3.

Health Hazard Identification

Contents

LIST OF TABLES

3. Health Hazard Identification

Since work occupies a central place in most lives, it is not surprising that it is related to many afflictions, nor that in one form or another it contributes to diseases of every system of the body.

Some diseases are relatively easily linked to workplace conditions, either because the diseases themselves are distinct or relatively rare, or because the particular workplace conditions differ greatly from ordinary conditions of daily life. Other diseases are associated with either the workplace or other activities, or with both; pinning down causes and preventive strategies of those diseases is more complicated.

Occupational diseases have been recognized for centuries, although definitions of disease and ill health have changed over time. Society—less willing to accept adverse effects of any kind and knowing that much disease is preventable—no longer believes poor health to be a necessary concomitant of work.

While attention often focuses on new hazards, and in identifying and preventing more subtle, previously unnoticed effects, professionals in occupational safety and health also continue to deal with many cases of well-known occupational diseases. The still-frequent occurrence of many of these older diseases represents a failure to use already available knowledge.

Health hazards include those identified as present in the workplace, those present but unidentified, and new hazards, not yet introduced there. The identified hazards include exposures to physical agents such as radiation and noise, and exposures to some substances, including chemicals, metals, minerals, and vegetable dusts. Present, unidentified hazards may be many or few. Continued observation of workers and testing of substances are necessary to determine what exposures are hazardous. Testing of new substances should reduce the number of hazards introduced unknowingly into the workplace.

Traditionally, physicians and groups of workers have been the sources of information leading to the association of particular hazards with disease. “Factory fever” (typhus), “mad hatters” (victims of mercury poisoning), and “wrist drop” (lead poisoning) were related to workplace exposures through observation. Recent years have seen increasing importance being given to epidemiology—the study of the distribution of diseases—and toxicology— the study of the dangerous properties of substances—in identifying workplace hazards.

Case reports from doctors, workers, and employers can be valuable sources of information on hazards and serve to generate hypotheses for larger studies. But inadequacies in the training of physicians, both those who practice occupational medicine and those in general practice, limit identification hazards through case reports.

Epidemiology relies on observations or suggestions of possible associations between exposures or behaviors and disease for hypothesis generation. It has limitations in the kinds and magnitudes of effects it can detect, but it can provide the most convincing evidence of associations between exposures and behaviors and health. The strengths of epidemiology still remain to be exploited, and much remains to be learned about diseases and syndromes that are widespread in the population.

Toxicology can garner useful information about the possible effects of substances, but large toxicologic studies are expensive, require years to complete, and produce information that is sometimes difficult to apply to human exposures. Making risk assessments from animal data involves both technical problems and assumptions. Although continued attention to toxicology and risk assessment may reduce technical controversies, the assumptions about the predictive value of various tests are likely to remain in dispute.

Epidemiology and toxicology have not been the panacea for solving workplace health problems that some envisioned. The limitations of both argue for a continuing role for occupational medicine in hazard recognition as well as treating workers. That role can be enhanced during the education of physicians.

Computerized information about workplace exposures and workers' health forms the basis for surveillance systems that aim to identify health hazards. Occupational health surveillance is the source of both great promise and great controversy. It can be used to identify the causes of occupational illness, setting the stage for preventing further illness. But there are practical difficulties in implementing systems that will be statistically useful, concerns about company liabilities after discovering a possible relationship, and concerns that efforts will be made to substitute surveillance activities for preventive efforts and installation of appropriate controls.

OCCUPATIONAL DISEASE

Some diseases are always or nearly always caused by conditions at work. These diseases represent relatively easy cases for health and safety professionals because they can be readily linked to particular working conditions. In general, identification of workplace hazards is facilitated by:

- conditions at work that differ greatly from the normal conditions of daily life, and
- the presence of distinctive or very rare diseases in these exposed workers.

Examples from the early part of this century are the occurrence of "phossy jaw" among phosphorus match workers, the diseases of radium dial painters, and "wrist drop" caused by lead poisoning among adult workers. More recently, mesothelioma and liver angiosarcoma both occur so rarely in the nonexposed population that when cases were observed among asbestos and vinyl chloride workers, respectively, questions of occupational causation were immediately raised and relatively quickly answered.

But relationships between work and diseases are not always so clear-cut. In fact, it is probably more frequent that working conditions directly cause or contribute to diseases that are also related to other human activities. In other words, workplace exposures c ause workers to suffer an *increased incidence* of disease, even though these diseases also regu arly occur in the general population.

For example, most lung cancer occurs in smokers, and it is accepted that there is a causal relationship between cigarettes and lung cancer. Some substances encountered in the workplace are also known lung carcinogens because they increase the occurrence of lung cancer in nonsmokers as well as in smokers. In addition, smoking and other carcinogens may also act together to cause cancer. However, deciding which exposure(s) caused lung cancer in a particular smoking worker is a difficult task.

Hazards that increase the incidence of common diseases can be best identified using the techniques of epidemiology. But even after studies have shown a link between exposures and increased disease incidence for a *group* of workers, it often remains impossible to determine, for any *individual* worker, that his or her disease was caused by occupational exposures.

MAJOR CLASSES OF OCCUPATIONAL DISEASES

Occupational diseases have been recognized as such for centuries. References to almost all classes and types of diseases appear in the works of Ramazzini, the 18th-century physician often called the father of occupational medicine. Since then, the definition of disease in general has changed,

as has the perception of work-relatedness. Society is less willing to accept adverse effects of any kind. Because so much disease is known to be preventable, poor health is no longer taken as a concomitant of certain occupations. Our increasing ability to detect subtle effects allows us to broaden our efforts in prevention.

There is something seductive about new risks, and a tendency to focus on new hazards. Although in one sense occupational health is dealing with new and ever-subtler effects, the old diseases are still around, in greater numbers than is generally perceived. In **1979,** an estimated **84,000** active workers suffered from acute byssinosis and at least 35,000 employed or retired workers were disabled from cotton dust-related disease. In 1978, an estimated 59,000 workers were thought to suffer from silicosis. Even as new and perhaps scientifically and medically more intriguing conditions become issues in occupational health, the old problems require continued vigilance.

To guide its research priorities, the National Institute for Occupational Safety and Health (NIOSH) has developed a list of 10 groups of occupational diseases (table 3-1). Although termed the "Ten Leading" work-related diseases, the list includes nearly all categories of health effects that have ever been linked to workplace conditions.

Six of the categories of diseases listed by NIOSH are discussed in this chapter. Traumatic injuries are the subject of the next chapter, and noise-induced hearing loss is discussed in chapter 8. The reader is referred to the recent textbooks by Levy and Wegman **(269)** and Rem, et al. **(396),** for details of disease and hazard identification.

Respiratory Disorders

The lungs and other parts of the respiratory tract come in contact with all manner of airborne materials in the workplace. Gases, vapors, fumes, fibers, and particles all may be inhaled, Of all health effects, occupationally related cancers of the respiratory tract receive the greatest attention, but they are not the only serious respiratory conditions associated with the workplace, and certainly not the most widespread. Other responses of the respiratory system may be acute irritation, immunologic or allergic reactions, or chronic changes in the tissues that line the respiratory

Table 3.1 .—The Ten Leading Work-Related Diseases and Injuries: United States, 1982[a]

Type of disorder/inju"~	Exam Dies
1 Occupational lung diseases	asbestos is, byssinosis, silicosis, coal workers' pneumoconiosis, lung cancer, occupational asthma
2 Musculosketal injuries	disorders of the back, trunk, upper extremity, neck, lower extremity; traumatically induced Raynaud's phenomenon
3, Occupational cancers (other than lung)	leukemia, mesothelioma; cancers of the bladder, nose, and liver
4. Amputations, fractures, eye loss, lacerations, and traumatic deaths	—
5. Cardiovascular diseases	hypertension, coronary artery disease, acute myocardial infarction
6 Disorders of reproduction	infertility, spontaneous abortion, teratogenesis
7, Neurotoxic disorders	peripheral neuropathy, toxic encephalitis, psychoses, extreme personality changes (exposure-related)
8, Notse-induced loss of hearing	—
9. Dermatologic conditions	dermatosis, burns (scaldings), chemical burns, contusions (abrasions)
10, Psychologic disorders	neuroses, personality disorders, alcoholism, drug dependency

[a]The conditions listed u rider each category are to be viewed as *selected* examples, not comprehensive defin lt lons of the category

SOURCE (563)

tract. Some conditions that begin as acute problems progress to chronic states, perhaps the best known being byssinosis–or "brown lung" disease.

NIOSH has made formal recommendations for maximum exposure levels to 60 substances, based on their effects on the respiratory system. That number is greater than the substances cited for any other organ system.

Chronic Conditions

The most serious conditions are pneumoconioses, chronic conditions occurring generally after years of exposure to very fine dusts. The tissue reacts by thickening, producing a condition called "pulmonary fibrosis. " The best known pneumoconioses are asbestosis, silicosis, and coal workers' pneumoconiosis ("black lung"), but similar conditions may be produced by a number of different materials, such as talc and kaolin. Pneumoconioses are characterized by coughing and shortness of breath, which grow worse over time, followed in the later stages by signs of heart failure and eventually ending in death.

Chronic bronchitis can be caused by a number of occupational hazards but, as the commonest chronic response of the respiratory tract, is also brought on by nonoccupational causes. It may also be multicausal, as many diseases are, with nonoccupational factors (particularly cigarette smoking) interacting with occupational exposures to cause disease.

