Occupational toxic inhalations

Douglas Henry Linz, MD
Assistant Professor of Medicine
Department of Internal Medicine

Alan F. Barker, MD
Associate Professor of Medicine
Department of Internal Medicine

William E. Morton, MD, DPH
Professor of Environmental Medicine
Environmental Medicine Division

Patricia L. deGarmo, ANP
Adult Nurse Practitioner
Ambulatory Care Nursing
School of Nursing
Oregon Health Sciences University
Portland, Oregon

THOUSANDS OF POTENTIALLY toxic agents are in daily industrial use. Recognition of occupational disease in the emergency department is made easier when affected persons are transported directly from the work site, having had an acute unprotected exposure to a known injurious substance in an industrial accident and when symptoms and signs differ from those associated with other common nonoccupational diseases. If there is a lag period between exposure and clinical illness, if potential toxins are unknown or multiple, or if the resultant illness mimics common diseases, recognition and appropriate management of acute toxic inhalations may be delayed.

Efficient diagnosis and treatment of occupational toxic inhalations will be facilitated if emergency department personnel maintain a high index of suspicion for the possibility of work-related inhalation injuries, familiarize themselves with the industrial processes and toxic substances used in local industries, maintain an adequate reference library, and obtain occupational histories from patients. Ideally, emergency department staff should make site visits to neighboring industries accompanied by an occupational hygienist. A list of toxic substances can then be compiled.

Standard reference books[1-9] are available in soft-cover editions.[3,4,9] Selected offprints from the medical literature that address the diagnosis and management of inhalation injuries caused by toxic agents used locally should be obtained and stored in a reference file that is easily accessible within the emergency department. Thus, emergency staff need not become experts in occupational medicine or industrial toxicology; they need only educate themselves about those injuries likely to occur in the local area.

The complete occupational history is too cumbersome and time-consuming for use as a screening instrument in emergency evaluations. Key elements of the occupational history for emergency care providers include:

- current job title and specific work activities;
- known exposures to fumes, dusts, aerosols, and mists;
- the temporal relationship of the chief complaint to work activities;
- similar problems in coworkers;
- protective equipment used;
- work site ventilation;
- nonwork-related environmental exposures; and
- hobbies and habits, especially tobacco smoking and use of alcohol and other recreational drugs.

PHYSIOLOGY

Airborne hazardous agents are deposited at various levels of the respiratory tract as a function of particle size and density, the velocity of airflow, and the amount of airway turbulence. Once deposited, substances are subject to the influence of the following pulmonary defense mechanisms:

- mechanical filtration by nasal cilia;
- sneezing and coughing as a result of smooth muscle contraction triggered by stimulation of irritant receptors;
- the buffering and barrier function of respiratory mucous as well as its ability to rapidly clear suspended particles via mucociliary escalator;
- the phagocytic function of alveolar macrophages; and
- activation of both humoral and cellular immune mechanisms.[10-12]

Toxic manifestations are a function of the inherent chemical reactivity of the hazardous substance, its concentration in inspired air, and the intensity and duration of exposure balanced against the functional state of the pulmonary defenses. Inhalation of highly irritating substances causes prominent eye irritation, rhinitis, sneezing, and coughing. It may result in little serious pathology, however, because the exposed person has ample warning and evacuates the site. Substances of small molecular size, which are less irritating even at high concentrations, may pose a serious and unsuspected health risk. Inhaled doses may be high, with deposition characteristics that favor systemic absorption. Agents that concomitantly cause dysfunction of one or more pulmonary defense mechanisms present additional toxic potential.

ACUTE PULMONARY TOXICITY

A patient who has had occupational toxic inhalation often presents with evidence of acute respiratory dysfunction as the sole or a predominant manifestation of poisoning. The respiratory tract, including the upper airway, tracheobronchial tree, and pulmonary parenchyma, has a relatively limited repertoire of reactions to toxic insult. As a result, a number of agents produce the same or similar reactions.

Respiratory reactions to inhaled toxins are a function of the deposition site. Toxicity to the upper airway is most often manifested as acute inflammation with edema; in severe reactions, mucosal sloughing and upper airway obstruc-

tion may ensue. Acute or delayed bronchospasm may follow stimulation of mucosal irritant receptors or initiation of immunologic hypersensitivity reactions. Acute alveolar injury usually causes accumulation of exudative fluid within the alveoli and is clinically evident by acute or delayed pulmonary edema. Although more than one of these respiratory reactions may occur simultaneously, in the majority of cases a single clinical response will predominate.

IMMUNOLOGIC REACTIONS

Hypersensitivity pneumonia

Hypersensitivity pneumonia[13] is an example of immunologic pulmonary disease caused by repeated exposure to any one of a number of inhaled antigens including various thermophilic bacteria, fungal and bacterial products, animal proteins, and a few organic chemicals (boxed material, Occupations Associated With Hypersensitivity Pneumonitis).

