CHAPTER 53

Indoor Environmental Quality and Health

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Approximately 71 million employees work indoors in the United States and the U.S. Bureau of Labor Statistics estimates that more than 21 million of these are exposed to some degree of poor indoor environmental quality (1). The Occupational Safety and Health Administration (OSHA) estimates that 69,000 severe headaches and 105,000 respiratory problems may be caused by poor indoor environmental quality (1). Employees working in service industries, in wholesale and retail trades, and in government jobs make up the bulk of those at risk (Table 53-1) (1).

Changing energy use strategies in the 1970s resulted in construction of buildings with improved energy efficiencies and tighter sealing to prevent energy loss. As a consequence, health complaints relating to indoor environments began to increase, and the term *tight building* or *sick building syndrome* (SBS) was adopted to describe this problem. Complaints relating to the environment had previously been attributed to either poor working conditions or psychological factors. It soon became apparent, however, that health complaints could also be attributed to inadequate ventilation, mold overgrowth, lack of fresh air exchange, excess biological and chemical contaminants, dampness, or inadequate dilution of indoor contaminants (1–9). The phrase *poor indoor air quality* is used to describe environmental conditions indoors that can result in signs and symptoms attributable to the buildup of airborne contaminants. Such illness, however, is often multifactorial. Symptoms commonly expressed in cases of poor environmental air quality are as follows:

- Mucous membrane irritation
  - Eye irritation
  - Nasal symptoms
  - Throat irritation
  - Drying of mucous membranes
  - Drying of skin
  - Rashes
  - Sinus congestion
- Respiratory symptoms
  - Cough
  - Chest tightness
  - Sore throat
  - Voice changes and hoarseness
  - Asthma
  - Difficulty breathing
  - Bronchial hyperresponsiveness
- Constitutional
  - Nausea
  - Abdominal complaints
  - Myalgia
  - Arthralgia
- Neurologic and neurobehavioral
  - Headache
  - Fatigue
  - Dizziness
  - Lethargy
  - Difficulty concentrating
  - Memory problems

TABLE 53-1. Occupational Safety and Health Administration sites of poor indoor air quality

Occupational field	Employees working indoors	No. of buildings with air quality problems	No. of employees exposed to air quality problems
Agriculture, forestry, fishing	279,050	51,956	83,715
Mining	180,700	4,554	54,210
Construction	1,643,750	128,091	493,125
Manufacturing	5,748,000	77,573	1,724,400
Transportation	3,412,350	48,563	1,023,705
Wholesale and retail trade	15,744,000	384,466	4,723,200
Finance, insurance, real estate	7,248,150	104,863	2,174,445
Services	26,926,000	385,235	8,077,800
Government	9,473,561	173,100	2,842,068
Total	**70,655,561**	**1,358,400**	**21,196,668**

From ref. 1, with permission.

For example, increased incidences of allergic diseases, coughing, wheezing, shortness of breath, asthma, bronchitis, headaches, eye irritation, muscle aches, fever, chills, nausea, vomiting, and diarrhea are reported among children and adults exposed to indoor biological contaminants, but biologicals encompass a wide array of contaminants and biochemical by-products (1–9).

The World Health Organization (WHO) characterized SBS in 1983. Since then, health complaints associated with poor indoor air quality have been classified as either SBS or building-related illness. Although arbitrary and archaic, this classification serves to categorize illness as traceable or untraceable to a defined cause or source.

SBS defines a set of symptoms whose origin is uncertain or related to ill-defined factors in the environment. Affected individuals experience multiple and sometimes vague health complaints. In such cases, health complaints tend to cease when the individual leaves the site and recur when the individual reenters the site.

The term *building-related illness* applies to a definable medical condition able to be traced to a single source and documented by specific signs and symptoms consistent with a known disease. Examples include *Legionella pneumophila*, hypersensitivity pneumonitis caused by organic dusts and bioaerosols, carbon monoxide poisoning, and allergic-mediated asthma caused by identifiable allergens. The seriousness of building-related illness became apparent in the *Legionella pneumophila* infection of 182 American Legion members attending a convention in 1976 in Philadelphia, resulting in 29 fatalities. The dissemination of this bacterium from contaminated ventilation systems emphasizes the contribution of the multiple factors of humidity, biological growth, and ventilation to causing illness.

SOURCES AND CAUSES OF POOR ENVIRONMENTAL QUALITY

Studies indicate that vague complaints relating to mucous membrane irritation, respiratory symptoms, and headache occur more commonly in office environments (3,4,9,10). But sources and causes of such health complaints are multiple and can be difficult to identify. Investigations of these sites show that dete-

rioration of the environmental quality indoors is most often caused by problems with airborne contaminants traceable to one or more of the following general sources:

- Chemical
- Biological
- Physical
- Psychosocial

A dynamic mixture of chemical, biological, and particulate pollutants arising from a variety of sources circulates in indoor air:

Chemical sources
  Chemicals volatilizing from building materials and furnishings
  Cleaning materials and disinfectants
  Chemicals emitted from office machines and materials
  Pesticides
  Tobacco smoke
  Combustion products from cooking and fireplaces
Physical sources
  Ventilation problems
  Dusts
  Particulates
  Fibers, such as asbestos or fiberglass
Biological sources
  Pollen
  Mold and fungus
  Biological by-products of microbes
  Bacteria
  Viruses
  Dander from pets
  Insects and insect parts
  Human skin particles
  Dust mites

These pollutants are influenced by air movement, ventilation, temperature, and humidity. Most of the chemical sources of indoor contaminants are comprised of volatile organic chemicals (VOCs). Analyses of indoor air samples demonstrate between 50 and 300 different VOCs present in low levels in nonindustrial environments, such as offices, homes, shopping centers, and malls (11–13) (Table 53-2).

Biological sources of indoor pollution include mold, fungus, pollen, spores, bacteria, viruses, and insects, such as dust mites and roaches. Water reservoirs and damp areas provide nutrient sources for microorganism growth. Relatively high humidity and moisture allow biological agents to amplify to levels that when disseminated indoors can trigger illness and allergies. Reports indicate that indoor dampness and mold growth are associated with increased respiratory illness in adults and children (5,7,8). High relative humidity also encourages growth in the dust mite population, which can cause allergies and asthma. More attention is being focused on biochemical products of microorganisms as potential causes of indoor-related respiratory illness, such as endotoxin, 1,3-β-glucan, mycotoxins, peptidoglycan, and VOCs emitted from fungi (9).

Physical factors, the third source of indoor-related illness, include dusts, fibers, particulates, and overall comfort factors, such as ventilation, lighting, temperature, humidity, noise, and vibration. Dust and particulate matter are ever present indoors. Each cubic meter of air contains small concentrations of millions of particulates, of which 99% are invisible to the eye (9).

Psychosocial factors, the fourth source of illness indoors, include elevated stress from perceived or real environmental threats and illness, lack of control over the environment, the nature of the work itself, and conflict arising from adversarial stances of management or coworkers. Psychosocial factors can be particularly complex. Frequently, however, some employees may be improperly labeled as *psychogenic* or their illness as *psychological* without a proper or thorough investigation of environmental causes (14–17).

TABLE 53-2. A partial list of volatile organic chemicals identified indoors

Xylenes	Chlorobenzene
Ethylbenzene	Pinene
Toluene	Carbon tetrachloride
1,1,1-Trichloroethane	Chloroform
1,1,2-Trichloroethane	1,2-Dichloroethane
Dichlorobenzenes	Methylene chloride
Styrene	1,2,4-Trimethylbenzene
Hexane	1,1-Dichloroethylene
2-Butanone	Naphthalene
1,1-Dichloroethane	1,3-Dichloropropane
Alkyl benzenes	1,3,5-Trimethylbenzene
Ethyltoluene	Hexanol
Methylcyclopentane	Heptadecane
2-Methylhexane	Ethyl acetate
Methylcyclohexane	Isopropylbenzene (cumene)
2,2,5-Trimethylhexane	*n*-Propylbenzene
Ethylene dibromide	1,2,3-Trimethylbenzene
Bromodichloromethane	Acetone
Methyl butyl ether	*n*-Heptane
Undecane	*n*-Butanol
Dodecane	Benzyl chloride
Decane	Dimethyl phthalate
Tridecane	1,1,2,2-Tetrachloroethane
Tetradecane	1,1,2,2-Tetrachlorethylene
m-Ethyltoluene	Dibutyl phthalate
Cyclohexane	Butyl acetate
3,4-Dimethylheptane	2-Ethoxyethelacetate
Pentadecane	1,4-Dimethylethylbenzene
Hexadecane	2-Propanol
1,2,4-Trichlorobenzene	2-Methylbutane
Nonanal	2,2,4-Trimethylpentane
Limonene	1,4-Dimethylcyclohexane
Nonane	Pyridine
Chloroethyl vinyl ether	Propane
4-Methyl-2-pentanone	2-Vinyl pyridine
Carbon disulfide	Diethyl phthalate
Benzene	Ethylene dichloride
Tetrachloroethylene (perchlorethylene)	Dichlorethylene
Trichloroethylene (trichloroethene)	Camphene
Octane	Isopropyl ether
	Trichlorofluoromethane (Freon)
	Methyl chloride

INDOOR ENVIRONMENTAL QUALITY AND COMFORT FACTORS

Overall comfort in the indoor environment of home or work directly affects perceptions of health. Research shows that human comfort levels in the work environment are second in importance only to satisfaction regarding the nature of the work itself (14). Human well-being indoors is a result of multiple interacting factors that collectively contribute to perceptions of comfort and indoor environmental quality. But these factors can also contribute to illness and discomfort indoors.

Energy Conservation

Energy conservation strategies dating from the 1970s have contributed to declining indoor air quality (4,8,10). Building design and operational changes focused on decreasing energy con-

sumption to comply with goals of reducing American dependency on foreign energy sources. But energy-efficient buildings may sacrifice ventilation effectiveness to reduce overall energy costs (17–20). Such efforts may result in better-insulated buildings but reduce the performance capacity of ventilation systems. The overall result is often inadequate fresh air exchange for building occupants that allows airborne chemical contaminants and pollutants to concentrate.

Building Materials and Furnishings

Products used in construction contain chemicals that can outgas into the indoor environment. Building materials are constantly changing and new products are entering the market, so it is difficult to keep track of the large variety of volatile chemicals contained in these products. Building products, ranging from structural materials to coatings, contain chemicals that are emitted indoors (11–13,21). Emissions of VOCs from building materials depend on the nature of the material, the chemicals, and the location of the material in the structure. Emission rates can vary from an initial high release in minutes or hours to long-term degassing over weeks, months, and even years. Such products include wood, insulation, plastics, sealers, caulking, adhesives, paints, varnishes, waxes, finishes, lacquers, fabrics, and carpets.

Furnishings and fabrics can act as sinks to absorb airborne chemicals, releasing them slowly back into the indoor environment, depending on temperature, humidity, and ventilation. In general, warmer temperatures and higher humidity increase the rate of emission of VOCs.

HUMAN FACTORS

Human activity contributes to indoor contamination by introducing irritating cleaning agents, pesticides, solvents, tobacco smoke, particulates, dust, fibers, mold, and allergens. Humans also shed millions of skin particles and microbes indoors. Cooking and other combustion sources introduce carbon monoxide, nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and particulates into indoor air (22,23). Computers, copiers, fax machines, laser printers, and other office machines emit volatile chemicals and ozone.

Smokers contribute to the indoor chemical and particulate pollutant load. Whereas environmental tobacco smoke (ETS) has previously been thought of as a nuisance to most nonsmokers, the U.S. Environmental Protection Agency (EPA) considers it to be a substantive risk factor for cancer and heart disease (24,25). The EPA classifies ETS as a group A carcinogen, meaning that it causes human cancer. Although the EPA's cancer conclusions are being questioned, ETS remains a prime contributor to cough, shortness of breath, and chest tightness in exposed asthmatics (26). ETS also contributes to significant formaldehyde exposure indoors (27,28).

VENTILATION SYSTEM

Up to 50% of poor indoor air quality cases can be traced to a ventilation problem (19,20). A properly functioning ventilation system provides adequate fresh air and dilutes and removes pollutants. It also balances indoor air quality with comfort. Ventilation is a dominant cost of building maintenance and energy use, and decreasing ventilation is sometimes used as a cost-saving measure. Such approaches, however, can lead to the buildup of pollutants indoors.

Breathing produces carbon dioxide (CO_2) as a by-product, and its concentration indoors is a useful measure of air freshness. Accumulation of CO_2 concentrations of more than 800 parts per million (ppm) of air indicates inadequate fresh air supply and can be associated with health complaints, such as fatigue, headache, lethargy, and general discomfort. The American Society for Heating, Refrigeration and Air-Conditioning Engineers (ASHRAE) recommends that indoor CO_2 concentrations do not exceed 1,000 ppm (19,20,29,30). Elevated CO_2 concentrations of more than 800 ppm, however, may signal the buildup of other indoor pollutants because of their inadequate removal or dilution. ASHRAE has issued a number of indoor air quality standards including 62-1999, Ventilation for Acceptable Indoor Air Quality (superseding 62-1989), and projects 62.1P and 62.2P.

Air ducts contaminated with dirt, dust, and moisture can provide sources for microbial growth that may cause illness. The 1976 discovery of legionnaires' disease in Philadelphia underscores the fact that serious illness and death can result from a contaminated ventilation system.

Humidity

Excessive moisture and dampness indoors increases the risk of childhood asthma and other respiratory symptoms (5,7,8). Relative humidity values indoors more than 60% are associated with overgrowth of fungus and bacteria that can contaminate ventilation systems, carpet, wall spaces, insulation, ceiling tiles, window seals, and other areas of the indoor environment. Humidity less than 20% can cause drying of skin and mucous membranes, leading to irritation. High relative humidity increases upper airway moisture, allowing dusts and water-soluble toxic chemicals to dissolve more easily, contributing to upper airway irritation, inflammation, and cough.

A humidity range of 45% to 50% is recommended by ASHRAE and the EPA (24). Properly functioning ventilation systems help to maintain relative humidity between 20% and 60% (20).

Noise and Vibration

Whereas *sound* applies to the form of energy that produces hearing, *vibration* is the term applied to nonaudible sensations of touch and feeling. Noise is an unpleasant sound.

Noise is generated by vibrations transmitted as mechanical energy through air, solid, or liquid. It includes a spectrum ranging from infrasound to audile sound to ultrasound. Sound is measured in frequency (cycles per second) called a *hertz* (Hz). As an example, a sound frequency of 100 Hz means the period of vibration is $1/100$ of a second (0.01 seconds). The *wavelength* of sound is the distance it travels in one cycle. Wavelength is an important property of sound and ranges from high frequency to low frequency. The term *decibel* (dB) is used to express the level of loudness associated with sound. A decibel reference level of zero is assigned to the sound heard by a person with excellent hearing in a quiet location. A sound of 140 dB is considered a pain threshold (31,32). The human ear is more sensitive to high frequencies, and sounds audible to the human ear range from 35 to 20,000 Hz.

Excess or chronic noise can cause health effects (31,32). Low-frequency noise between 20 and 100 Hz can produce health complaints, ranging from general annoyance and distraction to physiologic and psychological effects (31,32). Noise less than 100 Hz can be felt as vibration. Vibrations that interact with body receptors of touch and pressure can interfere with human performance. Sounds in the 40- to 60-Hz range have effects on the respiratory system because of the resonance characteristics of the chest wall. Sound between 0.1 and 20 Hz can cause dizziness and nausea, but usually only in decibels less than 120 (31,32).

The level (loudness) and the nature (frequency) of noise are important in producing symptoms. Prolonged exposure to low-frequency noise can result in fatigue, headache, difficulty concentrating, nausea, disorientation, cough, dizziness, and digestive problems. Most of these health effects occur around 7 Hz. OSHA regulates occupational exposure to noise by the Noise Control Act of 1972 that established the Office of Noise Abatement and Control

within the EPA. This act enforces noise control regulations for machines, railroads, interstate motor carriers, and aircraft. OSHA's threshold limit value (TLV) for noise is 85 dB for an 8-hour day or 80 dB for a 24-hour period. Hearing loss can occur in individuals exposed to 75 dB 8 hours per day over a lifetime (33).

Besides auditory effects, noise can cause physical and psychological health effects. Noise interferes with communication, can cause disturbances in sleep, induces stress, irritability, fatigue, and interferes with performance and productivity. The threshold for annoyance is approximately 30 to 40 dB. Excess noise can elevate blood pressure, cause irritability, decrease productivity, and be generally discomforting (32,33).

Lighting

Light is the portion of the electromagnetic spectrum visible to the human eye, and can affect physical and psychological health. Studies involving seasonal depression demonstrate a relationship between a person's mood and lighting. Visual stress can be caused by inappropriate lighting, inadequate contrast, or glare. In addition, suboptimal lighting can cause eye irritation, stress, fatigue, headaches, and affect moods and performance. Studies demonstrate that performance and satisfaction rise with an increase in luminescence. However, bright light can cause feelings of dissatisfaction (32,34).

Because a relationship exists between lighting design and energy use patterns, architects and engineers have sought to minimize energy consumption with increased use of natural light and more energy-efficient light sources. The health consequences of artificial lighting are a subject of much research, adding to the complexities of indoor comfort and health.

Odors and Irritancy

Odors may range from tolerable to objectionable, and odors that seem satisfactory to the human nose generally have not been a concern for the majority of people indoors. Frequently, odors are associated with respiratory symptoms and mucous membrane irritation. The common chemical senses (CCS) formed by trigeminal nerve endings in the nose and upper airways detect irritants, pungent chemicals, and irritating particulates. The olfactory nerves detect odors. Different chemicals give rise to different olfactory responses that may give rise to different human responses. Health complaints associated with odors are a complex issue, and some individuals may complain of odor intolerance or an increased sensitivity to certain odors from indoor sources.

Stress

Poor indoor air quality can be a chronic stressor. How an individual adapts or maladapts to such stresses determines if health problems develop. Stress also occurs when an individual cannot control the environmental source of their illness. If the environment is perceived to be a threat, fears can develop and stress levels may rise. Another common cause of stress is the conflict that often surrounds indoor air quality problems and the adversarial stances of supervisors toward an individual's complaints about air quality.

Other stressors include the nature of the job and negative employee relationships. Workplace stress continues to be a growing concern because of its high financial and health care. Stress from all causes is estimated to cost $150 billion a year in lost productivity and worker's compensation claims (16). Most stress claims are the result of cumulative events, not single events. Environmental stimuli, such as chemicals, odors, and irritants, and recurring illness from unknown sources can precipitate chronic stress in some susceptible individuals.

Activity and Clothing

The level of human activity indoors determines metabolic rate and, thus, is related to thermal comfort. ASHRAE publishes a table of metabolic rates associated with a variety of activities and levels of work. Most office workers are sedentary and ASHRAE's thermal comfort standards are based on this level of relative activity. Dissipation of heat caused by activity is necessary to maintain thermal comfort, and clothing is a prime factor related to heat loss or gain. ASHRAE has a table of clothing values for thermal comfort. These values are expressed as *clo* units of thermal resistance. One clo unit = $0.88°F \times ft^2 \times h/BTU$ (32). Various articles of clothing represent different clo values: trousers plus short-sleeve shirt = 0.5 clo units.

BIOLOGICAL MECHANISMS OF INDOOR ENVIRONMENT–RELATED ILLNESS

Pollutants, thermal comfort, humidity, adequacy of ventilation, and air movement combine to play interacting roles in perceptions of health in work and home environments. Studies estimate that between 20% and 35% of office workers perceive indoor air quality problems in their work environment (17–20). But health complaints, such as headache, sinus congestion, and fatigue, may be difficult to separate from general symptoms experienced by the overall population. Therefore, establishing a cause-effect relationship between the indoor environment and illness is often difficult because of the numerous variables involved (35). Also, the definition of what constitutes SBS varies. WHO recognized this difficulty and combined various definitions into a singular summary to describe the syndrome as follows (33):

1. A majority of occupants indoors report symptoms.
2. Symptoms appear more frequently in one building or part of a building than any other.
3. Six categories of symptoms cover the majority of health complaints:
   - Sensory irritation
   - Neurologic symptoms
   - General health symptoms
   - Skin irritation
   - Unspecific hypersensitivity reactions
   - Odor and taste problems
4. Mucous membrane, nose, eye, and throat irritations are the most frequently expressed symptoms.
5. Other symptoms tend to be less expressed.
6. No singular causality can be identified.

Still, patterns of illness can be correlated with environmental clues. Poor indoor environmental quality should at least be considered if typical symptomatology occurs in a site characterized by one or more of the following (Table 53-3):

- Presence of chemical odors
- Recent remodeling
- Newly constructed building
- Presence of moisture or water damage
- Heavy use of cleaning agents
- Indoor combustion sources
- Mold contamination and discoloration of walls and ceilings
- Musty or stale odors
- Excess dust or particulates on walls or other surfaces
- New carpet odors
- Office machines in unventilated areas or in direct sunlight

Affected persons express improvement of symptoms when they are away from work and over weekends, with recurrence of symp-

TABLE 53-3. Clues to potential indoor air quality problems

Odors
Chemicals
Musty
Stale
Tobacco smoke
New carpet
Pesticides
Diesel or gasoline engine exhaust
Remodeled site or new building
Paints
Varnishes
Glues
Lacquers
Thinners
Adhesives
Roofing materials
New carpet
Grouts
Caulking
Sealants
Pressed woods
Solvents
Office machines
Placed in unventilated area
In warm rooms
Located in direct sunlight
Water and moisture damage
In ventilation system
In subbasements
Involving floors, ceilings, or insulation
Involving carpet or walls
Involving wallboard or sheet rock
Combustion sources
Tobacco smoke
Fireplace flue not working properly or in need of cleaning
Unvented gas heaters and gas appliances
Internal combustion in a confined space
Combustion sources near ventilation intake vent
Space heaters unvented
Charcoal grills indoors
Accumulation of dust and particulates
On surfaces such as desks and walls
In ventilation system
On ventilation grills
Overuse of cleaning agents or disinfectants
On large surface areas
In poorly ventilated areas
Containing irritating chemicals
In small or confined spaces
Ventilation problems
Poor air movement
Stale air
Microbial contamination
Dirty vents
Lack of air filtration
Pollutant source near fresh air intake
Environmental factors
Too humid
Too warm
Harsh or glaring light
Excessive noise
Vibrations

toms on returning to work. The time factor of exposure duration seems to be important in determining how quickly symptoms resolve in anecdotal cases. The longer the exposure, the slower the resolution of symptoms seems to occur. The search for biological models to explain the causes of these signs and symptoms has focused on the following mechanisms (11–14,22,23,35–40):

- Inflammation involving upper and lower airways
- Mucous membrane irritancy
- Neurobehavioral and neurologic effects of VOCs
- Allergic reactions and hypersensitivity to chemicals and biologicals
- Stress and psychological reactions
- Infections
- Effects of chemicals and biological toxins on the immune system

Inflammation and irritation of mucous membranes are primary mechanisms at the root of many indoor air quality–related health problems. Underscoring the complexity of the problem, environmental factors, such as temperature and humidity, can interact with airborne contaminants to trigger illness (35,36). Also, why some people are more susceptible than others may partially be explained by their atopic status and their heightened susceptibility to inflammation (36,37). Still, symptoms associated with poor indoor air quality are sometimes difficult to delineate from those caused by common allergies because allergens and nonallergens share similar pathways of inflammation and illness production.

