAL AIRWAY DISEASE.\***

**Bronchitis**

- Sulfur dioxide (used in chemical manufacturing)
- Rock and mineral dusts (used in road construction and digging of foundations)
- Cement dust
- Smoke from welding or cutting with acetylene torch

**Bronchiolitis**

- Acetaldehyde
- Ammonia (used in farm-crop preservation)
- Chlorine gas
- Hydrogen fluoride
- Hydrogen sulfide (used in oil refining)
- Nitrogen dioxide (generated by freshly stored hay in silos), nitric acid, nitrous acid, and nitric oxide
- Phosgene (used in chemical manufacturing)

**Asthma**

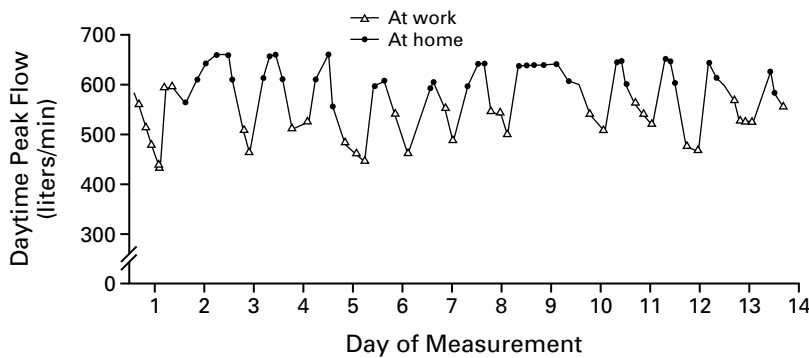
- Asthma with latency
  - Acid anhydrides (used in epoxy adhesives and paints, coatings, circuit boards, polymers, polyesters, and plasticizers)
  - Aldehydes
  - Acrylates (used in paints and adhesives)
  - Animal proteins (in laboratory animals, farming, and veterinary medicine)
  - Cobalt (used in carbide-tipped tools)
  - Dusts from flours and grains (found in bakeries)
  - Dusts from wood (used in furniture making and cabinetry)
  - Ethylenediamine, monoethanolamine, and other amines
  - Formaldehyde and glutaraldehyde (used in sterilizing medical instruments)
  - Isocyanates (hexamethylene diisocyanate, diphenylmethane diisocyanate, and toluene diisocyanate) used in polyurethane paint (used in auto-body repair) and the manufacture and application of foam (used in roofing foams)
  - Latex (used in health care facilities)
- Asthma without latency (irritants that cause the reactive airway dysfunction syndrome)
  - Contaminants in metalworking fluids
  - Chlorine gas (pulp from paper mills)
  - Bleach (sodium hypochlorite)
  - Strong acids

**Chronic obstructive pulmonary disease and chronic airflow limitation**

- Coal dust (causes emphysema with nodular fibrosis)
- Crystalline silica (causes chronic airflow limitation)
- Cotton dust (causes chronic airflow limitation)
- Cadmium (causes emphysema) (used in electronics, metal plating, and batteries)
- Toluene diisocyanate (causes chronic airflow obstruction)

\*Causes of bronchitis are discussed in Morgan<sup>19</sup> and Fishwick et al.,<sup>20</sup> causes of bronchiolitis in Wright,<sup>24</sup> causes of asthma in Chan-Yeung and Malo,<sup>25</sup> and causes of chronic obstructive pulmonary disease and chronic airflow limitation in Hendrick,<sup>26</sup> Christiani et al.,<sup>27</sup> and Davison et al.<sup>28</sup>

weight substances (less than 5000 daltons) can cause sensitization without producing specific IgE. Among these substances, the isocyanates, which are used widely in polyurethane foams and paints, are a frequently recognized cause of asthma. Exposed French workers in whom the disease developed were more likely to be positive for HLA-DQB1\*0503 and the allelic combination HLA-DQB1\*0201/0301, whereas HLA-



**Figure 2.** Rates of Peak Expiratory Flow in a 42-Year-Old Man with Asthma and Work-Related Symptoms. The patient used a portable peak expiratory flowmeter and a daily calendar. The early-morning peak flows showed the diurnal morning dip usually seen with asthma. The peak flow values were consistently lower when the patient was at work than when he was at home, a finding that confirmed that the asthma was related to work.

