

# Occupational Diseases

NIOSH Instructional Module



**SHAPE**

Safety/Health Awareness  
for  
Preventive Engineering



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Centers for Disease Control  
National Institute for Occupational Safety and Health

**CDC**  
CENTERS FOR DISEASE CONTROL



# **OCCUPATIONAL DISEASES**

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## ABSTRACT

The objective of this educational module is to familiarize engineering faculty and students with some basic principles underlying the development of occupational diseases. This self-contained instructional module can be studied separately or as a component of an upper-level engineering course. The courses appropriate for the information contained in this work include occupational health and safety courses as well as laboratory design courses. In addition, this instructional module could serve as a suitable addition to a survey course on pollution control.

In this module, a qualitative, conceptual model describing the interaction of a worker with an environment containing potentially harmful inputs is presented. In this model, dose (the amount of the hazardous agent received by the worker) is the driving force for the physiological, biochemical, or biomechanical responses. The potential outcomes of the exposure, as well as the roles of the body defense mechanisms and means of elimination of harmful agents, are discussed. Some implications of development of occupational disease as interpreted with the aid of the model include: effect of differences in human susceptibility, aspects of medical intervention and surveillance, and rational approaches to setting of safe standards of occupational exposure.

Quantitative approaches describing the response of a worker to exposure are discussed. Basic concepts concerning dose-response relationships and dynamic models describing the fate and distribution of potentially harmful agents in the body are reviewed. The nature of laboratory, clinical, and epidemiological information used in analyses of occupational diseases and related issues is considered.

In the last half of this educational module, the specific anatomy, physiology, and defense mechanisms associated with several of the more important human systems are discussed. Some examples of occupational disease which affect these systems are discussed. For each of the human systems, a table lists typical occupational diseases along with the causative agents and the industries or processes where they can be found. Included in this analysis by physiological system is a discussion of ergonomics.



**Unit I**  
**INTRODUCTION**

- PURPOSE:** To introduce, in general terms, the scope of issues related to occupational diseases.
- OBJECTIVES:** To acquaint the reader with:
1. The multidisciplinary aspects related to occupational diseases
  2. The complexity of issues involved in occupational diseases
  3. The role of scientific information in studying occupational diseases
- SPECIAL TERMS:**
1. Occupational exposure
  2. Work environment
  3. Pathophysiology
  4. Body burdens
  5. Homeostasis
  6. Susceptibility
  7. Epidemiology
  8. Biases
  9. Medical history
  10. Extrapolation
  11. Regulatory policy

### **BACKGROUND**

In the last decade, a greater public awareness of occupational diseases and their consequences has created a broad-based involvement with issues related to worker health and safety. Studies related to occupational diseases are no longer restricted to health-care professionals, and the field of industrial hygiene contributed significantly to this change.

As scientists have increased their ability to analyze for minute concentrations, those who study occupational disease have established that materials, biological agents, or energies existing in very low concentrations may nonetheless be harmful to humans. Exposure to materials that exist as minute contaminants of other industrial raw materials may also represent a risk to worker health.

Engineers who, as a profession, are often responsible for the design and construction of industrial facilities and the protocols relating to their operation must now become more involved with worker health-related issues. New materials or new or improved processes, or both, that are constantly being introduced to industry require greater awareness of their health effects at the design stage. Engineers should not relegate health considerations to retrofitting practices. Increased public awareness has also had positive results, e.g., greater worker awareness of health-related issues; setting new standards of exposure and adjustment of old standards to reflect a more up-to-date understanding of occupational diseases; recognition of the need to instruct professionals such as engineers in health-related issues. This volume is directed to this last need in the expectation that through greater understanding, engineers will be able to contribute to improving the conditions that influence the well-being of workers.

Occupational diseases are preventable. An understanding of the nature of occupational diseases (identifying the causal agents, quantitatively assessing the human exposure, and learning the interaction of hazardous agents and the human body) should result in a safer work environment. In this enlightened situation, arrived at partly through the actions of engineers, health effects associated with a specific operation will be considered in the overall engineering design. Being aware of the interaction of a worker with his/her work environment will affect process design, including engineering controls; decisions about safe operating practices; and the use of protective equipment. This educational module is intended to introduce engineering faculty and their students to some basic principles—principles that will form a foundation for their understanding the development and prevention of occupational diseases.

Before occupational diseases are discussed in greater detail, background information is presented to place in perspective the current scientific understanding about work-related disorders. In this manner, a basis for both the general and specific issues that follow will be established.

### **COMPONENTS OF THE SYSTEM**

When investigating the development of an occupational disease, one is concerned with the interface and interaction between the human body and the work environment. An additional and important concern is the nature of the disease process, including the structural and functional changes occurring in the human body that result in or are a result of a disease process (the study of human pathophysiology). Together, all these disciplines contribute to an understanding of occupational diseases. In this work, a systems approach will be used to investigate the behavior of the human body in an occupational setting. This requires a description of the interaction of the human body with potential disease-causing chemical, physical, or biological agents in the environment. Matters are complicated by the fact that only a fraction of a worker's time may be spent in an occupational environment and that exposure to potential disease-causing agents (including chemical agents, physical energies, or biological entities) may take place in the home environment or as a result of nonoccupational activities.

A thorough study of occupational disease requires a multidisciplinary approach. Physical sciences and engineering analyses are useful to describe the interface of the human with the work environment. Life sciences information, including biochemical, biomechanical,

toxicological, and pathological descriptions, is needed to assess physiological effects of occupational exposure. In addition, the social patterns of the workers (i.e., lifestyle considerations) may influence the outcome of exposure.

**COMPLEXITY OF THE ISSUES**

The central focus in discussing occupational diseases is the human worker and his/her body—a complex system of physiological and psychological (behavioral) components. Just as no two people will behave exactly alike in a work environment, they also will not have the same responses to stimuli. Not only can the range of human responses to physical, chemical, or biological agents be dramatic, so can the range of idiosyncratic behavior and personal hygiene. Cigarette smoking and willingness of a worker to wear protective equipment are two examples of personal habits that may influence the risk of occupational diseases.

**Human differences**

**Work history**

A person's work history may also influence his/her potential for developing an occupational disease. Past exposure to disease-causing agents may have resulted in the bodily accumulation of agents that are slow to be removed. Body burdens (the amounts of these agents in various body compartments) may stress normal physiological systems. Alternatively, previous work exposure may have affected homeostasis (the stabilizing tendency in the human body) and, thus, rendered the individual more susceptible to certain occupational diseases. Assessing the effect of work histories on the potential for developing an occupational disease is difficult and a subject of ongoing research.

**Susceptibility**

Generally, the differences in individual susceptibility to occupational disease can be related to general health, age, sex, race, diet, and heredity. These differences, as well as the limited information relating exposure and human response, significantly complicate the task of setting "safe" levels for potentially harmful agents. For these reasons, limits for occupational exposure cannot be considered as absolute levels of protection. Although limits are established, this is not assurance that individual workers may not show deleterious effects if they have unusual susceptibility (to be discussed below in greater detail).

**SCIENTIFIC FACTORS**

Many dilemmas exist concerning the role of scientific "information" and occupational disease. Most scientific information that relates exposure to diseases comes from three qualitatively different types of investigation discussed below:

- case studies of accidents or disasters,
- epidemiological studies, and
- basic and applied scientific research.

**Accidents and disasters**

Accidents/disasters such as occurred in Chernobyl and Hiroshima serve as unparalleled sources of information concerning human exposure to radiation. The human and environmental exposure after the industrial accident in Bhopal is and will remain under investigation for many years. While the moral, ethical, and legal implications of these accidents are being explored, scientists are gathering data from medical records and environmental measurements to assess human and environmental responses to ionizing radiation and widespread isocyanate exposure. Sometimes information from accidents and disasters is claimed to be "gained from experience." Nonetheless, perhaps the most useful outcome of these accidents/disasters are the corrective changes that diminish the probability of a recurrence.

**Epidemiology**

Epidemiological research attempts to relate exposure to harmful agents and the occurrence and distribution of disease or injury in segments of the society. Unlike clinical medicine, where the focus is on the diagnosis and treatment of an individual, epidemiology emphasizes the patterns of disease or injury in groups of individuals in order to identify causality. Interpreting causal relationships is made difficult because of systematic errors (called biases) introduced into a study or because individuals are exposed to factors other than a particular environmental agent—factors that may influence the outcome of a disease (a confounding factor). The epidemiologist's raw data may consist of monitored or

**Biases**

## OCCUPATIONAL DISEASES

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### **Risk**

estimated patterns of exposure, job titles and death records, or medical history records. The results of a study may be a description of an incidence rate for a particular disease, and it may be standardized to the general population or expressed in a proportional manner. The statistically determined increased risk of developing a disease based on exposure (degree and length of exposure) to a specific agent is often sought in these studies. Results of epidemiological investigations have been extremely beneficial in assessing causal relationships. They are, however, often clouded by imprecision because of faults with the data sets and the presence of confounding agents, and biases in the studies.

### **Laboratory studies**

Scientific laboratory research aimed at better understanding the interaction between exposure to an agent and a disease is limited primarily to animal experimentation. For example, laboratory tests seek to identify harmful agents that interfere with reproduction—in particular, agents that interfere with transferring genetic information from parent to offspring or that may produce physical defects in the offspring. The great complexity of and physiological differences between human and other animal reproductive systems is such that extrapolating laboratory information from one species to the other should be approached cautiously.

### **Animal experiments**

### **Extrapolation**

Because conducting animal experiments is expensive in terms of time and money, the usual approach is to subject the animals (usually rats and mice or other small mammals) to very high levels of the substance being investigated. This way a sufficient number of positive (disease producing) results can be obtained. The extrapolation procedure is subject to criticism, and some of the issues relate to:

1. differences between laboratory test animals and humans,
2. well-controlled administration of test agents in the laboratory versus uncontrolled occupational exposure of humans,
3. the often several orders of magnitude difference per mass of body weight of laboratory versus occupational exposure, and
4. the short-term laboratory exposure versus the chronic (long-term) occupational exposure.

Much of what we know about exposure to potentially harmful agents and the development of occupational diseases is obtained from laboratory experiments on animals. Regulatory policy relies heavily on such scientific endeavors. The drawbacks and weaknesses of this approach, however, continue to place medical professionals, other scientists, and policy makers in a dilemma.

**Unit II**  
**OCCUPATIONAL DISEASE AS A PROCESS**

<b>PURPOSE:</b>	To present a conceptual model to aid in interpreting issues related to development of occupational diseases.
<b>OBJECTIVE:</b>	To review aspects relevant to formulating the conceptual model including: <ol style="list-style-type: none"><li>1. Types of hazardous agents</li><li>2. How they may enter the body environment</li><li>3. Normal and defensive body processes</li><li>4. Elimination of potentially harmful agents</li><li>5. Altered body responses</li><li>6. State of health</li></ol>
<b>SPECIAL TERMS:</b>	<ol style="list-style-type: none"><li>1. Etiology</li><li>2. Latency period</li><li>3. Causality</li><li>4. Hazardous agent</li><li>5. Xenobiotics</li><li>6. Biological entities</li><li>7. Mode of entry</li><li>8. Environmental stress</li><li>9. Transcutaneous absorption</li><li>10. Dose</li><li>11. Sensitivity</li><li>12. Acute</li><li>13. Chronic</li><li>14. Immune system</li><li>15. Antibody</li><li>16. Cellular defenders</li><li>17. Inflammation</li><li>18. Biotransformation</li><li>19. Enzymes</li><li>20. Homeostasis</li><li>21. Elimination</li><li>22. Acclimation</li><li>23. Compensatory changes</li></ol>

**PROBLEMS WITH UNDERSTANDING OCCUPATIONAL DISEASES**

Occupational diseases develop out of the complex circumstances involving the pathophysiological response of a human exposed to harmful agents. Despite recent, rapid advances in science and medicine, much of the information describing the etiology (the study of factors that cause diseases) of occupational disease either does not exist or is poorly understood. The large variability among humans in their responses also contributes to this unclear situation. Still other factors have hindered the understanding of occupational diseases: the long latency period of some occupational diseases, the difficulty in establishing causality between exposure and development of a disease, the lack of emphasis on occupational diseases during medical training, the multifactorial nature of real life exposure.

From an engineering point of view, the development of an occupational disease may be considered a complex, incompletely understood process involving a contaminated environment (forcing function) acting on a physiological entity (the worker or physiological transfer function) with the potential of producing a pathological condition (a perturbed state). Occupational diseases are usually studied according to functional physiological units (e.g., organs) or according to hazardous agents (or materials). The approach here differs from the standard health-care-oriented approach; the emphasis is on system behavior including interaction with the local environment.

**Conceptual model**

As an aid to understanding occupational diseases, a conceptual descriptive model is presented in Figure II-1. This three-stage representation of the results of occupational exposure may be considered to be an input stage or forcing function; the response stage or processing of the stimulus or a transfer function stage; and an output or result stage. With this system representation of a human in an occupational setting, the discussion will involve how hazardous agents (including chemicals and biologicals [e.g., insects, viruses], or energies [e.g., the physical aspects of labor]) enter a body or its environment as well as some of the physiological and pathological responses.

In this simplified, schematic diagram, exposure to some potentially harmful agent (a chemical substance; a biological material; or an energy) becomes an input to the human body (dose) when it crosses the hypothetical surface separating the occupational environment from the internal milieu of the body. This dose now elicits the possibility of two initial responses: normal or altered body processes, each with their inherent defense mechanisms and elimination. The altered body process route may be in response either

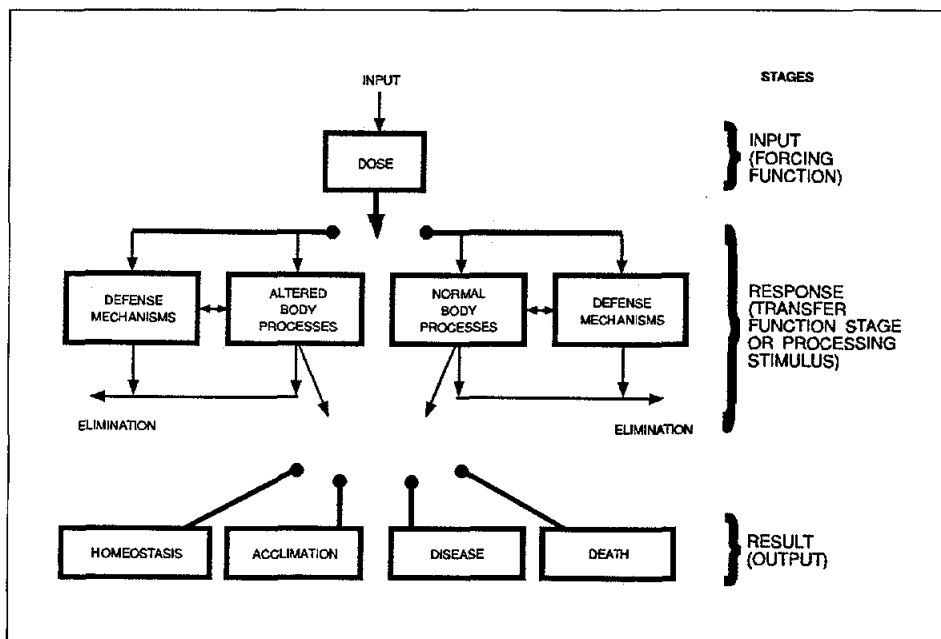


Figure II-1. Human input-response model.

to previous exposure or to genetic characteristics that predisposed the body to be hyper- or hyposusceptible to a stimulus. The final state of the body that results from the input and physiological and biochemical processing steps is: homeostasis where normal conditions are attained; acclimation in which changes occur that do not impede normal function; disease that differs qualitatively from acclimation only in that the changes that occur are greater and in that normal function is disrupted; or death.

## **POTENTIAL HAZARDS**

Chemical agents (including particulates, gases, vapors, liquids, and combined forms of these) probably represent the largest category of industrial hazards to health. In addition to these chemical substances, energies (including various forms of radiant energies, mechanical energies associated with physical labor, and biomechanical operation of the human body) may be hazardous. Climatic conditions such as temperature or humidity represent potential hazards. Biological agents (ranging from microorganisms to insects) may also be deleterious. In a negative sense, the deprivation of any normal input required to maintain normal human function (e.g., oxygen deprivation) is itself a hazard. Finally, physiological, and sociological stimuli are potential hazards.

## **MODES OF ENTRY**

Any of the potential hazards or circumstances above can affect the internal human body via inhalation, ingestion, transcutaneous transport, irradiation, or information exchange (information that may affect mental health). Where there is an energy transfer between the worker and the work environment, the form of exchange may result not only from environmental stresses such as climate, light, sound, and heat but from the physical aspects of labor. The physical aspects of labor are part of the worker-job interaction—that is, the study of ergonomics.

Hazardous agents usually enter the body via inhalation. Our respiratory system is a highly organized mass transfer apparatus; its primary function is oxygen exchange into the blood and carbon dioxide exchange from the blood to the outside environment. This physiological system is effective in removing particulates, gases, and vapors from inspired air. The specific effects and the site of action of these airborne materials are determined by the organization of the respiratory system, including the dynamics of breathing, as well as by the physical, chemical, and physiological properties of the agents being captured.

Ingestion is not considered a major pathway by which foreign agents enter the body; nevertheless, it is worth noting. Either accidentally (e.g., poor hygiene) or as a consequence of a contaminated environment (exacerbated by mouth breathing), foreign agents may be ingested. The ingested agents usually wind up in the stomach where they are exposed to an active physiological system characterized by low pH and high digestive enzyme activity.

Transport of agents across the skin to the internal body environment can occur via several distinct pathways. Transcutaneous absorption will depend on the barrier function of the skin and the physicochemical properties of the absorbing agent. Adsorption onto the skin may be a first step that results in the material eventually being transferred to the internal milieu (milieu interne). Abraded or punctured skin opens a direct entry route to the internal environment for hazardous agents. The direct route may provide an entry several orders of magnitude greater than that of adsorption. Biological agents such as ticks or microorganisms can also penetrate the skin and gain entry to the internal environment.

Irradiation (the exposure of the body to either ionizing or nonionizing radiation) may affect the skin surface or may penetrate to deeper layers. This form of energy exchange could be from sunshine or from exposure to radioactive agents.