Because humans breathe between 10,000 and 20,000 L of air daily, with most passing through the nose, upper airway, and respiratory tract, exposure to airborne contaminants is unavoidable (36). Thus, those with a predisposition to inflammation by either nonimmune stimuli or immune stimuli may be more prone to respiratory irritation and inflammation caused by airborne contaminants (37–39).

Irritancy and Pungency Caused by Airborne Contaminants

Airborne contaminants include particulates, bioaerosols, or chemicals, and respirable airborne particles of 10 μm in diameter or less can penetrate into the airways (see Fig. 52-3).

Detection of airborne chemicals and particulates by the nasal passages and upper airways involves the common chemical senses, a specialized network of nerves emanating from the trigeminal nerve with endings located in the face, eyes, and nasal passages (39,41,42) (Fig. 53-1). As the trigeminal nerve leaves the brain, it divides into three branches innervating both sides of the face and upper airways: the ophthalmic, the maxillary, and the mandibular. The ophthalmic branch innervates the interior part of the nose, the

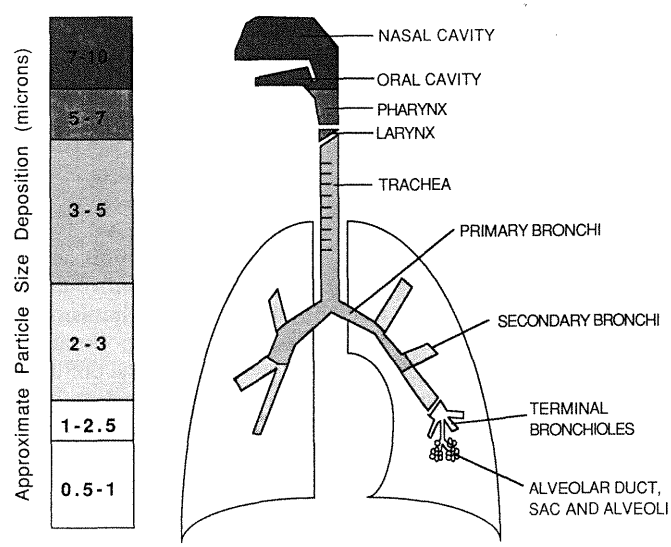

Figure 53-1. Schematic illustration of respiratory tract anatomy and approximate pattern of particle deposition.

conjunctiva, the cornea, and the iris of the eye. The maxillary branch innervates the posterior and inferior nasal passages. The mandibular branch innervates the tongue and the mouth. Activation of these chemical sensory pathways by airborne hazards serves to warn of danger by producing an irritancy reaction. If this CCS interaction with irritants is unregulated or a constant activation occurs, inflammation can result.

The CCS responds quantitatively and qualitatively to stimulation by chemical vapors and airborne particulates (39,43,44). Small changes in molecular structure among VOCs give rise to large differences in chemical potencies. The nerve receptors in the membranes of the nose and mouth are close to the surface, separated only by a thin film of moisture. Airborne chemicals can penetrate this moisture layer to react with nerve endings.

VOCs and low-molecular-weight chemicals can activate the CCS nerve receptors either by physical or by chemical reactions. Those that bind chemically produce a more potent reaction (39,41). Examples of such chemicals are formaldehyde, acrolein, chlorine, ozone, sulfur dioxide, and aldehydes.

The nerves of the CCS release neuropeptides in response to environmental irritants. This type of inflammatory response is termed *neurogenic inflammation* (39,41,43). Neuropeptides (also termed *neurokinins*) are found in nerve fibers of the nose, dental pulp, and the eyes and can be released by lung tissue. Therefore, volatile chemicals can produce irritant effects and release inflammatory neuropeptides at nerve sites around the body, throughout the nasal mucosa, lungs, and other sites that store such mediators (39,44,45). Neuropeptide release results in a cascade of events leading to more inflammation, swelling, pain, and the release of other inflammatory mediators from tissues, amplifying effects and producing symptoms:

Sneezing
Nasal stuffiness
Rhinorrhea
Facial pain
Eye irritation
Watery eyes
Headache
Sinus congestion
Cough
Fatigue
Throat irritation
Wheezing

Desensitization of these sensory nerves may also occur with a fading of the irritation response. No singular predictor dictates which response may occur in a given individual.

Disorders in the regulation of neurogenic inflammation can lead to prolonged and more intense responses from environmental stimulants. Control of neurogenic inflammation is through neutral endopeptidase, which degrades neuropeptides. Conditions that decrease neutral endopeptidase activity may increase neurogenic inflammatory responses (39,43,44). Irritant chemicals and respiratory viral infections that inhibit neutral endopeptidase regulatory activity, therefore, can contribute to a person's sensitivity to airborne pollutants. This mechanism may explain some individuals' symptoms to indoor air pollutants.

Another important relationship by which airborne pollutants cause respiratory symptoms is via the interconnection of the nasal airway and bronchial airways (46). Accumulating evidence supports the fact that nasal inflammation can aggravate asthma. Studies show that intranasal corticosteroid treatment for allergic rhinitis has a beneficial effect on nonspecific bronchial hyperresponsiveness and on asthma symptoms (46). Thus, induction of nasal inflammation by airborne contaminants is an important mechanism linked to lower airway respiratory symptoms.

CCS receptors respond to different types of stimuli besides chemical: thermal, mechanical, biologicals, particulates, dusts, and bioaerosols. At lower exposure levels, a summation effect occurs. That is, the more tissue and receptors that are exposed to irritants, the stronger the response. Time summation may also be an important event in symptom amplification from indoor pollutants.

Respiratory Irritation, Bronchial Hyperresponsiveness, and Asthma

The lungs also respond to airborne chemicals and hazards via inflammation. The surface epithelial cell layer of the lungs forms a physical barrier against inhaled toxins and hazards. These cells secrete a thin sterile moisture barrier over the surface of the lungs and bronchioles. Other specialized cells secrete a thick mucous layer on top of the water layer. Together, these layers form a gel phase that traps chemicals, particles, and dusts. The surface lining of the lower airway is made up of ciliated epithelial cells, forming a brush border that constantly pushes trapped substances toward the mouth where they can be expectorated or swallowed.

Besides epithelial cells that can release cytokines and other mediators of inflammation, nerve endings can be stimulated by irritants to cause bronchoconstriction. If the cell layer lining the airway is damaged by an inhaled hazard, nerve endings can react by constricting the airway. This may occur because of a high-level acute exposure or chronic low-level exposure. Also, pulmonary macrophages and epithelial cells release mediators in response to stimuli by irritants causing an inflammatory cascade resulting in an acute or chronic response (45,47,48).

Because the tissues of the airways form an interactive protective mechanism, irritants and toxins that affect one cell or tissue type affect others. Toxins and particulates that damage the protective mechanism and result in inflammation of the airway (referred to as toxic inflammation) can cause cough, shortness of breath, chest tightness, wheezing, and asthma. Once an inhaled hazard induces the inflammatory process, chemical mediators of inflammation are released by epithelial cells and macrophages [(interleukin (IL)-1, tumor necrosis factor-α (TFN-α), and IL-6]. Once released, these chemical mediators activate other cells, causing a cascade of inflammation (38,47,48).

Acute exposures produce inflammatory responses that differ from those of chronic exposures. Also, chronic exposures producing ongoing inflammation may result in pathologic alterations in airway tissues, including fibrosis and increased production of mucus (Fig. 53-2).

Exposure to airborne contaminants may also produce a hyperresponsiveness of the airways that can be either IgE mediated or non–IgE mediated. Some low-molecular-weight chemicals, such as acid anhydrides and isocyanates, may serve as haptens to generate type I immune-mediated asthma. Bioaerosols can act as antigens to cause type IV hypersensitivity reactions, such as hypersensitivity pneumonitis (see Chapters 25 and 97).

The term *reactive airways* or *nonspecific bronchial hyperresponsiveness* is used to describe nonimmune-mediated asthma caused by inhaled respiratory irritants. Once a person has developed reactive airways, exposure to chemically unrelated airborne irritants may trigger symptom onset via inflammation (49).

An entity termed *reactive airways dysfunction syndrome* has been described after a high-level exposure to irritant chemicals. Signs and symptoms of respiratory irritation occur quickly after such an exposure, with coughing, chest tightness, and throat burning. Reexposure to irritating vapors or fumes can precipitate symptoms of cough, wheezing, and shortness of breath. Pulmonary function tests may be abnormal but are usually reversible on treatment with a bronchodilator. Reactive airways dysfunction

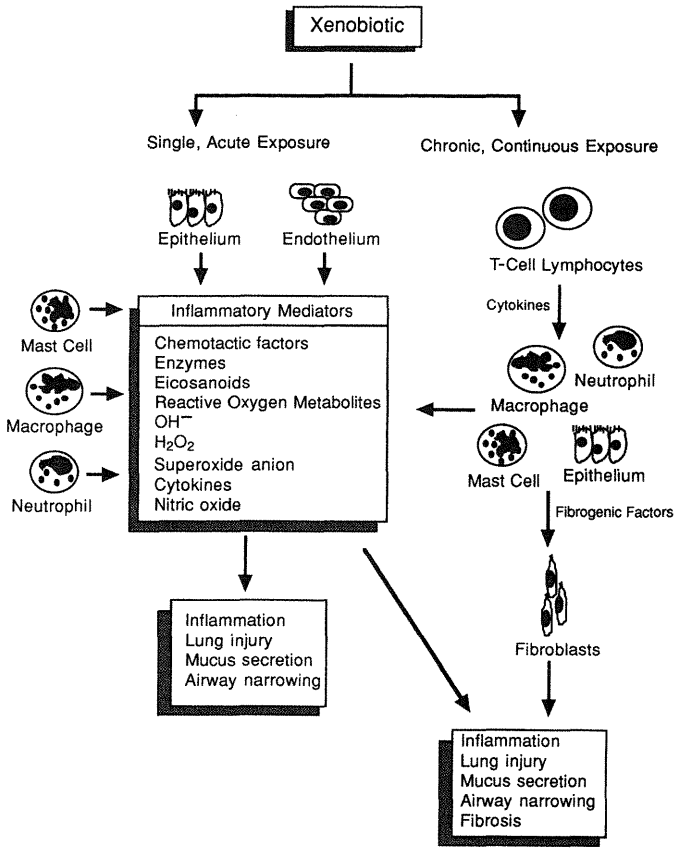

Figure 53-2. Pathways of xenobiotic-induced inflammatory events.

syndrome and other forms of hyperresponsive airways probably represent a spectrum of the same disease process and have as a common basis inflammation of the airway (38–40,47–49).

Another inflammatory syndrome of a nonallergic nature attributed to airborne pollutants is *reactive upper airways dysfunction*. It too has been described after an acute high-level exposure or after chronic low-level exposure to airborne contaminants (43). Reactive upper airways dysfunction is manifested by signs and symptoms of rhinitis (runny nose), nasal stuffiness, eye burning, sinus congestion, facial pain, and severe headache, almost of a migraine nature (see Table 53-3) (37,39,41,43).

Symptoms of bronchial hyperresponsiveness usually begin with cough, chest tightness, and may proceed to shortness of breath and wheezing. Such hyperreactive airways can last for weeks, months, or years, and is managed like asthma (49). Because of the lowered level of sensitivity of individuals with reactive airways or reactive upper airways dysfunction, common indoor air pollutants, such as perfumes, solvent vapors, tobacco smoke, physical irritants, bioaerosols, and irritating cleaning chemicals, can trigger respiratory reactions (49).

An important feature of upper and lower reactive airways is the potential loss of the protective cell surface barrier because of chronic inflammation. The loss of this protective lining increases the airway's susceptibility to chemical irritants and prolongs the disease process (43,49).

Irritant Vocal Cord Dysfunction

Irritant vocal cord dysfunction (IVCD) is a newly recognized medical disorder, often misdiagnosed as asthma (50). Cases of IVCD have occurred after acute high-level occupational or environmental exposures. Vocal cord dysfunction is a disorder of the larynx in which the vocal cords adduct inappropriately during an inspiration or expiration. Signs and symptoms and causes of IVCD are listed in Tables 53-4 and 53-5. The abnormality can occur in inspiration, expiration, or in both phases of the respiratory cycle. Patients with IVCD express a significant increase in chest complaints.

Vocal cord dysfunction often mimics asthma and, therefore, it is important to consider the diagnosis of IVCD in symptomatic patients after irritant exposures to distinguish it from hyperresponsive airways. The pathogenesis of IVCD is not known, but direct inflammation caused by irritants is suggested (50).

Vocal cord dysfunction may be associated with symptoms of panic, depression, and anxiety. Psychopathology can also occur. Chronic symptoms of sinusitis, rhinitis, and voice changes occur and can exacerbate vocal cord dysfunction (50).

The frequency of gastroesophageal reflux disease is higher in IVCD than other causes of vocal cord dysfunction (50). Gastroesophageal reflux disease must be managed appropriately to prevent acid reflux from causing further respiratory irritation and asthmatic episodes. The irritation caused by reflux of gastric acid onto the vocal cords may also have a role in the pathogene-

TABLE 53-4. Clinical criteria for vocal cord dysfunction

Irritant vocal cord dysfunction
Documented absence of preceding vocal cord dysfunction or laryngeal disease
Onset of symptoms after a single specific exposure or accident
Exposure to an irritating gas, smoke, fume, vapor, mist, or dust
Onset of symptoms within 24 h after exposure
Symptoms of wheezing, stridor, dyspnea, cough, or throat tightness
Abnormal direct laryngoscopy for vocal cord dysfunction either in the asymptomatic state, during symptoms, or with a provocative study
Exclusion of other types of significant vocal cord disease
Non-irritant–induced vocal cord dysfunction
Symptoms of wheezing, stridor, dyspnea, cough, or throat tightness
Abnormal direct laryngoscopy for vocal cord dysfunction either in the asymptomatic state, during symptoms, or with a provocative study
Exclusion of other types of significant vocal cord disease
Absence of onset of symptoms after a single specific exposure or accident

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TABLE 53-5. Vocal cord dysfunction–associated symptoms

Symptom	Irritant vocal cord dysfunction	Vocal cord dysfunction	*P* Value
Wheeze	9/11 (82)	26/33 (79)	.83
Cough	11/11 (100)	31/33 (94)	.40
Shortness of breath	11/11 (100)	30/33 (91)	.30
Choking or throat tightness	9/10 (90)	22/26 (85)	.68
Chest pain or chest tightness	6/6 (100)	17/30 (57)	.04
Stridor	4/6 (67)	6/8 (75)	.73
Gastroesophageal reflux	7/10 (70)	19/32 (59)	.55
Voice changes	11/11 (100)	14/16 (88)	.22
Dysphagia	5/9 (56)	8/30 (27)	.44
Rhinosinusitis	8/11 (73)	30/33 (91)	.13

Note: Expressed as number of patients reporting symptom/number of patients for whom the symptom was adequately recorded, with percentage in parentheses.
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sis of IVCD. Gastric acid reflux produces distinct symptoms of hoarseness, persistent nonproductive cough, a sensation of pressure deep in the throat, and a continual need to clear the throat. Causes of IVCD are listed:

Ammonia
Flux fumes
Cleaning chemicals
Odors
Smoke
Organic solvents
Machine fluid
Ceiling tile dust
Sulfur dioxide

The differentiation and correct diagnosis of vocal cord dysfunction are important because therapy for vocal cord dysfunction is different from that for asthma, and patients may benefit from speech therapy to retrain muscles that cause laryngeal dysfunction or biofeedback. Vocal cord dysfunction does not seem to benefit from inhaled corticosteroids, bronchodilators, or leukotriene inhibitors.

VOLATILE ORGANIC CHEMICALS INDOORS AND HEALTH EFFECTS

VOCs are an important category of chemical compounds found in the air of most indoor environments. The term *VOC* defines a mixture of VOCs with highly variable chemical and physical properties. WHO defines classes of VOCs: semivolatile, volatile, and highly volatile. VOCs have melting points below room temperature and boiling points from 50° through 100°C to 240° through 260°C. Studies of volatile organic hydrocarbons found indoors indicate that they are low in concentration, usually in parts per billion or parts per million, but may become more concentrated than in a typical outdoor environment.

Characterization of the quantity and types of indoor air chemical contaminants has been undertaken using gas chromatography-mass spectrometry (GC-MS) in an effort to delineate the chemicals to which humans are exposed. From 50 to 300 VOCs can be detected by air samples in nonindustrial environments, including offices, homes, public buildings, shopping centers, and malls (Table 53-6). VOC sources include building materials, solvents, paints, furnishings, office machines, cleaning materials, human activity, pesticide spraying, and remodeling. In clean environments, the total volatile organic chemical (TVOC) load is much less than 1 mg per m^3, with individual VOCs less than 1% of any recognized exposure standard (11–13,51–54).

TABLE 53-6. Sources of common volatile organic chemicals found in buildings

Compound	Source
1,1,1-Trichloroethane	Carpet glues, aerosol sprays, cleaners, dry-cleaned clothes
Freon	Refrigerators, propellants
Tetrachloroethylene	Dry-cleaned clothes
n-Hexane	Carpet glues, wallpaper, chipboard, insulation foam, smoking, gasoline
n-Heptane	Glass cleanser, traffic
Octane	Paints, tobacco smoke, traffic
Nonane, decane, undecane	Floor adhesives and waxes, paints, cleaners
Dodecane, tridecane, tetradecane	Waxes and polishes of floor
2-Methylbutane, 2-Methylpentane, 3-Methylpentane	Traffic
Dimethyl-cyclopentane, Methyl-cyclopentane, Methyl-cyclohexane	Solvent-based glues and waxes, traffic
2-Methyl-1,3-butadiene	Rubbers, oxidation of volatile organic chemicals
Benzene	Paints, carpet glues, particleboard, tobacco smoke, traffic
Trimethylbenzenes	Floor and wall coverings, paints, floor varnishes and waxes, chipboard, smoking, traffic
Xylenes	Floor covering, adhesives, wallpaper, paints, smoking, traffic
Toluene	Paints, adhesives, lacquer parquet, cleaners, tobacco smoke, traffic
Naphthalene	Antimoth products
Ethanol	Cleaners, varnish, floor covering (linoleum, lacquer)
2-Butoxyethanol	Floor cleaners, paints, wax strippers, and varnish removers
Acetone	Glues, carpets, particleboard, drapes, bioeffluents
Cyclohexanone	Resins, waxes
Benzaldehyde, nonanal, decanal	Cleaners, chipboard, photochemical oxidation of volatile organic chemicals, Tenax
Butyl acetate, ethyl acetate	Floor covering (parquet, PVC flooring)
Acetic acid	Varnishes, silicon sealant
Benzoic acid	Floor detergent
Dodecanoic acid	Wood glue, varnishes
a-Pinene, terpenes	Cleaners, air fresheners, wood products
Limonene	Lemon-scented cleaners, air fresheners, polishes, waxes

PVC, polyvinyl chloride.
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Chemical Emissions from Office Products

Concern over the impact of manufacturing processes and product waste streams on the outdoor environment has resulted in a wide variety of innovations dedicated to the development of sustainable manufacturing and consumption. Manufacturers expend much time and resource implementing programs devoted to pollution prevention, design for disassembly, recycling and reuse of recycled materials, and waste stream minimization. This emphasis on manufacturing and waste stream environments, however, ignores an important environmental niche between manufacture and disposal. That unique environmental niche is the indoor environment surrounding product use. Concern for the outdoor environment has influenced many companies to spend more resources attempting to understand how a product affects a sanitary landfill than on how that same product affects the indoor environment and its human occupants. Although traditional product safety is a major concern for most manufacturers, the impact of a product on the indoor environment is complex.

Although U.S. efforts to minimize air and water pollution have met with measurable success, an increasing public concern exists over a new generation of pollution-related human illness in the office, home, and transportation environments. High-speed printers, copiers, visual display terminals, duplicators, microfiche, and blueprint machines are point sources of indoor contaminants that cannot be disregarded, especially when used in inadequately ventilated facilities. Most modern electronic products emit low levels of volatile organic compounds into the indoor environment. These fugitive emissions arise from plastics, solvents, coatings, adhesives, and encapsulans associated with manufacture, as well as consumable supplies, such as toners, inks, paper, transparency films, and labels.

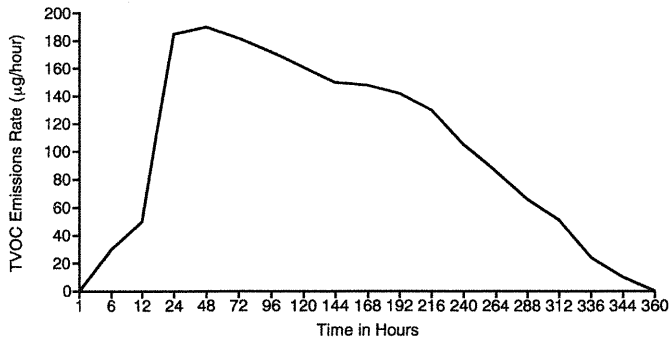

Figure 53-3. Bell-shaped chemical emissions profile from office electronic products. TVOC, total volatile organic chemical.

The newer an item of electronic equipment, the higher may be its potential rate of chemical emissions.

The chemical emission profile of an electronic product is largely dependent on the product itself. Those products that do not consume supplies (e.g., computers and monitors) typically produce a bell-shaped curve of emissions, resulting from a diffusion and evaporation of chemicals left over from manufacture that over time decrease to insignificance (Fig. 53-3). Those products that consume supplies (e.g., printers and photocopiers) typically produce higher levels of emissions, producing a sigmoidal curve that reaches a steady-state emission rate dependent on the supplies used and the duration and frequency of use (Fig. 53-4).

Whether a product's emissions impact significantly an indoor environment depends on two opposing factors: (a) the type and rate of chemical emitted, and (b) the rate and effectiveness of that environment's ventilation.

VOCs, ozone, and particulate emissions from electronic products can be measured in chambers or under field conditions. Clearly, chamber measurement in which variables, such as background VOC concentrations, temperature, humidity, air exchange rate, and mixing, can be controlled yields superior results. It is often impossible, however, to chamber-test certain products because of their size or mobility constraints. When field testing products for chemical emissions, it is essential to know product function and exhaust paths, ambient air VOC profiles, temperature, and humidity.

Whether samples are taken directly from products under field conditions, or are obtained from chamber studies, all sampling and analysis should be performed using validated and traceable techniques. Usually these techniques require GC-MS approaches to allow for the appropriate qualitative and quantitative resolution. Date requirements for product emission analyses include the chemical species involved, their concentration, and the rate at which they are emitted. These data can then be used to perform predictive modeling, formal quantitative risk assessments, and to determine the ventilation requirements associated with product use.