DQB1\*0501 and the HLA-DQA1\*0101, DQB1\*0501, DRI haplotype appeared to be in part protective.<sup>30</sup>

Because some patients continue to have asthma for years after the discontinuation of exposure, therapy emphasizes prevention, early diagnosis, and removal of the substance responsible for the exposure. For most patients, the best therapeutic intervention is to eliminate exposure. The treating physician must ultimately address this issue, because prolonging exposure can worsen bronchial hyperreactivity, symptoms, lung function, and prognosis. If the diagnosis of asthma is in question, nonspecific testing of bronchial responsiveness (e.g., the methacholine challenge) can establish the presence or absence of airway hyperresponsiveness, which is almost always present in asthma.

A history of onset after a new workplace exposure, or of preexisting asthma made worse in a new work environment, indicates that the asthma may be work related. Checking whether the substance in question is on published lists of the known causes of asthma can be helpful.<sup>25</sup> The measurement of specific IgE, by epicutaneous (skin-prick) testing or a radioallergen sorbent test, is now possible for a growing list of known causes of asthma. A positive test confirms systemic sensitization but does not demonstrate sensitization of the respiratory tract. Airflow obstruction that is temporally related to exposure in the workplace can be identified by having the patient record peak expiratory flows both at work and away from work (Fig. 2).<sup>31,32</sup> Diagnostic criteria that follow a physiologically based approach are now available.<sup>33</sup> Airflow obstruction is treated with inhaled beta-agonists for acute symptoms (e.g., taken as two puffs of albuterol sulfate every four to six hours, with each puff delivering 120  $\mu$ g) and with inhaled corticosteroids and other drugs as needed to pre-

vent chronic symptoms. Removal of the substance to which the patient has been exposed usually brings some improvement.<sup>34</sup>

#### Chronic Obstructive Pulmonary Disease or Chronic Airflow Limitation

Cigarette smoking remains the predominant cause of chronic obstructive pulmonary disease, but many occupational dusts can cause or contribute to chronic airflow limitation or emphysema (Table 2).<sup>26,35</sup> When chronic airflow limitation is caused by silica or beryllium dust,<sup>36</sup> there may be accompanying radiographic evidence of pneumoconiosis. With most other substances that cause chronic obstructive pulmonary disease (Table 2) there can be airflow obstruction with a clear chest film. With many substances (including coal and silica dust), the disease may progress for decades after the exposure has ceased.<sup>37</sup> Cadmium causes emphysema after prolonged exposure at levels lower than those for other mineral dusts.<sup>28</sup> Cotton dust, a complex mixture that contains bacterial endotoxin, can cause chronic bronchitis,<sup>38</sup> occupational asthma,<sup>39</sup> inhalation fever, and chronic airflow limitation.<sup>27</sup>

#### Lung Cancer

At least 12 substances found in the workplace are classified as human lung carcinogens (Table 3).<sup>40</sup> Occupational exposure is estimated to account for approximately 5 percent of lung cancers in the United States.<sup>41</sup> The majority of these cancers are caused by asbestos, followed by radon, silica, chromium, cadmium, nickel, arsenic, and beryllium.<sup>42</sup> Cigarette smoke and asbestos interact strongly in causing bronchogenic carcinomas, and the risk of carcinoma is greater in persons with the interstitial fibrosis of asbestosis.<sup>43</sup> Many asbestos-related lung cancers occur in