Emphysema is another chronic condition in response to many different stimuli. Though there are undoubtedly cases of occupational origin, few convincing, direct correlations between workplace exposures and this disease are known.

Beryllium disease (berylliosis) is an example of granuloma formation in response to foreign bodies in the lungs. Granulomas form when body cells responding to an "inciting agent" become surrounded by bundles of collagen (a type of connective tissue).

Acute Conditions

Inflammations and irritations of the tissues lining the respiratory tract occur in response to many inhaled substances. The upper respiratory tract—the nose, throat, and larynx-is the most frequent site of irritation, It is susceptible to highly soluble irritants, such as ammonia, hydrogen chloride, and hydrogen fluoride-gases commonly encountered in industry.

Irritants that are less soluble tend to travel farther down the respiratory tract before they are absorbed entirely, causing irritation in the middle as well as the upper respiratory tract. Chlorine, fluorine, and sulfur dioxide, all commonly used chemicals, have such properties, The major effect on the lungs is bronchoconstriction.

Irritants of low volubility may cause only minor upper respiratory tract problems, but their delayed reaction deep in the lungs, which may occur as much **as** a day later, can be very serious. Ozone, oxides of nitrogen, and phosgene—again, commonly encountered in workplaces—are the most important hazards in this class.

Asthma and "hypersensitivity pneumonitis" are two manifestations of immunologic or allergic type reactions. Bronchial asthma, a condition affecting perhaps 4 percent of the U.S. population, is also prevalent among certain occupational groups. Asthma is a generalized obstruction of the airways in an allergic type of response to some substance. Causes can be of bacterial or animal (e.g., animal dander, small insects, bee toxin) or plant (e.g., flour, grain dust, fungi, cotton, flax, tea fluff, wood dusts) or chemical (e.g., formaldehyde, certain pesticides, some metals, some acids) origin. Often the condition develops only after a period of sensitization, and for some agents, very high percentages of those exposed become sensitized. It has been reported that nearly all workers in power plants along the Mississippi River become sensitized to river flies *(396).*

The causes of hypersensitivity pneumonitis include a variety of organic materials, commonly fungi or bacteria. Beginning with coughing, but without the wheezing associated with asthma, these disorders can become chronic and disabling. Such conditions as "farmer's lung, " "mushroom picker's lung, " "cheese washer's lung, " and "paprika splitter's lung" fall into this category.

Byssinosis deserves particular recognition. (For further discussion of this disease, see ch. 5.) Though it has been known in some sense as a dis-

ease associated with cotton and other textile fibers for hundreds of years, it was ignored as an occupational disease in this country until fairly recently. The disease begins with tightness in the chest and a decrease in lung capacity upon exposure. The condition is most severe on Monday mornings. Over a period of years, chronic obstructive lung disease may develop, partially or totally disabling the worker. The earlier stages of the disease are thought to be reversible, but the later stages are not. The exact etiologic agent of byssinosis is not known, but various chemicals and organic substances have been suggested.

Musculoskeletal Disorders

Low back pain is responsible for more lost work-time than any other medical condition except upper respiratory tract ailments. In terms of treatment and workers' compensation, low back pain is the costliest occupational ailment. More than half of all workers will experience low back pain of some kind sometime in their working lives, but the percentage of those cases associated with the workplace is unclear.

Low back pain may develop progressively and insidiously, or it may come on with immediacy. Pain may be dull and aching, with fatigue and stiffness, or sharp and crippling. Surprisingly little is known about the physiologic and physical causes underlying back pain. Circumstantial evidence implicates intervertebral discs in many cases. (Discs are cartilaginous structures separating the vertebrae of the spine.) In extreme cases, a disc may rupture, but physical signs that would explain the pain are usually absent. Episodes of pain, which last usually from a few days to a few weeks, generally resolve with rest. Months or years may pass without another attack.

Muscles, tendons, ligaments, and bones can also be damaged by traumatic events or by repeated strains over a long period. Although muscle pulls and tears have been recognized for years, the "repetitive motion disorders"—those caused by repeated, often forceful motions, mainly of parts of the arm—have come to attention more recently (see "Carpal Tunnel Syndrome, " ch. 7), Much assembly-line work and food processing, for example, is characterized by repetitive, strenuous, awkward tasks. The prevalence of repetitive motion disorders is unknown, but more and more industries are recognizing that they have such problems.

Cancer

Table **3-2** is a list of recognized occupational cancer hazards. In most cases, there is convincing or very strong evidence that the listed substances have caused cancer in humans. Inspection of the table shows that many of these substances cause common cancers, for instance, of the lung and skin. Except for a few specific and infrequent cancers, there is no way to tell, from examining a cancer patient, what agent(s), exposure(s), or behavior(s) caused the tumor.

The most detailed information about an occupational cancer hazard involves asbestos. The unfolding of that story illustrates the time necessary for association to be accepted and some controversies about occupational illness. Individual case studies and reviews of case series relating exposures to asbestos with cancer began to appear in the literature in the 1930s (161). According to Selikoff (430), however, the establishment of an association between occupational exposure to asbestos and lung cancer depended on a classic study by Doll in 1955 (147).

Although asbestos **was** positively identified as a cause of lung cancer in the 1950s, and exposure to it **was** known to be widespread, no published estimate of its impact on nationwide mortality was available until 1978, when two estimates were made. Selikoff (555) estimated that the annual number of asbestos-related cancer deaths was about 50,000. His estimate elicited little public attention.

The other 1978 estimate (555), entitled "Estimates of the Fraction of Cancer in the United States Related to Occupational Factors, " was prepared by the National Cancer Institute, the National Institute for Environmental Health Sciences, and NIOSH. Ten employees of those institutions were listed as contributors to the "estimates paper, " which was placed in an Occupational Safety and Health Administration (OSHA) hearing record about that agency's proposed generic cancer

Table 3=2.—Some Occupational Cancer Hazards

Agent	Cancer site or type	Type of workers exposed
Acrylonitrile	Lung, colon	Manufacturers of apparel, carpeting, blankets, draperies, synthetic furs and wigs
4-aminobiphenyl	Bladder	Chemical workers
Arsenic and certain arsenic compounds	Lung, skin, scrotum, lymphatic system, hemangiosarcoma of the liver	Workers in the metallurgical industries, sheep-dip workers, pesticide production workers, copper smelter workers, vineyard workers, insecticide makers and sprayers, tanners, miners (gold miners)
Asbestos	Lung, larynx, GI tract, pleural and peritoneal mesothelioma	Asbestos factory workers, textile workers, rubber-tire manufacturing industry workers, miners, insulation workers, shipyard workers
Auramine and the manufacture of auramine	Bladder	Dyestuffs manufacturers, rubber workers, textile dyers, paint manufacturers
Benzene	Leukemia	Rubber-tire manufacturing industry workers, painters, shoe manufacturing workers, rubber cement workers, glue and varnish workers, distillers, shoemakers, plastics workers, chemical workers
Benzidine	Bladder, pancreas	Dyeworkers, chemical workers
Beryllium and certain beryllium compounds	Lung	Beryllium workers, electronics workers, missile parts producers
Bis(chloromethy l)ether (BCME)	Lung	Workers in plants producing anion-exchange resins (chemical workers)
Cadmium and certain cadmium compounds	Lung, prostate	Cadmium production workers, metallurgical workers, electroplating industry workers, chemical workers, jewelry workers, nuclear workers, pigment workers, battery workers
Carbon tetrachloride	Liver	Plastic workers, dry cleaners
Chloromethyl methyl ether (CMME)	Lung	Chemical workers, workers in plants producing ion-exchange resin
Chromium and certain chromium compounds	Lung, nasal sinuses	Chromate-producing industry workers, acetylene and aniline workers, bleachers, glass, pottery, pigment, and linoleum workers
Coal tar pitch volatiles	Lung, scrotum	Steel industry workers, aluminum potroom workers, foundry workers
Coke oven emissions	Lung, kidney, prostate	Steel industry workers, coke plant workers
Dimethyl sulphate	Lung	Chemical workers, drug makers, dyemakers
Epichlorohydrin	Lung, leukemia	Chemical workers
Ethylene oxide	Leukemia, stomach	Hospital workers, research lab workers, beekeepers, fumigators
Hematite and underground hematite mining	Lung	Miners
Isopropyl oils and the manufacture of isopropyl oils	Paranasal sinuses	isopropyl oil workers
Mustard gas	Respiratory tract	Production workers
2-naphthyiamine	Bladder, pancreas	Dyeworkers, rubber-tire manufacturing industry workers, chemical workers, manufacturers of coal gas, nickel refiners, copper smelters, electrolysis workers
Nickel (certain compounds) and nickel refining	Nasal cavity, lung, larynx	Nickel refiners
Polychlorinated biphenyls (PCBs)	Melanoma	PCBS workers