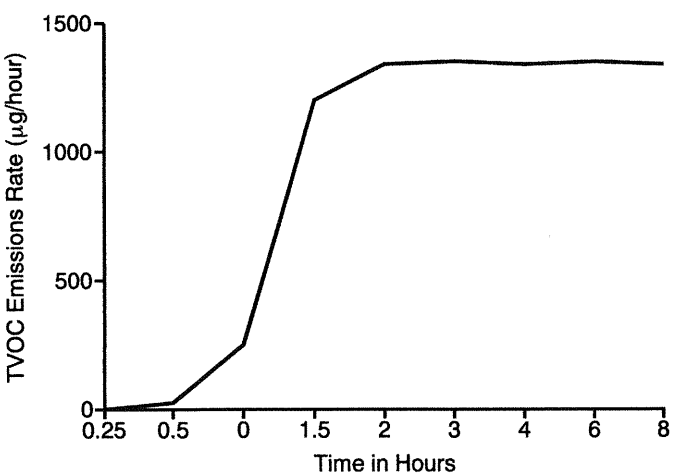

Figure 53-4. Sigmoidal chemical emissions profile from office products that consume supplies. TVOC, total volatile organic chemical.

Office and clerical work environments are common sites where poor indoor air quality frequently occurs (3,10–12,17). These offices are in modern or remodeled buildings and use computers, copiers, fax machines, laser printers, and paper products. They also depend on centrally controlled ventilation systems. Laser printers and copiers sitting in direct sunlight or in unventilated rooms release ozone and volatile irritant chemicals that can accumulate.

Carbonless copy paper is another source of chemical emissions in offices. The undersurface page of carbonless copy paper is coated with microcapsules of ink. The pH inside the capsule is acidic and the pH of the underlying sheets is alkaline. When the microcapsules are burst open by the pressure of writing or typing, the differences in the pHs cause color formation. Carbonless copy paper contains chemical allergens, solvents, and dyes that can produce eye irritation, rashes, and symptoms of respiratory irritation and allergy in office workers (55). Volatile organic chemicals and particulates from carbonless copy paper can accumulate in office environments because of the mass of paper used, handling of paper, filing, and shredding of documents. Adequate ventilation and control of paper dust and fibers can assist in preventing health complaints.

Chemical Emissions from Building Materials

Materials for building, remodeling, and construction vary from wet to dry. Most building products contain chemicals that can be emitted indoors (Table 53-7). Building products emit VOCs indoors at varying rates, and release is affected by volatility, temperature, humidity, air exchanges per hour, air circulation, reabsorbing sinks (reabsorbed by other materials in the environment to be slowly released over time), and air filtration (Table 53-8). Building products can be subdivided into short-term emitters versus long-term emitters.

Many covariables affect human response to low-level volatile chemicals, such as exposure duration, time of day, temperature, and humidity (35,53). Temperature and humidity act additively with the total volatile chemical load indoors to initiate symptoms (35).

Most outgassing of VOCs occurs when the building is new and slowly declines over time with a variety of half-lives, depending on the chemical, environmental factors, and the material. In addition, there may be odors associated with VOCs in a closed environment.

Building material, such as self-leveling-mortar containing casein, has been shown to release trace amounts of 2-ethyl-1-hexenol, ammonia, isoprophylamine, ethylamine, triethylamine, dimethylamine, trimethylamine, and dimethyl sulfide. Amines have been found in the 0.003- to .013-ppm range in indoor air after use of such mortar (56). In addition to the irritant effects from chemical emissions, an objectionable odor occurs because of the casein content of the mortar and possibly texturing materials for ceilings and outgassing of sulfhydryl compounds into the indoor environment (56).

The vapor emissions for building materials can vary from days to months and even up to years for formaldehyde emissions from particle board and pressed wood products (57). Sources of formaldehyde emissions are sealants, mortar, caulking compounds, paints, woods, plastics, vinyl products, foams,

TABLE 53-7. Volatile organic chemical emissions from building materials, interior furnishing, and office equipment

Material	Volatile organic chemicals emitted
Adhesives	Alcohols
	Amines
	Benzene
	Decane
	Dimethylbenzene
	Formaldehyde
	Terpenes
	Toluene
	Xylenes
	Nonane
	Undecane
	Dimethyloctane
	2-Methylnonane
	n-Propylbenzene
	Limonene
	Pinene
Caulking compounds	Alcohols
	Alkanes
	Amines
	Benzene
	Diethylbenzene
	Formaldehyde
	Methylethylketone
	Xylenes
	Butyl propionate
	2-Butoxyethanol
	Butanol
	Toluene
	Acetic acid
	Ethylbenzene nonane
Carpeting	Alcohols
	Formaldehyde
	4-Methylethyl-benzene
	4-Phenylcyclohexene
	Styrene
Ceiling tiles	Alkanes
Chipboard	Amines
Paneling	Benzene
Plywood	3-Carene
Gypsum board	Formaldehyde
Fiberboard	Terpenes
	Toluene
	Acetone
	Hexanol
	Hexane
	Propanol
	Butanone
	Benzaldehyde
	Isopropanol
	3-Methylpentane ethanol
	Methylethylketone
	Ethylbenzene
	n-Propylbenzene
	Limonene
	Pinene
Floor and wall coverings	Acetates
Wallpaper	Alcohols
Linoleum floor covering	Alkanes
Vinyl coatings	Amines
	Benzene
	Formaldehyde
	Undecane
	n-Propylbenzene
	Methyl styrene
	Xylenes
	3-Methylpentane
	Toluene
	Heptane
	Ethylacetate
	Methylethlketone
	Ethylbenzene
	4-Methyl-2-Pentanone
	Dodecane
	Nonane
	1,2,3-Trimethylbenzene
	1,2,4-Trimethylbenzene
Wood stains and varnishes	Acetates
Latex paints	Acrylates
Polyurethane floor finish	Alcohols
Floor lacquers	Alkanes
	Amines
	Benzenes
	Formaldehyde
	Limonene
	Polyurethane
	Toluene
	2-Ethoxyethylacetates
	2-Propanol
	Butanone
	Ethylbenzene
	Propylbenzene
	1,1'-Oxybisbutane
	Butylpropionate
	Nonane
	Decane
	Undecane
	Methyloctane
	Dimethylnonane
	Trimethylbenzene
	n-Butanol
	Hexanol
	Xylene
	Nonane
	Dodecane
Appliances	Carbon monoxide
	Nitrogen dioxide
	Sulfur dioxide
	Polyaromatic hydrocarbons
Computers and video display terminals	*n*-Butanol
	2-Butanol
	2-Butoxyethanol
	Butyl-2-methylpropyl phthalate
	Caprolactam
	Cresol
	Diisooctyl phthalate
	Dodecamethyl cyclosiloxane
	2-Thoxyethyl acetate
	Ethylbenzene
	Hexanedioic acid
	Toluene
	Xylene
Duplicating machines	Ethanol
	Methanol
	1,1,1-Trichloroethane
	Trichloroethylene
Electrophotographic printers	Ammonia
Photocopiers and related supplies	Benzaldehyde
	Benzene
Microfiche developers and blueprint machines	Butyl methacrylate
	Nonanal
	Ozone
	Styrene
	Terpene
	Toluene
	1,1,1-Trichloroethane

(continued)

TABLE 53-7. *(continued)*

Material	Volatile organic chemicals emitted
	Trichloroethylene
	Xylenes
	Zinc stearate combustion products
	Ammonium salts
	Polyolefin wax
	Carbon black
	Styrene-acrylate copolymer
Carbonless copy paper	Chlorobiphenyl
	Cyclohexane
	Dibutylphthalate
	Formaldehyde
	Kerosene
	Diethylethane
	Naphthalene
	Ammonia
Preprinted paper forms	Acetaldehyde
	Acetic acid
	Acetone
	Acrolein
	Benzaldehyde
	Butanol
	1,5-Dimethylcyclo-pentene
	2-Ethyl furan
	Heptane
	Hexamethyl cyclosiloxane
	Hexanal
	4-Hydroxy-4-methyl pentanone
	Isopropanol
	Paper dust
	Proprionaldehyde
	1,1,1-Trichloroethane
Typewriter correction fluids	Acetone
	1,1,1-Trichloroethane
Artificial essences fragrances	Nonane
	Decane
	Undecane
	Limonene
	Aromatic fragrances
	Ethylheptane
Room deodorants and fresheners	Acetaldehyde
	n-Butanol
	Ethylacetate
	Propylacetate
	Isobutylacetate
	Pinene
	Methylchloroform
	Isopropyl alcohol
	Isopropane/isobutane
	Triethylene glycol
	Propylene glycol
	Tertiary butyl alcohol
	Esters
	Terpenes
	Aldehydes
	Alcohols
	Brucine sulfate
	Propylene glycol
	Cyclomenaldehyde
	Benzyloacetate
	Hexanol
	Ether
	Lactones
	Acetols
	Resins
	Essential oils
	Hexylene glycol
	Nonylphenol
	Paradichlorobenzene
Sealants	Acetic acid
	Xylene
	Aliphatic hydrocarbons
	Toluene
	Petroleum hydrocarbons
	Hexane
	Methylethylketone
Cleaning agents and detergents	Pine oil
	Sodium hydroxide
	Ethylene glycol monobutyl ether
	Ethylenediamine tetraacetic acid
	Sodium carbonate
	Polyalkoxylated alcohol
	Sodium metasilicate
	Isopropanol
	Ethyl alcohol
	2-Butoxy ethanol
	Ammonium hydroxide
	Isobutane/propane
	Phosphoric acid
	Phosphates
	Dipropyleneglycol methyl ether
	Diethyleneglycol methyl ether
Glazing compound	Acetic acid
Dry cleaning	Trichloroethylene
	1,1,1-Trichloroethane
	Tetrachloroethylene
New clothing	Formaldehyde
Resins	Butylacrylate
Polymers	
Textile and leather finishes	
Carpet shampoo disinfectant	Pentachlorophenol
Wood preservative	Tetrachlorophenol
Fungicides	Pentachlorophenol
	Hexachlorobenzene
Insulation	Styrene
	Formaldehyde
	n-Propylbenzene pinene
Floor waxes	Trimethylcyclohexane
	α-Terpene
	Ethyltoluene
	o-Ethyltoluene
	m,p-Ethyltoluene
	m-Ethyltoluene
	1,2,3-Trimethylbenzene
	Decane
	Undecane
	Nonane
	Ethylmethylbenzene
	Dimethyloctane
Paint removers	Methylene chloride
Grease cleaner	Carbontetrachloride
Cleaning fluids	Trichloroethylene
	1,1,1-Trichloroethanol
	Ethylbenzene
	Xylene
	Undecane
Paint and lacquer solvents	Chlorobenzene
	Toluene
	Trichloroethylene
	Acetone
	Cyclohexane
	Xylene
	n-Butylbenzene
	Naphtha
Deodorizers	*o*-Dichlorobenzene
Moth balls	*m*-Dichlorobenzene
	p-Dichlorobenzene

(continued)

TABLE 53-7. *(continued)*

Material	Volatile organic chemicals emitted
Moulding tape	Toluene
Edge sealing	Isobutanol
	n-Butanol
Jointing compound	Ethylbenzene
	Styrene
	Xylene
	n-Butanol
	Isobutanol
	Formaldehyde
	Toluene
	Nonane
	1,2,4-Trimetholbenzene
Heaters	Formaldehyde
Unvented gas heaters	Carbon monoxide
Unvented gas ovens	
Carpet—latex backed	Formaldehyde
	Xylene
	4-Phenylcyclohexene
Plastics	Propylacetate
	Dibutylphthalates
Carbon paper	Mineral oil
	Stearic oil
	Oleic oil
	Carbon black
	Nigrosine
	Methyl violet
	Crystal violet
	Victoria blue
Paints	Waxes
	2-Ethyl-hexyl-acrylate
	N-Methylol-acrylamide
	Pentaerythritol triacrylate
	Trimethylpropane triacrylate
	Tripropulene glycol triacrylate
	Ethoxyethanol
	Ethoxyethylacetate
	Butylacrylate
	Epoxy acrylate
	Ethyl acrylate
	Titanium dioxide
	Latex

paper products, and insulation material. New homes release VOCs over a period of months, with a high concentration occurring immediately (Fig. 53-5) (Table 53-9) and then tapering off over a few months, with low levels persisting for years (57). Formaldehyde concentrations, however, tend to fluctuate, with higher indoor emissions occurring in warmer months (Fig. 53-6).

Human Studies of Volatile Organic Chemicals Indoors

Indoor air monitoring of homes and buildings free of health complaints show TVOC averaging much less than 1 mg per m^3 (11–13,51,53,54). These sites usually meet ASHRAE standards (62-1999) for ventilation, and health complaints are uncommon.

Human studies indicate that the average TVOC concentration in homes with indoor air quality problems ranges between 0.09 mg per m^3 and 13 mg per m^3 (11–13,51,53,54). Those with no problems average 0.36 mg per m^3, and range from 0.02 mg per m^3 to 1.7 mg per m^3. Human chamber studies show a TVOC threshold range for test subjects initiating symptoms between 0.2 mg per m^3 and 3 mg per m^3 (11–13,51,53,54). At a TVOC concentration more than 3 mg per m^3, discomfort and health complaints occur in test subjects (11–13,51–54). There were no health effects in test subjects at exposures less than 0.2 mg per m^3. At levels of 5 mg per m^3, objective and subjective health effects occurred. TVOC exposures of 8 mg per m^3 for 50 minutes caused irritation of mucosal membranes of the eyes and upper airways (11–13,51,53,54). Five human studies document sensory and neurobehavioral effects secondary to low levels of volatile chemicals indoors (51) (Table 53-10).

Headaches, neurobehavioral, and neurologic symptoms are noted in human test subjects at TVOC concentrations between 3 mg per m^3 and 25 mg per m^3 after an exposure of a few hours (51). Neurobehavioral performance tests confirm symptoms of drowsiness, fatigue, confusion, headache, and decreased attention occurring in subjects. Psychological performance tests indicate exposure-related impairment to learn new facts (51,53).

Neurologic symptoms associated with poor indoor air quality are puzzling and do not occur in every case of indoor air contamination. But in controlled human exposures, low-level mixtures of VOCs commonly found in indoor environments seem to be able to cause symptoms of irritancy and deficits in alertness, memory, and cognitive performance problems at concentrations below OSHA regulatory levels (51). A tendency to a stronger response in these studies was seen among prior SBS patients. Confusion, memory deficits, fatigue, drowsiness, and headache were associated with exposure to TVOC concentrations between 3 mg per m^3 and 25 mg per m^3 for only a few hours in test subjects (51), but seem to occur most often at the higher levels.

Overall, in most indoor environmental quality cases of the authors' experiences, neurologic symptoms usually tend to reverse quickly on leaving the contaminated environment. In some affected people, however, symptoms persist for no clear or plausible explanation. Theoretically, neurologic symptoms, such as fatigue and lethargy, might be explained by the action of inflammatory cytokines on the brain, but this remains to be proven (58,60).

Headache, fatigue, depression, anxiety, and chronic activation of the autonomic nervous system are adverse effects of chronic stressors of different varieties (61,62). Poor indoor air quality may also be acting as a chronic environmental stressor to cause such effects. Environmental exposures that escalate stress, to which people maladapt, may cause depression, irritability, mood alterations, difficulty concentrating, or difficulty sleeping (59,61,62). Identifying symptoms that are stress related and separating these from neurobehavioral toxicity require sophisticated neuropsychological testing.

Clinical cases report chronic fatigue and repeated respiratory infections associated with fungal contamination indoors (63). Airborne fungi and spores may incite inflammation via the 1,3-β-glucan component of their cell walls or release of VOCs (64). Thus, some environmental contaminants might serve as chronic stressors via activation of inflammation and activation of stress areas in the brain.

TABLE 53-8. Sources that emit volatile organic chemicals indoors at varying rates

Source	Volatile organic chemicals emitted	Rates $\mu g/m_2$
Building materials		
Plywood	Formaldehyde, terpenes, methylacetate, *n*-butanol, tetrachloroethylene, toluene, nonanol, *n*-undecane, tetradecane, naphthalene, *p*-dichlorobenzene, xylenes	40–2,400
Polystyrene foam	Styrene, ethylbenzene, aromatics	30–1,400
Rubber-backed nylon carpet	Toluene, benzene, *n*-decane, 4-phenycyclohexane	50–300
New vinyl flooring	Iso-alkanes, methylbenzenes, xylenes, ethylbenzene, toluene, 2-ethylhexanol, formaldehyde	120–43,000
Rubber floor covering	1,1,1-Trichloroethane, styrene, indene, 1,3/1,4-diisopropylbenezene, isodecane, acetophenone	410–1,400
Solvents and adhesives		
Solvent-based adhesives	Toluene, styrene, *n*-decane, *n*-undecane, cyclohexane, methylcyclopentane, alcohols	$5.1–16.5 \times 10^6$
Water-based adhesives	Nonane, decane, undecane, octane	$<10^4–2.1 \times 10^6$
Wall and flooring adhesive	Toluene, benzene, ethylacetate, styrene, ethylbenzene	2.5×10^6
Sealants	Methylethylketone, butylpropionate, 2-butoxyethanol, butanol, benzene, toluene	300–72,000
Wood stains	Nonane, decane, undecane, methyloctane, dimethylnonane, trimethylbenzene	17,000
Polyurethane varnish	Nonane, decane, undecane, methylethylketone, ethylbenzene, xylene	6,000
Solvent-based waxes and detergents	Alkanes, alkenes, terpenes	$<260 \times 10^6$
Water-based waxes and detergents	Alcohols, esters, alkoxyalcohols, terpenes, alcohols and acetates	1.2×10^5 to 1.2×10^6
Deodorizers	Nonane, decane, undecane, ethylheptane, limonene	$1.3–3.7 \times 10^6$
Liquid cleaner and disinfectant	Limonene, *p*-cymene, undecane, α-pinene, heptene, decane, nonane, heptane	1.1×10^6

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Another study in nonsmoking adult volunteers with nonspecific bronchial reactivity who were exposed to VOC mixtures at zero, 2.5 mg per m^3, and 25 mg per m^3 showed a decline in forced expiratory volume in one second at 25 mg per m^3, a VOC concentration not uncommonly found indoors (65). Such findings support an inflammatory basis for the respiratory effects seen.

Other studies exposed subjects to VOC concentrations of 10 mg per m^3 of different compounds common to indoor air, controlling for humidity, air changes, skin temperature, air temperature, and exposure duration (51,53,54). These studies included measuring swelling of the nasal cavity, detection of odor, tear film stability, and examination for inflammatory cells in tear secretions of subjects. The results showed subjects experienced inflammation from exposures lasting more than 60 minutes, which was most pronounced at usual indoor temperatures (51). These subjects perceived air quality deterioration when the VOC concentration reached 8 mg per m^3, causing dryness, itching, burning of the eyes, and upper airway irritation. As the concentration increased, the adverse responses increased. Neurobehavioral and neurologic effects of confusion and fatigue occurred at TVOC concentrations of 25 mg per m^3 after an exposure lasting 3 and one-half hours. Thus, VOC exposure and air temperatures appear to be interdependent variables contributing to symptoms, and reduction of indoor temperatures can sometimes reduce VOC-related symptoms (51).

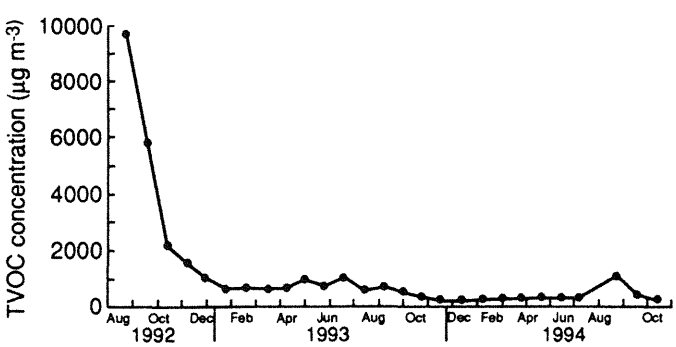

Figure 53-5. Total volatile organic chemical emissions profile from new home. TVOC, total volatile organic chemical. (From ref. 57, with permission.)

One double-blind study used 21 healthy subjects in comparison with a group of 14 subjects who had prior symptoms of SBS (53). The individuals who had prior symptoms had a tendency toward strong responses when exposed to low-level VOCs. Those with prior symptoms had exposure-related reductions in pulmonary functions, and both groups had an increased number of inflammatory cells in their tear fluids. Psychological performance tests indicated that the higher-exposure group had impaired ability to learn. The study concluded that low-level VOC exposure causes subjective complaints and objective effects in normal, healthy subjects, but more so in subjects who have had prior symptoms of SBS (53). Studies such as these demonstrate that the TVOC load in the environment probably plays an important role in initiating health complaints in a dose-related manner.

Gasoline refueling and driving expose people to VOCs in a confined environment (66). During refueling, the average TVOC in six studies ranged from 50 mg per m^3 to 150 mg per m^3. Gasoline emissions included *n*-pentane, *n*-butane, toluene, *m*- and *p*-xylene, and benzene. Main tailpipe emission of VOCs are methane, toluene, ethylene, *m*- and *p*-xylene, *n*-butane, and benzene (66). Inside automobiles, the VOC concentrations measured while driving were toluene (26 µg per m^3 to 56 µg per m^3), xylene (16 µg per m^3 to 23 µg per m^3), methylpentane (4 mg per m^3 to 18 mg per m^3), and benzene (9 µg per m^3 to 11 µg per m^3) (67,68).