**TABLE 3. SELECTED CAUSES OF OCCUPATIONAL LUNG CANCER.\***

Asbestos (used in boiler and pipe insulation)
Arsenic compounds (formerly used in pesticide sprays for orchards)
Bis(chloromethyl)ether and chloromethyl methyl ether (used in the manufacture of ion-exchange resins, bactericides, pesticides, water repellents, and flame repellents)
Cadmium and cadmium compounds
Chromium and certain (hexavalent) chromium compounds (used in alloys and metal plating)
Crystalline silica (produced by stone cutting, drilling, and tunneling)
Mustard gas
Nickel in nickel refining
Radon progeny (products of decay) and ionizing radiation
Soots, tars, and mineral oils (polycyclic aromatic hydrocarbons)

\*Causes of occupational lung cancer are discussed in the National Toxicology Program Report on Carcinogens.<sup>40</sup>

pipe insulators, building-construction workers, shipyard workers, and others with a history of prolonged, heavy exposure before the current workplace controls were instituted. Establishing a history of exposure that began more than 10 years before diagnosis and identifying indicators of the severity of the exposure (such as pleural plaques or a large number of asbestos bodies or uncoated asbestos fibers in resected lung tissue) are helpful in determining the cause of cancer.

Homozygous deletion of the glutathione S-transferase M1 (*GSTM1*) gene, or an *N*-acetyltransferase 2 (*NAT2*) slow acetylator genotype, may confer additional risk of lung cancer among persons exposed to asbestos.<sup>44</sup> Diffuse malignant mesothelioma of the pleura, peritoneum, and pericardium is also caused by asbestos, but the risk is not affected by smoking. The epidemic of asbestos-related lung cancers among persons heavily exposed through the 1970s is estimated to have peaked in the early 1990s at 1200 cases per year in the United States<sup>45</sup> and is expected to peak in the United Kingdom by 2010.<sup>46</sup> Reductions in the amount of exposure to these substances in the past 25 years, along with the beneficial effect of previous reductions in cigarette smoking, will contribute to the eventual decline in the incidence of lung cancer in these countries, whereas the frequency of the disease is expected to increase in countries with increasing occupational exposure and increasing prevalence of smoking.

**Interstitial Lung Disease**

Most inhaled dust is filtered out by the upper airways or cleared by the ciliated epithelium of large airways. If these defenses are overwhelmed by fine dust (less than 10 μm in diameter), however, the lung reacts with an alveolar and interstitial inflammation that may culminate in disease (Table 4).

**TABLE 4. SELECTED COMMON CAUSES OF OCCUPATIONAL INTERSTITIAL DISEASE.**

<b>Pulmonary fibrosis</b>
Asbestos
Crystalline silica (produced by stone cutting, drilling, and tunneling)
Kaolin (a clay used in china, ceramics, and pharmaceuticals)
Talc (magnesium silicate, which is used in the paint, ceramics, leather, fabric, and paper industries)
Tungsten carbide with cobalt (a hard metal used in carbide-tipped tools)
<b>Alveolar proteinosis</b>
Fine crystalline silica dust (found in silica flour and produced by sandblasting)
<b>Lipoid pneumonia</b>
Oily metalworking fluids (used in machining shops) <sup>47</sup>
<b>Hypersensitivity pneumonitis</b>
Amebae
Animal proteins (from pigeon, chicken, turkey, duck, and rat)
Fungi (e.g., <i>Aureobasidium pullulans</i> )
Metalworking fluid aerosols (used in metal-parts machining shops)
Thermophilic bacteria (e.g., thermoactinomyces, <i>Saccharopolyspora rectivirgula</i> )
Other bacteria ( <i>Bacillus subtilis</i> , <i>B. cereus</i> , and <i>Pseudomonas fluorescens</i> )
Toluene diisocyanate, diphenylmethane diisocyanate, and hexamethylene diisocyanate (in polyurethane paints, adhesives, and foam production)
Trimellitic anhydride and phthalic anhydride (in epoxy resins, coatings, and paints)
<b>Granulomatous disease</b>
Beryllium (used in the aerospace industry and in beryllium copper alloy machining)
<b>Inhalation fever</b>
Amebae, mixed bacteria, and fungi (endotoxin and beta glucans) from humidifiers and other sources of water aerosols <sup>48</sup>
Cotton dust
Freshly generated zinc oxide fumes (from vaporized, galvanized metal) <sup>49</sup>
Heated fluorocarbon monomers and polymers (e.g., polytetrafluoroethylene [Teflon])

