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Chapter 11

Health effects

There are beneficial as well as harmful aerosols. According to their nature, harmful particles can be classified into three categories: chemically toxic, infectious, and radioactive. In general, there is a relationship between the response and the dose received.

A biochemically active particle may contain only a small amount of active agents. In this respect, an inhaled particle simply acts as a carrier that facilitates delivery of deleterious or beneficial components to specific surface areas of lung airways. In view of the tortuous narrow passageways and sharp turns they have to go through, aerosol particles are an effective carrier. As an indication of their effectiveness, about one half of all 3-μm particles inhaled through the mouth deposit in the alveolar region.

11.1 ADVERSE HEALTH EFFECTS

In addition to respiratory disease, some types of deposited particles can cause systemic diseases following their dissolution and absorption.

The period between first exposure to an agent and the appearance of symptoms varies depending on the characteristics of the agent and disease. Some symptoms appear within hours from an acute exposure, whereas others may have latency periods as long as 20 years.

Synergistic or antagonistic effects play an important role. Synergism represents the interaction of two or more agents that produces an adverse effect greater than the sum of the effects resulting from exposure to each agent separately. Antagonism is an interaction between two or more agents that results in a reduction in adverse effect of each agent.

Host factors have a strong influence on biological responses to harmful particles. The main host factors include state of health, genetic trait, immunological status, and psychological state such as anxiety and stress.

11.1.1 Chemical Toxicants

Inhalation of particulate toxicants can lead to various types of responses including fibrotic, systemic, irritant, allergic, mutagenic, teratogenic, and carcinogenic responses. Injury of tissues may result from the inhaled compound or its metabolic products. Effects may differ considerably between direct exposure of epithelial cells to toxicants and exposure to the toxicants after phagocytosis. Toxicity also depends on particle size and physicochemical...
properties of the agent. Concentration of the agent and duration of exposure are two important factors influencing response. Acute and chronic exposure may result in different adverse effects.

Pneumoconioses, characterized by scars due to increase in interstitial fibrous tissue, are diseases resulting from retention of certain types of particles in the alveolar region. Different types of dusts may produce different patterns of fibrotic lesions. For example, crystalline free silica found in mines, foundries, blasting operations, and glass manufacturing can give rise to a nodular type of fibrosis (silicosis). On the other hand, asbestos fibers can cause a diffuse fibrosis (asbestosis) if they exceed 2 μm in length and 0.1 μm in width (Lippmann, 1990). Coal workers’ pneumoconiosis has a complicated form. Most pneumoconioses result in shortness of breath and chronic cough, but pneumoconioses from certain types of dust, such as iron oxide, may have no evidence of functional impairment.

Systemic response arises from chemical toxicants that affect certain organs or tissues. Target sites include respiratory tract, gastrointestinal tract, hematopoietic system, liver, kidney, bones, endocrine system, and nervous system. Herbicides, pesticides and heavy elements such as mercury, lead, cadmium, arsenic, molybdenum, and selenium are known systemic toxicants. An example of systemic response is metal fume fever, an acute flu-like illness with symptoms of throat irritation and dry cough. The symptoms appear within hours following heavy exposure to fumes of metal oxides.

Irritant response generally results from inhalation of particulate sulfates, pesticides, and droplets of sulfuric acid or other strong acids. They cause inflammation in affected regions such as rhinitis, pharyngitis, laryngitis, bronchitis, pulmonary edema, and pneumonia.

Allergic response involves sensitization by initial exposure and reaction to subsequent exposure. Such response can lead to bronchial asthma. Examples of allergens include nickel, cobalt, arsenic, chromium, organic dusts, herbicides, and insecticides.

Inhalation is a route of entry for airborne mutagens (agents that produce changes in DNA), teratogens (agents that cause developmental malformations), and carcinogens. Among known or suspected chemical mutagens are DDT, sodium arsenate, cadmium sulfate, and some lead salts. Examples of known or suspected chemical teratogens include dioxin, organic mercury, cadmium sulfate, and sodium arsenate.