Information is a psychosocial form of exchange with an environment that is very difficult to quantify. A conscious or subconscious input is received by the worker, and his/her mental health depends in part on information.

**Dose**

The amount of a hazardous agent that reaches the body's internal environment is referred to as the dose. For most agents, the notion of a dose may be easy to quantify (e.g., chemical agents); for others, the concept of a dose may be almost meaningless (e.g., as in the case of information). A dose may be referenced to a specific target organ or to a site of exposure, or it may be generalized to represent systemic contamination.

**NORMAL BODY PROCESSES AND DEFENSES**

Once a dose of some agent has entered, a normal biological response indicates that no altered sensitivities or hyper- or hyporesponse is initiated immediately following the dose. As part of the immediate and subsequent response to foreign agents or energies, defense mechanisms and eliminations are involved. These are related intimately with the normal body processes as shown in Figure II-1.

Normal body behavior or normal physiology is beyond the scope of this work, but many texts are available dealing with this subject. The normal biological processes following exposure to some potentially hazardous agent may depend on the quantity of the dose, the particular agent or energies involved, and the temporal pattern of the dose. As a result of either acute (short-term) or chronic (long-term) exposure to harmful agents, the state of health of the worker may change. The normal body process (see Figure II-1) should be considered as a starting point or as an initial condition in this dynamic system. That is, the "normal" processes can be changed as a result of inputs.

The human body is well equipped for defense against most foreign agents. For each mode of entry of agents or energies, the body has specific defenses or protective mechanisms. Examples of these are nasal filtration of particulates and the barrier function of the skin. Some specific defense mechanisms for each organ or body system will be discussed later. Once an exposure has resulted in a dose of an agent, the defense mechanism associated with the internal biological environment may be summoned. These internal mechanisms will be discussed only briefly. For a thorough description, refer to appropriate biological or medical sources (e.g., *Casarett and Doull's Toxicology*, 1980, see Bibliography).

The immune system, for example, is a complex defensive network that relies on specific cells to recognize foreign agents and to mobilize other cells (e.g., lymphocytes) to "attack" the foreign matter (biological or chemical). Concurrently, circulating antibodies (antagonists to specific materials) are synthesized, after recognition of the foreign agent, to enter the fray to destroy the foreign agents. As part of this system, a highly specific memory is developed from previous exposures to some agents. With the aid of this recall, the response time can be shortened and the degree of response increased for subsequent exposure.

Cellular defenders, other than lymphocytes as discussed above, can be found systemically in body fluids (e.g., blood or tissue fluids) or they can be associated with a particular tissue. The manner by which cells can defend against the presence of foreign agents, includes: engulfing or ingesting foreign agents (phagocytosis) and thereafter exposing these agents to internal cellular materials such as enzymes, which may chemically digest them; and producing and secreting substances, which aggressively coat or attack the foreign agent.

Inflammation, broadly defined, is a defensive reaction of tissue to injury characterized by redness, heat, swelling, and tenderness in the affected area. This reaction usually occurs along with other defensive mechanisms. Inflammation involves microvascular, cellular, body fluid-associated and systemic components. The term inflammation is somewhat arbitrary since, in reality, it is part of a process with ill-defined stages. Usually inflammation results from biological agents (e.g., bacteria), but energies such as those associated with sunburn, frostbite, or physical labor may produce inflammations. Inflammation is usually classified as acute or chronic. With an acute inflammation, the return to a normal condition can be expected in a matter of days and a specific population of defensive cells migrates to the inflamed area. Chronic inflammation is characterized by persistence over a long period of time, a cellular population in the injured area very different from that of the normal and the acute condition, and the excessive produc-



tion of tissue structural materials (e.g., collagen). Inflammation, even though it is involved in tissue response to injury and the subsequent repair process, may itself have harmful effects. Inflammation with excessive pulmonary edema (accumulation of fluid in the lungs) may be life-threatening.

The body can also transform agents foreign to its internal environment. This biotransformation results from the action of enzymes associated primarily with liver function and is classified into breakdown reactions (oxidation, reduction, or hydrolysis) and synthesis reactions (conjugation). Generally, biotransformations convert materials to other forms (metabolites) that are more easily eliminated from the body, or that are less toxic, or both. These effects are achieved generally by alterations in solubility and/or in chemical activity of the xenobiotics.

In addition to the primary defense mechanisms, above, protective characteristics can be attributed to the normal homeostatic (preservation of the stability of the system) mechanisms and to alterations in growth patterns. Altogether, the body can muster impressive defensive possibilities.

## ELIMINATION

Elimination (Figure II-1) is part of the dynamic and interacting system that determines the intake, distribution, and fate of agents that are potentially hazardous. As such, it can be considered an aspect of normal processing as well as a specific defense mechanism. The major excretion pathways are via urine and feces; materials can also be eliminated in sweat; in normal surface cell turnover (exfoliation), including loss of hair and nails; and in exhaled gases. More will be said about excretion and elimination in Unit IV as part of the discussion of dynamic mathematical (pharmacodynamic) modelling of the intake and distribution of potentially hazardous materials in the human body.

## ALTERED BODY PROCESSES

The pathway of altered body processes (Figure II-1) acknowledges the dramatically different response of an individual with altered susceptibility to a dose of some agent. Hypersensitivity can be found in a subpopulation of individuals whose immediate response to certain agents involves immune-mediated events not characteristic of the immediate response by the normal population. The relative response by the subpopulation of hypersensitive individuals can be extreme when compared with the response of normal persons. Also, the susceptibility of the otherwise normal population can vary significantly. Some individuals can exhibit extreme responsiveness to certain agents in the absence of action by the immune system. Both the hypersensitive and normal but hypersusceptible groups display altered body processes.

Altered body processes can involve a target organ, such as the skin or the lungs, or they can be systemic. The onset of the physiological response to a foreign agent may be rapid and exaggerated or, under specific conditions, it may be delayed. In any event, the eventual long-term outcome may be very similar to that result obtained following the normal body process route.

## STATE OF HEALTH

If the schematic in Figure II-1 can be considered to represent a system approach to the development of occupational disease, then the dose is an input (or forcing) function; the body processes, defenses, and elimination are analogous to a response (or transfer) function; and the result (or output) will be interpreted in terms of the state of health of the individual. The responses range from normalcy (return to homeostatic control) to death. A convenient paradigm by which to interpret these results comes from the analysis by Hatch (in: *Occupational and Industrial Hygiene: Concepts and Methods*, Esmen and Mehlman, eds. 1984, p. 54) in which impairment (consequence of the processing part of the system) is related to disability or other medical circumstances. For small doses (on a relative scale), the body processes are able to respond and to maintain the health of the individual without significant alterations. This normal adjustment, which is the most favorable outcome, eventually results in homeostatic conditions (Figure II-1). As the dose increases, a greater burden or stress is placed on the body's physiological/biochemical system. Changes to the characteristics of the system may result, but reasonably normal function can be maintained. In this case, the body's system has acclimated to the

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input and no disease results. As dose is further increased, the limits of the compensatory processes are reached; beyond this, some normal functions will not be maintained. Breakdown of some human systems occurs, and a disturbed function or a disease state results. Repair is possible in these conditions. If the dose is increased still further, irreversible changes may follow. Finally, failure of the system (the most extreme impairment) caused by too high a dose will result in death, the most severe consequence. The distinctions in both impairment and medical consequences are qualitative. This reflects the state of knowledge of medical science in general and occupational medicine in particular.

Now that a generalized, descriptive, hypothetical model relating to the development of occupational diseases has been formulated (Figure II-1) and its components and means by which to interpret results for the state of worker health have been discussed, it may be instructive to investigate the practical implications of the model with respect to engineering controls, medical surveillance, and treatment. A discussion of other practical approaches that can be used to understand causes and effects of occupational diseases will follow.

**Unit III**  
**INTERPRETATION OF THE MODEL OF DEVELOPMENT OF OCCUPATIONAL DISEASE**

- PURPOSE:** To use the conceptual model presented in Unit II as an aid in interpreting events related to the development of occupational disease.
- OBJECTIVE:** To examine, with the aid of this conceptual model, the following:
1. Potentially harmful agent dose reduction
  2. Monitoring a worker with respect to his/her state of health
  3. Medical intervention
- SPECIAL TERMS:**
1. Engineering controls
  2. Substitution
  3. Process modification
  4. Ventilation
  5. Isolation
  6. Primary prevention
  7. Administrative control
  8. Audiometry
  9. Spirometry

## OCCUPATIONAL DISEASES

### **USE OF CONCEPTUAL MODEL**

The model depicted in Figure II-1 is now examined with respect to: reducing the dose of harmful agents received by workers, monitoring of worker health, and finally treating the workers medically.

### **DOSE REDUCTION METHODS**

Two of the ways to reduce the dose of a harmful agent or energy are environmental control or restricting the mode of entry. In the first case, the engineering controls of substitution, process modification, ventilation, and isolation are considered.

#### **Substitution:**

Substitution involves replacing a harmful agent in an occupational setting with a harmless or a less harmful one that also satisfies the process requirements. Organic solvents, which produce harmful vapors, have been replaced by innocuous water-based cleaning solutions that perform the same function. Substitution may only reduce the potential for harm if a hazardous agent is replaced by another, less hazardous one. For example, silica-free abrasives have replaced silica sand in abrasive blasting operations, and fibrous glass insulation has been substituted for the more harmful asbestos. Whenever possible and practicable, substitution is a recommended procedure for reducing environmental and occupational hazards.

#### **Process modification**

Modifying process design or the manner by which the process is carried out may offer a simple, yet effective, way to control undesirable environmental factors. Additionally, well-considered changes might improve not only working conditions and product quality but decrease the cost associated with the process. Examples of process modification are the use of: automatic electrostatic paint spraying rather than manual compressed air spraying, and for cleaning parts, vapor degreasing with temperature control rather than hand washing with solvents.

#### **Ventilation**

Ventilation is by far the most widespread approach to reducing airborne hazards in the work environment. General ventilation in work areas relies on dilution and removal of process emissions to prevent the buildup of toxic substances. This type of control is used commonly when dealing with substances that are not very hazardous in low concentrations. When, because of the nature of a process and/or the characteristics of the emissions, the concentration and/or health hazard is great, then local ventilation is indicated. Local ventilation is designed to collect air contaminants at the source and carry them away before they reach the worker's breathing zone. As part of design considerations, enclosing parts of the emission producing process is often appropriate, and sometimes, either the worker or the process should be isolated.

#### **Isolation**

Isolation as an engineering control is not always involved with ventilation. For example, the problem of noise, which may be dangerous to the workers' auditory system, can be solved by physical isolation of the noisy equipment with the use of acoustic tiles and enclosures. Many industries are incorporating automatic and semi-automatic equipment in their operations—equipment that can be controlled from an external point (e.g., a control room). In this fashion, workers are not exposed to a potentially harmful work site and can control a process from an isolated computerized work station.

The above-mentioned engineering controls all serve to protect the worker by reducing the input (see Figure II-1) of harmful agents; i.e., environmental factors are controlled. The method of choice is, however, primary prevention, i.e., applying engineering methods and procedures to reduce or eliminate the hazard. Worker protection is usually most successful when control of health hazards is considered at the design stage.

#### **Restricting the mode of entry**

Restricting the entry of harmful agents is best done with the proper use of personal protective equipment. This equipment, which may be needed when engineering controls are not feasible, ranges from respirators, to ear plugs, to protective clothing including gloves. The cost can vary from minor (for ear plugs) to major (for elaborate respirators). The proper use of some of this equipment requires educational and maintenance programs and, in some instances, overcoming worker resistance based on perceived discomfort.

**Administrative control**

In addition to engineering controls and restricting the mode of entry, administrative controls can be helpful in worker protection. Educational programs may assist workers, through their own actions, to decrease the dose of potentially harmful agents received while at work. Administrative scheduling and encouragement of good housekeeping also serve beneficial roles. Taken together, all of the above mentioned practices have the potential to reduce the dose of harmful agents encountered occupationally.

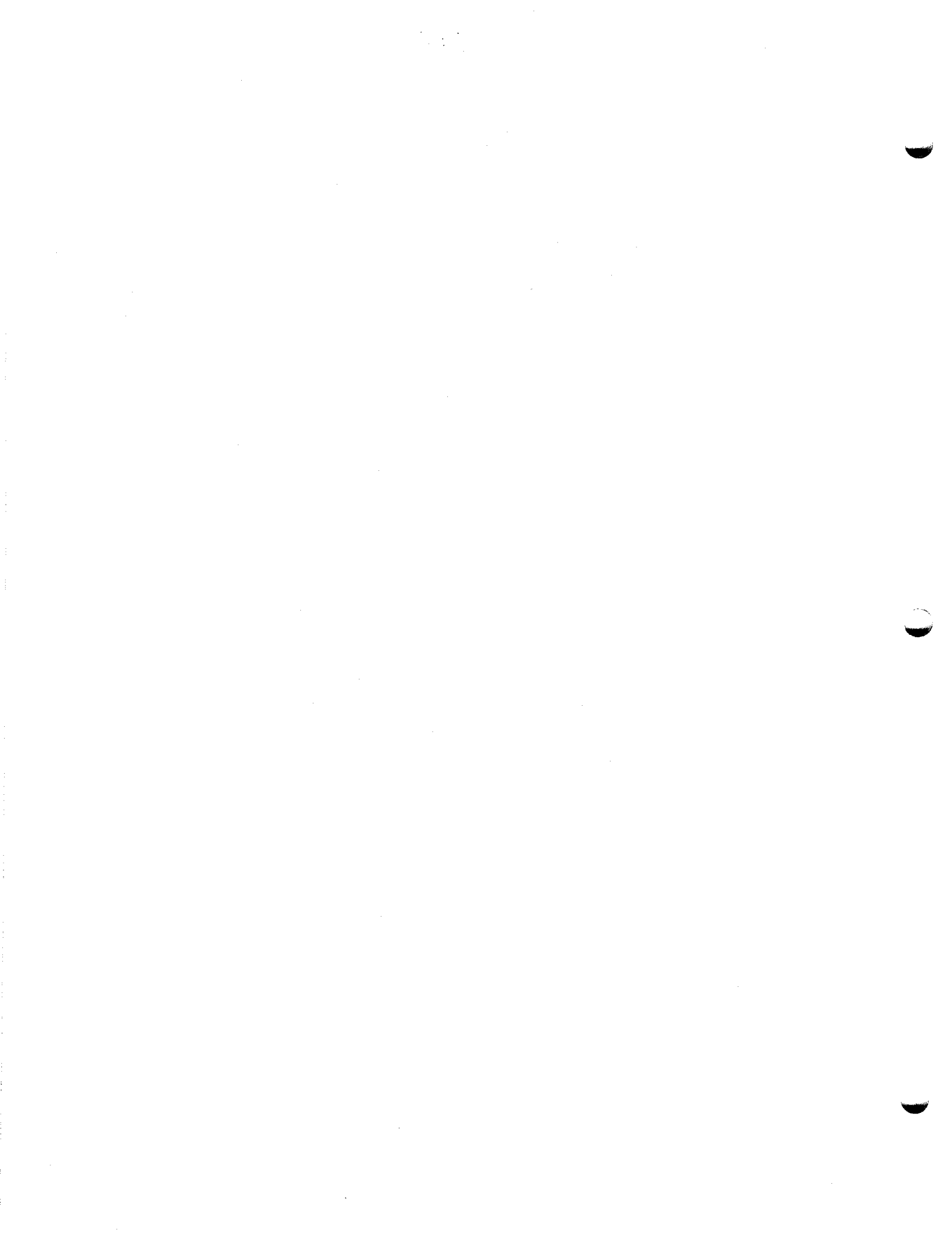
**MONITORING OF WORKER HEALTH**

Worker health is monitored for occupational diseases for several reasons: early detection of disease, compliance with standards (e.g., blood lead levels must be below specified values), determination of the adequacy of control measures, epidemiological studies, or pre-placement studies (establishing baseline health status of the worker). Monitoring can consist of a thorough physical examination including chest x-ray, pulmonary function testing, audiography, and similar noninvasive analyses, or it can involve biochemical analysis of human tissue, biological fluids, or excreta. Blood and urine are two very important sources of information; they can reveal human exposure to harmful agents or their metabolites and/or development of disease. Analysis of specific biochemical materials in these fluids can be interpreted in terms of changes in physiological function, early stages of pathology, or the presence of hypersusceptibility. Examples of health monitoring of workers in specific areas of concern include audiometry (testing of hearing sensitivity) and spirometry (measurements concerned with breathing). Also, the integral operation of the nervous system can be investigated by testing reflexes and mental skills. Breath analysis as performed by law enforcement officers with the objective of a quantitative determination of ethanol blood level is another example of biological monitoring.

Biological (worker) monitoring occurs at the response and result stages (Figure II-1). Analysis, whether invasive or noninvasive, can relate to normal body processes, defenses, eliminations, or outcome states. Medical science is becoming increasingly more sophisticated at these types of analyses.

**MEDICAL INTERVENTION**

A discussion of medical intervention (therapeutic actions to maintain, restore, or improve worker health) is outside the scope of this work. Medical intervention occurs at the level of normal or altered body process or defense mechanisms, i.e., response stage (Figure II-1). In Figure II-1, body processes may change as a result of a dose of a harmful agent, and it may be this change, depicted as a result in the Figure, that is the target of medical intervention.