**Fibrotic Disease**

In the 25 years from 1968 through 1992, a total of 100,890 death certificates in the United States listed pneumoconiosis (dust-associated disease of the lungs) as a contributing or primary cause of death. The majority of these cases were coal worker's pneumoconiosis, silicosis, and asbestosis.<sup>4</sup> The rate of death from pneumoconiosis is declining, but silicosis remains prevalent in many regions and industries and has recently been recognized as a disease of construction workers who perform surface-rock drilling and cutting. Dusts such as coal, cobalt, talc, and kaolin,<sup>47</sup> which are encountered less frequently in industry than silica, are important causes of new cases of disease.

The number of deaths from asbestosis has increased over the past 20 years but appears to have plateaued. Benign pleural disease is often the only manifestation of exposure to asbestos. Asbestosis usually has an indolent course and may be present subclinically for many years before becoming symptomatic in late middle age, with dyspnea, inspiratory crackles, and

bilateral basilar interstitial densities. A diagnosis is based on the history of exposure, chest examination and film, and pulmonary-function tests. Because there is no effective therapy, open or thoracoscopic lung biopsy is reserved for patients in whom a treatable disease such as pulmonary vasculitis (often accompanied by evidence of systemic inflammation) is part of the differential diagnosis or for patients with advanced disease who are being evaluated for lung transplantation.

Diffuse alveolar-filling disease (presenting as dyspnea with interstitial abnormalities on the chest x-ray film) due to the overproduction of surfactant by type II alveolar pneumocytes may be caused by intense exposure to fine silica dust, and it has been reported after several other types of occupational exposure to dust. Lipoid, alveolar-filling pneumonia can be caused by the inhalation of fine oil mist.<sup>50</sup>

#### **Granulomatous Disease**

Hypersensitivity pneumonitis, an acute febrile pneumonitis with peripheral leukocytosis, is caused by immunologic reaction to a variety of inhaled substances. It may have acute, subacute, and chronic forms, depending on the degree of exposure, the duration of exposure, and the susceptibility of the patient. A growing list of workplace substances have been identified as capable of causing this response<sup>51</sup> (Table 4). Cigarette smoking and intense exposure predispose workers to sensitization to some substances.<sup>52</sup> An acute episode often has its onset late in the day or in the evening after exposure in the workplace. Recurrent episodes become more severe as sensitization increases. Early episodes resolve spontaneously, and corticosteroids (60 mg of prednisone taken orally every day or the equivalent, tapered over a period of 10 days) may hasten their resolution, but if episodes are allowed to recur repeatedly, permanent damage caused by interstitial fibrosis may result.

Clinically and pathologically similar to sarcoidosis, beryllium disease can be diagnosed on the basis of a history of exposure, the finding of noncaseating granulomas in lung tissue, and T-lymphocyte sensitization to beryllium in peripheral blood or fluid from bronchoalveolar lavage.<sup>53</sup> Systemic corticosteroids are beneficial for relieving acute symptoms, but their long-term efficacy is uncertain.