There is a broad variety of chemical carcinogens including cigarette smoke, soot, asbestos, arsenic, chromates, and certain petroleum products. Changes in lung tissues can begin when an individual is exposed to a cancer-causing substance. A few abnormal cells may appear in the lining of bronchi. If
exposure to the carcinogen continues, more abnormal cells can appear and lead
to formation of a tumor.

In addition to asbestosis, asbestos fibers can cause bronchial cancer and
mesothelioma. The latency period is 20 years or longer. To have chronic
toxicity, inhaled asbestos fibers must exceed the following critical length limits:
5 \mu m for mesothelioma and 10 \mu m for lung cancer. In addition, fiber width must
be less than 0.1 \mu m to induce mesothelioma and larger than this limit to cause
lung cancer (Lippmann, 1990).

Cigarette smoke, containing particles and vapors, has been identified to be
the cause of a plethora of diseases. In addition to cancers of the lungs, larynx,
esophagus, bladder, cervix, kidney, pancreas, and stomach, smoking can give
rise to emphysema, chronic bronchitis, pneumonia, chronic heart and
cardiovascular diseases, abdominal aortic aneurysms, acute myeloid leukemia,
cataracts, and gum disease. Central bronchial airways are the most common
sites for lung cancer in cigarette smokers (Schlesinger and Lippmann, 1978).

11.1.2 Ambient Particles

The diseases resulting from exposure to ambient aerosols include
pulmonary emphysema, bronchitis, and, perhaps, lung cancer. Asthmatics are
particularly susceptible to the adverse effects of aerosol acidity in ambient air.

Emphysema is a condition of over-inflation of structures in the alveolar
region. The over-inflation arises from a breakdown of alveolar walls. Early
symptoms of emphysema include shortness of breath and cough. The primary
cause of emphysema is cigarette smoking. There is also an inherited form of
emphysema due to deficiency of a protein called alpha 1-antitrypsin.

Bronchitis is an inflammation of the lining of bronchial airways. When
bronchial airways are inflamed, less air is able to flow to and from the alveolar
region and a heavy mucus or phlegm is coughed up. Cigarette smoking is the
number one cause of chronic bronchitis. Dusts and fumes in ambient air and
workplaces are other common causes of this disease. Higher rates of chronic
bronchitis are found among workers exposed to particles of high concentrations,
such as coal miners, grain handlers, and metal molders.

Emphysema and chronic bronchitis in combination comprise chronic
obstructive pulmonary disease (COPD). A COPD patient has difficulty
breathing because (1) the airways lose their elasticity and therefore cannot keep
open properly; (2) some alveolar walls are destroyed; (3) airway walls are
inflamed; and (4) cells in airways make more mucus than usual, which tends to
clog the airways.

Ambient aerosol is a mixture containing numerous chemical species of
natural and anthropogenic origins. These particles are either directly emitted
into the atmosphere from many different types of sources or formed in air by
gas-to-particle conversion processes. Harmful components identified in highly polluted air include acid sulfate species, heavy metals, reactive organic compounds, and peroxides. At sufficiently high doses these components can produce local respiratory diseases or systemic disorders. However, none of the harmful components mentioned above exists in ambient particles at sufficiently high concentration levels to cause a specific disease.

Ambient particles are harmful when their concentration exceeds a certain limit; epidemiological studies have indicated a strong association of increases in human morbidity and mortality rates with increased concentrations of ambient particles in a certain size fraction (Wilson and Spengler, 1996; Vedal, 1997). Complexity in chemical characteristics of ambient particles has led to considerable difficulty in identifying the components responsible for adverse health effects. Thus, it remains largely unclear which specific components are responsible. Concentration alone cannot explain the causal relationship. According to the threshold limit values recommended by American Conference of Governmental Industrial Hygienists, a worker can be exposed to nuisance or inert dust at the concentration of 5 mg/m\(^3\) in the respirable fraction without measurable injury.