## Unit IV

### QUANTITATIVE ASPECTS CONCERNING HUMAN RESPONSE

<b>PURPOSE:</b>	To discuss the quantitative approaches used to understand the relationship between the dose of potentially harmful agents and the human body response.
<b>OBJECTIVE:</b>	To review and discuss: <ol style="list-style-type: none"><li>1. Dose-response relationships</li><li>2. Threshold doses</li><li>3. Carcinogenesis</li><li>4. Pharmacodynamics</li><li>5. Simultaneous multiple exposures</li><li>6. Occupational exposure standards</li></ol>
<b>SPECIAL TERMS:</b>	<ol style="list-style-type: none"><li>1. Dose</li><li>2. Local toxicity</li><li>3. Systemic toxicity</li><li>4. LD<sub>50</sub></li><li>5. Threshold</li><li>6. Extrapolation</li><li>7. NOEL</li><li>8. Carcinogenesis</li><li>9. Mammillary model</li><li>10. Exfoliation</li><li>11. Binding</li><li>12. Body burden</li><li>13. Novel work patterns</li><li>14. Synergism</li><li>15. Potentiation</li><li>16. Antagonism</li><li>17. ACGIH</li><li>18. OSHA</li><li>19. NIOSH</li><li>20. TLV</li><li>21. TWA</li><li>22. PEL</li><li>23. REL</li><li>24. STEL</li><li>25. IDLH</li></ol>

**EXPOSURE AND RESPONSE**

In practical terms, when a stress producing agent enters an organism, a response can be expected. The response in terms of physiological impairment or disturbances may result from the direct effect of the agent, or it may result indirectly through an intermediary factor. The toxicity of an agent (i.e., its potential to do injury or harm to the body) depends on its chemical composition or physical properties and the manner in which the agent interacts with the body.

To appreciate the effects on the body of exposure to harmful agents, the properties of the perpetrating agents and also the physiological responses involved should be understood. Rarely is all of this information available. For practical purposes, several quantitative approaches to understanding the interactions between xenobiotic agents and the human body have been developed. Some of these will now be discussed.

**DOSE-RESPONSE RELATIONSHIPS**

The response of a system to a toxin (i.e., an agent with the ability to produce adverse effects in a biological system) is a function of the dose (the amount of energy or material received in the system). Dose-response relationships are a common way to express the results of toxicological research. In these studies, the input or dose is related to the output or result with no consideration for mechanistic behavior of the system or of the fate and distribution within the system of the causative agents. As such, this approach can yield practical information concerning the outcome of exposure to an agent without shedding light on the dynamic behavior or interaction of the agent with the system of interest, the human, or test animal.

**Dose**

Dosing depends on the route of entry, amount, and rate of administration of the agent under study. The infinite number of possibilities for the dose is usually studied in terms of discrete, well-defined dosing schemes. For laboratory test animals, two such schemes involve studying the effects of low doses over a major portion of the animal's life span (chronic studies) or high doses over a short period (acute studies). A considerable amount of disagreement exists concerning the ways to interpret results from these dosing schemes to more realistic, occupational exposure patterns in humans. It is prudent to remember that at some level of dose, all substances may be harmful. Usually a dose is reported as an amount of harmful agent received normalized to the body weight or surface area of the test animal. For inhalation studies, the dose may be related to the airborne concentration of the agent.

**Response**

Response characteristics in dose-response relationships must consider the site as well as the degree of response. With respect to location of a response, several broad categories are often considered. Local toxicity or response occurs at the site of application or exposure, whereas systemic toxicity may occur to a target organ or throughout the entire body via the blood.

The data from which dose-response relationships are constructed usually involve a range of doses as well as a statistical distribution of responses. Consider the straight-forward case where different individual doses of an agent are given to a biological population, and the response under investigation is whether the individuals live or die. Figure IV-1A represents the results for such a study. When the cumulative response for all of the doses is plotted against the logarithm of dose, the characteristic sigmoid-shaped curve results (Figure IV-1B). In panels A and B, data points for each dose show the average or probable response and information concerning the range of responses (i.e.,  $\pm 1$  standard deviation). Also shown in panels A and B is the lethal dose at which 50% of the test subjects die, LD<sub>50</sub>. One can define further, for comparisons or other reasons, the dose at which any specific percentage of subjects respond. For example, an LD<sub>5</sub> can also be established using dose-response characteristics.

Panel C (Figure IV-1) compares the cumulative lethal response of three agents (I, II, and III) and identifies both the LD<sub>50</sub> and LD<sub>5</sub> for each agent. The information in panel C indicates that the relative shape of each curve, as characterized by the near linear slope over the middle range of response, is an important feature when comparing the relative



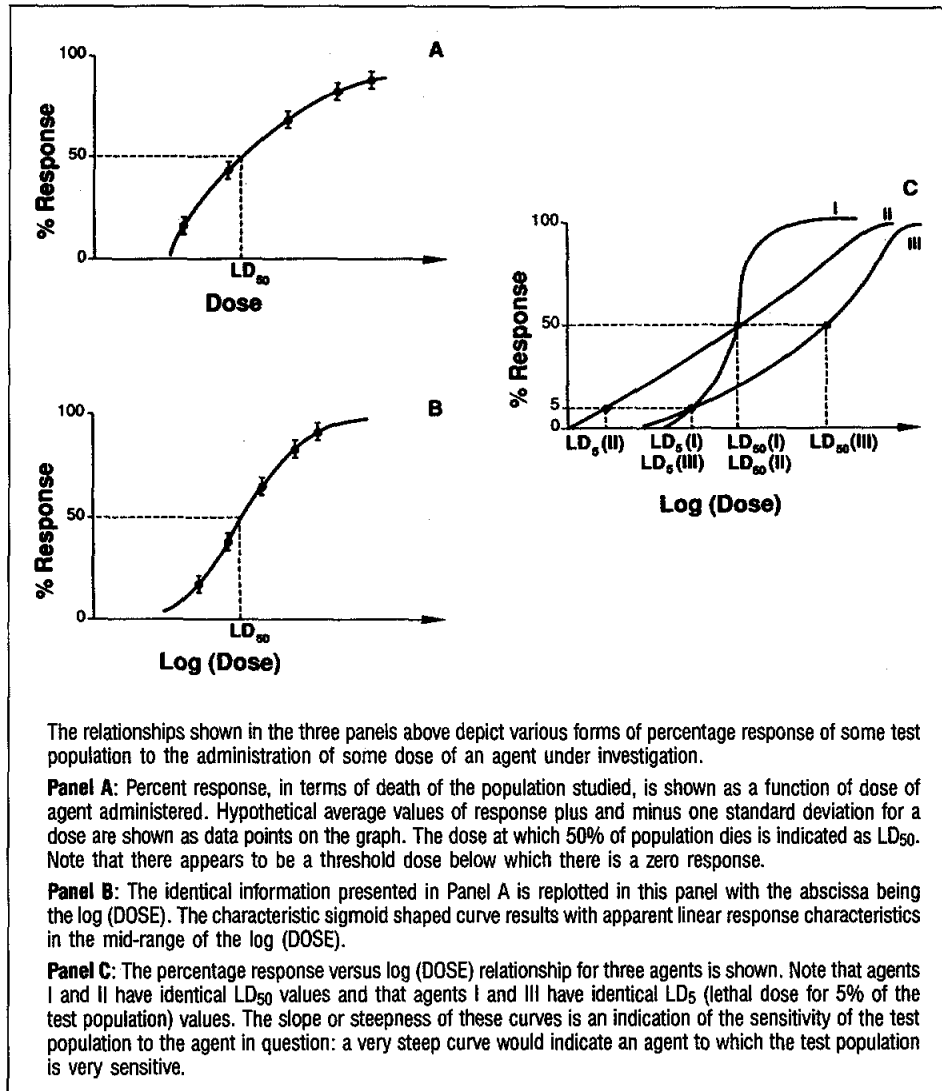


Figure IV-1. Dose-response relationships.

effect of different agents. For example, agents I and II have identical values of LD<sub>50</sub> yet lower doses of agent II are significantly more toxic than the same dose for agent I. Above the LD<sub>50</sub>, agent I is the more toxic of the two. When the LD<sub>5</sub> value is investigated, agent II has the lowest value and agents I and III have the same value. The LD<sub>50</sub> for agent III is much greater than for agent II, which indicates that a much higher amount of this agent or energy is required to kill 50% of the test subjects with a single dose. The slope of the dose-response relationship can be used to compare the sensitivity of the subjects to the agent and can be used to assess the margin of safety associated with a given exposure. A very steep curve would indicate an agent to which the test population is very sensitive.

Death as a response to a dose of some agent represents a very clear cut criterion or end point. Many other less well defined responses are of interest to the toxicologist, the health care professional, the industrial hygienist, or individuals involved with setting safe exposure standards. These responses of interest may be measures of: pathological change in some organ, body fluid content of foreign agents, or some biological agent whose levels of change are secondary to exposure to those agents; or the results of physiological function testing such as auditory testing, lung function analyses, or behavioral testing. For an acute response, the measured effect of some dose is usually an indication of the

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health risk and may be site specific or systemic. Understanding the results of chronic exposure is more difficult than understanding those for acute exposure. For chronic conditions, a response may build up over time and may be related to the accumulated exposure and to the dynamic exposure pattern.

Biological populations display responses that are usually characterized in a relative manner. For example, an agent that is considered relatively harmless to man may require a very large dose before it is considered lethal. On the other hand, an extremely toxic agent may cause death in milligram quantities. In between these extremes, agents may be slightly, moderately, or highly toxic.

### THRESHOLD CONCEPT

The threshold concept assumes that a sufficiently low dose of an agent will result in no injury, i.e., there will be no effect for the level of agent administered. For example, the defensive mechanisms and adaptability of the body can possibly neutralize or transform small amounts of xenobiotic agents or energies before damage is done. In Figure IV-1C, agents I and III are seen to have doses greater than zero that produce, on average, no response; the maximum dose with a nonproductive response is called the threshold. Also in that figure, agent II has no threshold value, i.e., there is no safe dose of agent II at which there is no observable response.

The existence of a threshold dose in animal experiments is sometimes used to set "safe" human dose levels. In the extrapolation of information from test species to humans, it is often assumed that, on a dose per weight (or surface area) normalization, humans and the test species behave similarly. That is, at or below the threshold value as determined in laboratory experiments, humans will also be "safe." Typically, a safety factor is incorporated in this determination so that the "safe" limit of the dose for humans is reduced further. This reduction is usually between 1/10 and 1/1000 of the no observed effect limit (NOEL) or threshold of the agent.

### CARCINOGENESIS

Carcinogenic materials are capable of accelerating the development of malignant or potentially malignant tumors or of increasing the rapid cell multiplication that may result in malignancies. The mechanisms associated with the development of cancers remain largely unknown. Cancer is thought to be a multi-faceted process for which no one model can explain all of the available information. Occupational exposures are estimated to be responsible for as many as 5% of all cancers.

A currently accepted occupational exposure paradigm has carcinogenesis modelled as a multistage process. The initiation stage involves genotoxicity (poisoning and changing of the cell's genetic materials) without a threshold dose. This means that any exposure to these initiation-stage carcinogenic agents may be unsafe, with risk generally assumed to increase with dosage. According to this model, once the carcinogen has changed a cell, that cell has been irreversibly changed to a cancerous or precancerous state. Mutational changes of this sort will alter the cell division process starting with the affected cell. One can consider that the response in the initiation phase is of an all-or-none variety, with risk somehow related to dose. Fortunately for the host, the initiated cell that produces heritable change in its progeny may go into a period of latency (a phase characterized by inactivity) or it may be eliminated by immune mechanisms. The second stage in the development of cancer is the promotional stage where exposure to certain other agents results in the growth of the initiated cells.

Clearly, according to this model of carcinogenesis, exposure to different causative agents at different stages of cancer development may have varied effects. Life-style characteristics may also intervene. These situations compound difficulties associated with understanding the disease process and with choosing appropriate biochemical testing for carcinogens. Very specific, elaborate, and stringent tests are now required to establish the carcinogenic potential of agents.

### PHARMACODYNAMICS

The previous discussions in this Unit have involved descriptions of doses and responses. The fate and distribution in the body of the causative agents, their derivatives, or

biochemical materials released because of the presence of the foreign agents have not been considered. If the time-dependent concentration of causative agents, their derivatives, or any released materials in tissues, target organs (selectively affected organ), body fluids, and excreta could be followed, the mechanisms and behavior involved in developing occupational diseases could be better understood. Pharmacodynamic models (also referred to as pharmacokinetic models) are used to quantify the intake, distribution, metabolism, and elimination of these materials. This type of mass exchange analysis of a kinetic, transient system does not attempt to describe toxicological effects associated with occupational exposure.

A schematic diagram depicting some of the compartments of the human body (Figure IV-2) is intended as an illustrative example of the basis of a pharmacodynamic compartmental model of the human body; it is not intended to be complete. In the representation, the blood compartment is in intimate contact with all the other compartments. (Models of this type, with a central compartment, are referred to as mammillary models.)

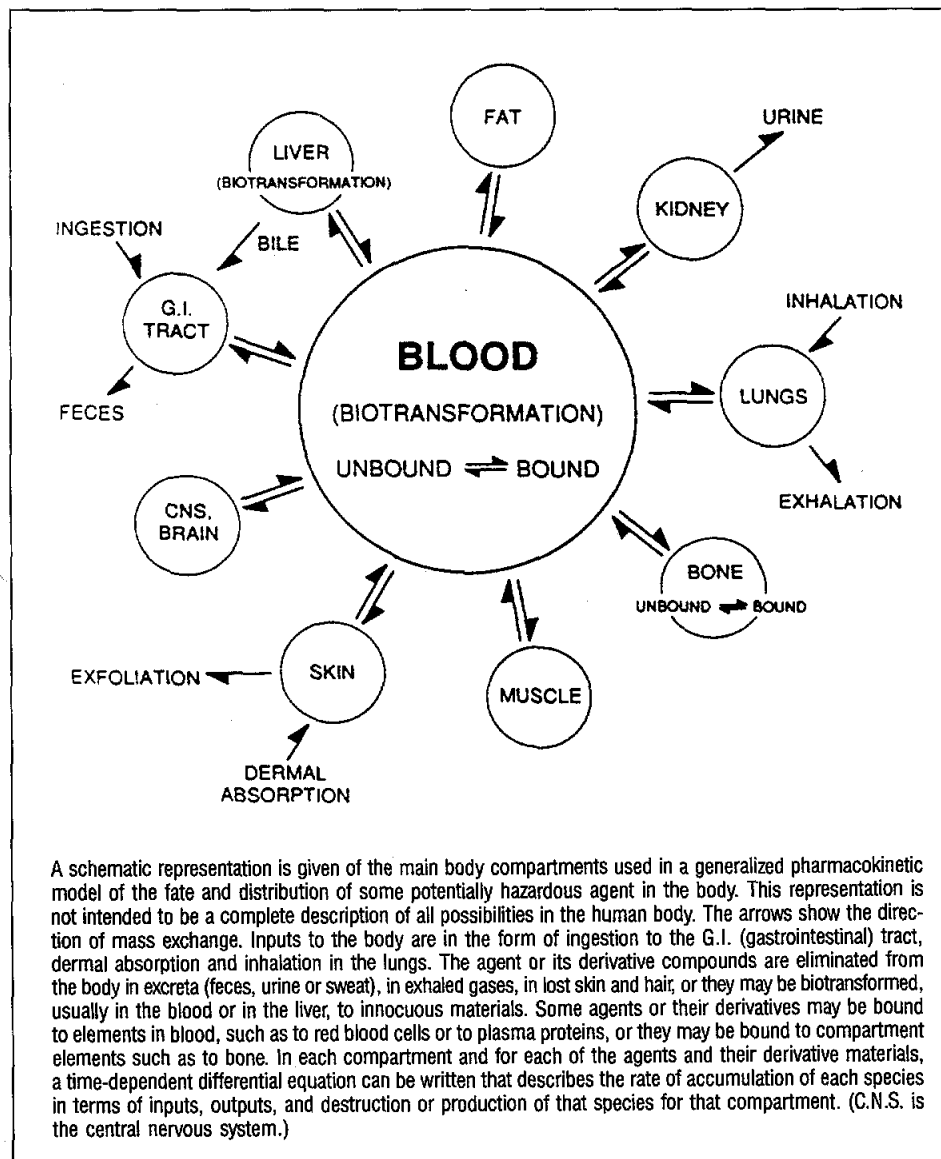


Figure IV-2. Compartmental distribution model.

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Each arrow in the Figure represents an exchange of the offending agent being studied so that between each compartment and the blood compartment there is both a forward and reverse exchange process. Exchange is not, however, assumed to occur between any two nonblood compartments except for the transfer of bile as a fluid from the liver to the gastrointestinal tract. Any materials contained in bile will also be exchanged in this bulk fluid transfer process. Other fluids can be exchanged within the body. For example, fluid cleared from the lungs or saliva from the salivary glands may be transported to the stomach on a regular basis.

Inputs of the studied agent(s) can occur through ingestion to the gastrointestinal (G.I.) tract (where a certain fraction of the material will be retained in the system), inhalation (the exhaled amount of the agent must also be considered), dermal absorption, or direct delivery of the agent to the circulating blood (via injection, as in some experimental studies). The agents under study are eliminated from the system in excreta, including potential losses in hair, skin exfoliation (loss of superficial layers), etc. The agent may also be transformed, particularly by the liver, into derivative materials that may or may not represent hazards to the body. Once in the blood, the agent may bind to elements of blood such as red blood cells or to specific plasma proteins.

The mathematical formula depicting these events and processes is really no more than a material balance for each compartment (or subcompartments, e.g., bound materials). The instantaneous rate of change in the amount of the agent within a compartment is equal to the amount of that agent that enters that compartment, minus the amount that leaves, minus any biochemical destruction or other such alteration of that agent in that compartment. Usually, for lack of better understanding, the exchange between compartments is assumed to follow first-order kinetics. That is, the amount leaving a compartment along any arrows is proportional to a constant exchange parameter times the amount of the agent in the compartment. Nonlinearities may exist concerning rates of exchange and content of agents in some of the compartments shown. These nonlinearities, however, are usually not understood well enough to quantitatively replace the linear approximation that is usually used.

The sum of the material balances for the agent is a set of time-dependent differential equations, one for each compartment and subcompartment for each agent. For a well-defined, determined system, these equations require: appropriate initial conditions; values for the multitude of exchange coefficients and binding coefficients; and a description of the pattern of exposure of the agent. Unfortunately, many, and perhaps all, of the exchange or other coefficients may not be known. The task of formulating a useful pharmacodynamic model then becomes one of estimating parameters with the use of the equations described above together with experimental or clinical data, which may describe the various compartment contents (body burden) or rate of elimination of the agent, all as a function of time post-exposure. For example, an experiment may have been done where blood, urine, and skin contents have been measured as a function of time following a specific dose of some agent. This type of information can be used along with other well-known information about the system to estimate parameters contained in the mathematical description. The variability in the estimated parameters decreases as more and different types of proper information are used in the mathematical analysis. The usual circumstance, unfortunately, is that sufficient (on an arbitrary scale) types and amounts of this kind of information are lacking for the task of quantitative parameter estimation. This is not an unexpected state of affairs because the experiments necessary to produce the types of information needed are usually varied, elaborate, time consuming, and expensive. Therefore, model parameters are usually estimated with the best available information; this involves statistical fitting procedures. After the parameters have been determined, along with some indication of their variance, the model can be used to predict the behavior of a typical individual with respect to his/her body burden of the agents following occupational or some other type of exposure.