A large number of workers involved in a variety of occupations are at risk for the development of hypersensitivity pneumonia. In many cases, as in patients with farmers's lung, the association of the acute illness with the occupation is relatively easy to determine. Symptoms begin within hours of work with compost containing thermophilic *Actinomyces*. In contrast, ventilation pneumonitis often requires rather specific questioning with regard to the work place exposure, and a large number of potential antigens have been implicated in its etiology. Patients who have this disorder generally are involved in a variety of "clean" occupations such as office work. Symptoms are likely to be attributed to recurrent respiratory infection. The fact that coworkers have similar illnesses may be seen as corroborating evidence of infectious etiology.

Byssinosis[14] in its acute form closely mimics hypersensitivity pneumonia in regard to symptoms and clinical findings. The most susceptible cotton workers are those who handle the raw cotton in preparation areas. A number of etiologic agents may be responsible, including cotton dust itself and products of bacterial or fungal contamination. Like workers in some other industries (boxed material, Occupations Associated With Occupational Asthma) cotton handlers may develop a syndrome of occupational asthma rather than hypersensitivity pneumonia.

Clinically, hypersensitivity pneumonia occurs in both acute and chronic forms, but acute reactions are more common and more likely to precipitate a visit to the emergency department. Acute hypersensitivity pneumonia is often mistaken for infectious bronchitis or pneumonitis.

Occupations Associated With Hypersensitivity Pneumonitis

Farming	Bird breeding
Mushroom farming	Malt working
Woodworking	Laboratory rat technicians
Cotton handling	Chemical manufacturing
Cheese processing	Sugar cane processing

Occupations Associated With Occupational Asthma

Detergent manufacturing	Platinum, nickel, chromium plating
Animal handling	Chemical manufacturing
Baking	Antibiotic manufacturing
Woodworking	Cheese processing
Plastic working	Hairdressing
Industrial painting	Beer brewing
Tobacco handling	Coffee and tea growing
Meat wrapping	Cobalt refining or alloy manufacturing

Although patients may appear to respond to antibiotic treatment, symptoms will improve without treatment within a predictable time following the last exposure. Symptoms, which begin four to six hours following the last exposure, include cough, dyspnea, and fever as high as 104° F with chills, malaise, and myalgias. On physical examination, patients appear to be acutely ill with fever, nonproductive cough, and tachypnea; basilar rales may be present but are not a necessary finding. Laboratory evaluation shows leukocytosis with an increased percentage of premature neutrophils. Chest roentgenograms may be normal or may show patchy reticulonodular infiltrates. Bedside spirometric examination and arterial blood gas determinations show variable reductions in forced vital capacity, 1-second forced expiratory volume, and arterial oxygen tension.

Treatment involves excluding other potential etiologies and giving respiratory supportive care that may include bronchodilators, oxygen supplementation, and glucocorticoids. Long-term care involves avoidance of the offending agent or use of effective respiratory protective equipment.

Occupational asthma

Workers in varied occupations who are exposed to animal, vegetable, and chemical agents are at risk for development of occupational asthma (boxed material).[1] Diagnosis of occupational asthma in the emergency department is important because there are implications for the prevention of further exposure, the necessity of frequent return visits, and the future employment of affected persons. Respiratory protection at work is mandatory, and a change in occupation may be necessary.

In view of the large number of at-risk occupations, an occupational history is a necessary part of the emergency department evaluation in all patients with adult-onset asthma or severe exacerbations of underlying asthma. Questions concerning hobbies and home exposure may also yield information implicating other potential antigens such as dust, mold, animal dander, and wood dust.

Diisocyanate-associated asthma is a recently recognized example of occupational asthma. Diisocyanates enjoy widespread industrial use; an estimated 100,000 workers are exposed in occupations including polyurethane manufacturing and some paint and linoleum applications.[15] Of the chemical forms of diisocyanates, toluene diisocyanate has been most carefully studied. It is estimated that 5% of exposed workers develop occupational asthma. Differences in work place exposure and individual responsivity account for a spectrum of pulmonary toxic effects.[16] Short-term exposure in high concentration causes a constellation of upper airway irritative symptoms. Susceptible persons may develop occupational asthma. Long-term low-level exposures have been associated with deterioration in pulmonary function. Rarely, persons who have short-term exposure develop a syndrome of hypersensitivity pneumonitis with pronounced systemic symptoms and alveolitis.