Questions have been raised whether ambient particles are a carrier of short-lived, difficult-to-quantify, but harmful compounds. Friedlander and Yeh (1998) have provided supporting evidence for the involvement of peroxides in the adverse health effects of particulate pollutants. Reactive oxygen species (ROS) in particles also have been shown to play an important role. Highly reactive oxygen-containing species, such as hydroxyl radical and hydrogen peroxide, are collectively described as ROS. In ambient air, photochemical reactions involving reactive organic gases can produce ROS, which are distributed in the gas and particulate phases. Combustion aerosols, such as vehicular exhaust, also contain relatively high concentrations of ROS. Hung and Wang (2001) have reported that the concentrations of particulate ROS in ambient air are strongly associated with photochemical activities. There is a good correlation between the concentrations of ambient ozone and ROS in submicron particles, especially in the ultrafine fraction that are freshly produced by either photochemical reactions in ambient air or combustion processes in vehicular engines.

Aerosol particles can serve as an effective carrier for ambient peroxides and reactive oxygen species to reach the alveolar region. In the absence of particles, inhaled peroxides and ROS mainly deposit in tracheobronchial airways because of their high solubility and diffusivity. When these reactive species are adsorbed on particle surfaces, they can easily reach the alveolar region and thereby lead to an adverse effect greater than in tracheobronchial airways.

Because of their small sizes and surface characteristics, ultrafine particles appear to be more toxic than larger particles. Respiratory effects are shown to
be associated with the number of ultrafine particles (Peters et al., 1997). A recent study indicates that ultrafine particulate pollutants are capable of inducing oxidative stress and mitochondrial damage (Li et al., 2003).

Pulmonary effects of ultrafine particles have been reviewed by Oberdörster (2001). Studies on rodents indicate that ultrafine particles administered to the lungs cause a greater inflammatory response than larger particles of the same total particle mass do. Surface chemistry appears to be an important contributing factor of their high toxicity. Furthermore, it appears that deposited ultrafine particles largely escape capture by alveolar macrophage and therefore have higher probabilities to enter the pulmonary interstitium. These results lend support to the hypothesis that ultrafine particles are causally involved in adverse responses seen in susceptible groups of the population. The need for further studies on ultrafine particles has been stressed in a couple of recent reports (National Research Council, 1998; Friedlander and Pui, 2003).

11.1.3 Bacteria and Viruses

Inhalation is an important route of entry for bacterial and viral pathogens. Single bacterial particles can remain airborne for a long time and therefore have high probabilities to be transmitted through air. Viruses in droplets generated by sneezing and coughing of a patient can survive for hours and gain access to another host while they are airborne.

Droplet size plays an important role in determining the atmospheric spread of infectious diseases. Sneezing and coughing can produce droplets of various sizes. The distance to which a droplet can be transported depends on the rate at which the droplet evaporates. Large droplets settle out of air quickly and, even if they are inhaled, may not reach the pulmonary region. For many pulmonary diseases, the susceptible part is the alveolar region of the respiratory tract. However, smaller droplets can evaporate rapidly to less than 10 μm in diameter. It is mainly these residual particles, named droplet nuclei (Wells, 1934), that can spread the diseases.

Tuberculosis and bacterial pneumonia are two common respiratory diseases caused by bacteria. Symptoms of tuberculosis include feeling tired, loss of appetite, fever, coughing up blood, and night sweats. Pneumonia is a serious infection of the lungs. When the lungs are infected, the alveoli fill with pus and other liquid, thereby greatly reducing the ability to transfer oxygen to the bloodstream.

Legionnaires' disease is a form of bacterial pneumonia. It has acquired its name, because the first known outbreak occurred in the Bellevue Stratford Hotel in Philadelphia where a convention of the Pennsylvania Department of the American Legion was held. In that outbreak, over 200 people contracted this previously unknown type of pneumonia as a result of exposure to mist from
contaminated water that was used to cool the air in the hotel's air conditioning system. The disease can also be contracted by inhaling mist from water sources such as whirlpool baths and showers that are contaminated with Legionella bacteria.

Anthrax is a disease caused by Bacillus anthracis, a spore-forming bacterium. Its symptoms are similar to a common cold initially, but progress to severe breathing problems and shock in a few hours to a few days. To contract the pulmonary form of Anthrax, it requires inhalation of 8 to 20 thousand spores into the alveolar region of the lungs. Droplets that deposit in the nose are not likely to cause the disease.