At present, toxicological results (that is, responses) cannot be directly related to the transient body burdens of causal agents. When such information and understanding are available, pharmacodynamic models will be able to predict directly the risk of disease associated with occupational exposure. The present pharmacodynamic models do serve a useful purpose in several fields related to occupational disease. For example, these models can be used to predict the blood level of some hazardous agent post-exposure where the exposure pattern may vary with respect to concentration and time. If health professionals have established a limit for the safe level of this agent in blood, then permissible occupational exposure levels for routine patterns of exposure can be determined with the appropriate models. These pharmacodynamic models are useful in establishing acceptable exposure limits, and these models can be used to predict the effects of nonstandard (novel) work patterns and recovery time once a body burden limit has been exceeded.

## **EXPOSURE TO MIXTURES**

It is usually unrealistic to assume that a worker is exposed to one potentially harmful agent at a time. More likely, a myriad of chemicals and energies abound in the workplace. The discussion to this point has involved only the effects of exposure to individual agents. When multiple exposures (in terms of number of agents) exist, the potential toxicological response may change dramatically.

The simplest possibility, when analyzing responses to multiple agents, is that their effects are additive—that the net effect will be the sum of the individual effects. If the effects of simultaneous exposure to potentially harmful agents result in an effect exceeding additivity, then the mixture is said to display synergism. Synergistic effects can increase the risk of exposure to agents by orders of magnitude above that of their combined individual effects. Nontoxic materials can sometimes increase the toxicity of toxic agents (potentiation). Both synergism and potentiation can make exposure to mixtures worse than exposure to individual agents. Sometimes, however, the combined effect of multiple exposures is to reduce the net toxic effect (antagonism). This positive effect may occur as a result of counterbalancing effects of various agents, interfering by blocking, or altering the fate and distribution of agents in the body.

All of these nonadditive net effects, which result after exposure to mixtures, complicate issues related to maintaining a safe working environment. Many of the mechanisms involved in the physiological interactions are unknown. Life-style exposures may also affect the overall human response. The situation is, indeed, very complex.

## **OCCUPATIONAL EXPOSURE STANDARDS**

The reasons behind setting standards for allowable occupational exposure to potentially harmful agents differ around the world. As a result, the specific quantitative nature of the standards also differ. In the United States and Canada, the underlying approach assumes that for most agents a threshold exists below which no injurious effects will result, even after repeated exposure. This concept has been mentioned previously in the discussion of dose-response relationships. Notable exceptions to the above premise involve exposure both to physical agents such as ionizing radiation and to carcinogens. For these hazardous agents, special standards have been formulated and no threshold is believed to exist. Exposure limits for carcinogens are, however, sometimes based on "safe" levels at which the risk (i.e., the circumstances under which adverse effects can be produced) to the worker is considered acceptable. This is, in part, because of difficulties and expense associated with trying to completely remove those harmful agents from the occupational environment.

The information used by organizations such as the American Conference of Governmental Industrial Hygienists (ACGIH) when recommending standards for permissible exposure include: human industrial experience, chemical analogy to other materials for which information is available, chronic animal inhalation studies, and human volunteer experiments. To a lesser extent, the following have been used: acute animal inhalation studies, chronic animal oral administration studies, and acute animal oral administration studies. With the aid of these laboratory, clinical, and epidemiological studies, the many different types of standards for permissible exposures have been developed. In the United

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States, the Occupational Safety and Health Administration (OSHA) is responsible for establishing mandatory safety and health standards. The National Institute for Occupational Safety and Health (NIOSH) is empowered to develop criteria to support revisions of standards or to recommend new safety and health standards to OSHA.

The typical employment scenario has a worker at his job for 8 hours per day for 5 days per week. The ACGIH recommended standard for exposure under these conditions is the Threshold Limit Value (TLV)—a concentration of a material in an occupational environment that will not result in adverse effects in most workers in typical employment patterns. Because of hypersusceptibility, as discussed previously, a small fraction of workers may be affected adversely at or below the TLV. For occupations that bring a worker into several different work environments, the time weighted average (TWA) exposure is calculated as the sum of the products of exposure times (8-hour workday and 40-hour work week) in different environments and the concentrations of the agents there, divided by the total work period. Safe practice requires that this computed TWA exposure should be below the TLV-TWA for that substance. Other standards set by other organizations that address the issue of an allowable concentration for normal work schedules are the OSHA permissible exposure limit (PEL), and the NIOSH recommended exposure limit (REL).

Exposures at concentrations higher than the ACGIH TLV are acceptable for some agents as long as the TLV-TWA is not exceeded and as long as:

- the higher exposure does not last beyond 15 minutes;
- no more than four periods of such elevated exposure occur daily; and
- the elevated exposures occur with at least a 1-hour break between them.

ACGIH's short-term exposure limit (STEL) is aimed at protecting workers from immediately acute effects; the limit is usually based on scientific information or on a biologic rationale.

For agents capable of producing extremely injurious effects rapidly and at concentrations higher than their TLV, other standards have been set. Occupational exposure concentrations that should not be exceeded even instantaneously for agents in this category are referred to as ceiling values. Other standards are used to classify agents as immediately dangerous to life or health (IDLH); for these, 30-minute single escape times are allowed.

A full discussion of setting standards, which is beyond the scope of this work, would also involve an understanding of the quantitative and mechanistic nature of the development of occupational diseases. Novel work schedules (i.e., other than 8 hours per day, 5 days per week) and nonoccupational exposures are just two issues that complicate the matter of setting appropriate standards to protect workers.

## UNIT V

### RESPIRATORY SYSTEM

**PURPOSE:**

To understand the role of the respiratory system with respect to the development of occupational disease.

**OBJECTIVE:**

To review briefly the following aspects of the respiratory system:

1. Anatomy/physiology
2. Defense mechanisms
3. Occupational diseases

**SPECIAL TERMS:**

1. Pharynx
2. Larynx
3. Trachea
4. Bronchi
5. Alveoli
6. Terminal velocity
7. Equivalent diameter
8. Conducting airways
9. Respiratory units
10. Mucociliary escalator
11. Phagocytic
12. Pulmonary edema
13. Alveolitis
14. Pneumoconiosis
15. Spirometry

**PHYSIOLOGICAL OVERVIEW**

For the reader to appreciate the responses of the different components of the body to harmful agents such as chemicals, biologicals, or energies, Units V–XII present brief physiological background information. Where appropriate, the discussion of system physiology is followed by a concise description of the relevant defense mechanisms. Each Unit contains a tabulation of the occupational diseases affecting the system, the causal agents, and the industries concerned.

**ANATOMY / PHYSIOLOGY**

The respiratory system is usually divided into two subcomponents based roughly on physiological function: the conducting airways and the respiratory units. The conducting airways consist of the nasal and mouth cavities, the pharynx (upper throat), larynx (voice box), trachea (wind pipe), and bronchi (see Figure V–1 Panel A). As the name implies, the function of this subcompartment is to conduct air to the lower respiratory subcompartment unit. The respiratory unit consists of the smaller bronchioles, the alveolar ducts, and the alveoli (terminal air sacs) (see Figure V–1 Panel B). The alveoli are the anatomical sites where gas exchange takes place between the inspired air and the blood. The inspired air, which travels along the conducting airways to the alveoli, experiences a dramatic decrease in average velocity as the cross-sectional area available for air flow increases. In the trachea of the normal adult, for example, the cross-sectional area may be about 2.0 cm<sup>2</sup> and, in the alveoli, about 700,000 cm<sup>2</sup>. This large change in area and the subsequent change in airflow velocities strongly influence the pattern of deposition of particulates and gases in the respiratory system. Between the trachea and alveoli are numerous subdivisions, branches, or generations of the tubular structure through which air is transported. At each branch, the cross-sectional area for air flow increases and the average air velocity decreases.

The respiratory system is very efficient at capturing and absorbing particulates and harmful gases from inspired air. The entire system, which is exposed to the environmental air en route to the alveoli and out again, is somewhat tortuous and covered with mucous-like fluids. These features increase the efficiency of both particulate deposition and gaseous absorption. After a material has been either deposited or absorbed in the respiratory system, a number of possibilities exist. If they are insoluble fibers or dusts, they can be removed from the lungs by local defense mechanisms or they can remain in position. Soluble gases, once absorbed, can be transported to the blood. Once in the circulation blood, these agents can be distributed throughout the body. They may, however, have evoked an unfavorable response at the site of deposition.

**DEFENSE MECHANISMS**

**Terminal velocity**

**Aerodynamic diameter**

**Convective deposition**

**Diffusive deposition**

**Mucociliary escalator**

The respiratory system is not passive with respect to contact with or deposition of foreign matter. For convenience, particulates are often characterized by their terminal velocity, i.e., the rate of fall of the particulate under the influence of gravity at steady-state. Specifically, an aerodynamic diameter is used such that the behavior of the particulate in air is the same as an equivalent sphere with the density of water and the hypothetical aerodynamic diameter. The nose is so designed that only particles with relatively low terminal velocities can be inspired. For normal nose breathing, particles with an aerodynamic equivalent diameter much greater than 25 μm cannot be inhaled and, therefore, do not represent a threat to the respiratory system. As particulates decrease in aerodynamic equivalent diameter below about 25 μm, they can be inspired and become deposited in the upper part of the respiratory system usually by convective transport mechanisms. Deposition of particulates less than 1 μm in aerodynamic equivalent diameter takes place primarily in the lower trachea, bronchi and lower respiratory units shown in Figure V–1. Absorption of gases (and very small particulates) occurs primarily as a result of a diffusive mechanism and occurs most significantly in the lower respiratory unit. Overall the deposition of particles in the respiratory system has the characteristics shown in Figure V–2.

Once in the respiratory system, particulates can be transferred out of the lungs and lower conducting airways by the action of the mucociliary escalator. This defensive process “sweeps” mucus containing particulates from within the lungs up to the throat, where the mixture may be swallowed or expectorated. If a particle is not removed in this fashion,



**Phagocytic**

it will be “attacked” by macrophages. These phagocytic (foreign-particle ingesting) cells rely on powerful enzymes to destroy foreign particles. Sometimes, the particles are not destroyed by the macrophages but, instead, the ingested particle eventually destroys the attacking cell. As a result, the chemical substances contained within the attacking cells become liberated. The lung tissue environment into which these chemicals are introduced

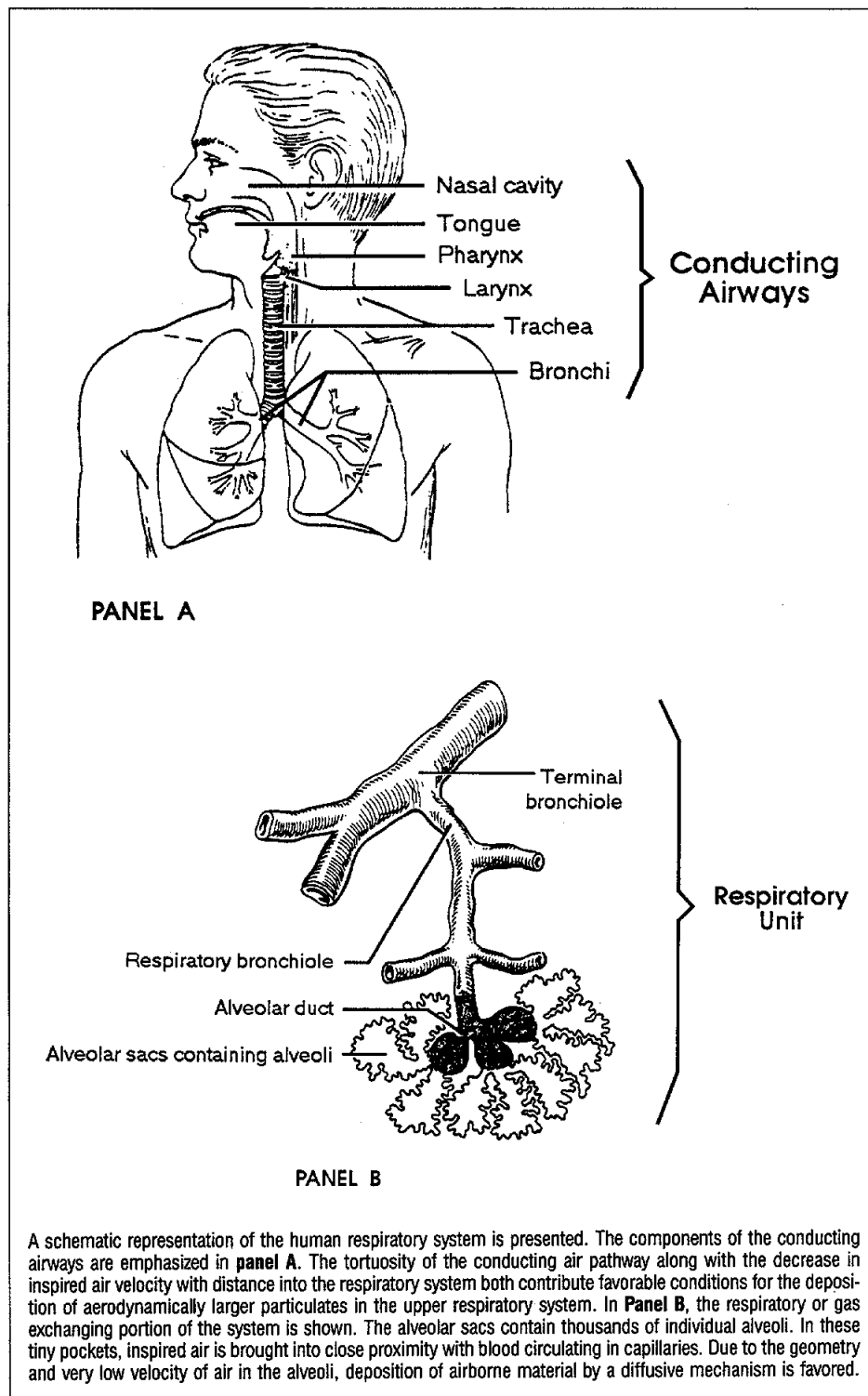


Figure V-1. Human respiratory system.

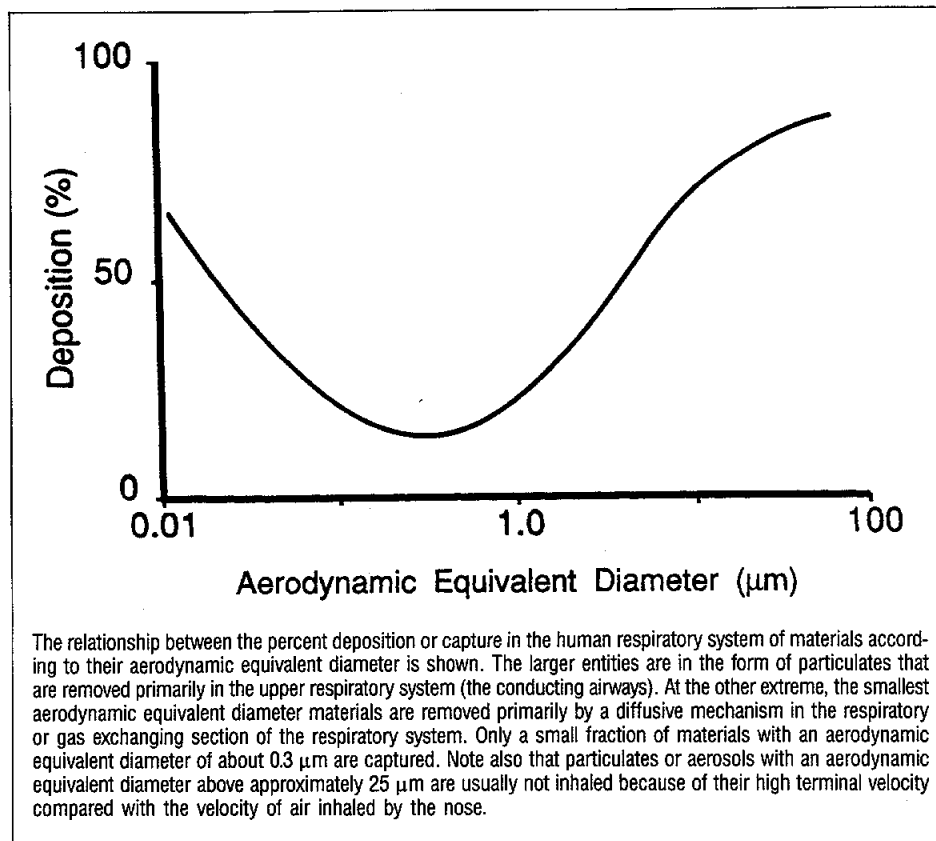


Figure V-2. Relationship of the aerodynamic equivalent diameter of particles to the percent deposition in the human respiratory system.

often responds by forming scar tissue, which can significantly alter the functional behavior of the respiratory system.

**OCCUPATIONAL DISEASES**

In the United States, occupational respiratory diseases represent approximately 10% of the chronic occupational diseases and have been designated as one of the 10 leading work-related disease and injury categories by NIOSH. The often profound effect that respiratory diseases have on the quality of life along with their prevalence makes occupational respiratory diseases a major concern for health professionals.

The development of occupational diseases and disorders associated with the respiratory system depends on the properties of the harmful agent, the pattern of exposure, and the physiological response of the system. The following are some examples of both acute and chronic respiratory problems associated with occupational exposure.

**Soluble gases**

The immediate effects of breathing some highly soluble gases (e.g., ammonia or hydrogen chloride) are severe irritation and discomfort of the upper conducting airways. If the exposure is at a very high single dose or if it is continuous, then the lower respiratory unit may be implicated. The normal physiology of the alveoli may be upset, and this can lead to tissue swelling and possibly to alveolar flooding (tissue fluids spilling into the air space). This latter situation compromises gas exchange and may be life threatening.