Table 3-2.—continued

Agent	Cancer site or type	Type of workers exposed
Radiation, ionizing	**Skin, pancreas, brain, stomach, breast, salivary glands, thyroid, GI tract, bronchus, lymphoid tissue, leukemia, multiple myeloma**	Uranium miners, radiologists, radiographers, luminous dial painters
Radiation, ultraviolet	**Skin**	Farmers, sailors, arc welders
Soots, tars, mineral oils	Skin, lung, bladder, GI **tract**	Construction workers, roofers, chimney sweeps, machinists
Thorium dioxide	**Liver, kidney, larynx, leukemia**	Chemical workers, steelworkers, ceramic makers, incandescent lamp makers, nuclear reactor workers, gas mantle makers, metal refiners, vacuum tube makers
Vinyl chloride	Liver, brain, lung, hematolymphopoietic system, breast	Plastics factory workers, vinyl chloride polymerization plant workers
Agent(s) not identified	Pancreas	Chemists
	Stomach	Coal miners
	Brain, stomach	Petrochemical industry
	Hematolymphopoietic system	Rubber industry workers
	Bladder	Printing pressmen
	Eye, kidney, lung	Chemical workers
	Leukemia, brain	Farmers
	Colon, brain	Pattern and model makers
	Esophagus, stomach, lung	Oil refinerv workers

SOURCE (542)

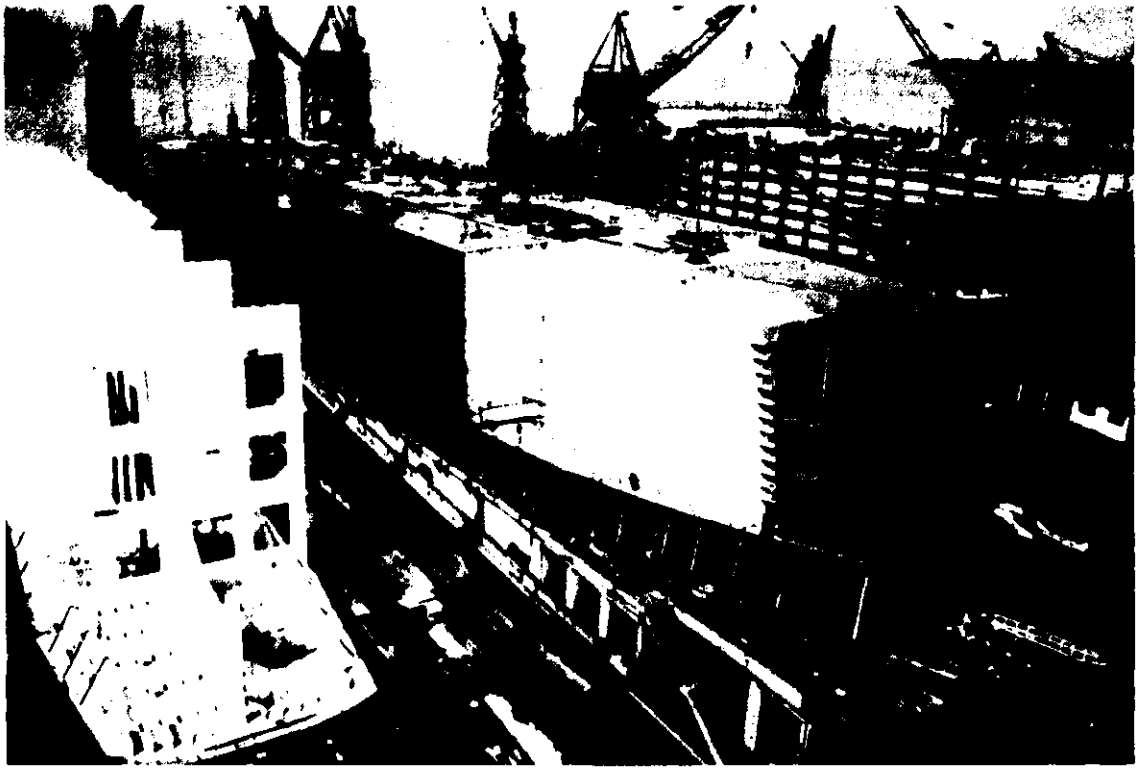


Photo credit OSHA, Office of Inforrnation and Consumer Affalrs

Shipbuilding operations present a variety of both safety and health hazards. During World War 11, many workers were exposed to asbestos in naval shipyards

policy (the "estimates paper" is available as an ap pendix in Peto and Schneiderman (371)).

Had the paper been only deposited in the hearing record it might have passed largely unnoticed. Its findings, however, were widely publicized when then-Secretary of Health, Education, and Welfare Joseph Califano cited them in a speech. Based on the "estimates paper, " he stated that workplace exposures caused at least 20 percent of all cancer in this country-with exposure to asbestos alone responsible for 13 to 18 percent. These projections were controversial as soon as they were publicized, and they attracted many critics. They also resulted in a spate of articles presenting other estimates of the cancer risk associated with occupational exposure to asbestos.

The subsequent papers can be divided into two general groups. One group used methods similar to the "estimates paper" to project numbers of cancer deaths based on estimates of workers exposed, exposure rates, and mortality observed among insulation workers highly exposed to asbestos. A second type of paper measured the number of deaths from mesotheliomas, which are closely associated with asbestos exposure, and then multiplied that number by some factor to estimate all asbestos-caused cancer deaths.

Methods similar to those employed in the 1978 paper generated three estimates of total asbestos cancer mortality. Those estimates, lower than the 13 percent figure in the "estimates paper, " were 1 percent (162), 2 percent (216) and 3 percent (331). The different numbers reflect the authors' different estimates about the numbers of heavily exposed workers—estimates that can be criticized because they were not made on the basis of actual measurements. As that sort of information does not exist, however, documented assumptions are the best that can be provided.

In the case of asbestos, scientists interested in extrapolating from study-generated data to estimates of national cancer mortality are aided by the fact that asbestos causes asbestosis and mesotheliomas. Both those diseases are reasonably rare and reasonably diagnostic for asbestos exposure. Although both are subject to undercounting that limits the accuracy of estimates based on them, the estimates from them are congruent with those based on the method used originally in the "estimates paper. " Calculations based on numbers of mesotheliomas and asbestosis produced estimates of between 1 and 2 percent of all cancer deaths being due to asbestos (148,212,294,370).

The consistency of the projections that asbestos causes between 1 and 3 percent of current cancer deaths (190) has a pronounced effect on estimates of total occupationally related cancers. Most, but not all, participants at an international conference about occupational cancer agreed that workplace exposures cause less than 5 percent *(20,000* annual deaths) of U.S. cancer mortality (371).

Although this number is not as frightening as saying asbestos causes 13 percent of cancer and that workplace exposures cause at least 20 percent, and perhaps twice that figure, it is still a large number of deaths. Furthermore, as representatives from all sides—academe, labor, and management—agree, those cancers are preventable.

The amount of cancer that is associated with workplace exposures is a significant part of the current debate about the relative importance of various factors in cancer causation (see (18), the exchange of facts and opinions in 'letters" Science 224:659 et seq., especially (154) and (19)).

Reproductive Disorders

The possibility that people's occupations are leading to problems for an unborn generation is frightening. It is increasingly a concern among workers, and attention to reproductive disorders on the part of scientists is intensifying. Few facts are available to either support or quell the fears that a great many reproductive hazards are present in the workplace. Relatively few instances of harm are known when compared with the known effects of workplace hazards on workers themselves.

Initial concerns about reproductive health focused almost exclusively on women. Exposure to the high levels of lead common at the beginning of this century were known to cause menstrual disorders, sterility, miscarriages, and stillbirths.

Much more recently, concern has been extended to males. One episode provided the catalyst. In

the late 1970s, a number of men working in the manufacture of dibromochloropropane (DBCP), a pesticide, were unable to father children, Investigation revealed severely depressed sperm production.

Damage can occur in males and females in a number of **ways.** In men, successful reproduction depends on proper functioning of the prostate, on libido, and on erection and ejaculation. The production and viability of sperm can be affected by damage to the sperm-producing cells or to the sperm as they develop.

In women, damage can occur in the reproductive cells, the oviducts, the endometrium, or to ovarian function. During fetal development in the uterus, humans are most vulnerable to environmental insults. Death, irreversible structural changes (teratogenesis), and growth retardation are the main classes of effects. More difficult to measure or prove are subtle deficits in intellectual capacity and functioning.

The effects of lead have been mentioned. At least one form of another heavy metal, mercury, is a known teratogen. Certain pesticides—DBCP and Kepone for instance-affect sperm production. Ionizing radiation has a variety of effects, particularly on fetuses—causing growth retardation, for instance, or microcephaly, or having latent effects, such as leukemias that develop during childhood. A few organic solvents and pharmaceuticals also are known to affect reproductive health. In all, relatively little is known about the extent of workplace-induced reproductive damage, but efforts to find out more are under way. A current OTA assessment scheduled for completion in 1985, "Reproductive Health Hazards in the Workplace, " addresses this issue.

Necrologic Disorders

A wide variety of metals and organic compounds act on the nervous system to cause physical and behavioral problems. Since many bodily functions require the participation of nerves, nerve impairment affects not only sensory abilities, but motor (muscular) ability as well as the functioning of organs.

Lead is the best-known neurotoxin in the workplace. More than a million American workers are exposed currently. Mercury, manganese, and other metals, **as well** as organic solvents and organophosphate insecticides, also pose neurotoxic risks. Table 3-3 lists some known neurotoxins and their effects.

Neurotoxins can damage the myelin sheath surrounding the nerve fiber or the nerve cell itself. Toxins can also interfere with the production and functioning of "neurotransmitters," chemicals produced in the body that are necessary for proper functioning of the nerves. 'some necrologic impairment is reversible, but damaged nerve cells have limited capacity for regeneration and repair.