As with hypersensitivity pneumonia, suspicion of an occupational etiology for an acute asthmatic attack is warranted when there is a short time between the onset of the attack and the last work place exposure. At least three patterns are recognized[1]:

1. an immediate asthmatic reaction, with onset of symptoms occurring 15 to 30 minutes after exposure;
2. a delayed asthmatic reaction beginning four to six hours after exposure and lasting 24 to 36 hours; and
3. a dual or combination asthmatic reaction pattern consisting of an early asthmatic response followed by improvement and exacerbation several hours after exposure.

Diagnostic procedures useful in establishing the diagnosis of asthma include evidence of a

reversible obstructive defect on spirometric testing and demonstration of heightened airway sensitivity to inhalation of a nonspecific pulmonary antagonist such as methacholine. Inhalation challenge testing may be required to establish a clear-cut causative relationship between occupational exposure and the asthmatic response. In such testing, persons undergo serial spirometric evaluation following exposure to a suspect antigen or a mixture of antigens. Treatment of occupational asthma includes oxygen supplementation and administration of bronchodilators, immunosuppressive doses of steroids, and intravenous (IV) hydration.

RESPIRATORY IRRITANTS

A number of chemically dissimilar substances have a common pattern of respiratory injury. In this group are a number of gases, including ammonia; chlorine; phosgene; hydrogen chloride; fluorine and hydrogen fluoride; bromine and hydrogen bromide; various oxides of nitrogen; ozone; sulfur dioxide; and ethylene oxide. In addition, a variety of metallic dusts and metallo-organic compounds cause respiratory irritation as a primary manifestation of acute industrial poisoning. In Table 1, potential industrial sources of the gases are listed; Table 2 identifies some sources of metal fume and dust exposure.

The mechanisms of respiratory toxicity for these agents are based on direct cellular injury. Some of the substances are strong oxidizing or reducing agents, others cause profound local acid-base disturbances, and still others damage tissues through unknown mechanisms. Several factors are important in determining the extent and location of respiratory pathology induced by these substances. Those materials with a distinctive color or odor or those that incite an irritant response at low concentration are likely to provide sufficient warning to exposed per-

Table 1. Industrial sources of respiratory irritants

Respiratory irritant	Industrial use
Ammonia	Fertilizer manufacturing; production of some chemicals, plastics, dyes, and explosives; industrial cleaning
Hydrogen chloride	Certain pharmaceutic, fertilizer, dye, and paint manufacturing; chlorinating rubber; electroplating
Hydrogen fluoride	Etching glass; cleaning metals; manufacturing some plastics and insecticides
Chlorine	Pulp, paper, and textile bleaching; solvent chlorinating; manufacturing certain plastics, resins, cosmetics, refrigerants, and pharmaceutics; sterilizing; deodorizing; sewage treating
Fluorine	Petroleum, ceramics, and uranium processing; production of fluorinated chemicals
Fluorides	Metal smelting; water fluoridation; certain pesticide production
Sulfur dioxide	Bleaching; fumigation; refrigeration, paper manufacturing, petroleum refining, smelting of sulfide ores; synthesis of sodium sulfide and sulfuric acid
Ethylene oxide	Hospital supply and grain sterilizing; chemical synthesis; polyester manufacturing
Hydrogen bromide	Bromide manufacturing; catalyst and reducing agent in chemical synthesis
Phosgene	Fire fighting; carbon dioxide welding; working with heated chlorinated solvents
Ozone	Formation from electrical sources; oxidizing; bleaching; disinfecting; aging liquor and wood; treating industrial wastes
Oxides of nitrogen	Oxyacetylene welding; glassblowing; nitric acid and fertilizer manufacturing, farming; fire fighting

Table 2. Industrial source of exposure to metal fumes and dusts

Metal Fume	Source
Zinc oxide	Galvanizing; electroplating; welding galvanized metals
Zinc chloride	Wood preserving; dye, deodorant, parchment paper, dental cement manufacturing; textile production; welding
Vanadium	Alloy manufacturing; catalyst in chemical manufacturing
Phosphine	Acetylene manufacturing; metal shaving and refining; fire fighting; pest control; welding
Pentachloride, trichloride, and oxychloride phosphorous	Farming; chemical manufacturing; manufacturing of dyes; gasoline additives
Nickel	Chemical manufacturing; welding; magnet and stainless steel manufacturing
Nickel carbonyl	Gas plating; nickel refining
Chromium	Chrome plating; ferrochrome and stainless steel manufacturing
Cadmium	Welding
Beryllium	Electronics; guidance system, navigation system, rocket part manufacturing; nuclear reactor production

sons to allow escape prior to the development of overwhelming acute toxicity.