In summary, symptoms of SBS appear to be able to be initiated in susceptible individuals when the total VOC concen-

TABLE 53-9. Whole house concentration (μg/m^{-3}) of total volatile organic chemicals during the first and second year

		Year 1 (August 3, 1992–August 3, 1993)			Year 2 (August 3, 1993–August 3, 1994)		Summer (March 16, 1993–September 28, 1993)	Winter (September 28, 1993–March 15, 1994)
House	Chemical	Mean	Max	Min	Mean	RSD (%)	Mean	Mean
1	TVOC	1,938	8,270	635	362	75	808	200
	Benzene	27	149	3	4	24	4	4
	Toluene	19	88	3	6	40	6	6
	Xylenes	81	289	59	25	59	42	16
	Undecane	75	261	32	18	61	34	10
	HCHO	59	122	29	42	33	63	37
2	TVOC	1,603	6,472	648	315	57	500	203
	Benzene	5	9	3	5	22	3	4
	Toluene	12	38	4	6	42	6	6
	Xylenes	64	227	32	21	48	36	15
	Undecane	70	276	32	17	54	33	11
	HCHO	51	91	28	37	48	52	28
3	TVOC	1,429	5,179	531	363	67	939	272
	Benzene	8	35	3	7	36	4	5
	Toluene	10	31	3	36	290	4	6
	Xylenes	30	94	14	20	136	19	8
	Undecane	57	176	26	16	59	39	10
	HCHO	41	106	17	40	43	53	30
4	TVOC	1,954	5,660	863	896	61	1,578	802
	Benzene	8	39	3	4	32	5	4
	Toluene	12	32	5	7	42	9	7
	Xylenes	33	85	16	45	183	25	26
	Undecane	82	202	41	37	61	70	31
	HCHO	43	111	15	45	45	59	35
Outside	TVOC	71	150	7	37	40	31	43
	Benzene	6	11	3	5	33	4	4
	Toluene	9	18	3	6	53	6	6
	Xylenes	7	11	4	4	40	4	5
	Undecane	4	24	6	1	20	2	1
	HCHO	3	5	2	2	63	3	2

HCHO, formaldehyde; RSD, relative standard deviation (i.e., standard deviation expressed as percentage of mean); TVOC, total volatile organic chemical.
Reprinted from ref. 57, with permission.

tration rises more than 3 mg per m^3 indoors (13,36,51,53,54). As the TVOC levels approach 25 mg per m^3, headache, psychological effects, fatigue, and adverse neurobehavioral effects are reported. Individuals with prior symptoms of SBS seem to have a tendency toward a stronger response in these studies. Thus, these studies provide guidelines for TVOC concentrations indoors that are associated with symptoms (Table 53-11). To relate TVOCs indoors to symptoms, however, it is important to convert TVOC measured in parts per million into mg/m^3 using the formula:

$$\text{mg/m}^3 = \frac{\text{ppm (molecular weight)}}{24.45}$$

Conversion of ppm to mg/m^3 allows the comparison of total VOC environmental contaminants using their average molecular weight to guidelines provided by human studies.

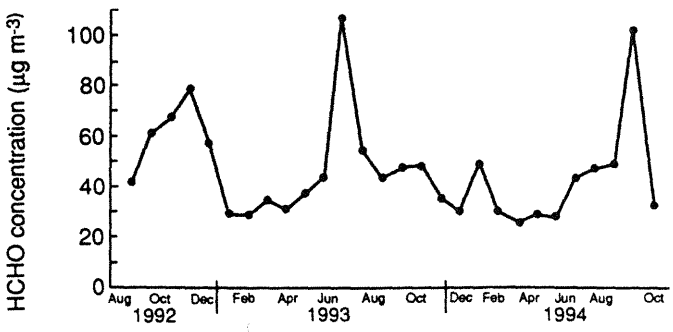

Figure 53-6. Formaldehyde concentrations indoors in newly built homes. HCHO, formaldehyde. (From ref. 57, with permission.)

Analysis of Volatile Organic Chemical Emissions Indoors

Monitoring of VOCs indoors is accomplished by a variety of techniques discussed extensively in Chapter 3. Some investigations of building-related illness include an approach termed *fingerprinting*, using GC-MS to characterize the chemicals in indoor air. Such techniques are used to identify potential chemical causes of airborne contamination and illness as distinct from background chemicals not causing illness. Such monitoring can also help determine the effectiveness of remediation activities.

Indoor VOC analysis in homes typically shows VOCs to be 10 times higher than those outdoors (57). Studies in homes show a variety of VOCs, from 85 detectable peaks up to 120 detectable peaks (57). VOC emissions and formaldehyde emission in homes studied are shown in Figures 53-5 and 53-6.

TABLE 53-10. Summary of five low-level indoor volatile organic chemical exposure experiments

Exposure		Population			
Type	mg/m³	Type	Number of subjects	Measure of effects	Reference
Twenty-two volatile organic compounds	0, 5, 25	Randomly selected but sick building syndrome–sensitive	64	Subjective sensory responses, indications of neurologic effects, and changes in eye and nose liquids	1
Twenty-two volatile organic compounds	0, 1, 3, 8, 25	Randomly selected and healthy	25	Sensory symptoms, headache, and general well-being	2
n-Decane	0, 40, 140, 400	Random, healthy	63	Sensory symptoms, tear film stability, leukocytes in eye liquids	3
Twenty-two volatile organic compounds	0, 25	Healthy Sick building syndrome subjects	21 14	Sensory symptoms, lung function Leukocytes in eye liquids and nasal secretions, performance	4
Twenty-two volatile organic compounds	0, 25	Healthy males	76	Sensory symptoms, neurobehavioral tests	5

1. Molhave L, Bach B, Pedersen OF. Human reactions to low concentrations of volatile organic compounds. *Environment International* 1986;12:167–175.
2. Molhave L. The sick building syndrome (SBS) caused by exposures to volatile organic compounds (VOCs). In: Weekes DM, Gammage RB, eds. *The practitioner's approach to indoor air quality investigations*. Akron, Ohio: American Hygiene Association, 1990a.
3. Kjaergaard SK, Molhave L, Pedersen OF. Human reactions to indoor air pollutants: *n*-decane. *Environment International* 1989;15:473–482.
4. Kjaergaard SK, Molhave L, Pedersen OF. Human reactions to a mixture of indoor air volatile organic compounds. *Atmospheric Environment* 1991;25A:1417–1426.
5. Otto DA. Neurotoxic effects of controlled exposure to a complex mixture of volatile organic compounds. Research Triangle Park, NC: US Environmental Protection Agency, 1990. USA.EPA/600/1-90/001.

Adapted from ref. 51, with permission.

Basically, most materials tested in homes emitted VOCs. Major chemical classes of emissions found in chamber tests were C_9 to C_{14} aliphatic hydrocarbons, C_5 to C_{10} aldehydes, toluene, xylene, terpenes (α-pinene, limonene, carene), naphthalene, ethylacrylate, texanol (paints), 2,2,4-trimethyl-1,3-pentanediol (flooring materials), 4-methyl-2-pentanone, camphene, nonane, dichloromethane, pentane, 1,2,3,5-tetramethylbenzene, hexanal, pentanal, ethylbenzene, 4-ethyl-1-methylbenzene, undecane, limonene, terpinene, 1-methylnaphthalene, biphenyl, acenaphthene, and styrene (56).

Also, the composition of VOC mixture and emission rates change with time. Timber and woods are long-term sources of terpenes and aldehydes. Wood used for framing maintained a high VOC emission rate for 2 weeks (57). The TVOC emission profile is used to classify materials as short-term or long-term emitters and as high, moderate, or low VOC emitters (57) (Table 53-12):

- High emitters: TVOC 100 mg/m²/hour
- Moderate emitters: TVOC 10 mg/m²/hour
- Low emitters: TVOC 0.01 mg/m²/hour

TABLE 53-11. Signs and symptoms of sick building syndrome correlated with volatile organic chemical concentration

Total volatile organic chemical concentration (mg/m³)	Health effects
0–0.3	Clean environment
0.3–3	Odors, threshold for health complaints
3–10	Discomfort, irritation, inflammation, headache
10–25	Neurologic symptoms

It is important to be aware that the multiplicity of environmental factors, such as temperature, humidity, ventilation, air exchanges, the location and nature of the building material, and sinks, all influence VOC emissions and TVOC airborne concentrations in the indoor environment.

GC-MS fingerprinting can also be used to determine whether removal of a chemical source is associated with abatement of health effects. An example of this approach is shown by a case

TABLE 53-12. Classification of materials based on rate of volatile organic chemical emissions

Long-term volatile organic chemical emitters		
High	**Moderate**	**Low**
Water proof bituminous emulsion	Waterborne emulsion paints, putty, treated timber	Vinyl flooring, carpet, underlay, chipboard, bituminised fiberboard, asphalt, plywood, untreated timber
Short-term volatile organic chemical emitters		
High	**Moderate**	**Very low or not detectable**
Spray-on adhesive, acrylic adhesive, wood stain, gloss paints and undercoats, caulk	Foam sealant	Plasterboard, polyvinyl chloride skirting board

Adapted from ref. 57, with permission.

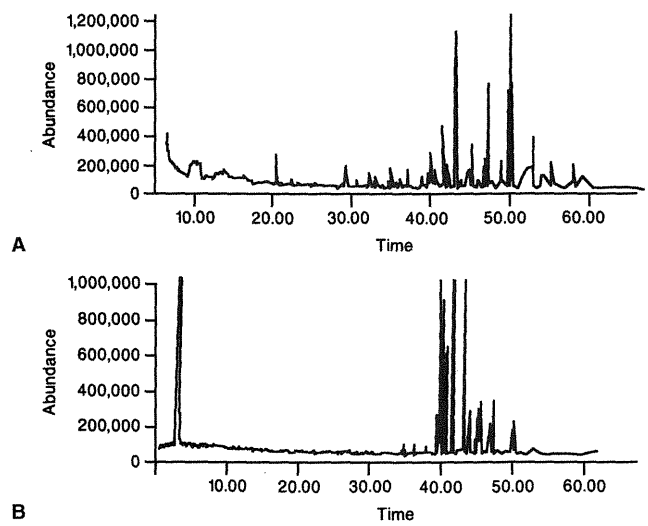

Figure 53-7. A: Identification of solvent in indoor air by gas chromatography–mass spectrometry. Air samples were collected in stainless steel canisters. A pesticide with a solvent-based carrier had been applied outside the home next to an exterior wall, and the occupants were experiencing irritant symptoms. **B:** Gas chromatography–mass spectrometry fingerprint of the solvent used with the pesticide confirms similar pattern to the samples collected indoors.

involving the presence of a solvent diluent of a pesticide that was injected along the perimeter of one area of a home. Indoor air samples collected in stainless steel canisters revealed a GC-MS fingerprint pattern similar to that of the solvent carrier. The presence of this petroleum solvent (Fig. 53-7A and B) was associated with irritant symptoms in the occupants. Attempts at remediation resulted in reduction of indoor air concentrations of the solvent after removal of exterior wall dirt where the pesticide was sprayed (Fig. 53-8A). Finally, cleaning the contaminated air return of the ventilation system resulted in almost total elimination of the airborne solvent as well as relief of health effects (Fig. 53-8B).

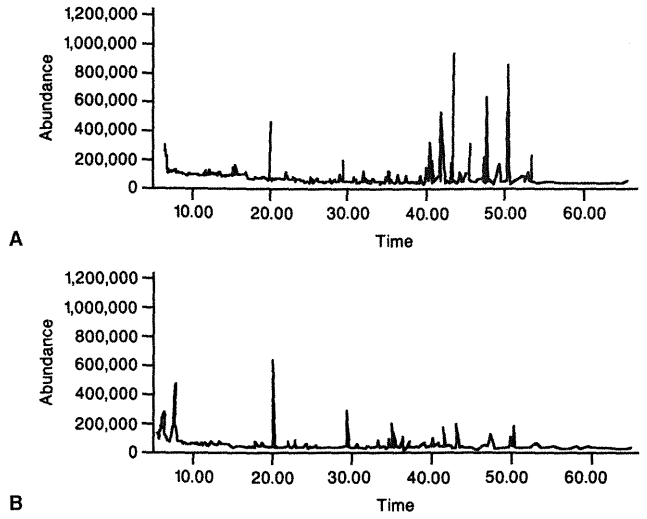

Figure 53-8. A: Repeat sampling results of the indoor air after removal of exterior wall soil contaminated with the pesticide and solvent. Results show failure to remediate contamination of the indoor air. **B:** Gas chromatography–mass spectrometry pattern demonstrates that cleaning of ventilation air duct returns in addition to removal of the exterior wall soil resulted in effective elimination of the air contaminant.

Volatile Organic Compounds in Human Blood

Human exposure to volatile chlorinated organic chemicals may result in low plasma concentrations of VOCs (69). Blood concentrations of volatile halogenated compounds may be higher in winter months, when residents spend most of their time indoors. Interpreting such plasma concentrations of organic chemicals is difficult in relationship to health complaints. The presence of such hydrocarbons in low concentrations is indicative of exposure from a wide variety of sources or environments, but does not necessarily constitute the existence of disease.

Sample collection can be a source of error in measuring VOCs in human blood. Studies show that VOC contaminants can be introduced into blood collection tubes (69). Studies have been performed to determine background VOC blood concentrations of nonoccupationally exposed individuals. Exposure to gasoline, tobacco smoke, and other sources of VOCs can account for levels in the parts per billion to parts per trillion range (69).

NEW CARPET

A variety of chemicals may volatilize from new carpets and the adhesives used to attach carpet to floors. The distinctive new carpet odor has been traced to the chemical 4-phenylcyclohexene (4-PC) (70,71). The source of 4-PC is styrene-butadiene rubber latex used to bind the backing of new carpet (Fig. 53-9). Production of styrene-butadiene rubber latex results in the formation of 4-PC as a chemical by-product via the Diels-Adler reaction. When isolated, 4-PC is a clear, oily liquid, possessing the distinctive new carpet odor (70,71).

Analysis of carpet pieces demonstrated that 4-PC was a common contaminant in several environments reported to cause health effects after new carpet had been installed (70,71). Acute and subacute exposure to low parts per billion of 4-PC may be responsible for symptoms of headaches, lethargy, and skin and mucous membrane irritation (72) (Table 53-13).

Air monitoring in office and home environments for 4-PC has revealed concentrations ranging from 0.3 to 40 parts per billion (ppb) (70,71). Data suggest that 4-PC air concentrations decay over several months from a high of 30 ppb to 1 or 2 ppb after carpet installation. Airborne concentrations of 5 ppb are odiferous. 4-PC concentrations less than 1 ppb have not been associated with illness after installation of new carpet in homes and work environments.

Studies of total VOC release from new carpet installation show a decline from the day of installation of approximately 11 mg per m^3 to approximately 1 mg per m^3 by 10 days (70,71). These TVOC levels exceed concentrations known to produce health complaints.

An investigation of an office space in which 21 of 34 workers complained of health effects showed 4-PC present as an air contaminant at 1.9 ppb as well as a variety of VOCs from the adhesive used to glue the carpet to the floor (72). Formalde-

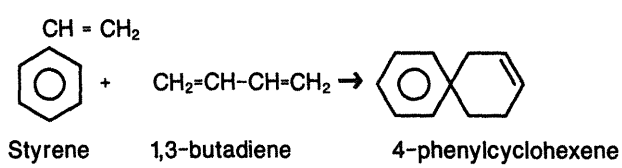

Figure 53-9. Diels-Alder reaction of styrene with 1,3-butadiene to produce 4-phenylcyclohexene as a by-product of styrene-butadiene rubber production.

TABLE 53-13. Signs and symptoms in 21 of 34 workers with 1.9 parts per billion of 4-phenylcyclohexene plus other volatile organic chemicals in the environment

Signs and symptoms	Number of workers	Percentage
Headache	14	67
Throat soreness	11	52
Fatigue and lethargy	10	48
Upper airway irritation	7	48
Nausea	10	48
Ocular irritation	8	38
Dizziness	6	29
Chest tightness	6	29
Skin irritation	5	24
Visual disturbance	5	24
Unusual taste	4	19
Myalgias	4	19
Shortness of breath	3	14

Sullivan J, Van Ert M, Krieger G. Indoor air quality and human health. In: Sullivan J, Krieger G. *Hazardous materials toxicology: clinical principles of environmental health.* Baltimore: Williams & Wilkins, 1992.

hyde, detected at 0.03 ppm, was not considered to be a source of worker illness. New carpet had been installed in this work area 1 week before employees moved into the site. No other source of indoor air pollution was found. Chemical odors were noted by the majority of workers occupying the site almost immediately. Within a few weeks of occupancy, health complaints were registered by the majority of the employees. The first indication of a health problem occurred when one of the workers presented to an emergency department with severe headache, vomiting, and upper airway irritation. The patient reported that headaches and nausea began within 3 weeks of moving into the new building. The patient also complained of ocular and skin irritation. These symptoms lessened during off-work hours. Surveys revealed 21 of the 34 workers (62%) occupying the building site had adverse health effects (see Table 53-13).

Of the 21 patients with symptoms, 10 described some form of past allergic condition, such as hay fever or seasonal rhinitis. The other 11 had no previous allergic manifestations. Smoking was not allowed in the work site, and six of the 21 affected workers were smokers. The building was a one-story modular type with a large open area partitioned into smaller cubicles. The area housed clerical staff with video display terminals used in the previous work area. The entire work area was open except for two administrative offices.

The illness experienced by these employees is similar to that seen in other building-related illnesses with the exception of more pronounced headaches and lethargy. Headaches (67%) and lethargy (48%) may be the result of central nervous system effects of 4-PC at low air concentrations. Prominent mucous membrane irritant effects were also apparent; sore throat (52%), eye irritation (38%), chest tightness (29%), upper airway irritation (48%), cough (24%), and skin irritation (24%) accounted for a large number of complaints, indicating the irritant nature of the mixed chemical exposure.

It is evident that 4-PC may be a chemical that could pose significant health effects for office workers and homeowners exposed to new carpet emissions. The extent of these health effects is not entirely known, but appears to be similar to other indoor air pollutants except that clinical symptomatology occurs in the low parts per billion range. 4-PC decays over several weeks to months in the indoor environment and even after 3 to 6 months may be detected in the 1 to 2 ppb range. The level of this compound can be reduced in the indoor environment by steam cleaning carpet and simultaneously improving ventilation. Explanation to workers of the expected health effects along with assurance that this and other chemicals can be removed from the environment should be part of the management plan.

Such factors as where samples are taken may cause variability in measurements when assessing health complaints. Steam cleaning new carpet along with improving ventilation can reduce vapors to a tolerable level for most people.

CLEANING AGENTS AND DISINFECTANTS

Many cleaning agents and disinfectants can contribute to poor indoor air quality. Material data sheets for these agents should be available. Cleaning agents and disinfectants contain a variety of irritating and sensitizing chemicals that can cause eye irritation, respiratory irritation, exacerbate reactive airways symptoms, cause dermatitis, and may cause asthma. Irritant chemicals in disinfectants and cleaning agents are as follows:

- Benzalkonium chloride
- Benzoyl peroxide
- Isopropanol
- Formaldehyde
- Glutaraldehyde
- Phenol
- Alcohols
- Chlorine compounds
- Potassium permanganate
- Free iodine
- Povidone iodine
- Thimerosal
- Gentian violet
- Hexachlorophene
- Chlorhexidine
- Phenylphenol
- Ethyl alcohol
- Ethylenediamine tetraacetic acid
- Quaternary ammonium chlorides
- Cationic detergents
  - Octyldecyldimethyl ammonium chloride
  - Dioctyldimethyl ammonium chloride
  - Didecyldimethyl ammonium chloride
  - *n*-Alkyldimethylbenzyl ammonium chloride
- Nonionic surfactants
- Sodium metasilicate
- Fragrances
- Colorants

The use of these agents in poorly ventilated areas or on large surfaces in enclosed spaces may result in exposure of occupants to low levels of sensitizers, such as quaternary ammonium compounds, surfactants, and alkyl benzyl ammonium chloride. Contact and allergic dermatitis may occur after exposure to some chemicals in these products. Also, chronic exposure may cause bronchial hyperresponsiveness and airway inflammation.

Disinfectants and cleaning products can be responsible for chemical odors in addition to being a source of respiratory irritation. Chemicals in these products are amines, surfactants, cationic and anionic detergents, ammonia, acids, hypochlorites, phenols, alcohols, and caustics. Substituting these cleaning agents for less irritating agents can be helpful in eliminating indoor pollution sources.

INDOOR COMBUSTION SOURCES

Natural gas is used by approximately 50% of households, potentially exposing occupants to by-products of combustion. Besides gas appliances, other combustion sources are fireplaces, tobacco smoke, cooking, internal combustion machines, and charcoal fires. Pilot lights, cooking, and gas appliance use contribute to nitrogen dioxide indoors, a respiratory irritant. Common pollutant by-products of combustion are the following:

Nitrogen dioxide
Sulfur dioxide
Formaldehyde
Carbon dioxide
Soot
Particulates
Volatile organic compounds

If wood stoves or coal stoves are not airtight, pollutants can escape indoors. Airflow patterns indoors may be altered, causing backdrafting of combustion by-products. Faulty design of fireplace flues can result in emission backdrafting.

CARBON MONOXIDE AND VEHICLE EXHAUST EMISSIONS

The most serious health threat from combustion is carbon monoxide. Thousands are seriously injured and killed yearly by this insidious poison. The following are carbon monoxide sources:

Automobile exhaust
Combustion processes
Gas stoves
Wood or coal stoves
Fireplaces
Tobacco smoke
Charcoal cookers
Space heaters
Gas hot water heaters, unvented
Unvented gas furnace
Methylene chloride in paint remover

Intake vents located in loading docks, garages, or busy traffic areas can bring outside exhaust pollutants indoors. Buildings with many story levels may have a negative air pressure on the lower floors as compared to upper floors, which causes exhaust pollutants from outdoors to be drawn inside the lower levels.

Improperly ventilated natural gas appliances contribute to concentrations of carbon monoxide, nitrogen oxides, and formaldehyde indoors. Inefficient and improperly ventilated natural gas appliances have resulted in cases of carbon monoxide poisoning in the home. Charcoal grills release high levels of carbon monoxide indoors and can be particularly dangerous in small spaces.

Carbon monoxide is a deadly gas that is odorless, colorless, and heavier than air. It can quickly fill a small space, such as a mobile home or bedroom. Mild toxicity produces headache, nausea, dizziness, and drowsiness that tend to influence a person to fall asleep, not allowing escape from the deadly gas (Table 53-14).

Carbon monoxide poisoning may elude diagnosis because it mimics other illnesses, like gastroenteritis. Carbon monoxide exposure should be expected if more than one person in a household is sick with similar symptoms, especially if a gas heater or space heater has been recently turned on because of cold weather.

TABLE 53-14. Carbon monoxide poisoning: signs and symptoms with increasing levels in blood

Level of carbon monoxide in blood (%)	Signs and symptoms
10–20	Headache, shortness of breath
20–30	Severe headache, dizziness, nausea, vomiting, difficulty concentrating
30–40	Lethargy, fainting on exertion, visual and auditory disturbance, dizziness, chest pain, fainting
40–50	Rapid heart rate, fainting, heart attack, seizures
50–60	Coma, brain damage, cardiac arrest
70 or more	Death

FORMALDEHYDE

Formaldehyde is a common indoor contaminant and a known upper airway, eye, and skin irritant. Formaldehyde exposure has become such a concern that OSHA issued a new formaldehyde standard in 1993 for medical evaluation of exposed workers. OSHA set the permissible exposure limit (PEL) for formaldehyde at 0.75 ppm in 1993.

Formaldehyde has many sources: carpet, fabrics, pressed wood products, tobacco smoke, phenolic resins, plywood and binders in fiberglass insulation, cosmetics, food, and combustion by-products. In studies, formaldehyde airborne concentrations in homes ranged from 0.1 ppm to 0.5 ppm, with an average of 0.07 ppm (73–75).

Formaldehyde is a colorless gas at room temperature, but also can be found in a liquid or solid form. Low concentrations of formaldehyde are present in ambient air, primarily because of burning of petroleum fuels and automobile exhaust.