Neurotoxins affect the parts of the nervous system to different degrees. The most commonly affected are peripheral nerves-those of the extremities. Hands and feet are often the first symptomatic zones, and numbness and tingling the first signs. Weakness in the hands and feet follows, and then difficulty walking and an inability to grasp heavy objects. Other symptoms include impaired vibratory sense, loss of touch perception, and tremors of the hand and other parts of the body.

A host of behavioral changes can also result from necrologic insults: Slow response time, impaired hand-eye coordination, irritability, lack of concentration, continual emotional instability, and impairment of recent memory area few such signs. (Lewis Carroll's "Mad Hatter" may have been a victim of the necrologic effects of mercury used in making felt hats.)

Most neurotoxins act through common pathways, though some have more specific effects: Carbon disulfide, for instance, acts at all levels on the central nervous system, but also causes conditions as extreme as acute psychosis.

Skin Disorders

The skin, the largest organ of the body, provides the first line of defense between workers and their environment. Because it is readily observable, recognition of a problem is relatively easy. For

Table 3-3.—Neurologic Effects of Occupational Toxins

Peripheral Effects

Effect	Toxin	Comments
Motor neuropathy	Lead	Primarily wrist extensors; wrist drop and ankle drop rare
Mixed sensorimotor neuropathy	Acrylamide	Ataxia common; desquamation of hands and soles; sweating of palms
	Arsenic	Distal parethesias earliest symptom; painful limbs, especially in calves; hyperpathia of feet; weakness prominent in legs
	Carbon disulfide	Peripheral neuropathy rather mild; CNS effects more important
	Carbon monoxide	Seen only after severe intoxication
	DDT	Only seen with ingestions
	N-hexane and methyl n-butyl ketone (MBK)	Distal paresthesia and motor weakness; weight loss, fatigue, and muscle cramps common
	Mercury	Predominantly distal sensory involvement

Other Manifestations

Manifestation	Agent	Manifestation	Agent
Ataxic gait	Acrylamide	Increased intracranial pressure	Lead
	Chlordane		Organotin compounds
	Chlordecone (Kepone)	Myoclonus	Benzene hexachloride
	DDT		Mercury
	N-hexane	Nystagmus	Mercury
	Manganese	Opsoclonus	Chlordecone (Kepone)
	Mercury (especially with methyl mercury)	Paraplegia	Organotin compounds
	Methyl n-butyl ketone (MBK)	Parkinsonism	Carbon disulfide
	Methyl chloride		Carbon monoxide
	Toluene		Manganese
Bladder neuropathy	Dimethylaminopro pionit ri te (DMAPN)	Seizures	Lead
			Organic mercurial
Constricted visual fields	Mercury		Organochlorine insecticides
Cranial neuropathy	Carbon disulfide		Organotin compounds
	Trichloroethylene	Tremor	Carbon disulfide
Headache	Lead		Chlordecone (Kepone)
	Nickel		DDT
Impaired visual acuity	N-hexane		Manganese
	Mercury		Mercury
	Methanol		

NOTE: This table Includes most, but not all, of the neurotoxic substances associated with listed conditions.

SOURCE: (39a)

both these reasons, skin disorders account for nearly half of all reported occupationally related illnesses in the United States. NIOSH has recommended maximum exposure levels for about *40* agents based on their effects on the skin (see table *3-4).*

Chemical, physical, and biological agents, mechanical factors, and plant and wood substances are known to cause occupationally related skin disorders (see table 3-5). There is probably no industry without some potential for exposure to one or more of these agents. The industries with the highest risk for skin disorders are listed in table 3-6. Although caused by a large number of agents, both biological and chemical, skin diseases are manifested in a relatively limited number of clinical symptoms: contact dermatitis, infection, pilosebaceous follicle abnormalities, pigment disorders, and cancers.

Contact dermatitis accounts for 90 percent of all occupational skin disorders. The most common manifestations of contact dermatitis are redness and swelling, and vesiculation (e.g., a poison ivy rash) in more severe cases. Contact dermatitis may be an allergic reaction or simply due to an irritant.

Bacterial, fungal, and viral infections may be contracted from customers or clients by such pro-

Table 3-4.—Substances for Which NIOSH Has Recommended Exposure Limits to Prevent Skin Disorders

Acrylamide
Alkanes:
Pentane
Hexane
Heptane
Octane
Arsenic, inorganic compounds
Benzoyl peroxide
Benzyl chloride
Carbon black
Chromium (Vi)
Coal tar products
Cresol
Epichlorohydrin
Ethylene dibromide
Fibrous glass (dust)
Glycidyl ethers:
Allylglycidyl ether (AGE)
n-Butyl glycidyl ether (BGE)
Di-2-,3-epoxypropyl ether (DGE)
Isopropyl glycidyl ether (lGE)
Phenyl glycidyl ether (PGE)
Hydrazines:
Hydrazine
1,1-dimethyl hydrazine
Phenyl hydrazine
Methyl hydrazine
Hydrogen fluoride
Hydroquinone
Nickel, inorganic and compounds
Phenol
Polychlorinated biphenyls:
Chlorodiphenyl (42°/0)
Chlorodiphenyl (54°/0)
Refined petroleum solvent
Thiols:
Butyl mercaptan (1-butanethiol)
Methyl mercaptan (1-methanethiol)
Ethyl mercaptan (1-ethanethiol)
Tin, organic compounds
Tungsten:
insoluble compounds
soluble compounds
Vanadium

SOURCE Adapted from (**128a**)

Table 3-5.—Workpiace Agents That induce Skin Disorders

Chemical **agents**
Rhus oleoresin (poison ivy and oak)
Acids
Alkalis
Solvents
oils
Soaps and detergents
Plastics
Resins
Paraphenylenediamine
Chromates
Acrylates
Nickel compounds
Rubber chemicals
Petroleum products not used as solvents
Glass dust
Plant and Wood Substances
Pink rot celery
Citrus fruit
Physical Agents
Ionizing and nonionizing radiation
Wind
Sunlight
Temperature extremes
Humidity
Biological Agents
Bacteria
Viruses
Fungi
Ectoparasites (mites, ticks, fleas, etc.)
Biting animals
Mechanical factors
Pressure
Friction
Vibration

SOURCE: (23a).

fessionals as barbers and hairdressers and by hospital workers. Staphylococcus and streptococcus bacteria may cause a range of skin conditions from superficial to those of deep skin layers. More serious bacterial infections, such as anthrax in sheep handlers and animal hide workers, are rarer.

Fungal infections often arise in moist, warm environments. Ringworm and *Candida albicans* infections are common examples. Candida infection is common in workers, such **as** dishwashers, who are frequently exposed to water, because moist conditions favor the fungus' growth. Viral infections are acquired by contact with other people and are a particular hazard for workers exposed intimately to other individuals in the course of their work, such as health care workers.

Pilosebaceous follicle abnormalities, generally acne-like lesions, occur after exposures to heavy oils and certain chemicals, particularly chlorinated aromatic hydrocarbons. The example currently most discussed is chloracne after exposure to chlorinated dioxins, either in the manufacturing process, or, most dramatically, after industrial accidents involving the generation and release of large amounts of the chemical. Chloracne may persist for **10** yearn or more after exposure ceases.

Table 3-6.—industries at Highest Risk for Occupational Skin Diseases

Industry	Annual reported incidence rate (per 1,000 workers)	Target population (rounded to nearest 1 ,000)	Severity [a]	Duration [b]	Incidence of lost workdays per = industry per year
Poultry dressing plants	16,4	89,800	030	10.0	4,405
Meat packing plants	72	164,300	0.31	4,3	1,561
Fabricated rubber products	55	103,200	0.22	11,5	1,424
Leather tanning and finishing	21,2	22,900	0.34	8.3	1,392
Ophthalmic goods	8.5	38,000	0.52	8.3	1,390
Plating and polishing	8.3	61,400	0.28	9.0	1,270
Frozen fruits and vegetables	7,2	43,200	0.31	12,1	1,153
Internal combustion engines	5.5	75,700	027	8.8	999
Canned and cured seafoods	5.6	19,700	0,36	23,7	934
Carburetors, pistons, rings, valves	70	29,400	024	17.9	895
Chemical preparations	8.3	36,700	0.23	12.3	855
Boat building and repairing	11.1	48,000	0.22	7,4	854

[a] Severity is defined by number or lost-workday cases divided by total number of cases in that industry
[b] Duration is the number of lost workdays per lost workday case

SOURCE (23a)

Pigment disorders occur when melanin production is either increased or decreased through exposures to chemicals or from a traumatic event—a burn, for instance. Loss of pigment may be reversible or not, depending on the causative agent and on the severity of the insult. Other changes in skin color are due to staining of various layers by such substances as heavy metals.

KNOWN AND UNKNOWN HEALTH HAZARDS

Health hazards are agents that can cause disease in people exposed to them. In terms of occupational health, there are three kinds:

- identified hazards known to be present in the workplace;
- hazards that are present in the workplace but that have not been identified as causes of disease; and
- new substances or processes not yet introduced into the workplace, that will be hazardous to human health.

This section reviews the findings that led to some associations being made between particular diseases and workplace hazards, as well as the methods currently employed to identify hazards.

Identified Hazards

Diseases associated with mining and metalworking have been recognized for many years, to some extent because of the antiquity of those trades. Some industrial chemicals are known to cause a variety of diseases, and energy from all parts of the electromagnetic spectrum is a hazard under particular circumstances. As the following examples show, associations between agents and diseases have been made by people from all sectors of society based on laboratory information as well as observations of human illness.