Irritant gases

The highly water-soluble gases—ammonia, hydrogen chloride, and hydrogen fluoride—have a tendency to cause early upper airway irritation because they react with mucous membranes. Most of an inhaled dose is delivered to the upper airway. In contrast, chemical pneumonia and noncardiogenic pulmonary edema are more likely to develop with intense exposure to gaseous substances that induce little upper airway irritation. Exposure to gases with low water solubility—phosgene, ozone, and the oxides of nitrogen—commonly cause chemical pneumonitis because a greater fraction of the inhaled dose is delivered to the alveoli. This disorder may also occur, however, with profound exposure to highly noxious agents.

Clinically, persons exposed to water-soluble gases present with symptoms ranging from mild mucous membrane irritation, headache, nausea, and vomiting to laryngospasm and bronchospasm for individuals who have more intense exposures. Burns of the eyes and nose are common. The airway may be obstructed early as a result of glottic edema or later from mucosal sloughing. Physical examination findings include conjunctival erythema, tearing, nasal discharge, and coughing. Gasping, choking, and inspiratory stridor portend the development of upper airway obstruction. Management of acute symptoms includes maintenance of an adequate airway and, in patients who have had intense exposures, hospital observation for evidence of impending respiratory failure.

The clinical presentation of patients exposed to gases of low water solubility is exemplified by silo-filler's disease,[17,18] which may be a fatal consequence of inhalation of high concentrations of nitrogen dioxide and nitric oxide. Within 2 weeks of the storage of fresh silage, generally in the late summer or autumn, the farmer enters the silo and, after a period of time that varies with exposure intensity, develops flulike symptoms including fevers, chills, cough, and a choking or smothering sensation

from acute chemical pneumonitis. Physical findings include tachypnea with variable degrees of respiratory distress and rales. Chest roentgenograms may initially be normal but usually reveal patchy alveolar infiltrates; the adult respiratory distress syndrome may occur.

Therapy is supportive; it may include oxygen supplementation and mechanical ventilation with or without positive end-expiratory pressure. Development of methemoglobinemia secondary to nitric oxide inhalation is a potential concomitant risk. The IV administration of methylene blue (2 mg/kg) is indicated for treatment of significant methemoglobinemia.

It is important to realize that these descriptions of the clinical responses to agents that are soluble or insoluble in water represent two extremes. A spectrum of clinical toxicity exists, and many patients have evidence of both upper airway and pulmonary parenchymal pathology. Factors such as the inherent chemical reactivity of the inhaled toxin, the exact nature of the exposure, and individual susceptibility as a result of underlying pulmonary disease and tobacco smoking weigh heavily in determining the nature and severity of the respiratory response to inhalation of irritant gases. Evaluation and management must be individualized.

There are several potential late effects of inhalation of these substances. These include bronchiolitis fibrosa obliterans, bronchiectasis, chronic bronchitis, and varying degrees of pulmonary fibrosis. Bronchiolitis fibrosa obliterans[19] is most likely to result in a visit to the emergency department. Weeks to months following apparent clinical recovery from a severe pulmonary insult, affected persons develop progressive tachypnea and dyspnea. Although the onset of symptoms is often insidious, symtpoms may become acute, prompting an emergency department visit. During recovery from the original insult, the body's reparative response results in fibrotic occlusion of small airways, causing a dramatic decline in alveolar ventilation. There is no effective therapy for this dreaded late complication, although immunosuppressive doses of steroids have been used.

Metals

Metals constitute the final group of inhalant respiratory irritants. They include cadmium, arsenic, beryllium, chromium, nickel, copper, zinc chloride, vanadium, tungsten, chlorinated phosphorous compounds, and phosphine. Exposure to fumes of some of these metals has been associated with the development of occupational asthma. Long-term exposure to beryllium and tungsten dust may result in granulomatous pulmonary disease simulating sarcoidosis. Inhalation of the fumes of these metals, usually as oxides, is associated with mucosal and upper-airway irritation. Chemical pneumonitis and delayed noncardiogenic pulmonary edema have been caused by nickel carbonyl, hexavalent chromium, phosphine, cadmium, beryllium, and zinc chloride. Potential industrial sources of exposure to these metals are listed in Table 2.

Development of severe chemical pneumonitis associated with nickel carbonyl inhalation can be predicted on the basis of elevated (>0.5mg/dL) levels of spot urinary nickel; this can be prevented by early administration of sodium diethyldithiocarbamate.[20] Cadmium fume poisoning[21,22] results from inhalation of highly toxic cadmium oxide, formed when cadmium metal or alloys are heated, as in welding or flame cutting. The fumes are only mildly irritating, and thus, unsuspecting workers commonly receive a substantial dose in poorly ventilated areas. A few hours later, fever, cough, shortness of breath, myalgias, and arthralgias develop. Patients may develop evidence of progressive pulmonary insufficiency with severe, often fatal hemorrhagic pulmonary edema. Central nervous system and renal toxic effects may be superimposed.