**Insoluble gases**

On the other hand, exposure to insoluble gases, e.g., phosgene and ozone, usually produces no immediate effects on the conducting airways. After exposure to these agents, there is often a several hour time lag before symptoms associated with pulmonary edema (swelling in the lungs) are noticed.

<b>Asthma</b>	Occupational asthma, which can be caused by hundreds of chemical agents, results in airway obstruction and difficult breathing. Onset can be immediate or delayed. Asthma develops as the respiratory system responds immunologically to the presence of causative agents. Following exposure, a chain of events is initiated that results in the release of physiologically active materials, such as histamine, that constrict the conducting airways.
<b>Alveolitis</b>	Extrinsic allergic alveolitis, which occurs in a different part of the respiratory system, is similar in its effects to asthma and results from a hypersensitivity reaction. Usually extrinsic allergic alveolitis is caused by biologic agents such as mouldy hay or wheat, but it can also result from exposures related to the chemical production industries (e.g., diisocyanates).
<b>Pneumoconiosis</b>	The most common occupational exposure involving the respiratory system occurs as a result of breathing air containing dusts and fibers. Pneumoconiosis (“dusty lung”) is the catch-all term categorizing the respiratory changes that result from inhaling these agents. The four most important diseases in this class are silicosis, asbestosis, byssinosis, and coal workers’ pneumoconiosis (the suffix “osis” denotes a process, in this case, pathological manifestations associated with the agents in question). The exact pathogenesis (development) of each of these respiratory impairments remains hypothetical.
<b>Silicosis</b>	When silica (quartz or flint, primarily) is deposited in the lungs, an excess production of collagenous fibers leads to the formation of nodules of fibrotic tissue. The compliance or elasticity of lung tissue then decreases. In the past, this disease, which has been recognized for many centuries, has been called dust consumption and grinders’ rot. In extreme cases, the disease may be fatal. Usually this form of pneumoconiosis is progressive over a period of years.
<b>Asbestosis</b>	With asbestosis, which is similar in many respects to silicosis, the harmful agent is the filamentous asbestos fiber. Physical impairment resulting from occupational exposure to asbestos may be progressive and take several decades to manifest itself. General population exposure to asbestos is also recognized as a potential problem. Asbestos has been linked to the formation of malignant tumors in the lining of the lung (mesothelioma). Cigarette smoking in conjunction with significant asbestos exposure further increases the likelihood of the disease occurring.
<b>Byssinosis</b>	Byssinosis is the acute or chronic respiratory condition resulting from inhaling cotton, flax, or hemp dusts. The specific agents responsible for respiratory impairment have yet to be identified.
<b>Coal workers’ pneumoconiosis</b>	Coal workers’ pneumoconiosis results from coal dust deposition in the lungs. As a consequence of exposure to coal dust, the lungs show specific and distinguishable areas of high coal dust content, formation of nodules, and eventually progressive massive fibrosis.
<b>Lung tests</b>	To assess the “health” of the respiratory system, lung function tests or spirometry are used. These tests measure lung capacity for air, rates of expiration, and gas exchange rates. From these tests, broad categories of the various respiratory diseases can be recognized. These tests can be used as routine screening procedures to alert an individual to developing problems, or they can be used as part of a preplacement evaluation of the worker. These lung function tests together with radiographic measurements (chest X-rays) give vital information concerning worker health.

The causative agents, industries in which workers may be exposed to these agents, and the effects on the respiratory system are briefly listed (Table V-1). (This and subsequent tables have been compiled from material in the bibliography cited at the end of the text; they are not intended to be complete.)

## OCCUPATIONAL DISEASES

Table V-1  
Occupational Respiratory Diseases

Causative Agents	Industry/Process/Worker	Disease or Effect
Inorganic dusts	Miners, construction, sand blasting, grinding operations, woodworking, insulators	Pneumoconiosis (silicosis and asbestosis, coal workers' pneumoconiosis)
Organic dusts (cotton, flax, hemp, grain)	Textile industry	Byssinosis, shortness of breath, chest tightness
Diisocyanates	Plastics, paints, coatings	Asthma
Solvents, thinners	Chemical process industries, painting, degreasing, hospital work, artwork, plastics industry	Irritation, inflammation, fibrosis, pulmonary edema
Chromates	Plating, alloying, tanning agents, pigments	Irritation, inflammation, cancer
Ammonia, hydrogen chloride, hydrogen bromide, hydrogen fluoride, chlorine, phosgene, nitrogen oxides, sulfur dioxide	Heavy chemical industry, pulp and paper production, petroleum refining	Irritation, inflammation
Formaldehyde	Morticians, laboratory workers, photographic film makers	Irritation, asthma
Insecticides	Insecticide production, farming	Bronchitis, pneumonia
Arsenic	Pigment industry, herbicide production, metal refining	Cancer
Nickel, nickel carbonyl	Nickel refining, petroleum refining, electroplating	Lung and nasal passage cancer

**Unit VI**  
**SKIN**

**PURPOSE:** To understand the role of skin with respect to the development of occupational disease.

**OBJECTIVE:** To review briefly the following aspects of skin:

1. Anatomy/physiology
2. Defense mechanisms
3. Occupational diseases

**SPECIAL TERMS:**

1. Epidermis
2. Dermis
3. Subcutaneous layer
4. Dermatitis
5. Photosensitivity
6. Pigmentation disorder

**ANATOMY / PHYSIOLOGY**

Skin is the largest organ in the human body with a surface area of about 2.0 m<sup>2</sup> and a weight of about 3 to 4 kg. It comprises several layers and its primary function is to separate and to maintain a resistance to mass exchange between the external environment and the internal milieu of the body. The schematic diagram (Figure VI-1) illustrates the three principal layers of the skin: the epidermis, the dermis and the subcutaneous layer. Together, the epidermis and dermis layers are usually no more than 1-2 mm thick in the normal person. The surface of the epidermis is composed of a densely packed layer of dead cells and hair. A rich blood supply is beneath the epidermis. The thickest layer of the skin is the dermis, which contains connective tissue components, hair follicles, sweat ducts, oil-producing sebaceous glands, and other components not shown. The subcutaneous layer is a less well organized layer and usually has a higher fat content than the dermis. The skin also contains fat cells, blood vessels, nerve cells, and heat, cold, and pressure sensing apparatuses.

**Epidermis**

On the surface of the skin is an oily layer. The outermost layer of the epidermis, the stratum corneum (horny layer), is composed of dead epithelial cells. This layer is a very effective barrier to aqueous materials, but it offers significantly less resistance to the passage of lipid-soluble materials. Below this layer is a rich supply of blood vessels.

**Dermis**

The location and characteristics of these vessels influence temperature control in the body. The dermis is a fibrous connective tissue that is both resilient and tough. The sub-

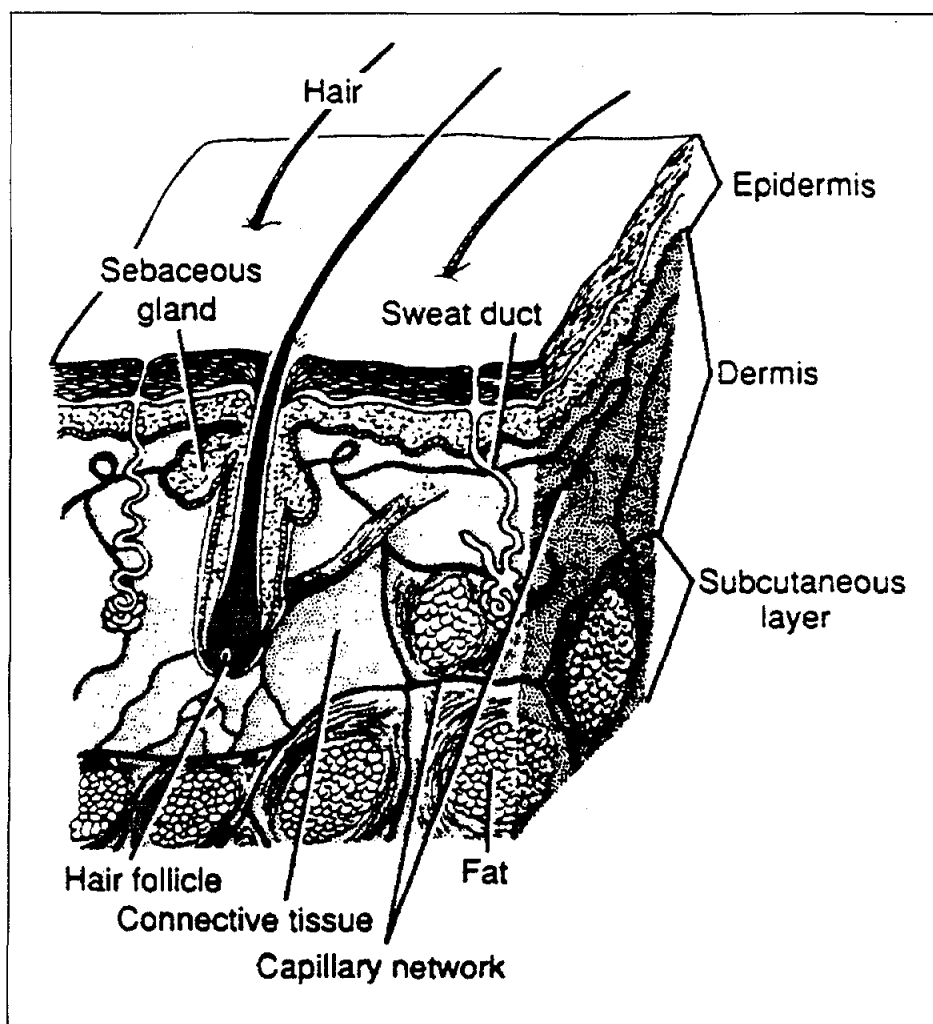


Figure VI-1. Human skin.

**Subcutaneous tissue** cutaneous tissue is less well organized than the dermis, has a relatively high fat content, acts somewhat as a thermal insulator, and offers shock absorbing qualities.

Just as in the case of the respiratory system, the skin may be in direct contact with the occupational environmental and with all of the potentially harmful agents contained therein. Exposures that may affect the skin adversely are: mechanical factors (e.g., friction or trauma); physical factors or energies (radiant energies, heat or cold); chemical materials; and biological materials (plant matter, microorganisms, insects, etc.).

**DEFENSE MECHANISMS** The toughness and flexibility of the skin, the oily surface layer, and the hair all afford protection to the skin against mechanical force. Repeated application of mechanical forces often produces calluses, which serve to protect underlying tissue. The location of a rich blood supply near the skin surface coupled with the action of sweat glands affords protection against excessive heat loads. The skin is not a very effective barrier against certain forms of radiation (e.g., sunlight). Ultraviolet waves may penetrate the skin, depending on its pigmentation, and affect underlying cells. The anatomy of the skin is such that it tends to prevent internal loss of body fluid while inhibiting external chemical penetration. The oily surface layer, the dense matrix of the stratum corneum, and the continual turnover of these materials at the skin surface are the primary protective mechanisms. These defenses fail when the skin has been abraded or punctured.

**OCCUPATIONAL DISEASES** Human differences that affect occupational diseases of the skin relate to race, age, sex, skin thickness, personal hygiene, sweating, and medications. Other factors such as seasonal and climatic considerations also play a role.

**Dermatitis** Contact dermatitis (an acute inflammation of the skin) results from direct exposure to a number of chemicals, is usually confined to the area of contact, and accounts for the great majority of occupationally induced skin problems. Irritants that elicit this response can produce a range of symptoms: e.g., erythema (blotchy red patches), hives, blistering, eczema or rashes that may weep, skin thickening, dryness, and roughness. Common agents such as soaps or detergents, solvents, acids, bases, petroleum products, and oxidants can produce irritant contact dermatitis. In addition, plant materials and animal substances may evoke a skin dermatitis. Direct irritant contact dermatitis is reversible.

Allergic contact dermatitis (also known as sensitization dermatitis) results from contact with a causal agent by hypersensitive individuals and may manifest itself at a site other than where contact took place. This form of the disease, which accounts for 20% of occupational contact dermatoses, is preceded by an induction period during which sensitization takes place (usually 10 days to a month). Causative agents include chemicals, plant or animal materials, and physical agents. Allergic contact dermatitis often looks very similar to irritant contact dermatitis, even though the underlying mechanism may be different. Once affected, the sensitized person will react after exposure to either the allergy-producing agent or to some chemically similar materials. Some chemicals, such as coal tar, may produce photosensitivity. When affected in this manner, an individual reacts more severely to light and may sunburn more easily. Both forms of dermatoses and photosensitivity reactions may predispose the worker to skin infections.

**Photosensitivity**

**Pigmentation disorder** Though technically not a disease, skin pigmentation disorders may result from occupational exposure. These skin color changes result from adsorption (e.g., dyes), inoculation (e.g., heavy metals as in tattooing), and altered melanin pigmentation (e.g., as a result of chemical burns).

Less common skin diseases include ulcerations (exposure to specific materials, e.g., arsenic trioxide dust), occupational acne (exposure to polyhalogenated biphenyls), and skin cancer (exposure to ultraviolet light or the products of incomplete degradation of tar, coal, and wood).

Diseases of the skin account for approximately one-third of all chronic occupational diseases. The incidence rate is, however, decreasing because of greater awareness, im-

## OCCUPATIONAL DISEASES

proved hygiene, and increased use of protective equipment including prophylactic creams. Examples of causative agents according to industry and the occupational skin diseases that result are listed in Table VI-1.

Table VI-1  
Occupational Skin Diseases

Causative Agents	Industry / Process / Worker	Disease or Effect
Soap, detergents	General working population, soap manufacturers	Dishpan hands (irritant contact dermatitis)
Turpentine	Painters, furniture polishers	Eczema, allergic contact dermatitis
Sodium hydroxide	Chemical industries, plastic production, laundering, paper making	Burns, ulcers, irritant contact dermatitis
Chromic acid	Plating, dyestuffs	Burns, ulcers, allergic contact dermatitis
Plastics, epoxies	Plastic workers, varnish makers	Allergic contact dermatitis
Chlorophenols	Insecticide manufacture, wood treatment	Irritant contact dermatitis
Creosote	Wood preservative manufacturers, construction workers	Irritant contact dermatitis, skin discoloration
Fibrous glass	Insulators, construction workers	Irritant contact dermatitis
Petroleum oils	Mechanics, petroleum workers	Irritant contact dermatitis, acne, burns
Cement	Construction workers	Burns, irritant contact dermatitis



## Unit VII KIDNEYS

- PURPOSE:** To understand the role of the kidneys with respect to the development of occupational disease.
- OBJECTIVE:** To review briefly the following aspects of the kidneys:
1. Anatomy/physiology
  2. Occupational diseases
- SPECIAL TERMS:**
1. Cardiac output
  2. Detoxification
  3. Fluid regulation
  4. Filtration
  5. Nephron
  6. Urine
  7. Glomerulus
  8. Enzymatic mechanisms
  9. Renal failure
  10. Ischemia
  11. Proteinuria

## OCCUPATIONAL DISEASES

### ANATOMY/PHYSIOLOGY

The kidneys in the normal adult weigh about 300 g; that is, about 0.5% of total body weight. Yet, they receive about 25% of the total cardiac output of blood flow. This latter fact strongly affects the pathogenesis of occupational kidney diseases. In physiological terms, the kidney plays a vital role in all of the following key functions: metabolic waste product removal from the blood, body fluid detoxification, total body fluid regulation, acid-base balance, electrolyte balance in the blood, erythropoiesis (production of red blood cells), and blood pressure regulation. To accomplish these tasks, the kidney uses a disproportionate (when compared with the remainder of the body) amount of energy, performs sophisticated filtration functions, is enzyme dependent, and employs active transport and active secretory mechanisms. In Figure VII-1A, the overall structure of the kidney is shown.

The functional unit within the kidney that regulates fluids and electrolytes is the nephron (Figure VII-1B). There are approximately one million of these nephrons per kidney. This multi-effect filtration device actively controls the composition and amount of urine formation. About 125 ml/minute of an ultrafiltrate of blood passes across the glomerulus into Bowman's capsule. This fluid then flows along the proximal tubule, the loop of Henle, and the distal tubule. In these structures, approximately 99% of the glomerular filtrate is reabsorbed and returned to the blood stream. In this fashion approximately 1 ml/minute of urine is formed and is delivered to the bladder before elimination. As a result of active transport mechanisms, a large fraction of the waste products in the blood ultrafiltrate remain in the urine and are eventually excreted. Most of the fluid and certain essential electrolytes in the blood ultrafiltrate are returned to the blood circulation by the sophisticated mass transport mechanisms of the nephron. These functional characteristics predispose the kidney to occupational diseases because:

1. Blood-borne toxins have intimate contact with the kidneys.
2. These toxins are usually concentrated in fluids by the action of the kidney.
3. Toxins have more opportunity to interfere with normal kidney functions as a result of the kidney's high metabolic rate.
4. The kidneys are vulnerable to the effects of toxins as the result of their reliance on enzymatic mechanisms.

### Kidney function measurement

Kidney function can be clinically evaluated by measuring exchange of materials between the blood and urine. By determining urine production and the relative amount of various materials in urine compared with those in the blood (termed clearance), the selectivity and transport properties of the nephrons can be assessed. Also, the blood flow rate to the kidneys and the operation of active transport and secretory mechanisms in the kidneys can be evaluated.

The kidney processes are very well controlled and regulated. In particular, many of the nephrons can be damaged or destroyed, and the remaining kidney will still appear by analysis of urine to be operating within an acceptable range. If even more nephrons are damaged, then the entire fluid and electrolyte balance system along with the toxin and metabolic waste product elimination system may start to fail. As a result of the well-controlled nature of kidney function, early-stage kidney diseases, including those of occupational origin, may be difficult to detect.

### OCCUPATIONAL DISEASES

The kidneys do not contact hazardous agents directly as does the skin or the respiratory system. Kidney contact with toxins is mediated through the blood. As mentioned, kidney blood flow is disproportionately large. As a result of this pattern of contact, effects of toxins at sites other than the kidneys may occur simultaneously with nephrotoxicity (toxicity to kidney cells).