Physical Agents

Sources of ionizing radiation are increasingly common in the workplace. X-ray apparatus and radioisotopes are widely used, and nuclear powerplants and scientific research also involve potential exposures to ionizing radiation. Very high doses of radiation can kill workers within a few days, but of greater concern, because the events are more likely, is low-level exposures, which may last for several years and may cause cancer. The deleterious effects of radiation were discovered from observations of disease among early workers in the field and confirmed by analyses of the survivors of Nagasaki and Hiroshima.

Nonionizing radiations include ultraviolet, infrared, microwave, and laser. All present hazards for workers' eyes, and there is continued interest in and study about other effects from microwave radiation. Ultraviolet and infrared radiation as well as intense visible light are generated in welding, and welders' goggles and helmets are designed to protect against such hazards.

Also in the category of physical agents is noise, which, especially if it is loud and continuous, causes progressive hearing loss. The impact of occupational noise is difficult to separate from the effects of aging, but many studies have shown workplace noise is a hazard to hearing. (See ch. 8 for a discussion of the role of personal protective equipment in preventing hearing loss.)

Vibration, often experienced as a result of the use of handtools, causes a number of musculoskeletal disorders (see ch. 7).

Heat, cold, and pressure encountered in underwater work are also hazards. These have been associated with particular jobs for a very long time, and many of their effects are visible during or soon after exposure.

Metals

Hunter (218) divides hazardous metals into three groups. Those known since ancient times, such as lead and mercury, were long ago associated with disease. According to Hamilton (1922, quoted in 218), the first legislation directed against an occupational hazard was drafted in 1665 in Idria, now part of Yugoslavia. The workday for cinnebar (mercury ore) miners was restricted to 6 hours as a preventive measure to reduce the occurrence of tremors. Mercury continues to cause concern today as an environmental contaminant, and it is especially dangerous in the organic (methylmercury) form.

Hunter's second group, the "other metals, " are arsenic, phosphorus, and zinc. He points out that the grouping is arbitrary in that arsenic is a metalloid and phosphorus a nonmetal. These three elements have been in common industrial use for a few centuries, and all have caused illness and death. The recognition of phosphorus as the cause of "phossy jaw" among matchmakers (see box A) led to the substitution of a safe form of phosphorus in matches. These three metals still occupy important places in industry and in agricultural products.

The third group of metals are those recently introduced into commerce, including some important in advanced metallurgic technologies and the nuclear industry. Toxic effects are definitely associated with some—beryllium, cadmium, chromium, manganese, nickel, osmium, platinum, radium, ruthenium, selenium, tellurium, thallium, thorium, uranium, and vanadium. In some measure, because these substances were introduced into the workplace when industrial hygiene measures were more common, exposure to many of them

Box A.—"Phossy Jaw"

Phossy jaw was a disease that resulted from inhaling yellow or white phosphorus fumes that penetrated any defective tooth and killed cells in the jaw and surrounding tissues. Invasion of the dead areas by germs from the mouth led to suppurating infection, swelling, and intense pain. Death could result from blood poisoning; surgical treatment, which often included removal of the jaw, was incapacitating and disfiguring. The **disease was** first diagnosed in workers in European match factories in the middle of the 19th century.

Up through 1908, there was no recognition of phossy jaw as an occupational health problem in the United States. A Bureau of Labor study that year of the wages of women and children in the match industry revealed 150 cases of phossy jaw. Two years later, the Bureau issued "Phosphorus Poisoning in the Match Industry in the United States."

One of the surest forms of controlling exposures to hazardous substances is to substitute a less hazardous chemical. Phossy jaw was conquered by substituting a different form of phosphorus for the "white phosphorus" commonly used in matches. The Diamond Match Co., which held the American patent for the safe form (sesquisulphide), waived its patent rights and made the safe substitute available to the entire industry (199). In 1912, Congress passed the "Esch Act," which levied a tax on white phosphorus matches, driving them from the market.

has been well controlled (218). Also important to controlling exposures to some of these metals is their great expense; uncontrolled losses through spills or into the atmosphere as vapors, fumes, or dusts entail financial losses as well as health hazards.

Many metals are worked in industry with no reported toxic effects. Cesium, cerium, columbium, gallium, germanium, hafnium, iridium, lanthanum, molybdenum, rhenium, rhodium, rubidium, strontium, tantalum, titanium, tungsten, and zirconium, for example, have not been associated with illness in workers (218). Exposures to many such metals are controlled by standard industrial hygiene practices, and the fact that some of these metals are very expensive also encourages reduced exposures.

Hunter (218) is a good source of historical information about the uses and effects of the various metals and about British approaches to controlling exposures. Rem, et al. (396), discusses clinical symptoms and treatments as well as U.S. approaches to control, and Levy and Wegman *(269)* provide a lively introduction to the occupational health and industrial hygiene problems associated with the metals, with less emphasis on clinical detail than Rem. Tyrer and Lee (483) summarize information about acute and chronic health effects of the metals and list recommended and regulatory limits to exposure.

Dusts and Fibers

The hazards of mineral dusts have been known since mining began. Both silica dust and coal dust cause lung diseases. The widespread use of silica as an abrasive for "sand blasting" and other polishing results in many thousands of American workers being exposed to mineral dusts that are associated with lung diseases. In addition, cotton dust and asbestos are important as causes of byssinosis and asbestosis, respectively.

Chemicals

Because of the explosion of organic chemistry (chemistry that involves carbon) in the last 100 years, thousands of new chemical substances have been introduced into the workplace. Currently there are more than 55,000 chemicals listed in the Environmental Protection Agency's (EPA) *inventory of Chemical Substances,* which is a compilation of chemicals in commerce. About 100 new chemicals are introduced to commerce each month (547a). Many of these substances–pesticides of various kinds and drugs-are designed to alter normal biological functions, and it is no surprise that some have been found to cause cancer and other diseases, and that these substances are of special concern **(542).**

Some of the now-known hazards, such as vinyl chloride monomer, have been discovered as a result of workers who have become sick. (See ch. 5 for a fuller discussion.) Several years before an alert physician noted an excess of rare liver tumors in vinyl chloride workers, the results of an animal test of the same chemical were announced at a scientific meeting. The animal tests also showed the chemical to be a liver carcinogen. It can be argued that had the animal results been taken seriously, exposure to vinyl chloride would have been reduced sooner. As it happened, the existence of the animal studies may have been a factor in the rapid regulatory process that led to significant reductions in vinyl chloride exposures.

Acrylonitrile is a commonly used plastic that, like vinyl chloride, presents little hazard after it is polymerized. However, animal studies showed that acrylonitrile monomers are carcinogenic, and a follow-on epidemiologic study showed an excess of cancer among acrylonitrile production workers. Regulations restricting exposures to the substance were drafted by OSHA; unlike most other OSHA health regulations, the final standard for acrylonitrile was not challenged in court. There must have been a number of reasons for that success, and included in them were probably the congruence between the results of the animal and human studies and the fact that the methods developed to control vinyl chloride exposures were directly applicable to the control of acrylonitrile.

Methods for Detection of Present, Unidentified Hazards

Epidemiology, toxicology, and occupational medicine provide the means for identifying the causes of occupational illnesses. In the traditional,

idealized view of the process, physicians generate hypotheses about possible associations between workplace exposures and subsequent disease. Hypotheses are tested in epidemiologic studies so that the associations can be characterized in statements of statistical probability.

The traditional role of toxicology has been to provide information about the mechanisms of disease causation, the end results of which are detected by physicians and studied by epidemiologists. Toxicology today is generally thought of in different terms. Since the late 1960s and particularly through the 1970s, toxicology has been seen as a way to identify chemical hazards before their effects appear in humans. The most visible toxicologic activities are the testing of chemicals for carcinogenic properties in laboratory animals, mainly rats and mice **(542).** The Federal Government, through the National Toxicology Program, spent $31.6 million in 1983 on bioassays for that purpose.

There is also a certain amount of research now going on in development of short-term tests (so named because they require significantly less than the 2 to 5 years for an animal bioassay) as eventual replacements for and supplements to bioassays,

One of the most powerful methods of identifying associations between workplaces and diseases is through workers themselves. For instance, the pesticide dibromochloropropane was identified as a cause of male sterility by workers talking to each other. A possible relationship between office work involving video display terminals and fetal malformations that is now being actively investigated similarly derives from workers' observations. In many cases, workers' comments to their physicians lead to epidemiologic and toxicologic investigations and to medical surveys to decide whether a suspected association is real.

Toxicology

Toxicology is the testing of chemicals in animals, plants, or lower forms of life to detect biological effects. In addition to questioning what kinds of effects are produced and under what exposure conditions, toxicologists also investigate the mechanisms by which substances cause damage. That information is especially important in efforts to predict the likely toxic effects of substances that have not yet been tested. Toxicology can be subdivided in a number of ways. Here, testing for acute toxicities is discussed first, followed by a section on methods for investigating chronic toxicities—carcinogenesis, mutagenesis, and teratogenesis.

Acute Toxicity Testing. —Chemical burns and immediate difficulty in breathing as a result of inhalation of a substance are examples of acute toxic effects. Animal testing of chemicals for toxicity has produced a voluminous data set.