Treatment is the same as that for noncardiogenic pulmonary edema. Emphysema is a potential late development in survivors.

METAL AND POLYMER FUME FEVERS

The syndromes of metal and polymer fume fevers are flulike illnesses developing after exposure to a variety of hot metallic oxides, most commonly zinc oxide[23] or, in the case of polymer fume fever, after exposure to heated fluorocarbons such as polytetrafluorethylene (Teflon). Operations involving exposure to molten zinc, such as galvanizing and electroplating or welding on galvanized metal, are most frequently associated with metal fume fever. Zinc is alloyed with other metals in brass, bronze, and certain nickel and aluminum compounds, and work with any molten metal except aluminum may produce a similar clinical syndrome.

Following a delay of four to 12 hours after the last exposure, often on Monday evenings, metal workers note the onset of throat irritation, cough, shortness of breath, a sweet or metallic taste, and systemic symptoms including weakness, myalgias, and arthralgias. Later, cycles of high fever with profuse diaphoresis and rigors develop; severity is a function of intensity of exposure. Symptoms abate in 24 to 48 hours. Tolerance develops during the work week, only to be lost on the weekend, with recurrence of symptoms the following Monday. These symptoms are nearly indistinguishable from the early symptoms of cadmium fume poisoning. To exclude any possibility of cadmium oxide exposure, careful questioning of the patient and coworkers is indicated in cases of suspected metal fume fever. Symptoms and duration of illness are similar for polymer fume fever.

The importance of these syndromes for emergency department personnel involves recognizing and differentiating them from acute infectious diseases. Correct diagnosis obviates the need for antibiotics and frequent return visits to the emergency department. Treatment is supportive, and workers should be advised to improve work site ventilation or use respiratory protective equipment.

ASPHYXIATION

Inhalant asphyxiants can be divided into two groups: those that cause simple asphyxiation, and chemical asphyxiants. In both groups, the basis for toxicity is impaired oxygen delivery to tissues. Simple asphyxiants include smoke, nitrous oxide, argon, helium, hydrogen, nitrogen, carbon dioxide, methane, and ethane. As concentrations of these substances in ambient air increase, the fractional inspired oxygen concentration and partial pressure of oxygen in circulating blood decrease. Signs of mild tissue hypoxia include tachycardia, tachypnea, and incoordination. These symptoms progress to emotional lability, nausea, vomiting, lethargy, and unconsciousness as the concentration of oxygen in inspired air falls. Fractional inspired oxygen concentrations below 6% result promptly in seizures, apnea, and cardiac arrest. Treatment of simple asphyxiation involves delivery of supplemental oxygen and support of respiration.

Chemical asphyxiants include carbon monoxide, hydrogen cyanide, and hydrogen sulfide. These gases interfere with cellular respiration: Carbon monoxide combines with hemoglobin, and hydrogen cyanide and hydrogen sulfide bind to oxidative enzymes, especially cytochrome oxidase.

Fire fighters, coal miners, smelter workers, caisson workers, toll booth attendants, and traffic police, all have risk of carbon monoxide toxicity. Workers exposed to methylene chloride, a commonly used solvent that is rapidly metabolized to carbon monoxide, are also at risk. Industrial uses of hydrogen cyanide include extraction of gold from ore, manufac-

ture of phosphoric and oxalic acids, use of acrylonitrile, and metal plating. Hydrogen cyanide is an ingredient in some pesticides. Hydrogen sulfide exposure is associated with paper making; gas drilling; coal, lead, and sulfur mining; sewage treatment; felt making; and animal skin and sugar beet processing. Hydrogen sulfide is used in brewing and in manufacturing nylon and various synthetic rubbers.

Inhalation causes symptoms of mucous membrane irritation and noncardiogenic pulmonary edema. Onset of symptoms 24 to 72 hours after exposure is not unusual. Emergency management[24] is similar to that for acute cyanide poisoning,[25] except that only the nitrites are used. Thiosulfate is used in cases of cyanide poisoning to convert cyanide to thiocyanate. Controlled levels of methemoglobinemia induced by the nitrites inactivate sulfide as sulfmethemoglobin. Additional measures include administration of supplemental oxygen and hospitalization to observe for delayed-onset pulmonary edema.

ACUTE NEUROLOGIC AND BEHAVIORAL TOXICITY

Occupational neurologic diseases may be manifested as peripheral neuropathies, encephalopathies, seizure disorders, movement disorders, or combinations of these conditions. Most industrial neurotoxins, including lead, arsenic, mercury, manganese, nickel, organotin compounds, organic solvents, chlordane, chlordecone, acrylamide, and dimethylaminopropionitrile, generally cause neurologic disease of insidious onset, developing after months to years of exposure.