Formaldehyde emissions indoors from building materials is in the following order of decreasing emission rate: chipboard, carpet, plywood, plasterboard, bituminised fiberboard, 15-mm plywood, mineral wool insulation, and curtains (57).

Formaldehyde releasers are used as preservatives in many commercial products, including cleaning agents, shampoos, soaps, paints, lacquers, cutting oils, cosmetics, coloring agents, skin care products, toilet cleaners, automotive cleaning agents, disinfectants, dishwashing liquids, and descaling agents (Table 53-15).

It is impossible to escape formaldehyde exposure because it is contained in a normal diet. Smoked foods and foods prepared on grills can have high concentrations of formaldehyde, up to 1,000 ppm. Formaldehyde is common in fruit, such as apples and tomatoes, and is found in dairy products, vegetables, baked goods, and food preservatives.

The hazards of formaldehyde are mainly from inhalation and dermal contact. General exposure occurs through the use of formaldehyde-containing products, burning fuels, tobacco smoke, or formaldehyde releases as preservatives. Formaldehyde in the air at a home or work arises from burning of organic fuel, such as wood, coal, natural gas, oil, and gasoline or diesel fuel. Resins used as glues and adhesives in the manufacturing of wood products, such as furniture and paneling, are prime sources of formaldehyde. Formaldehyde is also used in the manufacture of carpets and permanent pressed clothing. Sidestream tobacco smoke is said to contain up to 40 ppm of formaldehyde (76).

Health effects from formaldehyde include upper airway irritation and eye irritation. Symptoms of throat irritation, fatigue, headache, eye irritation, and nausea have been reported in indoor air concentrations of formaldehyde between 0.1 and 1.0 ppm (74,75). The respiratory irritation threshold and ocular irritation threshold are 0.8 to 1.0 ppm (74,75). Because of formaldehyde's water solubility, it is absorbed in the upper airway and does not usually reach the lower airways. Some individuals, however, experience asthma exacerbations on exposure to formaldehyde. Patch testing can determine if a person has an allergic hypersensitivity skin reaction to formaldehyde.

TABLE 53-15. Examples of formaldehyde releasers in common products

- Benzylhemiformal
  - Cleaning agents
  - Polishes
- Bioban CS-1246
  - Cutting fluids
- Nitrobutyl morfoline
  - Cutting fluids
- Bromonitrodioxane
  - General cleaners
  - Dishwashing liquids
  - Automotive cleaners
- Bromonitropropanediol
  - Automotive cleaners
  - Dishwashing liquid
  - Disinfectants
  - General cleaners
- Chloroallylhexaminium chloride
  - Cleaning agents
  - Coloring agents
  - Paints and lacquers
  - Polishes
  - Shampoo
  - Hair care products
  - Soap and skin care products
- Diazolidinyl urea
  - Soap and skin care products
- Dimethylol urea
  - Cleaning agents
  - Cutting fluids
- Dimethylol dimethyl hydantoin
  - Shampoo, hair care products
  - Soap and skin care products
- Dimethoxymethane
  - Cleaning agents
- Formaldehyde
  - Cleaning agents
  - Coloring agents
  - Curing agents
  - Cutting fluids
  - Paints
  - Lacquers
  - Polishes
  - Shampoo
  - Hair products
  - Soap
  - Skin care products
  - Surface active agents
  - Toilet cleaners
- Hexamethylenetetramine
  - Cleaning agents
- Imidazolidinyl urea
  - Shampoo and hair care products
- *N*-Methylolchloroacetamide
  - Coloring agents
- *N*-Methylolethanolamine
  - Paints and lacquers
- Trihydroxyethylhexahydro *S*-triazine
  - Disinfectants
- Paraformaldehyde
  - Disinfectants
  - Descaling agents

ENVIRONMENTAL TOBACCO SMOKE

The burning of tobacco indoors introduces chemical pollutants and particulates. A report published in the *Journal of the American Medical Association* in 1992 reviewed evidence that exposure to ETS contributed to excess deaths from heart disease and cancer (24,25). If the epidemiologic evidence is valid, then ETS may be responsible for 35,000 to 40,000 excess deaths from heart disease annually (25). However, this estimate is based on 1980s data and is being questioned.

Tobacco smoke is made up of more than 4,000 toxic substances, including carcinogens (Table 53-16). The EPA has classified ETS as a group A carcinogen, meaning that sufficient evidence exists to prove that it causes cancer in humans (24). OSHA has also classified ETS as a potential occupational carcinogen.

Exposure to ETS exacerbates asthma, causing more than a 20% decline in forced expiratory volume in one second (26). ETS is an irritant of the eyes and upper airway also and is a significant source of formaldehyde exposure indoors (27).

NITROGEN OXIDES

Nitrogen oxide sources are burning of fossil fuels, industrial processes, and motor vehicles. NO_2, the most common of the oxides of nitrogen, is a reddish brown to yellow gas with an acrid irritating odor. Nitrogen oxides are involved in the photochemical generation of ozone.

Indoor exposure to nitrogen oxides occurs from gas-burning appliances, unvented furnaces, stoves, hot water heaters, tobacco smoke, kerosene space heaters, and influx of outdoor air contamination from vehicle exhaust.

Gas stoves are a principal source of nitrogen dioxide indoors and when a gas stove is used for cooking, the peak nitrogen dioxide concentration in a kitchen can be 1 ppm or higher.

Nitrogen oxides are insoluble in water and, therefore, can penetrate to the lower respiratory tract. Children are particularly susceptible to NO_2 because of their developing respiratory system. Studies have linked NO_2 exposure and increased respiratory illness in children (22,23). Low levels of NO_2 cause rhinorrhea, throat irritation, eye irritation, and cough. Asthmatics are sensitive to low NO_2 levels. Mild exposure causes shortness of breath, headache, cough, fatigue, nausea, and dizziness that can persist up to 2 weeks postexposure. Exposure to massive concentrations can produce severe lung damage, asphyxiation, laryngospasm, and death. The irritant effects of NO_2 do not occur until concentrates reach approximately 13 ppm (23).

After a severe exposure, individuals may develop permanent respiratory impairment. Exposure to NO_2 concentrations as low as 0.10 to 0.60 ppm can enhance airway responsiveness in asthmatics (77). At concentrations greater than or equal to 1.5 ppm, NO_2 increases airway reactivity in healthy subjects (78). Epidemiologic studies suggest an association between NO_2 exposure and the susceptibility to respiratory illness (79,80). Nitrogen dioxide exposure limits are as follows:

TLV [American Conference of Governmental Industrial Hygienists (ACGIH) 8-hour time-weighted average (TWA)], 3 ppm
PEL (OSHA 15-minute ceiling), 5 ppm
Immediately dangerous to life and health, 20 ppm
National Ambient Air Quality Standard (EPA annual average), 0.053 ppm

SULFUR OXIDES

The main source of SO_2 is burning of sulfur-containing fuels. SO_2 is a component of indoor and outdoor pollution arising from automobile exhaust. It is found in lower concentrations indoors than outdoors. The use of kerosene space heaters can generate significant concentrations of indoor SO_2.

SO_2 is soluble in water and tends to be absorbed in the upper respiratory tract. Nasal breathing filters out most inhaled SO_2, preventing its passage into more sensitive areas of the lungs. Mouth breathing tends to increase the amount of SO_2 that reaches the lungs.

SO_2 is highly irritating to the eyes and airways. Its odor is detectable at 0.5 ppm. Concentrations more than 6 ppm induce symptoms of irritation, including eye irritation, tearing, runny nose, coughing, shortness of breath, bronchospasm, chest tightness, and a choking sensation. Prolonged and chronic exposure to SO_2 can produce chronic bronchitis, airway inflammation, chronic cough, increased mucous excretion, and clearing of the throat. Massive exposure to SO_2 can result in severe permanent pulmonary damage. SO_2 concentrations in the indoor environment and outdoors in the air are associated with decreases in pulmonary functions. Exercise in polluted environments with low humidity increase health problems to those susceptible, such as asthmatics. SO_2 exposure limits are as follows:

TLV (ACGIH) (8-hour TWA), 2 ppm
PEL (OSHA 8-hour TWA), 5 ppm
Immediately dangerous to life or health, 100 ppm
National Ambient Air Quality Standard (EPA), 0.14 ppm

OZONE

Ozone (O_3) is a naturally occurring colorless or light blue gas with a pungent electrical-type odor. It is a potent chemical respiratory tract irritant and is the principal oxidant in photochemical smog. Exposures occur more commonly in urban and

TABLE 53-16. Examples of pollutants in the vapor phase of environmental tobacco smoke

Compound	Concentration/cigarette	Compound	Concentration/cigarette
Nitrogen	280–320 mg (56–64%)	Nicotine	1,000–3,000 μg
Oxygen	50–70 mg (11–14%)	Nornicotine	40–150 μg
Carbon dioxide	45–65 mg (9–13%)	Anatabine	5–15 μg
Carbon monoxide	14–23 mg (2.8–4.6%)	Anabasine	5–12 μg
Water	7–12 mg (1.4–2.4%)	Bipyridyls	10–30 μg
Argon	5 mg (1.0%)	*n*-Hentriacontane (n-$C_{31}H_{64}$)	100 μg
Hydrogen	0.5–1.0 mg	Total nonvolatile hydrocarbons	300–400 μg
Ammonia	10–130 μg	Naphthalenes	3–6 μg
Nitrogen oxides	100–600 μg	Phenanthrenes	0.2–0.4 μg
Hydrogen cyanide	400–500 μg	Anthracenes	0.05–0.1 μg
Hydrogen sulfide	20–90 μg	Fluorenes	0.6–1.0 μg
Methane	1.0–2.0 mg	Pyrenes	0.3–0.5 μg
Volatile alkanes	1.0–1.6 mg	Fluoranthenes	0.3–0.45 μg
Volatile alkenes	0.4–0.5 mg	Carcinogenic polynuclear aromatic hydrocarbons	0.1–0.25 μg
Isoprene	0.2–0.4 mg		
Butadiene	25–40 μg	Phenol	80–160 μg
Acetylene	20–35 μg	Other phenols	60–180 μg
Benzene	12–60 μg	Catechol	200–400 μg
Toluene	20–60 μg	Other catechols	100–200 μg
Styrene	10 μg	Other dihydroxybenzenes	200–400 μg
Volatile aromatic hydrocarbons	15–30 μg	Scopoletin	15–30 μg
Formic acid	200–600 μg	Cyclotenes	40–70 μg
Acetic acid	100–1,700 μg	Quinones	0.5 μg
Propionic acid	100–300 μg	Solanesol	600–1,000 μg
Methyl formate	20–30 μg	Neophytadienes	200–350 μg
Volatile acids	5–10 μg	Limonene	30–60 μg
Formaldehyde	20–100 μg	Other terpenes	200–250 μg
Acetaldehyde	400–1,400 μg	Palmitic acid	100–150 μg
Acrolein	60–140 μg	Stearic acid	50–75 μg
Volatile aldehydes	80–140 μg	Oleic acid	40–110 μg
Acetone	100–650 μg	Linoleic acid	60–150 μg
Volatile ketones	50–100 μg	Linolenic acid	150–250 μg
Methanol	80–180 μg	Lactic acid	60–80 μg
Volatile alcohols	10–30 μg	Indole	10–15 μg
Acetonitrile	100–150 μg	Skatole	12–16 μg
Volatile nitriles	50–80 μg	Quinolines	2–4 μg
Furan	20–40 μg	Benzofurans	200–300 μg
Volatile furans	45–125 μg	Stigmasterol	40–70 μg
Pyridine	20–200 μg	Sitosterol	30–40 μg
Picolines	15–80 μg	Campesterol	20–30 μg
3-Vinylpyridine	10–30 μg	Cholesterol	10–20 μg
Volatile pyridines	20–50 μg	Aniline	0.36 μg
Pyrrole	0.1–10 μg	Toluidines	0.23 μg
Pyrrolidine	10–18 μg	Other aromatic amines	0.25 μg
N-Methylpyrrolidine	2.0–3.0 μg	*N*-nitrosamines	0.34–2.7 μg
Volatile pyrazines	3.0–8.0 μg	Glycerol	120 μg
Methylamine	4–10 μg		
Aliphatic amines	3–10 μg		

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suburban environments, particularly during air pollution alerts. O_3 is a common outdoor pollutant and is consumed in the transformation of nitrogen monoxide into nitrogen dioxide. Consequently, the levels of atmospheric ozone may be higher in rural areas as compared to urban areas.

O_3 concentrations are higher outdoors than indoors, but indoor levels can increase when windows or doors are open. Average concentrations indoors range from 0 to 0.02 ppm (0 to 40 mcg per m^3), with peak levels approaching 0.1 to 0.2 ppm (200 to 400 mcg per m^3). Photocopiers and laser printers can produce peak O_3 concentrations of 0.2 ppm indoors and breathing zone levels of approximately 0.10 ppm (81,82).

One-half of the U.S. population lives in areas that cannot meet or have not met federal ambient air quality standards for O_3. Therefore, millions of people are exposed to this respiratory irritant. O_3 is formed by the action of ultraviolet light on nitrogen oxides and hydrocarbons in the atmosphere. Because O_3 formation depends on ultraviolet radiation, its formation is greatest on warm and sunny days. In heavily populated areas, typically the pattern of O_3 formation occurs mainly in the late mornings, lasting until late afternoon or early evening. O_3 is also formed at higher altitudes by ultraviolet light action on oxygen. Environmental exposure limits and guidelines to ozone follow:

National Ambient Air Quality Standard, 0.12 ppm (1-hour average), 0.08 ppm (8-hour average)
TLV (ACGIH), 0.10 ppm (8-hour TWA)
PEL (OSHA), 0.10 ppm (8-hour TWA)
Immediately dangerous to life and health, 10 ppm

Ozone is used as a disinfectant and bleaching agent. Copiers, laser printers, and electrostatic air filters are sources of ozone indoors.

Ozone has a short half-life and, consequently, interaction with humans is limited to an air-fluid interface, such as the mucous membranes of the upper airway, the respiratory tract, or the eye. Because ozone has little water solubility, it can penetrate to deep areas of the respiratory tract. Fifty percent of ozone is taken up in the upper airway and nasal passages. O_3 that reaches the lower airways can actually be absorbed into the blood to a small degree. Because O_3 has a potent oxidizing agent, it can damage tissues.

Signs and symptoms of O_3 exposure are cough, headache, chest tightness, chest pain, chest tightness on deep inspiration, shortness of breath, a dry throat, wheezing, and difficulty breathing. O_3 has been documented to significantly impair the ability to perform sustained exercise, probably through the discomfort that it produces on inspiration during intensive periods of exercise. Other symptoms include extreme fatigue, somnolence, dizziness, insomnia, decreased ability to concentrate, acrid taste and smell, and eye irritation. If an individual increases his or her breathing rate or engages in exercise for long durations of exposure, symptoms can be provoked at O_3 concentrations lower than the federal ambient air quality standard.

Studies link ambient O_3 concentrations with exacerbation of asthma. In some people, acute respiratory responses to O_3 become attenuated with repeated daily exposures (see also Chapter 97).

Environmental Sampling for Biologicals

Sampling for biologicals in the indoor environment requires a strategy related to the health effects exhibited by the occupants and the characteristics of the environment as determined by inspection. Characterization of biological growth and bioaerosols may include analyses for some or all of the following:

- Microscopy (characterizing spores, pollen, or particulates)
- Species identification of microorganisms
- Airborne colony-forming units per cubic meter (CFU/m^3) of viable organisms
- Antigen content of dust
- 1,3-β-glucan in dust samples
- Peptidoglycan (gram-positive bacteria)
- Ergosterol analysis of spores
- Endotoxin
- Mycotoxin
- 3-hydroxy fatty acids/phospholipid ester-linked fatty acids

The physical and aerodynamic properties of bioaerosols affect their collection and assay. The aerodynamics of bioaerosols are determined by particle size, diameter, shape and density, hydrophobic or hydrophilic properties, electrical charges, and their chemical nature (83). For spherical particles, the aerodynamic properties are related mainly to their diameter. For elongated or spherical-shaped particles, the smallest diameter may better represent its aerodynamic properties.

Large particles fall faster than smaller ones. Therefore, collection assays may overestimate large particles compared to small particles. Also, small particles flow around a surface, whereas larger particles impact onto a surface. Hydrophilic particles may be more easily collected into a liquid impinger than hydrophobic particles, which would pass through the liquid. Also, more water-soluble particles dissolve in the liquid. The electrostatic charge also affects behavior of particles with respect to surface interaction. Charged particles may be more attracted to surfaces with opposite charges.

Sampling may be for viable fungi and bacteria, total fungi and bacteria, or fungal and bacterial chemical substances. When sampling for biological contaminants indoors, simultaneous sampling outside serves as a source of comparison and may also reveal an outdoor source of contamination.

Standard biological sampling for microorganisms is divided into the following:

1. *Representative sampling*: Refers to only a portion of a population of biologicals that are selected for a study, such as a single bacterial or fungal species.
2. *Observational sampling*: Involves onsite inspection and sensory perception of an expert to determine information about sources, dispersion, and exposure of individuals to biologicals. Observational sampling can result in immediate decisions regarding the health and safety of an environment and the relationship of signs and symptoms to environmental conditions.
3. *Bulk sampling*: Refers to collection of a physical sample on a surface or from a specifically identified biological source, such as in a ventilation system. Bulk sampling allows for determination of an amount of antigen per gram of dust. This, however, does not consider the total amount of dust in the environment or the amount that might be aerosolized. To have meaning, bulk samples must be collected from the primary source of the causative agent in the environment.
4. *Wipe or surface sampling*: With wipe or surface sampling, a defined area is swabbed and the swabbing material is treated in the same manner as the microporous filter. This, however, only gives a measure of concentration for a given area, not a volume of air. This technique may be useful for evaluating ventilation ducts.
5. *Dust sampling*: Similar to air sampling, except a coarser filter is used to collect dust. This indicates the concentration of viable fungi and bacteria adhering to dust, which may not be accounted for in other sampling techniques.
6. *Air sampling*: This is more representative of human exposure to bioaerosols. Variables of air sampling are the aerodynamics and the physical nature of the particles, electrical charge, and chemical nature. Collecting a sample representative of the bioaerosols in certain space over time to make determinations regarding health effects is critical to interpreting results and health implications. Particle size of biologicals can vary from less than 1 μm to more than 100 μm. Attempting to characterize the sample for such a range of particle sizes can be difficult with a single collecting device. Respirable bioaerosols of health concern, however, generally are from 0.1 μm to 10.0 μm in diameter. Focusing on these sizes provides a better human exposure representation.

AIR SAMPLING FOR BIOLOGICALS

Three ways in which viable fungi and bacteria may be collected from air follow:

1. *Filtration*: Involves drawing air through a microporous filter, resulting in microorganisms being intercepted by the filter. This filter is then placed in peptone water and shaken. This suspension is used to inoculate growth media or is serially diluted into the media and then spread onto culture plates. After incubation, the bacterial or fungal colonies are counted; each colony represents 1 CFU or viable organism. These data allow investigators to calculate the concentrations of airborne viable fungi and bacteria. Nonviable spores and microorganisms that can also cause health problems are not detected by this method.
2. *Impaction*: Involves drawing air through an impactor, an instrument that places a maximum limit on the size of par-

ticles collected. The air drawn through the impactor is impacted onto an agar plate, depositing fungi and bacteria. The agar plate is incubated and the resulting colonies are counted. This method underestimates the number of viable cells, because the force involved in sampling may destroy many of them.

3. *Liquid trapping*: Trapping of fungi and bacteria in a liquid is accomplished by bubbling air through water. Two instruments used are the impinger and cyclone scrubber. This causes airborne microorganisms to become entrained in the water that is then used to inoculate growth media. The media are then spread on culture plates and incubated, after which colonies are counted.

To determine the total fungal or bacterial count in air, not just viable count, microscopy may be used. Air is drawn through a microporous filter, and the filter is viewed under a microscope. This allows a visual count of viable and nonviable cells and spores.

Sampling time is another important feature. Continuous sampling over an exposure period of interest might be ideal; however, it may not be achievable. Many times sampling is done for a specified period, such as for 5 minutes.

SAMPLING FOR CHEMICALS

Because culturing techniques may significantly undercount viable organisms, assays for biochemicals derived from microorganisms are being investigated as a means to characterize biocontaminants. Research shows that fungal biomass may be determined by ergosterol analysis (84–86). Ergosterol is stable and is found in living and nonviable spores. Air is collected on a microspore titer and spores are extracted with methanol. Analysis is by gas-liquid chromatography–mass spectrometry or high–pressure liquid chromatography. One study showed 3.2 μg of ergosterol per milligram of spores. *Aspergillus* and *Penicillia* produce 1.4 μg per mg to 6.0 μg per mg.

A modified LAL analysis is used to assay for airborne (1,3)-β-glucan content (87–91), which research is showing can correlate with respiratory symptoms.

Volatile chemicals generated by fungi are being used to help determine fungal presence and the nature of fungal contamination indoors. Detection of 3-methylfuran indicates fungal growth and amplification (87,88). Detection of 1-octen-3-ol indicates dormant fungal mass. Geosmin presence indicates fungal mass presence and active growth (87,88). Volatile chemical by-products can be sampled with a portable air sampler (Anasorb 747 carbon tube). Samples should be obtained in areas of concern and near ventilation intakes outdoors with control samples. GC-MS with selected ion detector is used to analyze for volatile chemicals.

When sampling for airborne mycotoxins, a microporous filter should be the collection medium or, if sampling for mycotoxins in dust, a coarser filter may be used. After sampling, the mycotoxins are extracted from the filter and the extract is tested for cytotoxicity to certain cellular preparations (87,88). This reveals the presence or absence of mycotoxins but does not provide a quantitative measurement.

Endotoxin sampling is similar to mycotoxin sampling in the collection stage. Endotoxin is extracted from microporous filters or dust filters and may be analyzed in two ways: The extract may be analyzed for lipopolysaccharide content using GC-MS, or the extract may be analyzed using an LAL assay. Either approach may provide a quantitative measurement of endotoxin concentration (87,88).

Detection of dust mites may be accomplished by using two methods, microscopy and feces detection. A microscope with tenfold magnification should be used to identify mites, and samples for viewing should be collected from bedding and carpets. Detection of dust mite feces may also give an indication of the concentration of the population. This is performed by collecting dust and mixing with reagents that change color according to the amount of feces in the sample (87,88).

Spore traps can provide a continuous recording of spores that collect onto a greased tape that can run for days. This allows recording of four sizes and the analyses of spores, looking for fluctuations in concentrations and the nature of spores throughout a time course. Identification of fungal, bacterial, and spore species is critical to assessing health risks.

CULTURE MEDIA

Biological air sampling requires nutrient media, such as potato dextrose agars and blood protein agars. Potato dextrose agars are used to quantify airborne fungi, and blood protein agars are used to quantify airborne bacteria. The agars are used in conjunction with a high-flow air-sampling pump and a single-stage viable impactor. Air samples for each agar are collected over a 5-minute period.