Increasing concern about animal welfare is causing reconsideration of animal testing methods. For instance, one of the most venerable acute toxicity tests is the LD_{50} test. Designed in the 1920s, the test involves the use of 50 to 100 animals to decide what amount of substance will cause the death of 50 percent of the animals. This method is coming under increased attack, however, as being imprecise and causing more animal suffering than is necessary. OTA is studying the use of alternatives to animals in research and testing. The report from that project, expected in 1985, will discuss the pros and cons of various animal tests and alternatives to animal tests.

NIOSH's 1980 Registry of Toxic Effects of Chemical Substances lists 45,156 substances. Included for most of the substances is the LD_{50} estimate of the amount that will kill half of a population of test animals. In addition, information about the toxic effects of the substance on animal skin and eyes is also commonly reported.

Dosages of ingested or injected substances necessary to cause effects in animals are expressed as the weight of the substance administered divided by the animal's body weight, i.e., milligrams of substance/body weight in grams or kilograms. When the substance is inhaled, the dangerous concentrations are expressed as parts per million in air or as the weight of the substance per cubic meter of air. These values provide data for making estimates of the biological effects of the substance in humans. Almost always, safety factors of 10 or 100 are used in setting acceptable limits for workers. That is, if 100 parts per million of **a** substance causes breathing difficulties in animals, a prudent policy would be to limit worker exposures to 10 or 1 part per million.

Chronic Toxicity Testing.—Structural activity relationship (SAR) analysis, chronic animal bioassays, and short-term tests are the main tools of toxicology (see table 3-7) as it relates to carcinogens, and, in general, chronic health hazard identification (542,547a). Finding a toxic effect in humans is far more convincing evidence about the seriousness of a hazard than detecting a toxic effect in animals, which, in turn, is more convincing than results from short-term tests. The weakest evidence is that derived from projections from structural activity relationships. Although the Federal effort devoted to chronic toxicities-mutagenicity and teratogenicity as well as carcinogenicity—is largely directed toward identifying carcinogens, there are some minor stirrings of effort to broaden beyond cancer (595).

Carcinogenicity has received the lion's share of OSHA's attention to health hazards. Of the fewer than two dozen chemicals regulated through new, permanent OSHA standards, all but two—lead and cotton dust—have been carcinogens.

Extrapolation problems—that is, how knowledge of effects in animals are projected to make predictions for people and how exposure levels in test animals are related to human exposure levels–bedevil the use of animal test data. OTA (542) has already discussed those problems and various approaches to reconciling them.

1) Structural activity relationship analysis, SAR uses known information about the properties of a substance to gain insight into the possible and probable effects of the substance on human beings. It is a new and still uncertain technique. Substances whose molecular structures resemble those of known toxic substances come under greater suspicion than those whose structures do not. No firm conclusions can be made based on these analyses except in the rare cases where all previously known members of an entire class of chemicals are known to be hazardous. In general, positive results are taken to indicate a need for further testing,

SAR has found most use in making estimates of the toxicity of "new" chemicals, when no test data are available. However, even there the scientific underpinnings of SAR are considered by some to be very weak, and the conclusions based on it are hotly argued (547a).

2) *Short-term tests.* Short-term tests encompass a large collection of methods for measuring toxicity in lower life forms-viruses, bacteria, and lower plants and animals, such as fruit flies-in cultured cells, or, in a few cases, in specific organ systems of laboratory rodents (542). Since their introduction about 15 years ago, they have been characterized as holding great promise for toxicology. A cynic might say that they always will.

Table 3-7.–General Classification of Tests Available to Determine Properties Related to Carcinogenicity

Method	System	Time required	Basis for test	Result	Conclusion, if result is positive
Structural activity relationship(SAR) analysis	'Paper chemistry"	Days	Chemicals with like structures interact similarly with DNA	Structure resembles (positive) or does not resemble (negative) structure of known carcinogen	Chemical may be hazardous; that determination requires further testing
	Basic laboratory tests	Weeks			
Short-term tests	Bacteria, yeast, cultured cells, intact animals	Generally few weeks (range 1 day to 8 months)	Chemical interaction with DNA can be measured m biological systems	Chemical causes (positive) or does not cause (negative) a response known to be caused by carcinogens	Chemical is a potential carcinogen
Bioassay	Intact animals (rats, mice)	2 to 5 years	Chemicals that cause tumors m animals may cause tumors in humans	Chemical causes (positive) or does not cause (negative) Increased incidence of tumors	Chemical is recognized as a carcinogen in that species and as a potential human carcinogen
Epidemiology	Humans	Months to lifetimes	Chemicals that cause cancer can be detected m studies of human populations	Chemical is associated (positive) or is not associated (negative) with an increased incidence of cancer	Chemical is recognized as a human carcinogen

SOURCE Adapted from (542)

Running counter to that lack of enthusiasm, recent spectacular advances in molecular biology suggest that short-term tests will grow in importance. As more and more insight into the molecular basis of carcinogenesis accumulates, along with rapid advances in methods to manipulate DNA and other cellular components **(542,548),** improved short-term tests should follow. The limitations and uncertainties of testing substances in whole-animal bioassays are built into the method itself. No such limits bound potential short-term tests for discerning interactions between chemical and cellular components. Of course, it will always be possible to argue that the short-term test system is not sufficiently parallel to human biology to serve as a guide to human risk estimation.

The critical issue for development of short-term tests is defining their current and ultimate value in policymaking. The first step is to find out how well the results of a test represent the "truth," a process referred to as validation. Truth is usually relative, and in the case of the carcinogenic potential of chemicals, the convenient measuring stick for truth is the bioassay, with its attendant limitations **(542).** The acceptability of bioassay results as a guide to making decisions about health hazards appears, sometimes at least, to be tied to the financial interest or disinterest of individuals and organizations in the substances identified as carcinogens.

There is little hope that a single short-term test will ever suffice as a reliable predictor of toxicity in human beings, and hope is pinned on the development of a battery of tests. Years of discussion and argument will undoubtedly precede the acceptance by scientists and regulators of any set of tests. And even then, a "generally accepted" test battery will be challenged in specifics, much as evidence from bioassays currently is.

The development of reliable short-term tests may actually enhance the value of bioassays, which will always find a place in toxicologic testing. Short-term tests can increase the knowledge base for deciding which chemicals should be tested in animals, and can shed light on the probable mechanisms of action of each chemical.

3) Bioassays. The bioassay is the mainstay of toxicology today. For some questions, answers involving the biology of whole animals are essential. The technique involves exposing a population of laboratory animals, usually rats and mice, to a suspect toxic agent. After an appropriate time, about 2 years for carcinogenicity, the disease incidence in the the treated population is compared with the disease incidence in a population of untreated controls. The premise underlying the mammoth effort in bioassays is that evidence of disease in animals is applicable to predictions for people; in fact, substances known to be carcinogens in humans also cause cancer in animals.

An entire branch of risk assessment has grown up around the quantitative predictions of effects in human beings based on animal evidence, In the combination of bioassay and risk assessment has lain the hope of perfectly protecting workers and the public from chemical carcinogenesis before effects appear. On general principles, this appealingly simple system may still hold promise for setting and defending regulatory goals, but its systematic failure to guide regulatory efforts in specific instances has led to disillusionment.

The technical problems encountered in conducting bioassays--including questions about high doses, and the impossibility of knowing which extrapolation model is most appropriate—plague risk assessment. Equally or more important are the assumptions involved. For instance, apparently endless arguments have gone on about whether liver tumors in mice mean anything in terms of human risk; the argument has not been settled by experimentation but is silenced by convention **(542).**

Formaldehyde is a case in point. There is general agreement that formaldehyde is an animal carcinogen. The bioassay was carried out by industry's own toxicology laboratory. But in the final analysis, industry objected to regulating formaldehyde on the basis of the bioassay, and assessments produced by different organizations varied in the amounts of human risk they predicted.

Epidemiology

The importance accorded epidemiology reflects a trend toward more systematic, scientific study of disease. The desire to base conclusions about causality on something more than individual observation and intuition-the two most valuable tools of the clinician—calls for describing associations quantitatively, both in terms of strength of association and in terms of the probability that the association is not simply one of chance. Careful epidemiologic investigations have confirmed important suspicions about work-related illnesses. The now universally acknowledged case against asbestos is built on epidemiologic studies.

The strengths of epidemiology still remain to be exploited. A great deal needs to be learned about diseases and **syndromes that are widespread in the population. Certain chronic conditions (cancers in particular) and heart disease are known** to be associated with various occupations. The means exists, through the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute *(542,683),* to enter about one-tenth of all U.S. cancer cases on tumor registries as they are diagnosed. This system provides the ability to set up large case-control studies with relative ease. (See box B.)

Cohort studies of large industrial populations—which can be assembled by corporations and/or unions and facilitated by workplace surveillance systems that have been installed by many companies to track and store various sorts of data—also yield valuable information. (These surveillance systems are discussed further in the "Occupational Medicine" section.)

Government Records. —An important and frustrating feature of epidemiology in the United States is the difficulty of locating and tracking people. In a cohort study, it is critical that the maximum number of cohort members be located. If the cohort contains workers employed at a particular site s, 10, or 20 years ago, many will have moved. In a case-control study, members of either population may be identified through hospital records, and the recorded addresses may no longer be current. In either type of study, the epidemiologist often needs to locate people for interview and examination.