Affected persons are unlikely to seek initial medical care in the emergency department. Acute neurologic and behavioral symptoms, including headache, coma, syncope, seizure disorder, psychosis, and central nervous system depression, may also accompany other intoxications. Cerebral hypoxia may occur either (a) from decreased cardiac output as a result of occupational cardiac disease or (b) as a result of impaired cellular respiration, as occurs with asphyxiation, through decreased oxygenation of blood. In these cases, although neurobehavioral symptoms and signs may be the most obvious and troublesome, diagnosis and treatment for the primary disorder is the key to effective management.

Workers with intense exposure to volatile organic solvents may develop symptoms of acute intoxication.[26] These symptoms, including headache, ataxia, dysarthria, confusion, disorientation, light-headedness, and occasionally, syncope, resolve over a period of minutes to hours with no specific therapy. Affected painters, degreasers, furniture strippers and refinishers, and other workers exposed to organic solvents should be advised to improve work site ventilation and use personal pulmonary protective equipment to prevent development of chronic central and peripheral nervous system impairments.

ACUTE CARDIAC TOXICITY

Occupational cardiac diseases may take the form of coronary ischemic events, arrhythmias, or congestive cardiomyopathies. A few agents have been implicated in the acceleration of atherosclerosis, including carbon disulfide and possibly carbon monoxide; however, this is a long-term process. Similarly, chronic exposure to cobalt in alloy makers may be associated with an increased risk of congestive cardiomyopathy. Among the causes of acute cardiac toxicity, asphyxiants and agents that induce hemolytic anemia may induce myocardial ischemic events secondarily, particularly in workers with subclinical coronary arterial occlusive disease.

Workers in the pharmaceutic and explosives manufacturing industries may have excessive exposure to aliphatic nitrates, including nitro-

glycerin and ethylene glycol dinitrate.[27,28] These persons are at risk for development of two clinical syndromes, one resulting from acute nitrate toxicity and the other from nitrate withdrawal. Symptoms of acute nitrate overdose include headaches, nausea, dizziness, diaphoresis, and palpitations. Tolerance to these effects develops within 1 week. Withdrawal symptoms occur 24 to 72 hours after exposure is interrupted. Anginal chest pains, lacking the usual provocative influences of exercise and emotion, may occur. Angiographic studies performed at this time have demonstrated coronary arterial spasm that is reversible with nitrate administration. Acute myocardial infarction and death have been reported in otherwise healthy young persons with normal coronary arteries at autopsy.

A second cohort of workers at risk for acute cardiac events are those exposed to fluorocarbons[29] and other halogenated hydrocarbons. The cardiac manifestations of short-term exposure to these substances result from their arrhythmogenicity, and sudden death may result. Occupations associated with potential exposure to fluorocarbons include: operating room personnel; solvent workers; plastic, rocket fuel, and drug makers; aerosol bomb and fire extinguisher workers; metal conditioners; and dry cleaners.

Emergency department personnel and rescue workers need to be cognizant of the potential cardiac effects of the nitrates and fluorocarbons if they are to avoid ascribing cardiac symptoms to noncardiac causes in otherwise healthy young workers. Treatment is the same as the treatment of myocardial ischemia and cardiac arrhythmias of other causes. Affected persons should be given advice with regard to the potential consequences of re-exposure.

HEMATOLOGIC TOXICITY

Acute hematologic toxicity from occupational inhalants takes the form of hemolytic anemia. Pharmaceutic and chemical workers are at risk for the development of hemolysis in response to the same medications and drugs that may cause this response in patients. Certain inborn errors in metabolism, most notably the X-linked glucose-6-phosphate dehydrogenase deficiency, confer a heightened susceptibility to methemoglobinemia and hemolysis in response to exposure to certain oxidants. Among the chemicals associated with this response are aniline, naphthalene, naphthol, phenylhydrazine, trinitrotoluene, methylene blue, and naphthoquinones and quinones. Acute hemolytic anemia may develop in workers exposed to explosives, dyes, photographic developers, and perfumes, as well as in pharmaceutic and chemical producers. If exposures are sufficiently intense, hemolysis is an expected outcome, regardless of genetic susceptibility.

Another group of agents that can produce hemolytic anemia are metals, including lead, mercury, arsenic, and copper. Generally, hemolysis occurs as a result of long-term exposure and is mild. Arsine is a potent cause of severe, acute hemolytic anemia.[30] This extremely toxic gas has no industrial uses but is a by-product in metal pickling and dross-removal operations and a number of other industrial processes in which arsenic is in contact with hydrogen.