Examples of diseases due to viruses include influenza, common cold, viral pneumonia, and severe acute respiratory syndrome (SARS). When a person is infected by influenza virus, the tissues of respiratory tract become swollen and inflamed. Prominent symptoms of flu are high fever, muscle aches, severe headache, dry cough, and sore throat. Patients with common colds have milder fever, stuffy nose, sneezing, coughing, and also sore throat. Flu and common colds mostly spread through transfer of virus-containing droplets by inhalation or hand-to-hand contact.

SARS is a respiratory disease due to a type of coronavirus. First reported in Asia in February 2003, its symptoms include high fever (temperature higher than 38.0°C), shortness of breath, headache, coughing, diarrhea, and malaise. Most SARS patients develop pneumonia. According to the World Health Organization, a total of 8,098 people worldwide were infected during the 2003 outbreak. Of these, 774 died. A probable transmission route of the SARS virus is the spread of droplets produced by the cough or sneeze of a patient. Infection can occur if these droplets deposit on the mucous membranes of the mouth, nose, or eyes of persons who are nearby.

11.1.4 Radioactive Particles

The most common radioactive particles in ambient air are radon daughters. After release from soil, radon gas continues to decay and generate a series of radioactive products. These radon daughters easily attach to ambient particles and become a source of radiation exposure for the general population. Occupational exposure to radioactive particles mainly occurs in uranium, tin, and hematite mines.

The primary health effect from inhalation of radioactive particles is cancer. Damage caused by ionizing radiation at the cellular or molecular level can give rise to uncontrolled growth of cells. This is a stochastic effect resulting from long-term, low-level exposure to radiation. Increased doses lead to increase in probability of occurrence. All regions of the respiratory tract are susceptible, but
the frequency of incidence differs from region to region. The types of radiogenic tumors and target tissues have been reviewed by ICRP (1994).

Soluble radionuclides in deposited particles can be absorbed into bloodstreams. Depending on their metabolic behavior, these radionuclides can be retained in various organs for different periods of time.

11.2 THERAPEUTIC AGENTS

A broad variety of pharmaceutical agents can be effectively delivered through inhalation to treat respiratory and systemic diseases. Examples of aerosolized agents for treating respiratory disorders include bronchodilators and mucolytics. Antibacterial and antiviral agents have been used in aerosol form for treating pulmonary infections. For aerosol therapy of systemic illnesses, various degrees of success have been achieved with hormones, vaccines, antibiotics, and cardiovascular drugs. Among the agents tested for systemic medication, aerosolized insulin and heparin appear to be very promising.

Two proven classes of aerosolized drugs for treatment of asthma and chronic obstructive pulmonary disease are \( \beta_2 \)-adrenergic agonists and glucocorticoids. Inhalation of \( \beta_2 \)-adrenergic agonists can relax bronchial smooth muscle, stimulate skeletal muscle, and inhibit release of inflammatory mediators. Short-acting \( \beta_2 \)-adrenergic agonists can provide bronchodilation within minutes of inhalation. Glucocorticoids are useful for treatment of inflammation.

Anticholinergics are among other common agents for treatment of asthma and chronic obstructive pulmonary disease. As bronchodilators, anticholinergics agent have a slower onset but a comparable duration of action as \( \beta_2 \)-adrenergic agonists.

Aerosolized formulations of corticosteroids have become commonly used agents in treating respiratory diseases such as asthma, cystic fibrosis, and obstructive lung disorders. These formulations are able to influence existing inflammation.

Mucolytics such as N-acetylcysteine can give rise to rapid liquefaction of viscid mucus. When administered in aerosol form, they can help maintain adequate mucus viscosity in patients with chronic obstructive airway disease.

PROBLEMS

11.1 A review of the SARS epidemic in 2003 indicates that, in some countries, a majority of cases were caused by nosocomial infection. Discuss possible transmission routes of the SARS coronavirus in hospitals.
11.2 A potential terrorist weapon is the release of plant and animal pathogens in aerosol form. These pathogens can have devastating effects on agriculture if they are released at points where they can spread out rapidly. What strategies can be used to protect agriculture from such terrorist attacks?

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