There are standard methods for locating people in this mobile society. Asking at places of employment and using telephone and city directories are common. Mail sent to the last known address frequently reaches the person. In difficult cases, the epidemiologists can hire private detectives or credit bureaus to locate persons. The so-called NIOSH-window facilitates some occupational epidemiology studies. Investigators who are allowed to use it can supply a name and some other identifying information (such as the Social Security number) to the Internal Revenue Service, and the agency provides the person's current address. Members of the OTA Advisory Panel for this assessment reported that there is some confusion about who can and cannot use the NIOSH window and under what conditions.

The Federal Government collects information about places of employment and about what hazards or substances are present in them. Such records have obvious usefulness for epidemiology, providing a quick method for identifying persons who may have been exposed to a substance. However, all the record systems have flaws that restrict their usefulness **(542,557).** The recommendations made by the Committee to Coordinate Environmental and Related Programs (CCERP) of the Department of Health and Human Services provide an excellent grounding for questions about the current systems and suggestions for changes.

The National Death Index (NDI) can tell epidemiologists that a person is dead and which State (or other) department of vital statistics holds the death certificate. This speeds up the retrieval of information for studies, but the NDI does not actually provide information on the cause of death and underlying causes.

Section 8(e) of the Toxic Substances Control Act (TSCA) requires that manufacturers report to EPA on chemical substances that pose significant risks to human health or the environment. Some companies voluntarily report these results to NIOSH and OSHA. In practice, this reporting requirement means that an employer that carries out a short-term test, a bioassay, or an epidemiologic study that shows a health risk must report it to the EPA. EPA prepares a report on each 8(e)

Box B.—Epidemiology

Cohort Studies

A cohort study starts with a group of people—a cohort, considered free of the disease under study and whose exposure to a risk factor is known. Usually the risk factor is an exposure to a suspect toxic substance or a personal attribute or behavior. The group is then studied over time and the health status of individual members observed. This type of study is sometimes referred to as "prospective" because it looks forward from exposure to the possible development of the disease characteristic. Cohort studies can be either concurrent or nonconcurrent in design. Concurrent ones count only cases of disease or other outcomes that occur after the start of the study. Nonconcurrent cohort studies also count any cases or other outcomes for which there are records.

Case-Control Studies

In a case-control study, persons with the disease under study (cases) are compared with individuals without the disease (controls) with respect to risk factors that are judged relevant. Some authors label this study design "retrospective" because the presence or absence of the predisposing risk factor is determined for a time in the past. However, in some cases the presence of the factor and the disease are ascertained simultaneously.

The choice of appropriate controls is rarely without problems. Often, for practical reasons, controls are chosen from hospital records. But they may not be representative of the general population, and they therefore may introduct "selection bias" (2$2).

General Considerations

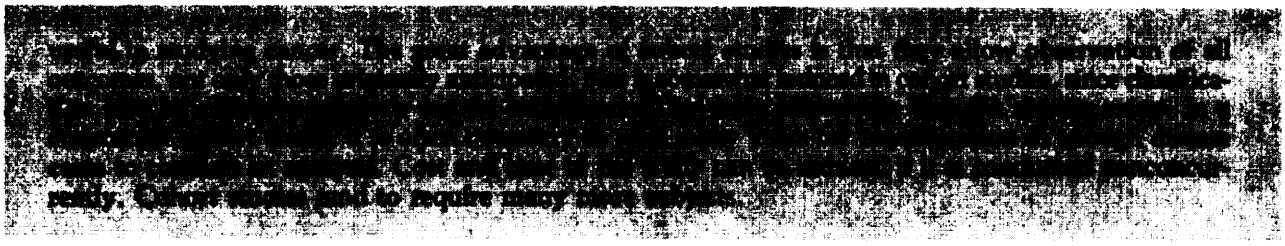
In case-control and cohort studies, the groups selected should be comparable in all characteristics except the factor under investigation. In case-control studies, the groups should resemble each other except for the presence of the disease; in cohort studies, the study and comparison groups should be similar except for exposure to the suspect factor. Since this rarely is possible in practice, comparability between groups can be improved by either matching individual cases and controls (in case-control studies) or by standard statistical adjustment procedures (in either case-control or cohort studies). Demographic variables such as age, sex, race, or socioeconomic status are most commonly used for adjustment or matching.

There are advantages and disadvantages in both types of study (see table 3-8). Case-control studies tend to be less expensive to conduct, require relatively fewer individuals, and often have been especially

Table 3-8.-Advantages and Disadvantages of Case-Control and Cohort Studies

Type of study	Advantages	Disadvantages
Case-control	Relatively inexpensive	Complete information about past exposures often unavailable
	Smaller number of subjects	Biased recall
	Relatively quick results	Problems of selecting control group and matching variables
	Suitable for rare diseaes	Only relative risk is yielded
Cohort	Lack of bias in ascertainment of risk factor status	Possible bias in ascertainment of disease
	incidence rates as well as relative risk are yieided	Large numbers of subjects required
	Associations with other diseases as by-product can be discovered	Long follow-up period
		Problem of attrition
		Changes over time in criteria and methods
		Very costly
		Difficulties in assigning people to correct cohort

SOURCE: (542).



notification and circulates it within the Agency and to other Federal agencies, including OSHA and NIOSH. In addition, periodically the reports received over a period of time are bound together for distribution to libraries. The 8(e) activities, therefore, provide a way to disseminate health hazard information rapidly.

Occupational Medicine

The field of occupational medicine has gone through a series of changes during this century. Not long ago, the clinician not only tended the sick but also filled a number of other roles, investigating possible disease relationships and fostering changes in the workplace. To a certain extent, the role of the occupational physician **was** altered by the rise of epidemiology and toxicology as separate professions.

Epidemiology and toxicology have not been the panacea for solving workplace health problems that some envisioned. Toxicology is limited to testing under conditions that cannot mimic complex human exposures and behaviors. Epidemiology cannot begin until it finds subjects for study, and it relies on outside input—in particular, clinical observations of possible associations between exposures or behaviors and disease—for hypothesis generation. It has limitations in the kinds and magnitudes of effects it can detect. The limitations of both toxicology and epidemiology argue for a continuing role for occupational medicine in hazard recognition as well as in treating workers.

Better use of physicians' experience and insights will depend on education. There are two categories: general education of physicians about occupational disease and injury, and specialized education and training for practitioners of occupational medicine. An orientation toward occupational health is minimal at best, in most U.S. medical schools. Levy **(269a)** reports that only **50** percent of U.S. medical schools provided some class time to occupational health during the 1977-**78 academic** year. This has risen to **66** percent in the 1982-83 academic year. However, the median number of required class hours devoted to occupational health remained at 4 hours. Postgraduate, specialty training in this country has traditionally been subsumed under preventive medicine, and centered in schools of public health. Recently increased emphasis has been placed on clinical experience in medical schools. The location of the specialty courses is less important than making sure the programs are well-taught and attractive and that they provide clinical experience. The NIOSH-supported Educational Resource Centers (discussed in ch. 10) provide postgraduate education for physicians.

In the United States, the occupational medical services are usually provided by physicians who are directly employed by or under contract to employers. Large companies frequently have on-site medical departments, staffed by physicians and nurses. Medium-sized companies might have the full-time services of an occupational health nurse, and possibly, the part-time services of a local physician. Small companies have only rarely provided occupational medical services.

An alternative organizational model is found in occupational medicine clinics, which have been growing in the last few years. These clinics are usually associated with a hospital or university and provide examinations and treatment to workers. Clinics might, because of a larger patient load and a staff that consequently sees more patients, be able to to provide more knowledgeable care, as well as improved physician training. In some cases, the clinics' staffs include not only doctors and nurses, but also industrial hygienists and safety engineers. The combination of staff from

different disciplines can provide a critical mass for a great deal of important activity in hazard identification and control.

These clinics also provide advantages to employers, especially small to medium-sized companies, that previously were not able to provide occupational medical services to their workers. In the words of the director of an occupational health department at one hospital:

> The larger corporations will undoubtedly continue to have in-plant occupational health services. But medium and smaller companies will be forced to make an economic decision on whether it is more advantageous to do it themselves or farm the occupational health service to others *(Daniel Conrad,* quoted in 338a).

Some hospitals are apparently establishing these clinics in order to develop new sources of revenue. The staff of these clinics expect to be able to conduct some research, as well as to provide advice about prevention and medical care to employees (338a).

Medical Surveillance Systems. —Computerized information systems have made it possible to store massive amounts of data. Information about exposures in the workplace and the health records of workers can form the basis for surveillance systems that aim to identify health hazards. Surveillance is defined as the "collection, collation, and analysis of data and its dissemination to those who need to know" (474). Public health surveillance techniques were developed in the last century to identify foci of pestilential diseases such as cholera, smallpox, plague, and yellow fever, so that appropriate control measures could be instituted. In the workplace, the value of surveillance is to alert workers and employers to unusual patterns of morbidity or mortality.

Concerns today center on chronic rather than acute diseases; the technical problems of linking cause and effect are heightened by the remoteness of disease from exposure. Computerized information systems in industry, including their *use* for medical and exposure records, have enabled massive amounts of information to be stored and correlations to be produced.

In the occupational setting, the necessary components of surveillance are:

- exposure information of some type;
- records of health outcomes, which may include causes of death; and
- background information about characteristics of each individual that might influence susceptibility to disease.

Variations in epidemiologic surveillance systems have to do mainly with the quantity and type of data in each category. "Exposure" can be quite basic: for instance, knowing the plant within a company, or the department within a plant, in which a worker is employed, and updating it perhaps yearly. At the more comprehensive end of the spectrum, exposure might contain continuous records of personal and area monitors measuring chemicals and other agents in the industrial environment.