Within several hours of severe accidental exposure, massive intravascular hemolysis begins, with symptoms of malaise, headache, abdominal pain, and vomiting. Passage of red urine followed by jaundice and oliguric renal failure comprise the classic triad of acute arsine poisoning. Pulmonary edema and myocardial and hepatic injury may occur, and death is common. The renal failure occurring with acute arsine poisoning is probably a consequence of a combination of the nephrotoxic effects of the products of hemolysis, as well as a direct nephrotoxic effect. Treatment for arsine poisoning is supportive and involves

recognition and management of the multiple organ system failure that may result.

ACUTE NEPHROTOXICITY

Recognition of acute occupational nephrotoxicity is severely hampered by the paucity of readily available tests measuring renal tubular function. Determinations of BUN, serum creatinine, urinalysis, and creatinine clearance give only a rough indication of the glomerular filtrative function and acute glomerular and tubular injury. Exposure to a number of industrial substances, including carbon disulfide, lead, cadmium, uranium, and chromium, may result in chronic renal failure. Workers exposed to high concentrations of certain organic solvents may develop rapidly progressive glomerulonephritis or an antiglomerular basement membrane disease virtually indistinguishable from Goodpasture's syndrome.[31]

Established causes of occupational acute renal failure include carbon tetrachloride[32] and inorganic mercury.[33] It is possible that acute renal failure might also result from the inhalation of heated ethylene glycol vapors, although the usual portal of entry for ethylene glycol is via ingestion. Carbon tetrachloride exposure is associated with its use as a solvent, as a dry-cleaning and fire-extinguishing agent, and as a fumigant. Large numbers of workers in varied occupations are potentially exposed. Inorganic mercury similarly has widespread industrial uses including manufacture of thermometers and barometers, electric equipment, mercury vapor and incandescent lamps, amalgams, felt, and various textiles, drugs, disinfectants, and solders. In addition, it is used as a chemical reagent in metal plating, photography, and taxidermy.

Acute renal failure occurring with both of these agents is generally seen in association with their toxic effects on other organ systems. Hepatocellular toxicity commonly occurs in the case of carbon tetrachloride, and neurotoxicity, including irritability, delirium, and psychosis, together with abdominal pain and vomiting, may follow short-term exposure to mercury vapors. Treatment is the same as that for acute renal failure and other associated organ system failures. Chelation using *N*-acetyl-*D*,L-penicillamine may be therapeutic in acute renal failure caused by mercury vapor inhalation if it is started early.[33]

ACUTE GASTROINTESTINAL TOXICITY

Although many industrial agents cause gastrointestinal toxicity when ingested, acute inhalant toxicity is virtually limited to acute hepatocellular or cholestatic hepatitis.[3] A variety of chemicals, including chlorinated hydrocarbons, aromatics, ethers, and nitrogen-substituted aromatics, can result in acute hepatocellular toxicity.[34] Acute cholestasis has developed in persons exposed to methylene dianiline and other epoxy resins in their work with synthetic fabric, rubber, and epoxy. Emergency care personnel should be able to recognize the occupational etiology of the hepatitis caused by these hepatotoxic chemicals, so that future exposure can be reduced or eliminated; they should also be able to differentiate between toxic hepatitis and the more common viral hepatitides. Treatment is supportive.

• • •

Categorizing inhalant toxins according to the organ system most likely to be affected in acute poisonings is a useful means for approaching the large number of potentially injurious industrial substances. The respiratory system, because of its large surface area and its intimate association with ambient air, receives the brunt of inhalant injury. The pulmonary defense mechanisms tend to protect or minimize these. Substances that reach the alveoli

are subject to absorption into the blood and are thus delivered to their target organs.

General recommendations to emergency department personnel include maintaining in the emergency department a reference file on occupational medicine and toxicology, as well as specific information regarding the recognition and management of acute occupational illnesses likely to occur at nearby industrial locations. Key to the successful treatment of occupational illness is consideration of potential industrial causes. Although acute occupational illnesses do not usually require specific treatment, establishing a work-related etiology is a critical first step in distinguishing among other common causes of similar illnesses and preventing recurrent short- or long-term injury.