The selection of culture medium is critical because different microbes may grow poorly or not at all in standard culture media and under certain conditions. Also, living organisms can be damaged by the collection technique and not grow. Air sampling for culture usually underestimates the true bioaerosol concentration (92). For comparison, air sampling should be conducted outdoors in close proximity to the fresh air intakes to service controls. Indoor air samples should be collected simultaneously near suspected sources of contamination before and after agitation of sources. Source agitation can produce a 1,000-fold increase in the indoor air bioaerosol concentrations.

Gravity or settling Petri dishes in culture media underestimate or may even fail to detect biological contaminants that can remain in the air for lengthy periods of time. Culture plate impactors used for bacterial sampling use general media, such as nutrient agar or casein soy peptone agar. Specialized media are sometimes used. Pathogenic bacteria grow best around 95°F (35°C). Thermophilic organisms grow best at 122°F (50°C) or higher, and most other common organisms grow between 25° and 30°C (77° and 86°F).

Legionella pneumophila may not be detected in air samples and, therefore, sampling from contaminated sources such as water is important to detect this organism.

Sampling of fungi is performed by plating air samples, bulk samples, or liquid samples onto appropriate culture media, such as potato dextrose, Sabouraud's dextrose, or malt extract agar. Malt extract agar has advantages because bacteria do not grow well on it, and it is also a medium that grows *Aspergillus* species. *Aspergillus fumigatus* generally grows at 45°C in incubation; otherwise, all other cultures for fungi are incubated at room temperature.

High-volume filtration sampling devices can be used to evaluate airborne antigens and mycotoxins. Volumetric sampling with sieve or slit impactors can be used over an interval of time in areas of suspected high fungal spore concentrations.

Air sampling is limited to detection of living microbial organisms, but nonliving particles can also produce illness and can be assayed. Nonliving biologicals, however, do not grow on culture media. Spore traps can be used to determine spore samples. Microscopy can assist in identifying particulates of biologicals. High-volume air samplers are required to collect enough airborne mycotoxins for detection by the analytical assay. Mycotoxin assay is by GC-MS.

Fungal spore counts are obtained by drawing air into a sampler and impacting them onto a moving sticky surface (Burkhard sport trap). The spores can be examined microscopically. Microporous filters are also used to sample spores. Spores are eluted from the filters and counted microscopically.

Guidelines for antigen environmental loads have only been established for dust mites. The detection of mycotoxins may only

be achieved in a culture medium. In some instances, however, mycotoxin can be collected from dust. Antigen concentrations can be measured with radioimmunoassay or enzyme-linked immunoassays.

Interpreting Results of Microbiological Sampling

Microbiological sampling results can be difficult to interpret. Analytic methods are not consistent across laboratories, and an accreditation program for laboratories that perform bioaerosol analysis does not exist. The ACGIH and the American Industrial Hygiene Association have published reference manuals for biological sampling (87,88).

No TLVs exist for bacterial or fungal bioaerosol concentrations in interpreting indoor sampling results. However, guidelines do exist. Concentrations of total culturable bacteria outdoors are typically 100 to 1,000 CFU per m^3; however, these numbers can vary quite dramatically in different geographic regions (93). Data for viruses, as measured in plaque-forming units, are similarly variable. Proactive monitoring is discouraged because of the difficulty of data interpretation.

In general, assaying environments for biological contamination should combine air sampling, bulk sampling, and inspection to characterize the extent of contamination and make decisions regarding health hazards. Decisions to measure for chemical byproducts are individualized on a case-by-case basis.

Indoor concentrations of less than 100 CFU per m^3 are usually not a concern, whereas those more than 1,000 CFU per m^3 deserve further attention. Concentrations between 100 and 1,000 CFU per m^3 are subject to interpretation on a case-by-case basis. The presence of any single type of fungus in levels exceeding 500 CFU per m^3 indicates a potential contaminating source.

Some investigators recommend that indoor levels of nontoxic and nonpathogenic microorganisms should be less than or equal to 300 CFU per m^3. Also, no microorganism should contribute individually to more than 50 CFU per m^3 of the total, with the exception of *Cladosporium*. Levels of fungi greater than 300 CFU per m^3 require further investigation for potential inadequate air filtration, excess humidity, and potential contaminant sources. Fungi of levels 300 to 500 CFU per m^3 appear to be normal and do not represent a health effects threshold, but rather a threshold for further investigation (94). These investigators state that indoor to outdoor ratios involving fungal CFUs per m^3 are not acceptable for evaluating indoor bioaerosol concentrations. Rather, sampling should identify individual microorganism components and compare indoor to outdoor ratios. These conclusions are based on evaluation of more than 900 indoor samples that show fungal and bacterial bioaerosol concentrations ranging from 0 to 6,077 CFU per m^3, with an average of 157 CFU per m^3. Eighty-seven percent of the measurements were less than 300 CFU per m^3 and only 6% were greater than 500 CFU per m^3 (94). Thirty-seven genera of fungi were identified in these samples.

Frequently occurring fungi in this study were *Cladosporium*, yeast, hyphae, *Penicillium*, *Aspergillus*, *Alternaria*, and *Curvularia*. One hundred eighty-two outdoor samples had fungal and bacterial bioaerosols in concentrations ranging from 0 to 12,668 CFU per m^3, with an average of 860 CFU per m^3. One-third of these samples were less than 300 CFU per m^3 and 51% were more than 500 CFU per m^3. Thirty-three genera of fungi were identified in the outdoor samples (Tables 53-17 and 53-18). This study showed that the average fungal concentration of 157 CFU per m^3 indoors is more than five times less than the average outdoor concentration of 860 CFU per m^3.

The ACGIH recognizes an indoor to outdoor fungi ratio of 33%. This ratio has been questioned because outdoor bioaerosol concentrations vary considerably (94). Therefore, using the 33% indoor to outdoor ratio results in a recommended indoor concentration of bioaerosols that may be too liberal as an accepted concentration limit (94). Indoor and outdoor populations of bioaerosols should be similar, with indoor concentrations lower than outdoor concentrations for individual microorganisms. Thus, concentrations less than or equal to 200 CFU per m^3 may be considered typical for indoor bioaerosol concentrations.

Other studies have reported that airborne concentrations of indoor fungi exceeding 500 CFU per m^3 are abnormal and should be investigated (95). A problem exists, however, when trying to determine whether the indoor source is coming from the outdoors as opposed to an indoor contamination source. Indoor sources are most likely when a significant difference exists between indoor and outdoor bioaerosol concentrations.

Techniques used to control biologicals include isolation systems, high-efficiency particulate air (HEPA) filtration, ultraviolet lights, carbon adsorption, electrostatic precipitation, negative air ionization, and heating and dehydration. Future technologies

TABLE 53-17. Frequency of occurrence and average colony-forming units per cubic meter of indoor fungi

Observed	Frequency (%)	Average (colony-forming units per cubic meter)
Total	100	157
Cladosporium	77	92
Yeast	56	52
Sterile hyphae	56	29
Bacteria	52	28
Penicillium	50	48
Aspergillus	33	20
Alternaria	17	30
Curvularia	7	20
Acremonium	30	8
Epicoccum	3	8
Geotrichum	3	18
Phoma	2	7
Fusarium	2	16
Paecilomyces	2	9
Dendryphiella	2	5
Drechslera	2	13
Absidia	2	1
Chaetomium	2	6
Nigrospora	2	10
Actinomycetes	1	3
Monocillium	1	17
Cunninghamella	1	11
Monilia	1	5
Rhizopus	1	5
Trichoderma	1	10
Gilmaniella	1	3
Hansfordia	1	3
Hyalodendron	1	3
Mucor	1	8
Stemphylium	1	5
Botrytis	1	2
Pleospora	1	4
Humicola	1	23
Pithomyces	1	10
Unidentified	1	6
Stachybotrys	1	3
Ulocladium	1	4
Basipetospora	<1	2
Gliocladium	<1	5
Oidiodendron	<1	2
Aureobasidium	<1	8

Adapted from ref. 94, with permission.

TABLE 53-18. Frequency of occurrence and average colony-forming units per cubic meter of outdoor fungi

Observed	Frequency (%)	Average (colony-forming units per cubic meter)
Total	100	860
Cladosporium	85	570
Sterile hyphae	76	87
Yeast	58	126
Penicillium	52	120
Bacteria	46	58
Alternaria	38	58
Aspergillus	27	277
Geotrichum	20	91
Curvularia	12	71
Fusarium	12	74
Epicoccum	8	17
Drechslera	6	62
Acremonium	6	43
Phoma	5	31
Trichoderma	2	35
Cunninghamella	2	21
Paecilomyces	2	22
Pleospora	2	35
Basipetospora	2	15
Nigrospora	2	22
Monilia	1	89
Monocillium	1	56
Ulocladium	1	10
Botrytis	1	22
Phoma	1	24
Pithomyces	1	3
Rhizomucor	1	9
Rhizopus	1	7
Mucor	1	14
Humicola	1	14
Stachybotrys	1	7
Actinomycetes	1	106
Absidia	1	36
Aureobasidium	1	12
Chrysosporium	1	36
Gonatobotrys	1	24
Gliocladium	1	35

Adapted from ref. 94, with permission.

include passive solar exposure, photocatalytic oxidation, ultrasonic atomization, air ozonization, ultraviolet lasers, agglomerators, and virus detection systems.

VIRUSES

Assaying for the presence of viruses requires specialized culture media. Viral culture media are generally tissue cultures. If collection is delayed beyond an hour, the samples should be refrigerated.

VENTILATION AND INDOOR ENVIRONMENTAL QUALITY

The ventilation system or air-handling unit of an office or home is frequently referred to as the *HVAC* system. The HVAC consists of the mechanical and functional components of duct work, air filter, air conditioning, and heating unit. The primary functions of the HVAC are to maintain indoor air pollutants at a minimum, control odors, maintain oxygen and carbon dioxide levels at acceptable concentrations, provide humidifying, cooling and heating, and maintain overall comfort. Although ventilation systems for homes and offices share common features, an additional function for commercial sites is to maintain a balance of positive air pressure in work areas. This positive pressure forces air to circulate to prevent the build up of pollutants.

HVAC systems in commercial office buildings and some homes are installed to service zones. As the number and size of zones increase indoors, so does the cost of ventilation. A zone is typically defined by the presence of a thermostat. Zones also allow for individual control of the HVAC and, therefore, the comfort level of that zone.

The HVAC is frequently cited as a cause of indoor air quality problems. The National Institute for Occupational Safety and Health (NIOSH) categorized the following major causes of ventilation-related health problems in studies of more than 1,300 cases of poor indoor air quality (20):

- 50% of cases related to deficiencies in ventilation, lack of outside fresh air, poor air distribution, uncomfortable temperature, or uncomfortable humidity.
- 30% of cases related to indoor chemical or biological contaminants.
- 10% of cases were attributed to an outdoor pollutant introduced to the indoors.

NIOSH also discovered patterns in these cases:

- Forced ventilation was common in sites with health problems.
- Health complaints increased as people density indoors rose.
- Problem buildings were energy efficient, thus creating a tight envelope.
- Workers perceived little or no control over their environment.

Understanding HVAC functioning is critical to indoor air quality evaluations:

Outside air is supplied to the interior of the building via ventilation ducts.

Contaminated or used air is removed from the building interior through air return ducts, or a plenum, located in the ceiling or wall, to a central return duct.

A portion of stale air is then exhausted outside and an equal portion of fresh outdoor air is introduced through the air handler, mixing with and diluting any pollutants in the stale air.

The mixed air then passes through an air filter.

The air is then conditioned by heating or cooling through a cooling coil or heat exchanger.

The introduction of fresh air is balanced with the exit of stale air.

HVAC systems have an outside air intake on the top or side of a building that brings outdoor air inside. The outdoor air is then mixed with recirculated air from the occupied area. The mixed air usually passes through a filter to remove gross contaminants. This filtered air then passes through a fan that creates a positive pressure to force the air through coils that either cool or heat. A drain pan beneath the coils collects water that condenses on the cooling coil. Air leaving the coil may be humidified or dehumidified, depending on the circumstances. This conditioned air then moves through a ventilation duct at a speed of 10 to 20 mph to a distribution box. The supplied air then travels from the distribution box through small ducts to terminal ducts and diffusers and into the rooms. The supplied air migrates throughout the room and eventually enters an air return vent, also called a *plenum*, where it is recirculated or exhausted outdoors (20).

HVACs can be broadly divided into *constant air volume system* or *variable air volume system*. Constant air volume HVAC systems vary air temperature for comfort control, and, depending on the sophistication of the HVAC system, a single constant supply system can provide ventilation and comfort control in multiple

zones. Thermostats allow for more individual control of comfort, but generally cause increased energy use.

Variable air volume HVACs control the amount of air delivered to the interior work space to maintain temperature. If temperatures are too high inside, the system delivers a higher volume of cooler air. Thus, airflow varies with the temperature. A variable volume HVAC is more energy efficient but may not always deliver enough outside fresh air. Sophisticated HVAC systems in modern office buildings may have combinations of multiple zones, variable air volumes, and complex duct work (20).

Ventilation processes can also be divided into *active* or *passive*. Homes frequently have active air exhaust features and passive air supply. Commercial building ventilation systems usually involve active exhaust and active air supply.

Inadequately functioning HVAC systems allow indoor contaminants to accumulate, contributing to stale and stagnant air, and may even introduce outdoor pollutants and allergens into the indoors, especially if the air is unfiltered. A frequently occurring problem is an imbalance in the flow of fresh air versus outflow of stale air. This can create *dead zones* of no air circulation indoors. These dead zones are essentially stale air that escapes being recirculated.

HVACs can be sources of moisture, allowing mold and other microorganisms to amplify and be circulated indoors. Over time, dust, dirt, and debris build up in the ventilation system. Proper maintenance can help prevent accumulated dirt and dust from being circulated indoors.

Indoor Air Quality Guidelines for Ventilation

ASHRAE has promulgated four standards dealing with the indoor environment:

- ASHRAE 62-1999: Ventilation for acceptable air quality with proposed 62.1P and 62.2P.
- ASHRAE 62-1989: Ventilation for acceptable air quality
- ASHRAE 52-1992: Thermal environmental conditions for human occupancy
- ASHRAE 52-1992: Air filtration

The ASHRAE standard (62-1999) on ventilation has as its objective to provide clean, fresh air in which contaminants do not exceed the limits set by the National Primary Ambient Air Quality Standard for outdoor air. This includes pollutants, such as sulfur dioxide, nitrogen dioxide, ozone, carbon dioxide, total particulates, lead, chlordane, and radon.

Whereas the ASHRAE standard is a practical guide oriented to providing comfort and air quality, it does not address air pollutant sources. If ASHRAE ventilation standards are met, however, and sources of pollutants controlled or eliminated, indoor contaminants are minimized to a level of comfort for the majority of people.

Ventilation systems have traditionally been designed to provide odor control and thermal comfort under the assumption that the air in a building is perfectly mixed. Increasing experience demonstrates that nonuniform mixing is common and that the task of predicting pollution transport produced by the ventilation systems is not simple. In the United States, building ventilation adequacy is measured and compared with ASHRAE guidelines.

To date, the home environment has escaped guidelines and regulations for indoor air quality, but is under consideration in 62.1P and 62.2P. Agencies in the United States and in other countries, however, are examining guidelines for residential indoor air quality.

ASHRAE standard 55-1992 provides the specific conditions in which 80% to 90% of indoor occupants should find the environment thermally comfortable. It does not address air quality or ventilation. The standard combines the variables of humidity, temperature, clothing, activity and movement, and radiant heat sources to achieve an 80% satisfaction rate among all indoor occupants and a 90% satisfaction rate for any one variable. ASHRAE standard 62-1989 actually addresses the relative humidity indoors, calling for a range of 30% to 60% (20).

ASHRAE standard 52-1992, Methods of Testing Air Cleaning Devices Used in General Ventilation for Removing Particulate Matter, establishes important factors in selecting air filters and filter rating procedures (20).

VENTILATION ADEQUACY

A major function of the ventilation system is maintaining fresh clean air to match the comfort needs of the number of people in a particular indoor environment. The concentration of CO_2 measured in parts per million in indoor air is used as a general measure of air freshness and adequacy of outdoor air delivery. It is a common measurement obtained by environmental consultants to test the adequacy of ventilation.

Outdoor CO_2 concentrations are always lower than those indoors. CO_2 build up in the interior of a home or office is dependent on the number of people in the site and the ability of the ventilation to replace stale air with fresh air. If the number of occupants in an indoor environment remains constant, then measuring CO_2 can assist in determining the quantity of outdoor air being delivered. Continuously monitoring CO_2 concentrations over days or weeks can generate confidence in the result because ventilation needs fluctuate with population demands. An electronic device is used to monitor CO_2 continuously in parts per million. Taking spot checks of the CO_2 may not be representative of the ventilation adequacy because CO_2 concentrations fluctuate and tend to be low in the morning hours and rise in the afternoon (Fig. 53-10). CO_2 can rise during the mid-morning if the space is operating with minimal airflow. As the interior of the building is cooled further, the CO_2 concentrations may fall by the afternoon. Reviewing CO_2 concentrations over a period of time can provide a better determination of the ventilation system performance. If the ventilation system is working adequately, then the CO_2 concentration inside in the early morning is close to the outdoor CO_2 value

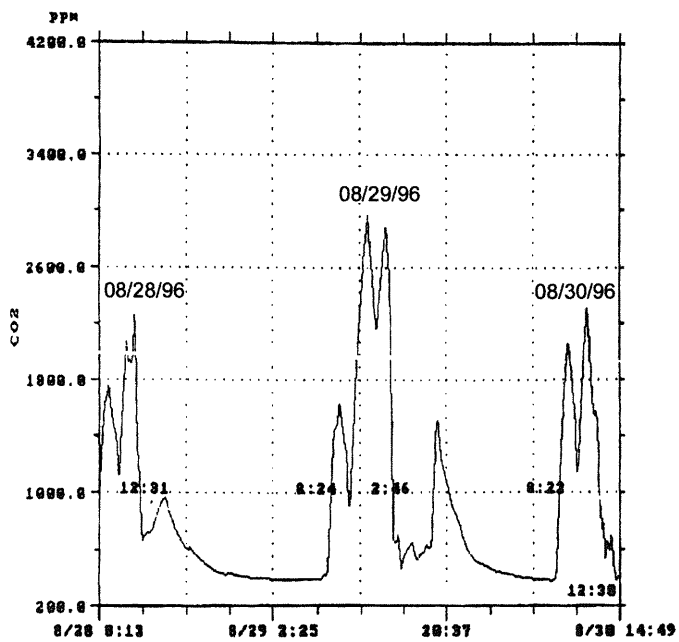

Figure 53-10. Carbon dioxide fluctuations indoors. Note the high levels, indicating inadequate ventilation.

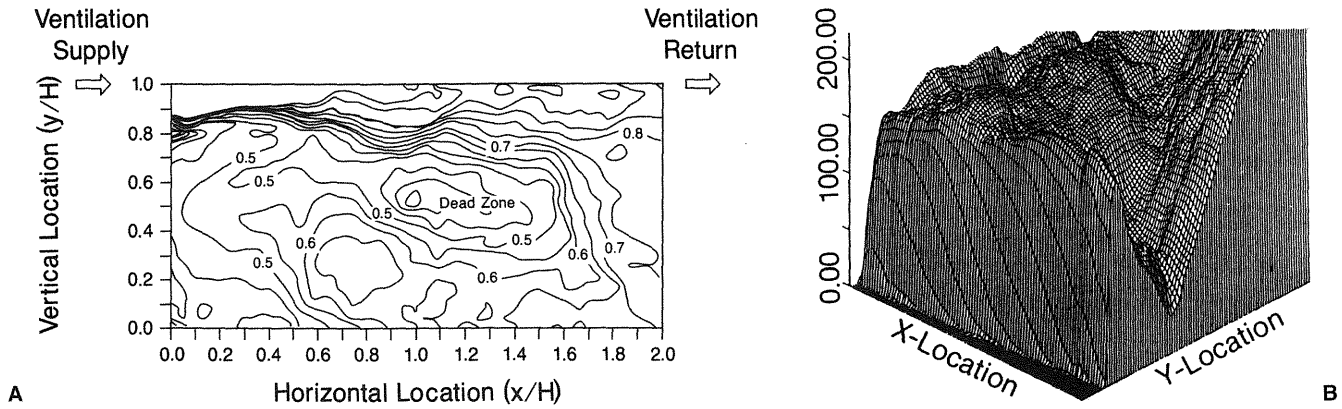

Figure 53-11. **A:** Two-dimensional mapping of the results of simulated airflow monitoring, identifying areas of no air movement. **B:** Three-dimensional model showing dead space areas representing little or no effective air movement as areas of depression. (Reprinted from Anderson R. Determination of ventilation efficiency based upon short-term tests. Golden, CO: US Department of Energy, National Renewable Energy Laboratory, 1988, with permission.)

at that time. If the CO_2 value is greater than the outdoor CO_2 value, then the ventilation may not be providing adequate fresh air.

CO_2 concentrations more than 800 ppm can be associated with health complaints. In many cases, people complain of headache, fatigue, and airway irritation when CO_2 levels exceed 800 ppm, signifying the buildup of pollutants. However, OSHA does not consider the CO_2 concentration indoors to be in violation of its regulatory control until levels rise more than 5,000 ppm. Such dichotomy between OSHA regulations and reality contribute to frequent conflict in some cases of poor indoor air quality.

One-half of NIOSH's indoor air quality health complaint investigations were related to inadequate ventilation. Although ventilation systems are designed primarily to provide control over thermal comfort, it has been assumed that airflow is evenly mixed by the ventilation system. This assumption, however, is not always true. Uniform distribution of fresh air via the ventilation systems for maximum dilution of indoor pollutants is not always a reality, and microenvironments of ventilation and distribution mismatches can occur. These mismatches can result in areas of poor air quality or dead zones, where the air may be stale (Fig. 53-11A and B).

With the advent of a strong emphasis on energy conservation, there has been a tendency to limit outdoor air intake as much as possible during adverse temperature conditions to avoid having to heat or cool incoming air. In modern buildings of tight construction that depend entirely on their ventilation system for outside air, this is relatively easy to accomplish. However, the persons designing the ventilating system are seldom the persons trying to reduce energy use, and so, after adjustments, it is not uncommon for the amount of outside air being introduced into the system to be considerably below what is necessary to maintain a comfortable indoor environment. Similar problems can occur if inadequate provisions have been made for exhausting air from the building or if the exhaust is blocked. In addition, occasionally the outside exhaust vent faces the fresh air intake portal. Thus, the HVAC perpetually recycles contaminated air. Careful sequential review and analysis of the HVAC system is always critical and should be exercised when investigating indoor environmental health complaints.