### Renal failure

Acute renal failure from an occupational exposure may result from: insufficiency of blood flow (ischemia) to the kidneys, toxic effects of products from the breakdown of blood, or direct effects of other toxins. A number of examples of these are discussed below. Prerenal (before the kidneys) ischemia (blockage of blood flow) can occur from poor

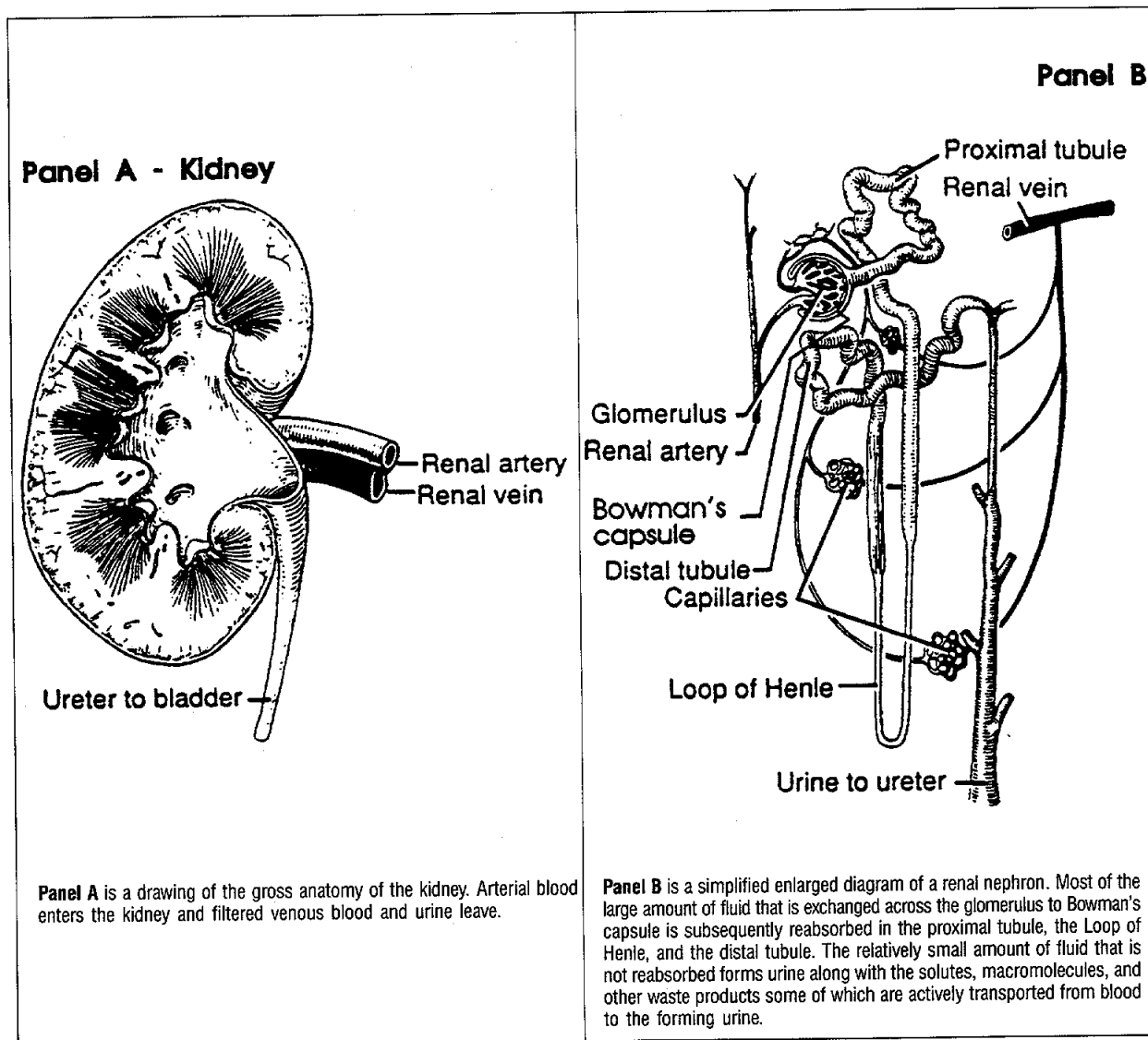


Figure VII-1. Gross anatomy of the human kidney and a simplified diagram of a renal nephron.

circulation, low blood pressure, or hemorrhagic shock (a circulatory failure due to loss of blood). As a result of these conditions, auto-regulatory mechanisms prevent blood from passing through the nephrons. The kidneys stop filtering and become damaged because of the presence and persistence of waste products. When red blood cells are broken down and hemoglobin is liberated into the plasma (hemolysis), the kidneys serve as a filter for these breakdown materials. Because of unknown mechanisms, the filtered hemoglobin may block subsequent urine production. The direct action of toxins on the kidneys varies. For example, when the kidneys are directly exposed to nephrotoxins, crystalline materials (such as oxalic acid crystals, the metabolic breakdown products of ethylene glycols) can be deposited in and damage the kidney tubules. Or, contact with halogenated hydrocarbons such as chloroform or carbon tetrachloride can interfere with the enzyme mechanism of the kidney.

**Renal disease**

Chronic renal disease resulting from occupational exposure is well known. Many heavy metals are causative agents. Chronic exposure to cadmium by inhaling cadmium oxides may interfere with the selectivity of the nephrons with respect to small plasma proteins. The result is that excessive amounts of low molecular weight plasma proteins are lost in the urine (proteinuria). This may influence the whole body fluid and plasma protein

## OCCUPATIONAL DISEASES

balances. After chronic exposure to lead, kidney tissue may become fibrotic, with irreversible dysfunction. Often a long latency period is associated with chronic exposure and damage to the kidneys; this makes identifying the occupational etiology difficult.

Work-related diseases of the kidneys are not a leading occupational health issue. Because of their predominant role in the production of urine, however, the kidneys may be involved in bladder cancer—an important (in terms of numbers and consequences) work-related disease. Even though the incidence of occupational kidney disease is relatively low, the severe consequences associated with these illnesses make prevention of kidney diseases an important consideration. A selected list of chemicals, industries in which workers may be exposed to these agents, and the effects on the kidneys appear in Table VII-1.

Table VII-1  
Occupational Kidney Diseases

Causative Agents	Industry/Process	Disease or Effect
Mercury, lead, cadmium	Battery manufacturing, pigment industries	Chronic renal failure, nephrotoxins
Chloroform, carbon tetrachloride	Solvent, chemical industries, painting, metal cleaning	Acute renal failure, nephrotoxins
Carbon disulfide	Solvent, rayon production, pesticide production	Chronic renal failure, nephrotoxins
Ethylene glycol	Solvent, cosmetics, auto industry, chemical industry	Acute renal failure, obstructive uropathy (obstruction of urine flow)
Therapeutic agents (drugs)	Pharmaceuticals, pharmacies, health care	Renal failure, nephrotoxins

## Unit VIII

### LIVER

**PURPOSE:** To understand the role of the liver with respect to the development of occupational disease.

**OBJECTIVE:** To review briefly the following aspects of the liver:

1. Physiology
2. Defense mechanisms
3. Occupational diseases

**SPECIAL TERMS:**

1. Protein synthesis
2. Energy production
3. Bile
4. Detoxification
5. Endogenous wastes
6. Intraperitoneal delivery
7. Clearance
8. Biotransformation
9. Hepatitis
10. Hepatotoxicity
11. Cirrhosis
12. Jaundice
13. Mixed function oxidase

**PHYSIOLOGY**

The liver, an organ well-perfused with blood that weighs about 1.5 kg, serves many functions: synthesis of plasma proteins and amino acids; utilization of free fatty acids to produce energy; energy and material storage; production of bile and bile salts; and breakdown and detoxification of endogenous wastes, drugs, and foreign chemicals to more acidic or more soluble forms that are more easily secreted. The liver is involved in complex biochemical reactions that often rely on complex enzyme systems. The position of the liver with respect to whole body circulation of blood (see Figure VIII-1), makes it particularly vulnerable to toxic attack. In particular, the liver is the first organ to receive blood flow from the stomach and digestive tract. Any substances transferred to the blood from the digestive system will encounter the liver on a "first pass" basis. Therefore, orally or intraperitoneally (within the abdominal cavity) administered drugs absorbed into the blood first encounter the liver. The liver biotransforms many materials into less bioactive, more water-soluble states. Unfortunately, because these enzyme mechanisms lack specificity, biochemical activity within the liver may convert an innocuous material into a more reactive, toxic, or even carcinogenic material.

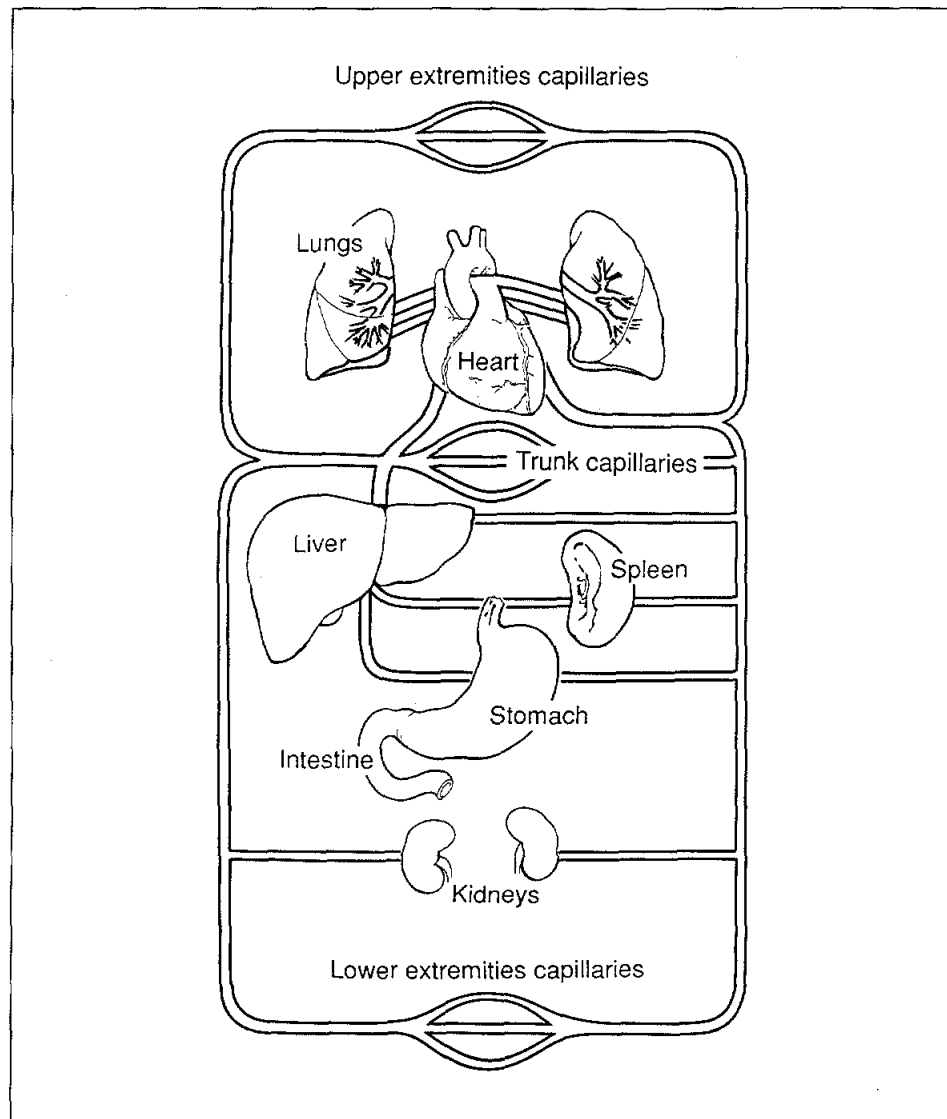


Figure VIII-1. Schematic of the human circulatory system indicating the relative position of the liver with respect to other body organs.

Health professionals have several tests to assess the liver's health: direct evaluation of liver enzymes in serum and liver clearance of dyes. Following acute upsets, individual evaluation tests are useful, but periodic testing over a long time period may be needed to detect chronic liver changes.

**DEFENSE MECHANISMS**

The defense of the liver against toxic materials has already been mentioned, i.e., its ability to biotransform and detoxify foreign matter. This ability depends on age, sex, genetic makeup, and nutritional status of the individual as well as the properties of the foreign substance. Favorable outcomes result when liver metabolism converts foreign materials to nontoxic metabolites, which are eliminated easily from the body, or when the production of a toxic material then undergoes further detoxification. If the toxic metabolite cannot be rendered harmless, cellular or tissue damage may result.

**OCCUPATIONAL DISEASES**

The liver, because of its physiological function and its position in the circulatory system, is susceptible to a wide variety of occupational diseases. These diseases generally fall into two categories: acute toxic hepatitis and chronic liver disease. The effects of occupationally induced pathological changes in the liver vary depending on the causative agents or site of action in the organ. Some hepatotoxic materials destroy liver cells whereas others may interfere with bile flow. Acute toxic hepatitis often results from inhaling a harmful material, with pathological changes usually appearing within 2 days post-exposure. Materials such as urethane and dimethylnitrosamines may cause acute toxic hepatitis.

Chronic liver diseases are often associated with a lengthy latency period—up to 30 years. Because of this long induction period, relating cause to effect is difficult. Several xenobiotic agents that produce chronic pathologies have been studied thoroughly. Often liver disease is characterized by damage to liver cells with the presence of nodules or fibrosis (cirrhosis); jaundice, with its characteristic yellow tinting of the skin, is symptomatic of this condition. Liver cancer may also result from chronic exposure to harmful materials.

Occupational exposure to vinyl chloride illustrates how liver metabolism may adversely affect the health of the host. Once the vinyl chloride monomer has entered the body, it is attacked in the liver by cytochrome P-450 (referred to as the mixed-function oxidase system). This very versatile and powerful liver enzyme system transforms the monomer into an aldehyde. This aldehyde may produce a very toxic acute hepatitis (inflammation of the liver) before eventually being converted further and then being excreted in urine.

As with occupational kidney diseases, occupational liver diseases are not very common. Because of their severity, however, occupational liver diseases, especially liver cancers, represent a significant risk to the worker.

A select list of causative agents, industries in which workers may be exposed to these agents, and the effects on the liver appear in Table VIII-1.

## OCCUPATIONAL DISEASES

Table VIII-1  
Occupational Liver Diseases

Causative Agents	Industry/Process/Worker	Disease or Effect
Carbon solvents, tetrachloride	Cleaning fluids, dry cleaners	Acute hepatotoxicity (liver cell injury)
Vinyl chloride	Plastics, vinyl chloride production	Acute toxic hepatitis, hepatic angiosarcoma (a liver cancer)
Arsenic	Smelting, insecticides	Chronic liver disease
Epoxy resins	Rubber, synthetic fabrics	Acute cholestatic hepatitis (inflammation and decreased bile flow)
Halogenated aromatics	Solvents, dyes, electrical transmission, insecticides, lubricants, paints	Acute toxic hepatitis
Chlorinated methylene dianiline	Resin hardeners	Acute cholestatic hepatitis



**UNIT IX**  
**CARDIOVASCULAR SYSTEM AND THE BLOOD**

- PURPOSE:** To understand the roles of the cardiovascular system, including blood, with respect to the development of occupational disease.
- OBJECTIVE:** To review briefly the following aspects of the cardiovascular system and the blood:
1. Physiology
  2. Occupational diseases
- SPECIAL TERMS:**
1. Heart
  2. Vascular system
  3. Lymphatics
  4. Pulmonary circulation
  5. Coronary artery
  6. Cerebral circulation
  7. Hydrostatic pressure
  8. Erythrocytes
  9. Atherosclerosis
  10. Rhythmical behavior
  11. Vasodilation
  12. Binding affinity
  13. Hemoglobin
  14. Metabolic inhibition

## OCCUPATIONAL DISEASES

### PHYSIOLOGY

The function of the cardiovascular system is to make blood available to virtually all parts of the body so that, through this fluid medium, oxygen can be delivered to tissues and cellular waste products including carbon dioxide from metabolism can be removed. The driving force for the circulation of blood is the pumping action of the heart—action based on the rhythmical cycle of contraction and relaxation of the heart chambers. The heart, which weighs approximately 300 g and is the size of a fist, is composed, primarily, of muscle and valves. The relative position of the heart with respect to other body organs is shown in Figure VIII-1.

#### Heart

#### Vascular system

The vascular system through which blood flows is a complex branching thoroughfare, the smallest anatomic segments of which are the capillaries. At the level of the capillary beds (the microvasculature), mass exchange between the intraluminal blood and external interstitial tissues occurs. The lymphatic system is another vascular system contained within the body. It emanates as small capillaries in tissues and culminates as larger vascular entity that returns tissue-derived fluids to the venous system of the blood circulation.

#### Lymphatic system

#### Pulmonary circulation

The human cardiovascular system is so designed that certain organs receive special attention. The pulmonary circulation (blood flow through the lungs) is the site where blood is oxygenated and gaseous wastes are removed. Since the action of the heart requires high metabolic activity, it also requires a considerable blood supply, which the coronary arteries supply from the heart's outer surface. This specialized circulatory system is highly regulated in an attempt to match metabolic need with delivery of oxygen. The cerebral circulation (brain blood flow) is also of specialized design. For this organ, important functional characteristics are maintaining blood flow and maintaining a relatively impermeable blood/brain barrier with respect to exchange of macromolecules. Throughout these organs and the remainder of the systemic circulation, the cardiovascular system is a very complex fluid dynamic network; it is very well regulated with respect both to blood flow (and therefore oxygen delivery) and to the hydrostatic pressure distributions. Defense mechanisms associated with this system are intimately related to its regulatory behavior.

#### Coronary circulation

#### Cerebral circulation

#### Blood

Blood is the fluid medium contained within the cardiovascular system. This non-Newtonian, aqueous suspension of cells serves several functions. The erythrocytes (red blood cells) contain the protein hemoglobin responsible for the blood's capacity to bind oxygen in a reversible manner. Platelets are relatively small blood elements that, because of their biochemical properties, help seal ruptures in the cardiovascular system and then participate in fibrin formation, which seals injured areas. Leukocytes (white blood cells), in general, act as circulatory defenders against invasion by foreign matter.