REFERENCES

1. Parkes WR: *Occupational Lung Disorders*, ed 2. London, Butterworths & Co, 1982.
2. Rom WN: *Environmental and Occupational Medicine*. Boston, Little, Brown, 1983.
3. Levy BS, Wegman DH *Occupational Health*. Boston, Little, Brown, 1983.
4. Mackison FW, Stricoff RS, Partridge LJ: *NIOSH/OSHA: Pocket Guide to Chemical Hazards*, US Dept of Health, Education, and Welfare publication No. (NIOSH) 78-210. Government Printing Office, 1978
5. Proctor NH, Hughes JP: *Chemical Hazards of the Workplace*. Philadelphia, Lippincott, 1978.
6. Finkel AJ, Hamilton A, Hardy HL: *Hamilton and Hardy's Industrial Toxicology*, ed 4. Boston, John Wright, 1983.
7. Gee JBL, Morgan WKC, Brooks SM: *Occupational Lung Disease*. New York, Raven Press, 1983.
8. Clayton GD, Clayton FE: *Patty's Industrial Hygiene and Toxicology*, ed 3. New York, Wiley, 1978.
9. Key MM, Henschel AF, Butler J, et al: *Occupational Diseases: A Guide to Their Recognition*, US Dept of Health, Education, and Welfare publication No. (NIOSH) 77-181. Government Printing Office, 1977.
10. Newhouse M: Lung defense mechanisms: I. *N Engl J Med* 1976,295:990-998.
11. Newhouse M: Lung defense mechanisms: II. *N Engl J Med* 1976;295:1045-1051.
12. Green G: Defense mechanisms of the respiratory membrane. *Am Rev Respir Dis* 1977;115:479-514.
13. Fink JN: Organic dust-induced hypersensitivity pneumonitis. *J Occup Med* 1973;15(3):245-247.
14. Merchant JA, Lumsden JC, Kilburn KH, et al: Dose response studies in cotton textile workers. *J Occup Med* 1973;15(3):222-230.
15. Butcher BT, Jones RN, O'Neil LE, et al: Longitudinal study of workers employed in the manufacture of toluene-diisocyanate. *Am Rev Respir Dis* 1977;116:411-421.
16. Chester EH, Martinez-Catinchi FL, Schwartz HJ, et al: Patterns of airway reactivity to asthma produced by exposure to toluene diisocyanate. *Chest* 1979;75(suppl):229-231.
17. Ramirez RJ, Dowell AR. Silo-filler's disease: Nitrogen dioxide-induced lung injury. *Ann Intern Med* 1971;74:569-576.
18. Scott EG, Hunt WB: Silo-filler's disease. *Chest* 1973;63:701-706.
19. Milne JEH: Nitrogen dioxide inhalation and bronchiolitis obliterans. *J Occup Med* 1969;11(10):538-547.
20. Sunderman FW: A review of the metabolism and toxicology of nickel. *Ann Clin Lab Sci* 1977;7(5):377-398.
21. Blejer HP, Caplan PE, Alcocer AE: Acute cadmium fume poisoning in welders: A fatal and a non-fatal case in California. *California Med* 1966;105(4):290-296.
22. Beton DC, Andrews GS, Davies HJ, et al: Acute cadmium fume poisoning: Five cases with one death from renal necrosis. *Br J Ind Med* 1966;23:292-301.
23. Drinker KR, Drinker P: Metal fume fever: V. Results of the inhalation by animals of zinc and magnesium oxide fumes. *J Ind Hyg* 1928;10:56-70.
24. Stine RJ, Slosberg B, Beacham BE: Hydrogen sulfide intoxication. *Ann Intern Med* 1976;85(6):756-758.
25. Wolfsie JH, Shaffer CB: Hydrogen cyanide: Hazards, toxicology, prevention and management of poisoning. *J Occup Med* 1959;1(5):281-288.
26. Elofsson S, Gamberale F, Hindmarsh T, et al: Exposure to organic solvents: A cross-sectional epidemiologic investigation on occupationally exposed car and industrial spray painters with special reference to the nervous system. *Scand J Work Environ Health* 1980;6:239-273.
27. Lund RP, Haggendal J, Johnsson G: Withdrawal symptoms in workers exposed to nitroglycerine. *Br J Ind Med* 1968;25:136-138.
28. Morton WE: Occupational habituation to aliphatic

nitrates and the withdrawal hazards of coronary disease and hypertension. *J Occup Med* 1977;19(3):197–200.
29. Mullin LS, Azar A, Reinhardt CF, et al: Halogenated hydrocarbon-induced cardiac arrhythmias associated with release of endogenous epinephrine. *Am Ind Hyg Assoc J* 1972;33(2):289–396.
30. Fowler BA, Weisberg JB: Arsine poisoning. *N Engl J Med* 1974;291:1171–1174.
31. Kleinknecht D, Morel-Maroger L, Callard P, et al: Antiglomerular basement membrane nephritis after solvent exposure. *Arch Intern Med* 1980;140:230–232.
32. Lewis CE: The toxicology of carbon tetrachloride. *J Occup Med* 1961;3(2):82–85.
33. Kark RAP, Poskanzer DC, Bullock JD, et al: Mercury poisoning and its treatment with *N*-acetyl-*D,L*-penicillamine. *N Engl J Med* 1971;271(1):10–16.
34. Zimmerman HJ: Occupational toxicity. *Hepatotoxicity*. New York, Appleton-Century-Crofts, 1978, pp 303–318.