#### **Inhalation Fever**

Inhalation fever is characterized by self-limiting fever after a single exposure, with peripheral leukocytosis but minimal or no lung inflammation (Table 4). Cytokines from resident lung cells cause demargination of pulmonary vascular leukocytes, and prostanooids that are produced by these cells act at the hypothalamus to produce the febrile episode, which usually begins up to 6 hours after exposure and lasts less than 12 hours.<sup>49</sup> The typical history of exposure

involves indoor work in the winter in which an organism-contaminated water-spray system is used to humidify air (humidifier fever)<sup>48,54</sup>; disturbing an accumulation of moldy hay, grass, compost, mulch, or wood chips; or heating zinc to the point of vaporization (e.g., in welding galvanized steel). Inhaled combustion products of polytetrafluoroethylene (Teflon) may cause fever and hemorrhagic pneumonitis.<sup>55</sup>

#### **DIAGNOSIS, DETERMINATION OF CAUSE, AND TREATMENT**

Most occupational respiratory illnesses can be diagnosed on the basis of the history,<sup>56</sup> physical examination, chest x-ray film, and pulmonary-function tests. An effective approach is first to determine the diagnosis and then to use the occupational history to identify possible causes (Tables 1, 2, 3, and 4). Higher-risk workplaces are those with obvious dust, smoke, or vapor or those in which there is spraying, painting, or drying of coated surfaces. Heavier exposure occurs when there is friction, grinding, heat, or blasting, when very small particles are generated, and in enclosed spaces. The association of the illness with work is suggested by a history of symptomatic improvement on weekends or vacations, followed by increased symptoms on return to work; it can also be suggested by the onset of disease after a new job is started or after a new material is introduced at the workplace. Asthmatic responses may be immediate (occurring within 2 hours after exposure), delayed (4 to 12 hours after exposure), or both, but after asthma is established, the symptoms may be constant. Episodes with increasing severity of symptoms are suggestive of immunologic sensitization.

The patient's history can be supplemented by Material Safety Data Sheets (from the employer or poison-control centers), which list the chemical components of commercial materials. The results of previous measurements of air from the patient's work area may be obtained,<sup>57</sup> or the physician may advise the employer to consult a certified industrial hygienist for air measurements and remediation.<sup>58</sup> Referral to an occupational-medicine specialist may be helpful for patients whose illness requires detailed investigation.

Employers often wonder why disease develops in only one of many similarly exposed persons. Polymorphisms in genes produce variation in the rate and pathway of metabolism, which results in marked differences in susceptibility to occupational substances among workers, just as polymorphisms affect responses to some medications. Interactions among occupational exposure, atopic predisposition, nutrition,<sup>59</sup> home or avocational exposure, and host factors (such as gastroesophageal reflux, cigarette smoking, and viral infections) are common, and they help to explain the occurrence of disease in certain persons. A lifetime occupational history is essential for the recog-

dition of some exposures, because 10 or more years pass from the initial exposure until the first manifestations of asbestosis, silicosis, disease from coal dust, lung disease from beryllium, and other illnesses. Immigrants may have had heavy exposure while working in unregulated industry in developing countries.

Treatment is usually identical to treatment for non-occupational forms of the illness. With the patient's permission, the employer should be notified of the hazard in order to prevent further occurrences, to initiate compensation, and to allow recording of the illness in logs, an action that is required by the Occupational Safety and Health Administration. If an ongoing hazard is suspected, health departments, the Occupational Safety and Health Administration, and the National Institute for Occupational Safety and Health can be invited by the employer, employee, or physician to conduct an investigation. Physicians are required by public-health law in 23 states to report certain specific illnesses or all occupational lung diseases to the state health department.<sup>60</sup>

Management of the disease includes either a change in the work practices that led to the disease or restrictions regarding what the patient can and cannot do. These measures can be discussed with both the patient and the employer in order to prevent future harmful exposures. Reasonable accommodation to allow a patient with a disability to keep working is now encouraged by the Americans with Disabilities Act. A work-related illness often threatens the patient's livelihood and health, and physicians can be instrumental in providing medical guidance for a transfer within the same workplace or, if necessary, job retraining through services provided by the government or the insurance company.

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