Air Filtration

Air filtration adds to the ability of the HVAC to prevent contaminants from entering indoor air. Depending on the type of air filter, the device may be more or less efficient in removing contaminants. The best filtration system is integrated with the ventilation system during building design. Retrofitting air filters to an older ventilation, however, can be easily achieved.

Most air filtration systems are designed to remove particulates, such as mold, pollens, spores, general allergens, dusts, and fibers. Some may remove chemicals and odors. Air filtration products range from single disposal filters to permanently installed air filtration systems. Filter efficiency is rated by its ability to retain particulates and dusts. The higher the efficiency rating, the more effective the filter is in retaining smaller and smaller particles that can penetrate deeply into the airways. Adequate air filtration helps to maintain a healthy environment by doing the following:

1. Preventing the entry of dust, particulates, and allergens into the indoors.
2. Preventing the accumulation of dirt and debris in the heating and cooling units, which would reduce performance and efficiency.
3. Preventing dust and dirt to accumulate in the ventilation ductwork, which can serve as a nutrient source for microbial growth.
4. Preventing entry of corrosion-producing pollutants, such as dust particles containing acid and alkaline chemicals.
5. Preventing entry of chemicals and odors from the outside.

Modern HVAC systems usually use two filters: a coarse filter that first removes large particles, followed by a finer filter to trap smaller dust.

Air filters come in a wide variety of designs and efficiencies with numerous suppliers. The type of filter should be based on a review of needs, filter efficiency, function, design and ease of installation, and maintenance. Filters vary from coarse to fine and inefficient to efficient. Coarse filters trap larger particles and are generally used as prefilters. Fine filters remove visible dust and irritant particulates. ASHRAE Standard 52 has two filter rating procedures:

1. *Dust spot efficiency test*: Used with filters that stop small particles.
2. *Arrestance test*: Used with filters that stop larger, coarse particles.

A filter with a high arrestance rating may be inefficient and ineffective in stopping small dust particles. The three performance

characteristics applied to any filter are (a) filter efficiency in removing particles from the airflow, (b) airflow resistance caused by the filter, and (c) time interval between cleaning and filter replacement.

Dust and particulate filters: These are usually disposable fiberglass filters and are not efficient at trapping small particulate matter. They do not remove chemical vapors or odors unless combined with a carbon-impregnated medium. Particulate filters vary with respect to the size of the particulates trapped, ranging from coarse filtration to fine particulate filtration. The least effective consists of a coarse prefilter placed at the air intake of the air-conditioning unit. This type of filter stops only the largest of dusts and particulates. Fine particles and dust that are in the respirable range are not stopped by this type of filter. A fine particulate filter is recognized by its pleated construction, providing more surface area to entrap fine particles.

Media filters: These filters are made of paper or fabric stretched over a frame and arranged in a pleated fashion to enlarge the surface area of contact. Check for filter efficiency, because some of these filters can be porous and inefficient. Media filters may be carbon impregnated to absorb gases and vapors of chemicals. Some filter products contain antimicrobial treatment to prevent microbial growth on the filter itself. Activated charcoal has been used for many years to adsorb chemicals. Carbon filters basically contain a medium impregnated with activated charcoal, which provides a massive surface area to adsorb gases, odors, and chemical vapors. Carbon can adsorb many different chemicals, but adsorbs larger molecules best.

Electronic air filters: Three types exist:

1. *Self-charging filters*: These are made out of plastic fibers that create static electricity by airflow passing through the filter medium. The static electric charge attracts dusts and particulate matter, trapping them in the filter. Static electricity generated by air movement through such a filter medium does not generate ozone. These types of filters generally trap only coarser particles, and efficiency declines rapidly as airflow increases or humidity increases.
2. *Electrostatic precipitators*: These filters operate in two stages: (a) Dust and particulates pass through a prefilter and then a charged electrical field, which applies a negative or positive charge to the particle. (b) The second stage involves a precipitating or collection section of the filter, consisting of negatively charged or positively charged areas that attract and deposit the charged particles. The efficiency of these types of filters varies, and they produce ozone, an irritant. Some electrostatic filters are combined with other media, such as charcoal or a coarse particle filter, improving their function.
3. *Charged medial filters*: Made from a dielectric material, such as fiberglass or cellulose, stretched across a frame. A direct current voltage is applied to the dielectric, creating an electrostatic field. This type of filter is not efficient because the electric current is not strong enough to place a charge on most particles to entrap them.

HEPA: HEPA filtration was a technology developed by the Atomic Energy Commission to remove radioactive particles from the air in manufacturing plants. By definition, HEPA filtration must remove at least 99.7% of all airborne particles of 0.3 μm in diameter (one-three-hundredth the diameter of a human hair). Air filters of 85% efficiency filter out most irritants affecting health. Higher-efficiency filters require more energy use and higher costs, but the reduction of health problems compensates for this.

Negative ion generator: This type of system is not a true air filter. It generates negative ions in the indoor air that attach to particulates and dust suspended in air, causing them to take on a negative electrical charge. The charged particles then attach to surfaces in the indoor environment, such as walls and furniture, thus being eliminated from the air but not from the indoor environment. It should not be used as a substitute for proper air filtration because dusts and particulates are not removed from the indoors.

Air purifiers and negative ion generators are portable units designed to clean and purify air in a room of a home or office. Both can be helpful in reducing the pollutant load in a room. Air purifiers recycle air; they do not provide fresh air. Portable air purifiers that come in self-contained units for use in individual rooms of a home or office are available, and their specifications should be reviewed to insure the unit suits the individual's needs.

Ion generators have shown conflicting results on preventing symptoms of asthmatics and those with SBS. Neither air purifiers nor ion generators are substitutes for proper air filtration and adequate fresh air.

Heating, Ventilation, and Air-Conditioning Contamination by Microorganisms

Microorganisms, such as bacteria and fungi, are common in outdoor and indoor environments, and their presence in low levels in a ventilation system is considered normal. Problems occur, however, when they amplify to high levels that can then be transported indoors as a bioaerosol. Fungus and bacteria require nutrients to amplify, and dirt and moisture are such nutrient sources. Growth sites for biologicals include the following HVAC areas:

- Air filters
- Humidifiers
- Cooling coils
- Condensation pans
- Moisture and debris in ventilation ducts

The presence of active microbial organism growth in the ventilation system is a potential health problem. The presence of microorganism overgrowth should be suspected if one or more of the following is noted: (a) musty or foul odors are present, (b) a discoloration of surface areas—green, black, white, or pink, (c) a presence of moisture that is slimy or cloudy, or (d) moisture damage to carpet or walls associated with odors.

Elimination of microbial contamination growth involves (a) removal of dust and debris and moisture, (b) correcting the cause of contamination, (c) preventing the spread of microorganisms from the contaminated area, and (d) treating the contaminated area with an appropriate chemical biocide, if necessary.

Air sampling for microorganisms can verify an airborne contaminant problem that may affect health. Sampling and interpretation of results, however, should be performed by qualified experts.

The use of chemical biocides to kill contaminating microorganisms should be undertaken by qualified experts. Biocides are toxic and are controlled by the Federal Insecticide, Fungicide, and Rodenticide Act. Six classes of biocides exist, and four are allowed for use in HVAC systems:

1. Sterilants that kill 100% of all forms of microbes.
2. Disinfectants that eliminate 99.999% of infectious, pathogenic bacteria.
3. Sanitizers that reduce, but not necessarily eliminate, 99.9% of microbes.
4. Fungicides intended to inhibit growth of or kill fungus pathogenic to humans or animals.

The surface to be treated must be cleaned, then thoroughly washed with the biocidal agent. The surface should not be

allowed to remain moist for more than 24 hours; otherwise, regrowth might occur. The EPA recommends that porous material, such as fiberglass insulation, that can serve as an amplifier source for microbe growth be first contained, then removed. Sanitizing such materials is virtually impossible.

Biocidal agents should only be applied by experts in a manner to minimize human exposure. These agents kill fungi and other microorganisms, and their proper use and efficacy require expert judgment. The manufacturer's instructions must be followed to avoid future problems.

Heating, Ventilation, and Air-Conditioning Codes and Professional Standards

Air concentrations of chemicals that result in SBS are usually two to three orders of magnitude less than PELs set by OSHA for a work site. OSHA PELs are based on air levels considered to be healthy for an industrial work environment and refer to airborne concentrations of substances to which employees can be exposed on a daily basis, without adverse health effects. OSHA does recognize that some workers may be more susceptible or hypersusceptible to much lower levels of chemicals than their standards. OSHA's PEL concept, however, is the only legally enforceable standard. Too many times an indoor environment has been judged to be clean based on such regulatory standards, yet the occupants continue to experience health problems.

In 1995, OSHA proposed the following regulations for indoor air quality for nonindustrial work sites, but these proposals have not yet been adapted (1). Specific guidelines that can help achieve high indoor air quality derived from OSHA's proposed standards are

- Keep CO_2 levels less than 800 ppm (25 to 30 cubic feet per minute of outside air).
- Keep relative humidity less than 60%.
- Obtain and maintain records on HVAC systems.
- Inspect, maintain, and operate HVAC systems in accordance with building codes in force at the time the building was constructed.
- Exhaust smoking areas to outdoors, and keep area under negative pressure.
- Provide local exhaust for specific pollutant emitters.

The growth of nonregulatory standards by professional organizations has helped to ensure better quality of air in home and work environments through HVAC design, construction, cleaning, maintenance, and quality of air delivered. Each of these organizations is dedicated to providing standards in its particular field to ensure a comfortable and healthy environment:

- *ASHRAE*: Ventilation standards for acceptable indoor air quality, ASHRAE standard 62-1999.
- *National Air Duct Cleaners Association*: Standard 1992-01 relates to standardized mechanical cleaning of nonporous air conveyance systems.
- *National Air Filtration Association*: Provides guides and technical assistance for proper air filtration.
- *North American Insulation Manufacturers Association*: Represents manufacturers of flexible duct liners and duckboard. The organization has produced guidelines for proper fabrication, installation, and maintenance of their members' products. The organization also provides fibrous glass duct construction standards.
- *Sheet Metal and Air Conditioning Contractor's National Association*: Has developed standards and guides governing the fabrication and installation of HVAC systems, HVAC Duct Construction Standard.
- *National Fire Protection Association*: Standard 90-A details construction materials, insulating materials, coatings, and other materials that may be used in construction and design of ventilation systems for fire safety.

Problems within the Heating, Ventilation, and Air-Conditioning System

HVAC systems are complex and have many mechanical parts with extensive branching duct work. Most HVAC problems can be categorized as mechanical, functional, or contamination.

- *Mechanical*: Examples are problems with fans, air handler units, air filters, or leaks around ventilation ducts.
- *Functional*: Examples are an imbalance of air, differences of air pressures within a building, insufficient fresh air, and exhaust air reentrainment, which causes odors.
- *Contamination*: Examples include dust, debris, mold, bacteria, or outside source brought indoors.

HVAC problems generally require the assistance of professionals, especially in large buildings. Ventilation specialists can use tracers or nontoxic smoke to evaluate airflow problems. A commonly used tracer is sulfur hexafluoride, which is chemically inert. Flow rates and air balances can be measured along with CO_2 concentrations to check for inadequate fresh air. Problems may arise in the following areas of the HVAC system, underscoring its complexity.

Outside air intake: A supply of outdoor air is drawn into an air intake vent and delivered to the air handler unit in the HVAC system either passively or actively to match the amount of stale air exhausted. The intake may be adjustable, so the amount of outside air admitted can be varied. The outdoor air supply delivered to the air handler unit of the HVAC system is presumed to be fresh and free of outdoor contaminants. This is not always the case. Outdoor air can be polluted by chemicals, pollens, automobile exhaust, and odors. Remember that the same chemicals outdoors can concentrate indoors.

The location of the intake vent is important to assuring fresh, clean air. Outdoor contaminants can be drawn indoors either by the air handler or through leakage in the ventilation system. The fresh air intake source should be away from any potential source of contaminants and pollutants, such as parked automobiles or trucks emitting vehicle exhaust near loading docks, exhaust from other combustible sources such as furnaces, or kitchens, or a congested urban area, street, or highway, or any other source of contamination and pollution.

Air supply ducts and distribution ducts: Ventilation ducts move outside air through the air handler and into the indoor space. Ventilation ducts can become contaminated by dust, moisture, microorganisms, and debris, which can be circulated into indoor air. Air leakage and imbalanced air pressure can occur. Normally occupied spaces in a building are under a slight positive pressure relative to return exhaust vents. This pressure differential allows air to move in the direction of the exhaust. Because the exhaust is under negative pressure relative to occupied spaces, any leaks around the return vents also draw air in from outside. If an occupied space does not maintain a positive air pressure relative to outdoors, then leaks can occur around doors and other potential leakage sites. Also, imbalance can result in areas of dead zones indoors, where stale air accumulates along with pollutants.

Air is distributed from the air-handling unit to the occupied indoor areas by multiple branching ventilation ducts. As the number of ducts increases, the rate of airflow in each decreases. The air enters through diffusers, which prevents the occupied areas from feeling drafty while mixing the air. The amount of air passing through a duct can be controlled by dampers, usually

set to respond to a thermostat. Unless the system is set to deliver at least a minimum of air, some individual areas may get no air exchange during times when the thermostat does not call for temperature modification. Air blowing from the end of a duct can travel as a stream from an appreciable distance without mixing uniformly in a room, creating dead zones that allow contaminants to build up in the environment.

Fans: HVAC fans create air pressure that moves air through the ventilation system. The main fans are usually located just after the air filters. Other fans may be located near exhaust vents. Fans are selected to deliver a quantity of air to meet ventilation requirements. The amount of air in cubic feet per meter and air pressure is a function of fan speed. Mechanical or electrical problems with a fan can affect air pressure and airflow throughout the HVAC system and, therefore, through the indoor environment. Fans can also become contaminated with dust or biologicals. Fans can move large quantities of air but can only work against a small pressure gradient. Obstructions in the ventilating system can reduce airflow even if the fan is working properly.

Air handler: This should be inspected to insure that it is clean and free of dust, moisture, and debris. Moisture problems can be caused by water leaks into the air handler through gaps or spaces in sheet metal joints. Also, condensation of water vapor in the intake system can occur when it operates during cooler hours with relative humidity high. The cooling coil should also be inspected for water condensation and dirt and debris. Any water condensation can result in the growth of microorganisms. Inspection of the filters, the cooling coil, and the pan for moisture can help eliminate many problems with aeroallergens from mold growth and bacteria in this area.

The room housing the HVAC system's air handler is usually under negative pressure relative to the unit itself. Contaminants can be drawn into the system from this point. It is important to note if the air handler unit is located near any source of contamination or pollution. In commercial buildings, the intake areas and handlers may be near traffic or a loading dock area, which are sources of vehicle exhaust and odors.

Air filters: Air filters should be inspected and either replaced or maintained according to manufacturers' recommendations. Gaps around the filters allow contaminated air to bypass. Filters should be inspected to determine if they need replacement and whether the filter fits tightly within its housing. Dirt, debris, or moisture on a filter is a source of nutrients for amplification of microorganisms.

Cooling and dehumidifying coils: Air is passed over cooling coils. If the air temperature is cooled below the dew point, water condenses on the coils. If the water is not adequately drained and the coils are not kept clean, mold and other microorganisms can grow, becoming a source of contamination.

Heating devices: These depend on combustion, and the products of combustion should be vented to the outside. This may not be the case, and dangerous carbon monoxide can build up indoors. Other sources of heat might be electric heating coils, a furnace, a heat pump, or even the cooling coils of a dehumidifier. Heated surfaces remain dry and should only cause problems if they collect dust or if they leak. In some new buildings, heat is primarily supplied around the outer walls to balance heat loss. The remainder of the building receives heat from the occupants, office machines, and lights, which generate heat as a by-product. In these situations, the main ventilation system is primarily called on for cooling.

Humidifier and evaporative cooler: In cold climates, heating outside air to comfortable temperatures reduces its relative humidity. Moisture is usually added to this dry air by spraying water into the airflow or passing the air over sources of moisture. Evaporative coolers pass warm, dry air through moist mats. As the water evaporates, it cools and humidifies the air. Moist surfaces support growth of biologicals and require maintenance and cleaning.

Air return: Rooms have a grillwork that allows air to move into return air ducts or plenums. These return vents may be located on the ceiling or near the floor. Even if a fan is present to aid this movement, measurable airflow in the room exists only close to the vent. It is quite common to use the space above a ceiling as the return air plenum. These grills should be inspected for dirt and dust, which could indicate buildup inside air vents.

Outside exhaust: In older buildings, sufficient air usually leaks out through cracks to make a general exhaust to the outside unnecessary. In newer buildings, exhausts are necessary. In addition to an exhaust on the main system, some local exhaust systems exist, which take air from a problem area (i.e., a restroom or a particular machine) and exhaust it to the outside. Most building codes require the restrooms and kitchens to have such exhaust ventilation.

Recirculation and air mixing: Because heating or cooling a building takes energy, and because draft-free temperature control requires that air entering offices be only a slightly different temperature than room air, it is the usual practice to circulate greater volumes of air than those needing to be drawn from the outside. Thus, ducts exist that allow much of the air returning from indoor areas to mix with outside air, pass through the filters, and return back into the indoors. A common ventilation in new buildings is the roof-mounted integrated unit that contains the intake, exhaust, and recirculating vents and controls. It is not uncommon that adequate makeup air has been neglected, particularly in manufacturing settings. Another common practice to save energy is to run the ventilating system only when the building is in use and for a limited period before and after hours. This may be automatically or manually controlled. This practice allows pollutants to build up, particularly over weekends.

Cooling towers: Cooling towers are used in commercial buildings to provide cool air. Warm water used in cooling towers favors the growth of biologicals, such as *Legionella pneumophila*, which is responsible for legionnaires' disease. Frequently, biocidal material is used to inhibit and control microbial growth. The proper cleaning and decontamination of cooling towers require the knowledge of professionals. Studies have shown that simple addition of biocides may be inefficient in controlling the growth of microorganisms. Dirt within the water and around the tower may make the biocide ineffective. If other organic materials are contaminating the system, then they can bind the biocide so it cannot reach concentrations to control microorganisms. The treatment of the cooling towers with chlorine-containing compounds has been more effective in controlling microorganisms.

Economizers: This is an energy-saving device that helps control the cooling of outside air coming indoors. Surveys should include a review of the economizer settings and testing of the operation of the economizer, including the damper movements. Economizers can result in lack of fresh air, allowing indoor air contaminants to build up.

EVALUATING INDOOR ENVIRONMENT-RELATED HEALTH PROBLEMS

Most businesses do not have a written and implemented indoor environmental quality plan that proactively addresses the indoor environment to prevent problems from arising. Affected employees usually have sought medical care for their symptoms long before the indoor environment is suspected. In other cases, employees may suspect that their work environment is causing their symptoms, but management ignores their claims. In these cases, workers may be blamed for being disgruntled or lazy. At this stage, adversarial relationships between company manage-

TABLE 53-19. Indoor air quality evaluation checklist

I. Building survey and environmental audit
   1. Building design and age
   2. Building location
   3. Building materials: exterior, mortar, flooring, ceilings, interior walls
   4. Interior furnishings: furniture, carpets, drapes, fabrics
   5. Interior finishing, paints, coatings, plastics
   6. Heating, ventilation, and air-conditioning: Location of intake and exhaust vents, coolers, last cleaning date, filters
   7. Recent renovations and changes to building
   8. Windows: Can they be opened and are they opened? Location of windows
   9. Movement of air mass when windows are opened

II. Interviews and health questionnaire
   1. Health survey and identification of ill workers
   2. Location of ill workers
   3. Location of workers relative to building alterations
   4. Identification of asthmatics and allergic individuals
   5. Description of syndrome
   6. Occurrence of syndrome relative to season
   7. Occurrence of syndrome relative to heating, ventilation, and air-conditioning

III. Pollution source identification
   1. Chemicals
   2. Volatiles, vapors, and semivolatile chemicals
   3. Cleaning agents
   4. Particulates, metals, dusts
   5. Biologics: mold, endotoxin, bacteria
   6. Inorganics
   7. Processes and reactions that produce pollutants
   8. Carbon monoxide and carbon dioxide
   9. Tobacco use
   10. Physical sources and thermal comfort factors (lighting, airflow, noise, humidity, temperature)
   11. Outside environmental sources (dust, odors, molds)
   12. Appropriate environmental monitoring

IV. Medical evaluation of employees
   1. Health evaluation
   2. Evaluation of signs and symptoms related to organ system
   3. Pulmonary functions if indicated
   4. Other studies as indicated

V. Remediation
   1. Heating, ventilation, and air-conditioning alterations and cleaning
   2. Engineering and technical controls
   3. Decontamination
   4. Removal of source
   5. Alteration of work habits
   6. Moving workers
   7. Control external sources
   8. Control psychogenesis

See EPA 1991 "Building Air Quality."

ment and the affected employees escalate, and employee trust regarding the company's ability or willingness to solve the problem wanes. Affected employees usually become angry and miss work. Some file worker's compensation claims at this point.

The evaluation of indoor environmental quality–related illness requires a systematic approach because of the complexity of potential causes. The objectives of the investigation are to gather information about the building, identify signs and symptoms of those with health complaints, locate and identify potential causes, determine work-relatedness of any illness, and remediate the cause by removing or isolating the source (Table 53-19).

Building Inspection

Regular building inspections can be preventive. Such an approach, however, is rare for a number of reasons. The building is usually leased, with the landlord off premise. Most business managers are not aware of what problems to look for in either preventing or reacting to a problem. In many cases, only a few workers are complaining of illness, and linking this with the indoor environment is usually not considered.

Building inspection involves collecting information about the site and its characteristics, and then performing a site survey. The inspection should be conducted by a qualified environmental specialist, such as an industrial hygienist, and includes the following basics:

1. Location of the building with respect to surrounding and outdoor sources of contamination.
2. Age of the building and construction materials.
3. Activities in the building.
4. HVAC system functioning, operation, filters, maintenance, and condition.
5. Adequacy of fresh air supply.
6. Number of occupants in affected areas.
7. Building maintenance, cleaning, and cleaning agents used.
8. Interior fabrics, building products, laser printers, copiers, drapes, carpets, and other sources of chemical emissions.
9. Presence of ETS.
10. Characterization and inspection of HVAC system, including humidification, location of ventilation ducts (exhaust and intake), movement of air, and air exchange.
11. Window locations and window openings.
12. Stagnant air and poor areas of air movement.
13. Physical factors, thermal comfort, lighting, noise, and humidity.
14. Dust and dirt on floors, desks, and in ventilation system.
15. Microbial contamination of ventilation system coolers and ducts.
16. Chemicals used in the environment.
17. Location of copying machines and other equipment in relationship to vents.
18. Renovations and building changes.
19. Changes to the immediate outdoor environment.
20. Location of outdoor air intake vents.
21. Odors.
22. Plumbing, water stains, and moisture damage areas.
23. Indoor pesticide application.