### OCCUPATIONAL DISEASES

Diseases of the heart and vascular system are primarily influenced by nonoccupation practices: e.g., cigarette smoking, diet, sedentary lifestyle, stress, and the presence of other diseases such as diabetes. Because of the overwhelming influence of these non-work related factors, establishing clear relationships between heart or vascular disease and occupational exposure has been generally difficult. Not only has research directed at establishing these causal relationships been limited, but no specific clinical manifestations exist to differentiate occupationally caused heart diseases from other heart disorders.

#### Atherosclerosis

Several examples of agents shown to have a direct effect on cardiovascular diseases will be discussed before occupational blood disorders are mentioned. The most convincing evidence concerning causality exists for the effect of carbon disulfide in coronary artery disorders. Chronic exposure to carbon disulfide is believed to result in atherosclerosis (material deposits in the arteries that restrict blood flow) of the coronary arteries. As a result of this condition, blood flow to the heart muscle is decreased and ischemia (lack of oxygen) results. The heart muscle becomes compromised, and the outcome can vary from pain in the chest area (angina) to death.

#### Heart rhythms

Another category of cardiovascular diseases relates to upsets in the normal rhythmical behavior of the heart. Abnormal heart rhythms are referred to as arrhythmias. High levels of exposure to solvents such as benzene or trichloroethylene have been implicated in

the etiology of cardiac arrhythmias. Physical symptoms of arrhythmias include dizziness, shortness of breath, palpitations, headaches, and nausea. Sudden death may follow.

**Vasodilation**

The last example of a cardiovascular disease of occupational origin involves exposure to nitrates such as ethylene glycol dinitrates or nitroglycerin. These materials have the ability to vasodilate the coronary artery (increase internal vessel diameter). When exposed workers are withdrawn from an environment containing these agents, they may experience a rebound phenomenon that results in spasmodic behavior of the vasculature. The outcome may be heart spasms, myocardial infarction (death of heart muscle after interruption of the blood supply), or fatal arrhythmias. Chronic exposure to nitrates may also increase the incidence of atherosclerosis.

**Hemoglobin**

In terms of occupational exposure, carbon monoxide is perhaps the most common chemical with the potential to alter normal blood characteristics and function. The hemoglobin in the red blood cells binds oxygen in a complex manner so that a maximum of four oxygen molecules can be associated with each iron-containing heme group. Carbon monoxide has a stronger binding affinity for hemoglobin than does oxygen. Therefore, carbon monoxide, if present in inspired air, will displace oxygen in red blood cells. The net result is that, in the presence of sufficient carbon monoxide, blood will lose its ability to transport oxygen. As such, carbon monoxide is a chemical asphyxiant (a material that decreases the blood's capacity to transport oxygen). Carboxyhemoglobin, the complex between carbon monoxide and hemoglobin, is a cherry color, just as is fully oxygenated blood. A person poisoned by carbon monoxide inhalation often has a pink to red flush to the skin. Other symptoms of carbon monoxide poisoning include headache, weakness, nausea, and dizziness. Depending on the concentration of carbon monoxide in the environment and the temporal pattern of exposure, the worker may experience angina, myocardial infarction, arrhythmias, or sudden death. Exposure to methylene chloride produces the same effects, as this solvent is metabolized to carbon monoxide in the body.

**Asphyxiant**

**Metabolic inhibition**

Another chemical agent that can interfere with oxygen delivery and utilization in tissues is cyanide. Cyanide compounds decrease oxygen uptake by hemoglobin, but more importantly, they act as tissue metabolic inhibitors by interfering with enzyme activity. Cyanide poisoning is often very rapid. Symptoms of acute exposure to cyanide include headache, palpitations, giddiness, possibly followed by unconsciousness and death.

Cardiovascular system diseases are the leading causes of death and disability in the United States. Fortunately, some types of these diseases have been declining even as the general distribution of the population becomes more weighted toward the elderly. Table IX-1 shows, for a selected list of chemicals, the industries in which workers may be exposed to these agents, and the effects on the cardiovascular system or blood.

OCCUPATIONAL DISEASES

Table IX-1  
Occupational Cardiovascular Diseases and Disorders of the Blood

Causative Agents	Industry/Process/Worker	Disease or Effect
Carbon disulfide	Degreasing, drycleaning, electroplating, rayon manufacture, resin manufacture	Coronary artery disease, atherosclerosis
Carbon monoxide	Many combustion operations, pulp and paper industry, petroleum refinery	Acute chemical asphyxia, possibly increased atherosclerosis
Methylene chloride	Degreasing, leather treatments, solvent processes, resin manufacture	Same as for carbon monoxide
Nitrates	Explosives, chemical industries	Angina, myocardial infarction, death
Fluorocarbons	Refrigeration, solvent workers, drycleaning	Arrhythmias
Halogenated hydrocarbons	Drycleaning, solvent workers, degreasing, paint industry	Arrhythmias
Heat	Bakers, furnace workers, smelters, kiln workers	Angina, acute myocardial infarction, death
Cyanide	Plastic making, pesticide production, coke oven workers, electroplating jewelers, steel production	Chemical asphyxiant
Arsenic	Smelting, agricultural use, pharmaceuticals	Coronary artery disease

**Unit X**  
**NERVOUS SYSTEM**

**PURPOSE:**

To understand the role of the nervous system with respect to the development of occupational disease.

**OBJECTIVE:**

To review briefly the following aspects of the nervous system:

1. Anatomy/physiology
2. Occupational diseases

**SPECIAL TERMS:**

1. Central nervous system
2. Peripheral nervous system
3. Sensory cells
4. Transmitting cells
5. Neuron
6. Axon
7. Myelinated sheath
8. Depolarization
9. Neurotoxins
10. Electrical transmission
11. Reflex function

## OCCUPATIONAL DISEASES

### **ANATOMY/PHYSIOLOGY**

The nervous system is usually divided into the central nervous system (CNS), which includes the brain and spinal cord, and the peripheral nervous system (PNS), which includes the sensory and transmitting cells that communicate information from the periphery of the body to the CNS. After information transmitted to the CNS is processed, outgoing signals may initiate bodily activities. In this fashion, the nervous system is organized to sense and transmit information to a central processing unit where a response is elicited. The nervous system then transmits this response, which will eventually be manifest in the form of control of motor functions.

### **Neuron**

The basic functional unit of the nervous system is the neuron. The neuron, composed of a main cell body and an axon along which impulses can be carried, can transmit electrical signals by a complex interactive system employing chemical neurotransmitters, electrical conduction, selective alternations in permeability of the axon, and conversion of electrical energy to chemical energy. Large nerve fibers are covered with a lipid structure called a myelinated sheath that serves to insulate the conducting fibers. This highly organized and sensitive control system can be disrupted by the action of chemicals at any site along the neuron. That is, potentially harmful materials entering the body as part of an occupational exposure may interfere with normal nervous system operation by a host of mechanisms including: demyelination, interference of transmission at nerve junctions (transmission or reception), depolarization of the axon, and cellular degeneration, to name a few.

### **OCCUPATIONAL DISEASES**

It is difficult to generalize about the action of chemicals on the nervous system. Many toxic materials primarily target other organs but still have significant secondary effects on the nervous system. The effects of neurotoxins can be conveniently distinguished according to their action on the central or peripheral portions of the nervous system.

### **Electrical signals**

Occupational diseases relating to the peripheral nervous system usually occur at two distinct anatomical sites: the myelinated sheath protecting the axon or the axon. The protective myelinated sheath of the axon can be destroyed while the central axon remains intact. Under these circumstances, conduction of electrical signals along the axon is compromised. Recovery is possible from this pathologic condition. The axon itself may also be attacked with ensuing degeneration. In this latter class of diseases, the myelinated sheath may, in a secondary manner, also be attacked. Recovery in the form of regeneration of partially degenerated axons is slow and may be incomplete. Symptoms of these diseases are usually first noticed as a numbness or tingling sensation in the hands or feet. These symptoms are followed by clumsiness and lack of coordination as sensory or motor apparatuses may be affected. These conditions may expose workers to accidents. The effect of most harmful agents can be characterized as above; there are, however, specific agents that produce specific effects. For example, when arsenic attacks the nervous system, it produces symptoms of painful limbs and, in particular, feet very sensitive to touch.

### **Neurotoxic agents**

CNS activity often decreases dramatically as a result of occupational exposure to neurotoxic agents. Heavy metals and many solvents have the capacity either to depress electrical transmission or to alter the effectiveness of physical activity. Many of the specific mechanisms involved in the action of neurological diseases remain unresolved. Excessive exposure to neurotoxins may have continuing behavioral and physical effects on the individual—effects ranging from mild symptoms of lack of energy or fatigue, to increase in response time for motor activities, to poor eye-hand coordination, to strong psychological effects such as emotional instability. Ethyl alcohol is perhaps the most common neurotoxin, and it can be encountered occupationally and also as part of a worker's lifestyle. Many organic chemicals are suspected or known nervous system toxins. The trend in the chemical production industry appears to be toward greater use of these materials which will, no doubt, result in the greater potential for worker exposure.

Assessing neurological damage is very difficult; the anatomical site of injury also poses great problems. A history of the patient and an evaluation of his/her mental status,

## Unit X—Nervous System

nervous system, sensory system, motor system, and reflex functions are required. Even with the above information, the health professional may still have difficulty discovering the occupational basis of a nervous system disorder.

Nervous system diseases have been identified as leading work-related illnesses, and proposed prevention strategies are being considered on a national basis in the United States. Of the almost 600 chemicals for which TLVs have been set, approximately one-third of these affect the nervous system. In addition, it is estimated that just below 10 million U.S. workers may have full-time exposure to these materials. A select list of chemicals, industries in which workers are exposed, and effects on the nervous system appears in Table X-1.

Table X-1  
Occupational Nervous System Diseases

Causative Agents	Industry / Process / Worker	Disease or Effect
Mercury (organic forms)	Agricultural industries	Central nervous system toxin, many effects including psychological disorders
Acrylamide	Plastics industry, paper, adhesives, dyes	Peripheral nervous system toxin (site of action is the axon, with motor and sensory effects)
Carbon disulfide	Rayon fiber production, chemical process industries, paints, fuels	Central and peripheral nervous system toxin, mental and many other disturbances
Arsenic	Smelter workers	Peripheral nervous system toxin, nerve condition abnormalities
n-hexane and MBK (methyl butyl ketone)	Chemical process industries, cleaning solvents, glues, adhesives	Peripheral nervous system toxin, impaired psychological function, impaired sensation weakness
Organophosphate insecticides	Farming, insecticide production	Central nervous system toxin, synaptic transmission decreased, multitude of physical effects
Solvents	Solvents, cleaning, coating	Peripheral nervous system toxin, narcotic effects, acute intoxication
Manganese	Steel fabrication, dry cell batteries, pigments	Central nervous system toxin, multitude of behavioral disorders, mimics Parkinsonism





**Unit XI**  
**REPRODUCTIVE SYSTEMS**

- PURPOSE:** To understand the role of the male and female reproductive systems with respect to the development of occupational disease.
- OBJECTIVE:** To review briefly aspects of the male and female reproductive systems that may result in the development of occupational disease.
1. Anatomy/physiology
  2. Occupational diseases
- SPECIAL TERMS:**
1. Sexual development
  2. Hormones
  3. Hypothalamus
  4. Pituitary gland
  5. Spermatogenesis
  6. Sterility
  7. Infertility
  8. Ovum
  9. Fertilization
  10. Fetus
  11. Embryonic development
  12. Teratogens

## OCCUPATIONAL DISEASES

### REPRODUCTIVE SYSTEMS

Long-term human survival demands reproduction. The male sperm, the female ovum, and the fertilized ovum are the most relevant components of the reproductive process that may be damaged as a result of occupational exposure. Since men and women play different roles and utilize different physiological systems in the reproductive process, they will be considered separately with respect to hazards associated with occupational exposure.

In general, knowledge concerning reproduction and the effects of occupational exposure to potentially hazardous agents can be characterized as being in a research stage. That is, many uncertain or unstudied aspects concerning reproduction and occupation represent practical problems, but they are currently being explored. Reproductive problems related not only to occupation but also to the environment in general have become prominent issues in the media and the courts. A large number of studies have involved reproductive or developmental effects of chemical, physical, or biologic entities on laboratory animals; however, only a few studies have involved the analogous human effects.

### MALE REPRODUCTIVE SYSTEM

#### Sperm

#### Testosterone

Sexual development in the male is a complex process that begins shortly after birth and reaches its goal during puberty when mature sperm cells can be produced. The developmental phase as well as the post-maturation period involves release of specialized hormones from the hypothalamus that interact with the pituitary gland to produce other chemical messengers. These hormones eventually stimulate the production of the testosterone needed for sperm production (spermatogenesis) as well as for sexual behavior, secondary sex characteristics, and other organ development.

#### Sterility

Perhaps the most critical process in the male reproduction system is the maturation of the sperm cell. This process takes between 2 and 3 months, involves constant cell division, and is susceptible to insult by foreign agents. Any agents causing hormonal imbalances or changes in the testosterone level may lower the sperm count and alter sexual behavior. The severe case of male sterility results when developing sperm cells are destroyed. Lifestyle may influence male reproductive toxicology. Habits such as cigarette or marijuana smoking, alcohol ingestion, and some leisure activities (e.g., pesticide exposure from gardening) may also affect the male reproductive system.

The extent of the problem is such that an estimated 10% to 15% of all couples in the United States cannot conceive a child within a 1-year period of normal unprotected sexual activity. No doubt male infertility contributes significantly to this situation.

Some of the agents that represent a hazard to the male reproductive system are given in Table XI-1.

### FEMALE REPRODUCTIVE SYSTEM

The female carries the burden in the human reproductive process. Once the ovum has been fertilized, a complex dynamic set of changes occur; these are depicted in Figure XI-1. After fertilization, the ovum becomes implanted in the uterus, and a rapid phase

Table XI-1  
Occupational Male Reproductive Disorders

Causative Agents	Industry /Process	Effect
Lead	Battery production	Reduced fertility, spontaneous abortion
Halogenated pesticides	Chemical industries, farming	Low sperm count, sperm precursor cell destruction
Organic solvents	Chemical industries, wood stripping	Reduced sperm count
Microwaves, X-irradiation	Electronics, research laboratories	Reduced fertility
Chemotherapeutic agents	Health care, research laboratories	Reduced fertility

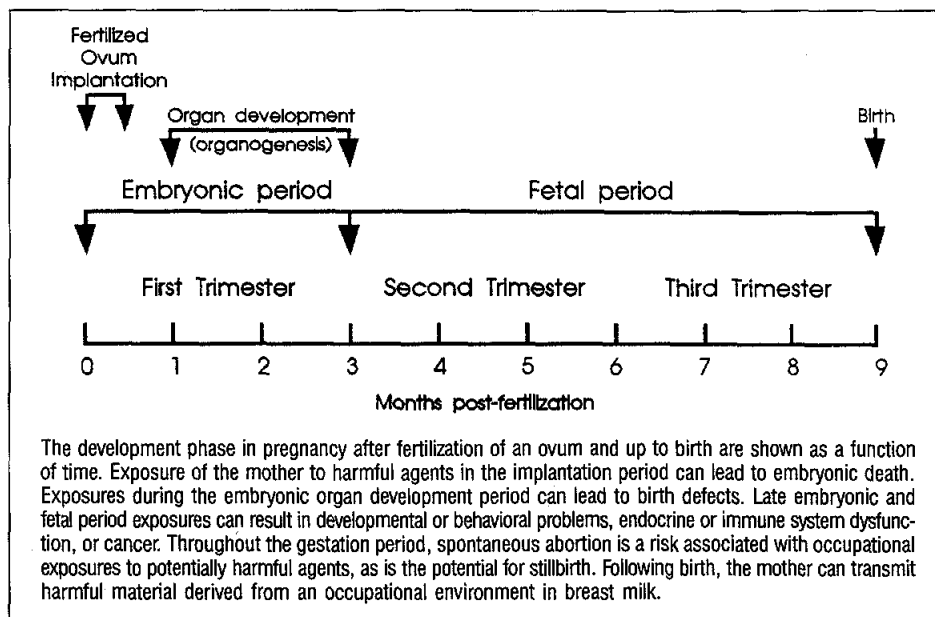


Figure XI-1. Time course of human pregnancy.

**Embryonic development**

of organ development ensues in which cells multiply and differentiate. Following this rapid developmental phase is a slower and longer maturation time during which the fetus is being functionally prepared for birth. In this stage-wise process, the well-being of the potential offspring is at risk from occupational exposure not only throughout the postfertilization period, but also prefertilization just as in the case for the male reproduction system. Perhaps the period most sensitive to abnormal influences is the early phase in the embryonic period where organs are developing as a result of cell differentiation. The time when a pregnant woman is exposed to a harmful agent is a critical factor with respect to the health of the embryo or fetus.

**Teratogens**

The potential for chemical, physical, or biological agents to interfere with normal female reproduction can occur at any stage in the process. The range includes prefertilization disorders such as menstrual disorders, alterations in sexual activity, and lowered fertility. After fertilization, genetic damage that existed prefertilization can be passed on to the embryo. The offspring can also be damaged during pregnancy as a result of harmful agents crossing the placental barrier or by a direct action on the fetus. The risk of spontaneous abortion, which may result from occupational exposure, exists throughout pregnancy but especially during the first trimester. During pregnancy, exposure of the mother to certain chemicals will result in death to the fetus (spontaneous abortion, miscarriage, or stillbirth) or in significant deformity. Harmful agents known as teratogens interfere with normal embryonic or fetal development. After birth, a breast-fed infant may be exposed to some chemicals transmitted from the mother to the infant via breast milk. This is particularly true for highly fat soluble chemicals. Social and personal habits also influence the health of the offspring.

**Reproductive risks**

Protocols for complex animal experiments have been formulated to test for potential occupational health risks associated with reproduction. Most of our present information concerning the risks associated with chemical exposure and reproductivity are as a result of animal model studies. Extrapolation of results from animals to humans remains of questionable value. Although epidemiological studies have proved useful in identifying reproductive risk, few chemicals used in an occupational setting have been identified as causing adverse reproductive effects in women. This fact along with other complexities involved with human female reproduction, has made the task of setting occupational exposure standards that ensure the well-being of the potential offspring very difficult.