Health outcomes may be ascertained from industrial health and accident insurance reports, which record only the most serious events, These can be supplemented by information gathered in preemployment examinations and nonroutine visits to physicians, as an intermediate approach. At the extreme, to the above information could be added the results of periodic medical screening for many diseases or other abnormalities. Basically, the simpler systems are considered passive, using data collected for other purposes (personnel records, insurance data); systems can be progressively more active in seeking data expressly for health surveillance **(312).**

Routine analyses of data collected in surveillance systems are seldom sufficiently rigorous to evaluate possible instances of occupational disease. Their broad, sweeping monitoring of health events is more of a hypothesis-generating device. It provides the means to make epidemiologic studies as targeted and as timely as possible.

A sign of growing interest and activity in occupational health surveillance, and medical information systems in general, was a meeting of the American Occupational Medical Association's Medical Information Systems Committee in 1981. Papers presented at that meeting, which described

19 such systems, were published as a supplement in the October 1982 issue of the Journal of Occupational Medicine (238).

In the same issue of that journal, computer software companies advertised their ready-made programs for instituting surveillance systems. The literature packets behind those systems, which appeared to be directed at smaller companies, describe convenient ways to classify and store large amounts of information about workplace exposures and employee health, What is missing, at least in the prospecti, are discussions about the ultimate value and potential contribution of such information to detecting problems in the workplace. Although the systems may facilitate record keeping that already goes on, they may fail to have a serious impact on safety and health, as they are promoted to do.

Occupational health surveillance remains a source of both great promise and great controversy. If it could be used just to identify the causes of occupational illness, setting the stage for preventing further illness, there would be little to say against the idea. As a purely scientific concept, it is unassailable. In practice, from the point of view of companies, the collection and particularly the analysis of data about exposures and health outcomes raises legal issues of responsibility and liability. From the employees' point of view, there is a fear that surveillance will be adopted as an alternative to installation of controls.

There is anecdotal evidence that some companies that had maintained surveillance systems have now dismantled them. Although the same data may still be collected for administrative reasons, they are not being assembled in a form for analysis of possible relationships between exposures and disease. This step may at least in part stem from the unknown consequences of finding the suggestion of a health problem—for instance, a slight excess of some particular cancer. Further study would certainly be necessary to confirm the association, yet the liability associated with even suspecting that a problem exists cannot be known at this time.

Some employers are concerned that discovering a possible association may make them liable in tort actions. In addition, section 8(e) of TSCA requires reporting of such findings, making them public and available to potential litigants. On the other hand, some companies expect that acting responsibly will provide some defense against tort action. The problem of deciding how to use suspicions that may be generated by routine matching of health and surveillance information is a very real one.

A second policy issue in this field concerns the proliferation of data collection systems for health and exposure information that are accompanying the microcomputer age. There appears to be little thought given to the ultimate value of these systems in improving workplace safety and health. Certainly for small companies, the targets of much advertising, the number of workers will be too small ever to detect all but the most obvious excesses of disease. There may be scope for using computer networks to pool data, but these activities bring their own problems. (See ch. 10.)

Another pertinent issue is the substitution of surveillance for prevention, particularly prevention in the form of controls on workplace exposures. Union officials and many health professionals fear that the creation of surveillance systems will lead to the impression that "something is being done" to improve health, resulting in less emphasis on controls and paralyzing action against hazards until large numbers of people become sick or die.

New Hazards

In some measure, "familiarity breeds contempt"-even when the subject is hazards-and there may be a human tendency to fear new hazards more than old ones. The emphasis placed on identifying and understanding "new" hazards grows partly from that psychology and partly from the realization that it is easier to control hazards before they become established in commerce and economically important.

Epidemiologic studies and occupational medicine are of no value in learning whether a new agent is hazardous before people are exposed to it. The introduction of a new substance or process into the workplace that is subsequently shown to be a hazard must be regarded as a failure of

preventive health measures. Analysis of the chemical structure of a new substance can be used to estimate what toxic properties are associated with it, but many people consider that technique to be unreliable. Toxicologic techniques can be used to learn about the hazards of new substances, but the associated costs place some restrictions on their use.

Toxicology costs money, and manufacturers will not spend great sums on testing a newly developed chemical before they know there is a market for it. Some manufacturers argued during the debate when the Toxic Substances Control Act was passed that they did enough toxicologic testing to be assured that new chemicals would not pose unreasonable risks. TSCA set up two programs to gather information about new chemicals.

The Premanufacture Notification Program

The Toxic Substances Control Act requires that manufacturers prepare a Premanufacture Notice (PMN) and submit it to EPA at least 90 days before starting manufacture of a chemical substance for use in commerce. The PMN is to contain any information available to the manufacturer about the toxicity of the chemical, Some PMNs contain many items of information bearing on the properties of the new chemical, while others contain none or only a few, and there are disputes about how useful the reporting has been to date (547a).

It is clear from EPA's experience with the PMN program that a common plain for potentially hazardous exposures to newly introduced substances is in their manufacture. EPA has used formal and informal regulatory procedures to reduce occupational exposures to chemicals described on PMNs (547a), and it has established informal communications with OSHA and NIOSH staff about controls. For instance, EPA has required the use of respirators in the manufacture of some new chemicals described on PMNs. According to EPA officials, the Agency consulted with NIOSH about appropriate respirators.

The PMN program provides an important opportunity to identify hazards before they become established in the workplace. Although EPA regulated pesticides under a licensing law before TSCA, its regulatory concern about other chemicals was restricted to those that became pollutants. Under the PMN program, it has authority to regulate chemical substances before they get into the workplace.

Significant New Uses

TSCA anticipated that the uses of a chemical described on the PMN might not be associated with an unreasonable risk, but that a different use, called a "significant new use, " might. TSCA directs EPA to write a significant new use order about new chemicals that fall into this category. In practice, EPA has restricted some chemicals to particular uses and required submission of more data about the chemical before it could be more widely used. One example of this process concerns a surfactant for cleaning. Concerned about possible dermatologic effects, EPA did not object to its use by professional cleaners, because those workers could be instructed in the proper use. However, if the surfactant is considered for use in consumer products-a significant new use—more information must be provided to EPA.

SUMMARY

Preventing workplace-related disease requires that associations between activities and exposures and diseases be identified. The known health hazards-extremes of heat and cold, radiation of various kinds, noise, and some dusts, fumes, and vapors from manufactured and naturally occurring substances—illustrate the diversity of exposures. In addition to identified hazards, present but so-far-unidentified hazards are also a concern. Finally, increasing attention is being focused on

assessing the possible hazards of new substances and processes before they are introduced into the workplace.

Some health hazards that have been known for centuries were obvious because of the particular nature of the diseases; for instance, lead poisoning symptoms were sufficiently distinctive to make the association between exposure to lead and disease apparent. Three disciplines—occupational medicine, epidemiology, and toxicology—have been important in describing associations. All three are currently used in investigations of current exposures that may be hazardous. Toxicology is especially important to learning about "new," possibly hazardous substances before they are introduced into the workplace.

Some of the most successful efforts at prevention, such as the marked reductions in exposure to vinyl chloride, began with a physician noting an unusual cluster of diseases. The importance of this source of information draws attention to medical school teaching about the role of work in health and disease. Unless medical students learn the value of taking an occupational history as part of the medical examination, associations may be missed. Occupational physicians, familiar with working conditions and exposures and often interacting with industrial hygienists and safety engineers, can be especially important in hazard identification. Workers' own observations and complaints, brought to the physician, are often the first indication of a hazard.

Epidemiology is important less in initial identification of hazards than in providing evidence for or against an association. In making decisions about which hazards are "real," positive epidemiologic studies are the most convincing evidence, but there are often protracted arguments about the appropriateness of study methods and the conclusions drawn. Companies, trade associations, unions, and government agencies all commission epidemiologic studies and comment on studies done by others. Government records, which contain information about vital statistics and locations, are especially useful in epidemiologic studies.

Toxicology provides information about the potential hazards of substances by testing them in animals or other systems. With the passage of the Toxic Substances Control Act, which requires that companies notify the Environmental Protection Agency of their intention to manufacture new chemicals, the government is in a position to obtain information about chemicals before they enter commerce. Although there are conflicts about how much information EPA needs to protect human health, it is clear that workplace exposures are being identified as concerns in the case of some new chemicals. Toxicology plays the central role in identifying hazards from new chemicals.

TSCA also requires that companies notify EPA about substances present in commerce that are substantial risks, and the Agency then disseminates that information. All three disciplines—occupational medicine, epidemiology, and toxicology—have contributed to the identification of substantial risks. The NIOSH Health Hazard Evaluation program investigates possible associations between exposures and illness at the request of employers or employees or on its own initiative (see ch. 10). It, too, relies on all three disciplines.

Hazard identification is not a smooth path; arguments and conflicts abound. Evidence that convinces some people leaves others unmoved. The methods that were used in the past, improved by better training and techniques, continue to be of value today. More attention during the education of physicians and other medical personnel to the influence of work on health, better use of Federal records, where appropriate, to facilitate epidemiology, and continual research to make toxicology more predictive all offer opportunities to improve hazard identification. However, as is made clear in other parts of this assessment, hazard identification alone is not sufficient. Making a decision to control a hazard requires that the hazard be identified, but identification, by itself, is not sufficient for control.