On concluding the building inspection, the investigators should provide a preliminary assessment of their findings, recommendations for changes, and recommendations for any further evaluations and monitoring. Easily identified causes of health complaints should be addressed immediately. At this phase, more in-depth investigation of particular problem areas may be conducted with appropriate monitoring.

Health Audit

A health questionnaire can be useful in determining the health status of employees and can help identify individuals who are manifesting symptoms associated with poor indoor environmental quality. The questionnaire should include location of the employee in the work site, dates the employee experienced illness, whether smoking is allowed, presence or absence of allergic conditions, and location where employees experience symptoms.

After employees complete the questionnaire, symptoms can be tabulated so the actual incidence and prevalence of illness can be determined and the location associated with symptoms identified. An example of a general health questionnaire is presented in the EPA's December 1991 publication, "Building Air Quality" (www.eps.gov/iaq/base).

TABLE 53-20. Checklist for ventilation problems

Yes	No	
❑	❑	Does the air in the room make people uncomfortable or sick?
❑	❑	Are odors present?
❑	❑	Is the space comfortable?
❑	❑	Too cold?
❑	❑	Too hot?
❑	❑	Too humid?
❑	❑	Too dry?
❑	❑	Can you feel the air moving or is the air stagnant?
❑	❑	Do office machines, copiers, printers, and such have adequate ventilation?
❑	❑	Is air distributed throughout the entire space?
❑	❑	Are dead zones of no air movement present?
❑	❑	Does the room have an air supply vent?
❑	❑	Does the room have an air return vent?
❑	❑	Is air moving out of the air supply vent? (Check with tissue paper.)
❑	❑	Is air moving into return vent? (Check with tissue paper.)
❑	❑	Are air vent diffusers open?
❑	❑	Is dust or dirt present on the air vent grill surfaces?
❑	❑	Does the heating, ventilation, and air-conditioning system operate when people are in the space?
❑	❑	Is the air intake of the ventilation system located near a contaminant source, such as a garage or vehicle parking area?
❑	❑	Has the heating, ventilation, and air-conditioning been inspected or cleaned recently?
❑	❑	Has the air filter been replaced or serviced?
❑	❑	Is there a lack of outside air?
❑	❑	Are there air pressure differences between rooms?
❑	❑	Is there excessive tobacco smoke?
❑	❑	Poorly vented heating equipment?
❑	❑	Poorly located intakes?
❑	❑	Is there visible mold, slime, or biological growth?
❑	❑	Is visible moisture or water present?
❑	❑	Is there water damage indoors?
❑	❑	Are cleaning chemicals stored in mechanical room or near air intake?
❑	❑	Is there deteriorated insulation around ventilation ducts?
❑	❑	Is there dirt debris in vents?
❑	❑	Is there improper exhaust ventilation?

See also EPA 1991 "Building Air Quality."

Identifying the prevalence rate of ill employees can help determine whether an excessive number of health complaints is related to a possible indoor air pollution cause. Because many individuals at a variety of times manifest a number of these vague complaints, however, it can be difficult to derive a true prevalence rate for indoor air pollution–related illness. Frequently, only one or a few individuals are voicing health complaints.

Strategies and Tactics

Symptoms can be generated by the buildup of low concentrations of multiple indoor contaminants, including off-gassing from building materials, emissions from office machinery, and solvents and other chemicals used in the office work and building maintenance. This synergy of low-level multiple pollutants is accentuated by a suboptimally performing HVAC system.

Because problems related to ventilation are responsible for 50% to 60% of indoor air quality problems, altering and adjustments in ventilation can result in improvement or resolution of symptoms (Table 53-20). The volume of fresh air should be increased if possible. Sometimes decreasing the occupancy numbers is helpful. Smoking should be eliminated totally. Local exhaust ventilation may also serve to reduce a pollutant source. Sometimes decreasing indoor temperature helps decrease volatile chemical emissions. Cleaning agents used indoors should be evaluated to determine if they contain irritants and sensitizers. If so, they should be replaced.

Inadequate outside air intake can be assessed by measuring the rise in CO_2 levels in the building over the day and subsequent fall in the evening with the building unoccupied but the ventilating system running at daytime levels. If the outside air intake is sufficient to adequately manage CO_2, it is assumed that other contaminants are managed also.

Temperature and humidity, and, if necessary, airflow at vents and return air grills, should also be checked. Although wet-and-dry bulb thermometers can be used, this level of accuracy is generally unnecessary. A desk thermometer and relative humidity meter should be adequate. Measurements for airflow assure that a vent is functioning and indicate if the airflow is directed in a suitable direction. In general, exact measurements of these parameters are less critical except in special circumstances.

These guidelines are based on whole building analysis rather than an analysis of the spatial distribution of the building's ventilation. Pollutant transport depends on building geometry, pollutant source characteristics, and thermo/fluid boundary conditions, such as flow rate, thermal stratification, duct location, and diffuser type. If the air in the room is well mixed, then the concentration can be predicted based on knowledge of the room ventilation rate, the pollutant source strength, and the concentration in the supply air. In situations in which the well-mixed assumption does not apply, knowledge of local concentration distributions is required to determine average ventilation system performance. Even if an acceptable average room concentration can be achieved at a given ventilation rate, the sensitivity of concentration to flow nonuniformities can produce localized areas (dead zones) with acceptably high concentration levels. As a result, a detailed knowledge of source strengths and local ventilation system performance is required to ensure that the ventilation system provides pollutant control at reasonable ventilation rates.

To properly evaluate indoor air problems, it is necessary to have some basic knowledge of ventilation. Because buildings are not constructed to contain air pressures significantly different from outside pressures, it is necessary to move air out of the building to move air into a building, and vice versa. If a system imbalance exists in a building, it may be noticeable when outside doors or windows are opened, resulting in a rush of air either into (excessive exhaust or insufficient intake) or out of (insufficient exhaust or excessive intake) the building. With the slight pressure difference between inside and outside, however, only as much air enters the building as is able to leave the building.

Inadequately functioning HVAC systems allow indoor contaminants to accumulate, contributing to stale and stagnant air, and may even introduce outdoor pollutants and allergens into the indoors, especially if the air is unfiltered. A frequently occurring problem is an imbalance in the flow of fresh air versus outflow of stale air. This can create dead zones of no air circulation indoors. These dead zones are essentially stale air that escapes being recirculated. HVACs can be sources of moisture, allowing mold and other microorganisms to amplify and be circulated indoors. Over time, dust, dirt, and debris build up in the ventilation system. Proper maintenance can help prevent accumulated dirt and dust from being circulated indoors.

Monitoring strategies for pollutants are based on the environmental assessment and health survey. Decisions regarding monitoring for VOCs and biologicals are driven by what is found on the inspection and the pattern of illness of the occupants. Monitored variables may include the following:

1. CO_2 (should be <800 ppm)
2. Relative humidity:

Winter 30% to 50%
Summer 40% to 60%
Plenum and ductwork <70%

3. Ambient air temperature (should meet ASHRAE standard 52-1992)
4. HVAC functioning and condition (should meet ASHRAE standard 62-1989)
5. TVOCs
6. Specific volatile chemicals
7. Combustion products, such as CO, NO_2, SO_2, and ozone
8. Biologicals, bioaerosols, and chemical by-products
9. Lighting level
10. Airflow: supply diffusers, return grills, and local exhaust systems
11. Airflow between spaces
12. Vertical air temperature
13. Air filtration
14. Noise and vibration

RADON INDOORS

Radon (radon-222), a naturally occurring nonreactive, colorless, odorless, and tasteless noble gas, is a product of the decay of trace amounts of uranium-238 found in soil and rock. Radon's eventual fate is to decay through a number of intermediates to lead-206, a stable end product. As a gas, radon can diffuse through soil and rock and enter home environments. In certain geographic areas, concentrations of radon can be higher in indoor environments compared to those outdoors.

Natural uranium found in the earth contains a predominance of the isotope ^{238}U. Uranium-238 decays through a series of isotopes, one of which is radium-226. Radium-226, an alpha emitter, and its daughter products are responsible for a large fraction of alpha emissions received by humans from the environment (96). Radium-226 present in soil and rock decays with a half-life ($t_{1/2}$) of 1,622 years to radon-222, which has $t_{1/2}$ of 3.8 days. Radon decay results in the generation of short-lived α- and β-emitting progeny. After six decay steps that produce isotopes with half-lives from 1.6×10^{-4} seconds to 26.8 minutes, the isotope of lead-210 is reached with a $t_{1/2}$ of 22 years (96). Lead-210 decays with a $t_{1/2}$ of 238 days to stable lead-206.

Because radon is a gas, it diffuses from its point of origin through soil and can enter a home or building via cracks or pipes. The porosity of the soil helps to determine its transfer. Thus, radon can move by diffusion and pressure differences into basements and indoor spaces. Radon-222 decays by alpha-particle emission to radon daughters: polonium-218 (radon A), lead-214 (radon B), bismuth-214 (radon C), polonium-214 (radon C^1) (97). Radon is not a health hazard by itself, instead health hazards are caused by the radon decay products (daughters) that emit alpha particles. Daughters are chemically active and can attach to particles, surfaces, and human tissue (98–100). Polonium-218 and polonium-214 are daughters that emit alpha particles.

A difference exists between radon activity indoors and exposure to harmful radon daughters. Radon activity is measured in either curies or becquerels, and typical air concentrations are expressed in terms of picocuries per liter or becquerels per cubic meter. Soil contains approximately 1 pCi of radium per g, which provides an emission of 0.5 pCi of radon per square meter per second (100). Outdoor radon concentrations average 0.20 pCi per m^3 (greater than Bq per m^3), and typical indoor air concentrations are 1.2 pCi per L (945 Bq per m^3) (97,100).

Radon exposure is expressed in terms of working levels (WL) or working levels per month (WLM), an accumulation measurement. One WL is any combination of radon daughters in 1 L of air that results in the release of 1.3×10^5 MeV of alpha energy (97). In general, 1 pCi of radon per L is equivalent to 0.005 WL (97,100). The WLM assumes 170 hours per month of exposure (not dose) (100).

Occupational exposure to radon in the United States was reduced from 12 WLM per year to 4 WLM per year in 1971 (98). The level for remediation activity in the home environment is considered to be 2 WLM per year (98). As of 1989, EPA monitoring has shown radon concentrations to be less than 4 pCi per L in 74% of homes across the United States (100).

The relationship of exposure to radon and actual dose of radon and its daughters remains complex. Therefore, most assays are designed to measure radon rather than the biologically active daughters. As mentioned previously in this section, radon is not hazardous by itself; instead, radon daughters that emit alpha particles create a health hazard when they attach to dusts and other aerosols because of their electrical charge and are inhaled, depositing in the tracheobronchial tree.

It is estimated that 9.25×10^{20} Bq per m^3 of radon is released from the earth on an annual basis (97). Variation in atmospheric radon concentration is dependent on meteorologic conditions and amount released from the soil. Outdoor radon concentrations are highest at midnight, with minimum concentrations occurring at noon because of air mixing.

The airborne radon concentration in a home is a factor of the earth surrounding the home containing radon gas, air changes per hour in the home, amount of radon in water and in natural gas, and construction of the home (100). Radon can diffuse through cracks in foundations and walls, openings for plumbing, and cinder block (100). Radon does not pass easily through solid concrete foundations. WHO has set limits of radon at 0.11 WL for existing buildings (100).

Ventilation reduces indoor radon concentrations if air exchanges average approximately four times per hour. Because this volume of air exchange is not easily achieved, radon concentration indoors exceeds that outdoors. Radon exposure also arises from contaminated water and natural gas and can be released from rock materials used to build houses. Action in the home is recommended if radon concentrations exceed 400 Bq per m^3 (11 pCi/L).

Health effects from excessive radon daughter exposure relate mainly to an increased risk of lung cancer from alpha particle exposure. Most studies of the relationship of lung cancer and radon exposure are from uranium miners. Studies indicate that all forms of lung cancer are increased by radon exposure (98). Also, the contribution of smoking to lung cancer is a confounding factor in determining the exact etiology. Radon exposure and smoking are thought to increase the risk of lung cancer tenfold over nonsmokers (98).

Over the lifetime of an individual, exposure to 1 WLM per year is thought to increase the number of deaths from lung cancer by a factor of 1.5 over the current rate in men and women (99). The National Council on Radiation Protection and Measurements has published guidelines on remediation and control of radon in indoor environments (National Council on Radiation Protection and Measurements report no. 77, 1984).

PSYCHOSOCIAL ASPECTS OF INDOOR AIR QUALITY

The presence of illness in the workplace can be unsettling to employees, stimulate anxieties about possible toxic exposures, and accentuate worker stress. An indoor environmental quality investigation can generate strong emotional responses, especially if results are negative but illness continues. The overall

effect leaves building occupants discouraged, suspicious, and unconvinced that the problem has been discovered and a proper solution found. Stress- and anxiety-related symptoms can occur after suspected exposure or actual exposure of employees to unknown environmental health threats. Thus, psychosocial factors are important to consider when investigating indoor environmental quality problems. Some of these are as follows:

- The environment itself
- Boredom associated with the job
- Pressure to produce
- Everyday relationship between labor and management
- Lack of communication and social support within the work environment
- Adversarial relationship between employees and management because of environmental quality problems

Stress and Environmental Threats

In the 1950s, Dr. Hans Selye expressed the concept that stress was a general response of living organisms to external or internal stimuli, which he termed *stressors*. Dr. Selye observed that chronic stress could lead to exhaustion, organ system failure, and even death. He confirmed what has been known for centuries, that stressful thoughts and feelings affect our physical well-being.

The phenomenon of acute reactions or triggering of symptoms when rechallenged with a stressor has been observed in animals and is termed the *generalized adaptation syndrome* by Selye in his 1950 book, *Stress*. The term *generalized* was introduced because he was able to show that chemicals and other stressors also lead to a maladaptive response.

The physiologic basis of stress involves interconnections between the brain and other areas of the body via the hypothalamic-pituitary-adrenal (HPA) axis. When activated, epinephrine, norepinephrine, and corticosteroid secretions increase. Whereas the stress response, referred to as the *fight or flight* reaction, is essential for well-being and survival, chronic stress can result in illness.

Poor indoor environmental quality can be a chronic stressor. The concept of pollutants as activators of the stress mechanism has research support. Biomarkers in the brain have been found that indicate that brain cells are activated in response to stressors.

Exposures to chemicals may evoke expression of brain biomarkers indicative of neuronal excitation response to stress. Pyrethroid insecticides administered intraperitoneally in animal models evoke c-Fos and c-Jun protein biomarkers in brain neurons in the thalamus, hypothalamus, hippocampus, and cortex to varying degrees (101). C-Fos and c-Jun proteins are transcription factors encoded by rapidly inducible protooncogenes (102,103). Such markers indicate changes in neuron activity and programming. C-Fos expression in homogenates is demonstrated after the administration of lindane. This expression of c-Fos and c-Jun biomarkers reflects an intense and lasting neuronal excitation. Such markers appear in the cells of the brain, which are functionally activated by stressors of all varieties. With the use of c-Fos and c-Jun markers, scientists can study areas of the brain that are activated by adverse stimuli (104).

Animals studied using conditioned stressors (stressors that produce fear or anxiety without pain or without some kind of insult) at the time of exposure show activation of areas in the hypothalamus that contain corticotropin-releasing hormones. Other areas activated in the studies included the amygdala, the basal ganglia, and thalamic nuclei (101–104). The areas of the brain activated by stressors are associated with the HPA and the sympathetic nervous system. The HPA pathway, thus, may be activated by a variety of stressors (physical, chemical, and psychological).

Stress can have effects on the human immune system although the neuroendocrine responses of the central nervous system are activated by the HPA (105–109). Although stress responses can cause release of endogenous opioids, cortisol, and catecholamines, which may alter the humoral and cellular immune system, this immune response is not chemically induced immunotoxicity, but rather a physiologic response of the immune system to stressors.

Studies show that stress can elevate numbers of T cells and B cells, impair responsiveness of lymphocytes to mitogens, decrease CD4 to CD8 (T helper to T suppressor) ratios, increase natural killer (NK) cell populations, and decrease NK cell activity (110–113). Individuals treated with β-adrenergic antagonist drugs, such as propranolol, show inhibition of immune alterations after stressful episodes (114).

Mood and anxiety disorders and other psychiatric conditions are associated with immune alterations. It is reported that a linear relationship exists between severity of depression and immune compromise, including a marked reduction in the response to mitogens by lymphocytes, reduced NK cell activity, and alteration of immune cell numbers, primarily an increase in CD8 T cell lymphocytes (113).

Marital discord, bereavement, and other such stressors are associated with immunosuppression and higher antibody titers to Epstein-Barr virus, lower NK cell activity, and reduced lymphocyte response to mitogens (111,112,115,116). The chronic stress of providing care to family members with debilitating disease is associated with decreases in CD4 T cells, lower helper to suppressor cell ratios, and increased antibody titers to Epstein-Barr virus (115,116). Bereavement, depression, and anxiety activate neuroendocrine functions, which reduce NK cell activity and reduce T cell numbers with CD4 markers.

Individuals under stress show higher titers of Epstein-Barr viral capsid antigen IgG. Plus, negative moods depress mitogen stimulation of lymphocytes. Studies also show that stressors increase the number of CD8 marker T cells, CD16/56 cells (NK cells), decrease mitogen response, and increase numbers of B cells (CD19) within 5 minutes of the stressor (106–108,117). These immune changes can persist for hours.

Chronic stress acts opposite of acute stress in producing immune function changes. Chronic stress reduces NK cell numbers and activity, whereas acute stress elevates NK cell numbers and activity. Acute stress elevates lymphocyte subsets. In contrast, chronic stress decreases lymphocyte mitogen responsiveness. Research has shown that moderate exercise modulates the effects of chronic diseases and has positive effects on immune function (118). Relaxation methods also positively modulate the immune system through stress reduction (114).

Chronic stress and associated somatic, behavioral, and psychological responses outlast their initiating cause, with symptoms persisting for long periods of time. Also, chronic stress is associated with a loss of personal control over one's health (119). Efforts to increase a patient's sense of control over aspects of their health should have positive health effects.

Control or lack of control is another feature affecting perceptions of stress, health, and well-being. Loss of control over one's environment, especially when it is suspected as a cause of illness, increases stress levels. In contrast to the industrial or occupational environment, residential environments allow significant personal control of thermal comfort factors as well as ventilation.

Psychogenic Illness

Certain features exist that suggest a psychogenic origin of indoor environmental problems as opposed to contaminant-induced illness (120–122):

1. An incidence of the problem in areas that are not consistent with ventilation patterns in the workplace or the environment.
2. A temporal sequence of events that is not consistent with ventilation flow patterns and ventilation flow rates or chemical sources.
3. An absence of medical findings compatible with exposures.
4. Outbreak of illness consistent with person-to-person transmission rather than transmission from a source.
5. Severe symptoms of sudden onset among a number of people, particularly if the symptoms begin after leaving the source of exposure or do not resolve on leaving the work site.
6. Moderate to severe symptoms that are unrelated to the nature of a contaminant found.
7. A diversity of symptoms without collaborating objective findings.
8. The discovery of individuals who are affected, not because they are near the source of the exposure, but rather become affected after learning of the exposure or learning that someone else is exhibiting signs of illness.
9. Pattern of the illness after a classic epidemic curve in which conversation is the vector of spread.
10. Managerial or supervisory change or changes in work flow or production volume, including deadline requirements.

The term *psychogenesis* has emotional connotations, and its cavalier use can further adversarial relations between management and workers in the investigation of indoor environment illness.

In general, organizations whose employees are more prone to develop psychogenic illness are generally rigid and authoritarian, with poor communication between workers and management (121,122). Workers may not believe that management is serious about the problem, and the worker believes he or she has an inability to control environmental conditions. Multiple stresses can affect a worker's ability to relate to the environment. These stresses may be fear of loss of job, external forces, and the thought of environmental contamination (123).

Threat of exposure to toxins can add to anxiety. Workers may become alarmed if they believe that a chemical contamination in an environment may cause them long-term health consequences. Also, heightened concern occurs if the source of the potential problem, such as an odor, cannot be established or identified and remediated.

Odors in the environment can create anxieties and stress. The psychologic responses to indoor air quality problems may relate more to an odor of a chemical than to its toxic effects. Odors, such as sulfur odors, odors of rotten eggs, or odors of chemicals or hydrocarbons, can be distressing to workers.

The relationship of management and employee can be greatly tested during these times. Sending workers to an emergency department unnecessarily may further serve to intensify anxiety. The use of a knowledgeable, single-source professional can help to prevent distortion of facts and decrease rumors. Closing the workplace is not recommended unless a serious and significant threat to the health of the workers exists. Once a workplace has been closed, it is difficult to reopen again.

Communication should be open and should be timely. Because rumor is the most common source of information, rumors should be dispelled by having frequent meetings and open discussions with employees regarding the investigation. Communication with the media may be important in some situations in which a public health concern is present. The media, if not properly educated, can help foster sensationalism and rumor.

WORK-RELATEDNESS OF POOR INDOOR ENVIRONMENTAL PROBLEMS

Illness associated with poor indoor environmental quality may range from vague and subjective to objective and easily recognizable. Environmental monitoring and investigations, however, may not produce evidence of a source.

Despite these difficulties, a medical condition, disease, or illness can be said to be work-related if the following criteria are met (124):

1. An employee-employer relationship exists.
2. The event is causally related to the work activity or work environment.
3. Medical conditions exist that are compatible with health effects secondary to exposure to an environment, chemical, industrial site, or other agents in question.
4. There was previously or is presently a sufficient exposure to agents in the work environment to produce illness or disease.
5. A preexisting disease is exacerbated by a previous or present work site exposure.
6. Evidence supports an occupational etiology.

Impairment and Disability

Impairment is present if an exposure results in a reduction or loss of use of a body part or reduction of function of a body system. This functional limitation may or may not prevent the individual from meeting the demands of his or her life's activities or conditions of employment. Disability results from a permanent impairment that cannot be overcome through retraining, use of accommodative procedures, or rehabilitation. Medical conditions, such as asthma, may result in episodic expressions of impairment. The medical condition may also result in a permanent impairment expressed on an episodic basis.

Individuals with health problems secondary to poor indoor environmental quality may fall under protection of the Americans with Disabilities Act (ADA), especially if one or more of their major life activities is substantially limited. Poor indoor air quality may be a reason why an employee may not be productive or be able to continue working in a specific environment. Accommodations may be required to make the environment healthy and safe for affected individuals, or the affected person may need to be relocated to another area of the work site or building.

The ADA, signed into law in 1990, has the purpose of eliminating discrimination against disabled individuals with the enforcement of federal law. Title I of the ADA applies to employment issues of qualified, disabled individuals. Disability is defined as mental or physical impairment that substantially limits one or more major life activities. Major life activities are defined as those activities that an average individual can perform with few or no difficulties. Under the ADA, employers are responsible for making reasonable accommodations to qualified individuals capable of performing essential functions of the job.

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