## OCCUPATIONAL DISEASES

Monitoring during the various stages of the female reproductive cycle has been suggested as a way to identify disorders: monitoring menstrual dysfunction may relate occupational exposure to an undesired physiological outcome, and analysis of amniotic fluid (the fluid surrounding the fetus during development) can be used to test for genetic defects.

Because of the complexity of the reproductive process, relating specific effects of occupational exposure to dysfunction has proved difficult. Lead exposure is an exception to this generality. Lead is known to adversely affect many of the stages in female reproductivity, ranging from preconception through embryonic and fetal development to birth. Parental exposure to lead increases birth defects including neurological damage and the chance of death within 1 year of birth.

Assessing the specific negative influence of occupational exposure on female reproductive function is difficult. As an example, although 1000 of the almost 3000 chemicals tested for teratogenic effects in animals gave positive results, fewer than 50 chemical agents are recognized as human teratogens. The need for considerable research related to female reproductivity and occupational exposure is obvious. Examples of causal agents known to produce problems involved with the female reproductive system are listed in Table XI-2.

Table XI-2  
Occupational Female Reproductive Disorders

Causative Agents	Industry/Worker	Effect
Lead	Battery production, mining industry	Reduced fertility, spontaneous abortion, behavioral or developmental disabilities
Anesthetic gases	Health care, nursing	Increased rate of miscarriage, birth defects
Polychlorinated biphenyls	Electrical industry, chemical industries	Passed on to infant in breast milk
Reinforced plastics	Plastics, construction	Suspected teratogens, stillbirth
Vinyl chloride monomer	Plastics, construction	Suspected husband-related effect on spontaneous abortion

## Unit XII

### ERGONOMICS

**PURPOSE:**

To understand the interaction of a worker with the work environment.

**OBJECTIVE:**

To review briefly the physiological, psychological, engineering, and human body aspects that relate to biomechanical, psychological, and environmental stresses associated with work.

**SPECIAL TERMS:**

1. Environmental stresses
2. Compatibility
3. Ergonomic checklist
4. White finger disease
5. Cumulative traumas
6. Fatigue

**THE WORKER  
AND WORK**

Occupational disease may result from biomechanical, psychological, or environmental stresses associated with work. Ergonomics is the interdisciplinary study of the interaction of the worker with the work environment. The objective of ergonomic studies is to make the human work experience more efficient while promoting the well-being of the worker. This involves establishing and maintaining compatibility between equipment, tools, tasks, and environmental factors on one hand, and human anatomical and biomechanic considerations and perceptual and behavioral characteristics on the other. Its interdisciplinary nature is a critical feature of ergonomics, which combines physiology, psychology, engineering, and anthropometry (measurements with respect to the human body). The nonpsychological aspects of ergonomics are sometimes referred to as human factors engineering. The range of subjects that can be studied from an ergonomic point of view is quite diverse and includes analyses of: static and dynamic human body biomechanics, metabolic and physical work requirements, use of tools, repetitive motion tasks, climatic and other environmental effects, lighting, equipment and process design, job demands, and mental and cognitive demands, to name a few.

**Human factors  
engineering**

Ergonomic considerations include aspects of safety program and managerial components as well as engineering, equipment, equipment maintenance, medicine, and training. To investigate the possibility of potential problems in a consistent, rational manner, ergonomic checklists have been designed. These devices are used to systematically examine the wide range of factors that may be involved in a system composed of a human working in an occupational environment. Common to many of the checklists are:

**Ergonomic checklist**

1. analysis of human capabilities with respect to work station design and layout,
2. investigation of equipment design regarding the reliability and ease of equipment use,
3. analysis of risk associated with physical workloads,
4. information handling and decision making,
5. a survey of environmental factors including illumination, noise, and vibration as well as climatic conditions,
6. consideration for work schedules.

NIOSH has proposed prevention strategies for the 10 leading work-related diseases and injuries. Included in this list are musculoskeletal injuries (including back injuries), traumatic injuries including death, noise induced hearing loss, and psychological disorders. The incidence of these injuries or diseases can be reduced by effectively applying ergonomic considerations.

**ADVERSE EFFECTS  
CAUSED BY WORKPLACE  
CONDITIONS**

Three examples of adverse effects on a worker serve to illustrate the scope of ergonomic problems.

**Cumulative traumas**

Cumulative traumas can result in disorders to:

1. the nervous system, such as damage to the peripheral nervous system;
2. the tendons and tendon sheaths, such as in carpal tunnel syndrome or in epicondylitis (tennis elbow), which may result from repeated hand/wrist movements;
3. the lower back, the site of some of the most costly occupational injuries based on number of injuries and associated medical expenses; and
4. joints, such as in bursitis and degenerative joint diseases.

The specific region associated with the symptoms of cumulative trauma is usually in the upper part of the body in either soft tissue or joints.

Workers who use vibratory equipment, such as jack hammers or chain saws, sometimes register such complaints as numbness and blanching of fingers, pain, loss of muscular control, or reduced sensitivity to heat and cold. These are the symptoms associated with Raynaud's or vibrational white finger disease. This condition can arise after prolonged and repeated minor insults (cumulative trauma) to the body such as from vibrations or from being struck by objects.

**Noise-induced hearing loss**

Noise-induced hearing loss can be either temporary or permanent. It can result from physical interference with the transmission of sound or it can result from neuropathologies. The causative agent is the sound power level or the level of impact noise. Industry abounds with equipment and operations that produce excessive sound pressure and noise impact levels.

**Fatigue**

Another example of an occupational disorder preventable by ergonomic considerations is that of fatigue. Though fatigue is not technically an occupational disease, it is so prevalent that it warrants mention. Fatigue is defined operationally as an impairment in the ability of a person to perform efficiently because of prolonged or excessive physical or mental exertion. Causes of fatigue include monotony, work intensity, and psychological and environmental factors. Fortunately, fatigue can be cured by rest. If insufficient rest follows bouts of fatigue, then complete recovery cannot be ensured and further relapse into unproductive work may result.

Table XII-1 is a selected list of occupational injuries or symptoms and the workers that fall within the field of study of ergonomics. As the average age of the workforce increases, so too will the potential for problems requiring ergonomic solutions.

Table XII-1  
Conditions Caused by Biomechanical and Environmental Stresses

Injury/Symptoms	Commonly Affected Workers
Back problems	Material handlers
Carpal tunnel syndrome or tendonitis	Clerical workers, assembly line workers, check-out workers, stamping job workers
Raynaud's syndrome	Forestry workers, construction workers
Degenerative joint diseases	Material handlers, forestry workers
Eye strain resulting in fatigue	Clerical workers, foundry workers, high precision assembly and inspection workers
Hearing impairment	Furnace operators, truck drivers, machinery operators, construction workers
Segmented vibratory diseases	Chainsaw chipper and jackhammer operators
Loss of strength, problems with hand-eye coordination, decreased mental capacity, fatigue	Most workers





## GLOSSARY

- ABORTION:** the premature expulsion from the uterus of the products of conception (including the fetus).
- ACCLIMATION:** the process of adapting to new conditions.
- ACUTE:** having a sudden onset, sharp rise; short and relatively severe course.
- ALLERGY:** a hypersensitive state in which abnormal responses occur to specific stimuli (allergens); the responses may be manifested in the skin, the gastrointestinal tract, or the respiratory system.
- ALVEOLAR FLOODING:** fluid accumulation in the air space of the alveoli.
- ALVEOLI:** the tiny respiratory air sacs of the lung.
- ALVEOLITIS:** inflammation of the alveoli.
- AMNIOTIC FLUID:** the fluid within the sac that surrounds the fetus *in utero*.
- ANGINA:** pain or pressure sensation of the chest, often associated with shortness of breath and a feeling of impending death, due to ischemia of the heart muscle.
- ANGIOSARCOMA:** cancer of the blood vessels.
- ANTHROPOMETRY:** the science dealing with measurements (size, weight, proportions) of the human body.
- ANTIBODY:** a protective protein that interacts specifically with the foreign material (chemical or biologic) whose presence stimulated its production.
- ARRHYTHMIA:** a variation from the normal rhythm of the heart beat.
- ASBESTOSIS:** a pneumoconiosis due to lung deposition of asbestos fibers; it evokes a fibrotic tissue reaction.
- ASPHYXIANT:** a substance capable of causing death from suffocation, i.e., from oxygen deprivation.
- ASTHMA:** a condition characterized by recurring, reversible bouts of spasmodic airway constriction causing wheezing and difficult breathing; may be due to allergies or a variety of factors including inhaled irritants, vigorous exercise, and psychological stress.
- ATHEROSCLEROSIS:** the thickening and loss of elasticity of the arterial wall and narrowing of its lumen due to deposition of yellowish fatty plaques.
- BILE:** a fluid secreted by the liver that is transported to the gastrointestinal tract where it aids in digestion and absorption of fats and fat-soluble vitamins.
- BODY BURDEN:** the amount of a harmful agent in the body.
- CANCER:** a malignant, invasive tumor produced by multiplication of abnormal cells that have escaped the normal controls of growth and replication.
- CARBOXYHEMOGLOBIN:** hemoglobin combined with carbon monoxide.
- CARCINOGEN:** a cancer-producing substance.
- CARCINOGENESIS:** the production of cancer.
- CARDIOVASCULAR:** pertaining to the heart and blood vessels.
- CENTRAL NERVOUS SYSTEM (CNS):** that part of the nervous system consisting of brain and spinal cord.
- CEREBRAL:** pertaining to the brain or to the main part of the brain.
- CHOLESTATIC:** relating to the suppression of the flow of bile from the liver to the gall bladder to the intestine.
- CHRONIC:** having a long protracted course; persistent.
- CIRRHOISIS:** a hepatic disease in which the normal liver tissue is disrupted and replaced by nodules and fibrous scars.
- CLEARANCE:** the removal of a substance (e.g., by the kidney) from a specific volume of blood per unit of time.
- CORONARY ARTERIES:** the arteries that supply the heart muscle.
- DERMATITIS:** inflammation of the skin.

## OCCUPATIONAL DISEASES

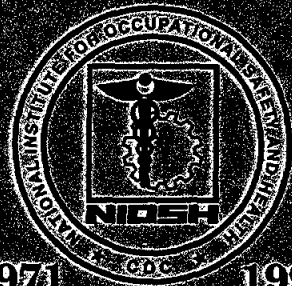
- DOSE:** the quantity of a toxic agent that reaches the body's internal environment.
- DYSFUNCTION:** impairment or disturbance in the normal functioning of a tissue or organ.
- ECZEMA:** dermatitis; an inflammation of the skin, with redness, itching, small blisters, oozing, crusting, and scaling.
- EDEMA:** accumulation of excess fluid in tissue spaces causing swelling.
- ENDOGENOUS:** originating within the organism.
- ENZYME:** a protein produced by the cell that, by its catalytic action, greatly accelerates a given chemical reaction.
- EPIDEMIOLOGY:** study of the relationship of factors determining human disease frequency and distribution.
- ERGONOMICS:** the interdisciplinary study of the interaction of man with all aspects of his work environment.
- ERYTHEMA:** redness of the skin produced by packing of blood in the local capillaries.
- ERYTHROCYTE:** red blood cell.
- ERYTHROPOIESIS:** the production of red blood cells.
- ETIOLOGY:** the cause(s) of a disease, or the study of the factors that cause disease.
- EXFOLIATION:** a peeling of scales or layers as in the shedding of small sheets of skin.
- EXPECTORATE:** to cough up and to spit out material from the lungs or throat.
- EXTRINSIC ALLERGIC ALVEOLITIS:** a respiratory hypersensitivity reaction mainly to inspiration of organic particles.
- FATIGUE:** a state of decreased capability and efficiency elicited by prolonged or excessive physical, mental, or emotional exertion.
- FIBRIN:** an insoluble protein in the blood essential in the process of blood clot formation.
- GENOTOXIC:** poisonous to the cell's genetic material.
- GESTATION:** the period of development of the fetus, from fertilization to birth.
- HEMOGLOBIN:** the oxygen-carrying protein of the red blood cell.
- HEMOLYSIS:** the breaking down of red blood cells with liberation of hemoglobin.
- HEMORRHAGIC SHOCK:** a state of circulatory failure due to loss of blood (hemorrhage).
- HEPATIC:** pertaining to the liver.
- HEPATOTOXIC:** toxic to liver cells.
- HIVES:** a transient, localized reaction in the skin in which changes in the local blood vessels allow excess fluid to leak into the tissues, forming smooth, itchy bumps.
- HOMEOSTASIS:** the tendency of the body to maintain the internal environment in its normal steady-state.
- HORMONE:** a chemical "messenger" substance, secreted by a specialized gland or tissue, that affects the function of another tissue of the body.
- HYPERSENSITIVITY:** a state of exaggerated response or extreme sensitivity to a foreign agent (allergen).
- HYPOTHALAMUS:** the part of the brain that coordinates the activity of the autonomic nervous system, the endocrine system (e.g., hormone glands), and many other body functions.
- IMMUNE SYSTEM:** a defensive system that relies on certain cells to recognize and to disarm a specific foreign agent.
- INFARCTION:** death of a tissue or organ due to ischemia, i.e., from obstruction of circulation to the area.
- INFLAMMATION:** a defensive reaction of the body to tissue injury—a reaction that involves changes in blood flow, body fluid distribution, and mobilization of phagocytic and other cells.
- INTRAPERITONEAL:** within the abdominal cavity.
- IRRITANT:** an agent that causes a state of overexcitation and undue sensitivity (i.e., irritation); a "primary irritant" affects the skin at first exposure.
- ISCHEMIA:** deficiency of blood flow due to constriction or obstruction of the blood vessel(s) supplying an area of the body.
- ITIS:** a word-ending denoting inflammation of the tissue indicated by the word stem with which it is used.
- LATENCY:** a state of seeming inactivity or dormancy between the time a stimulus occurs and the response becomes manifest.
- LEUKOCYTE:** a white blood cell.

- LUNG COMPLIANCE:** the ability of the lung to distend with pressure (volume change per unit of pressure).
- LYMPHATIC SYSTEM:** the system by which tissue fluid and proteins are removed from tissue and recirculated into the bloodstream.
- LYMPHOCYTE:** a type of white blood cell that participates in the body's defensive immune response.
- MACROPHAGE:** a highly phagocytic cell found in body tissues—a cell mobilized by inflammation to migrate to the site of injury.
- MELANIN:** the dark pigment that colors skin and hair.
- MESOTHELIOMA:** cancer of the tissue (pleura) lining the lung and the chest cavity; linked to exposure to asbestos.
- METABOLITE:** a substance produced by biochemical reactions in a living organism.
- MICROVASCULATURE:** the part of the circulatory system of the body composed of the finer blood vessels, e.g., arterioles, capillaries, and venules.
- MISCARRIAGE:** expulsion from the uterus of a non-viable fetus between 20 and 28 weeks of gestation.
- MYOCARDIAL:** pertaining to the heart muscle.
- NEPHROTOXIC:** toxic to kidney cells.
- NEUROPATHOLOGY:** study of aspects of disease of the nervous system.
- NEUROTOXIC:** toxic to nerve tissue.
- OBSTRUCTIVE UROPATHY:** a pathological change characterized by obstruction in the urinary tract.
- PALPITATION:** the subjective sensation of an irregular or rapid heart beat.
- PATHOGENESIS:** the sequence of events and pathologic mechanisms occurring in the development of disease.
- PATHOLOGY:** structural and functional changes that occur in the body with disease.
- PERIPHERAL NERVOUS SYSTEM (PNS):** the part of the nervous system outside the brain and spinal cord that consists of nerves and collections of nerve cell bodies.
- PHAGOCYTOSIS:** the ingestion of foreign particles or cellular debris by certain cells (phagocytes). The ingested substances may then be digested by enzymes or may be presented to lymphocytes to evoke antibody production.
- PHOTOSENSITIVITY:** an abnormally heightened reactivity of the skin to sunlight.
- PITUITARY:** a gland located within the skull that secretes hormones affecting growth, sexual characteristics, and other body functions.
- PLATELETS:** disc-shaped, cell-derived structures found in the blood, which are involved in blood clotting.
- PNEUMOCONIOSIS:** a condition characterized by permanent deposition of significant amounts of particulate matter in the lungs, e.g., "dusty lung."
- PROTEINURIA:** the presence of excess proteins in the urine.
- RENAL:** pertaining to the kidney.
- RISK:** this may involve both the potential for a disease to occur and its consequences.
- SENSITIZATION:** an immune response occurring on the first exposure to a chemical substance—an exposure that predisposes the individual to a heightened and more rapid response to further exposures.
- SILICOSIS:** a pneumoconiosis due to lung deposition of silicon dioxide (from stone, sand, or flint); it evokes nodular fibrotic changes.
- STILLBIRTH:** delivery of a dead fetus after 28 weeks of gestation.
- STRESS:** the reactions of a body to an adverse stimulus (physical, mental, or emotional) that tends to disturb the body equilibrium, or homeostasis.
- TERATOGEN:** an agent that causes defects during fetal development.
- TESTOSTERONE:** a steroid hormone responsible for development of male characteristics.
- THRESHOLD LIMIT VALUES (TLVs):** guideline values for airborne hazardous agents—designed to minimize health hazards to most workers.
- TOXICITY:** the degree of harm that an agent can produce in a biologic system.
- TOXIN:** a poison; any substance that may cause damage or disturb normal function in the body.
- ULCERATION (or ULCER):** a local destruction of a tissue surface caused by sloughing of dead inflammatory tissue.
- VASOLIDATION:** dilation of a blood vessel leading to increased blood flow.
- XENOBIOTIC:** a chemical agent foreign to the biologic system in question.

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The following list represents general texts and other compilations used in preparing this manuscript, including its tables and glossary. Taken together, these references offer an overview; the interdisciplinary nature of this field, however, often requires that information from other sources be consulted. When greater detail concerning any aspects of this work is required, the reader can consult occupational health and safety literature. A very useful source of technical information is NIOSHTIC, a computerized bibliographic data base. NIOSHTIC is updated quarterly and contains references on a wide variety of subjects relevant to occupational safety and health.

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