Survey of Contemporary Toxicology

volume 1

Anthony T. Tu

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Volume 1

Edited by

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SURVEY OF CONTEMPORARY TOXICOLOGY

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Preface

Toxicology is a science that deals with substances toxic to humans or to domestic animals. In ancient times, toxic substances were mainly of natural origins such as animal venoms, plant and marine toxins, and bacterial toxins. As human activity grew, so grew the problem of toxicology. In the affluent society in which we live, human activities are greatly focused on how to make living more comfortable. As industry booms, waste products are released into water and air, causing pollution. Food produced at a given place is transported for a distance; hence, food preservatives become important and, consequently, questions arise concerning the biological effects of these additives. As human society expands within the natural environment, interactions between human and poisonous creatures increase. Many other examples can be cited. This short list merely illustrates that the field of toxicology is expanding tremendously in our modern society.

Like any branch of science, toxicology becomes highly specialized. It is almost impossible for a single person to be knowledgeable in all aspects of toxicology. There are numerous toxicology books; many of these are excellent but are so specialized that only persons in the particular subfield can understand them.

Both the publisher and I feel that there is a great need for a book that individuals from interrelated fields can understand. Hence this book, *Survey of Contemporary Toxicology*, has been written by experts in the field and the contents are systematically organized. As mentioned, modern toxicology is extremely broad; it is not possible to be completely inclusive. For Volume 1, I selected seven chapters on such diverse topics as industrial toxicology, chemical pollutants in water (water pollution), food additive toxicology, foodborne diseases, bacterial toxins, plant toxins, and marine toxins. It is my intention that Volume 2, presenting other toxicological topics related to contemporary society, be published in due time. These volumes are also designed as textbooks for undergraduate students.

I hope this book achieves its purpose—that is to promote a general understanding of the different aspects of toxicology associated with contemporary living.

If you have any suggestions for improving the book, please write to me. All constructive suggestions will be carefully considered for future volumes.

Anthony T. Tu

March 1980 Fort Collins, Colorado

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Industrial Toxicology

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1. INTRODUCTION

Occupational disease of chemical origin dates back to ancient civilization. Lead was known to be toxic several centuries before Christ. Strabo, the Greek geographer and historian, who died in AD 23, described the arsenic mines in Pontus: "The air in the mines is both deadly and hard to endure on account of the grievous odour of the ore, so that the workmen are doomed to a quick death" (1). The first known paper devoted specifically to toxic vapors and fumes was written in 1473 (2). Goldsmiths and metalworkers were cautioned to avoid breathing the fumes from burning coal, mercury, silver, and lead. In 1700 Ramazzini presented the first comprehensive treatise on occupational disease. Record of occupationally induced cancer dates from around 1775, when Pott wrote his observations on cancer of the scrotum, found in the young boys who swept out chimneys (3).

Modern toxicology originated early in the nineteenth century (4, 5). The first applications of industrial significance came shortly thereafter. Marsh developed an analytic method for arsenic in 1836, and in 1850 Bernard found that carbon monoxide combines with hemoglobin. Concurrently came the expansion of the Industrial Revolution, and some new types of disability were readily pinpointed. For example, mercuric nitrate was used to "felt" animal fur; the chronic mercurialism that developed in hatmaking became known as "hatters' shakes" (see Section 4.4.2). In 1895 the German surgeon Rehn reported four cases of bladder cancer, a relatively uncommon disease, from workers in one factory engaged in the manufacture of fuchsin dye (6).

Today the volume of literature pertaining to toxicologic effects of occupational significance is enormous. This chapter outlines the highlights.

2. MONITORING THE INDUSTRIAL HEALTH HAZARD

Industry overall reflects the prevailing culture and technology. As technology changes, varying industrial health hazards are recognized. Evaluation of a specific industrial health hazard is essentially a stepwise progression. The first step of data collection is usually a literature search of the chemical toxicants or other stresses known to be involved, supplemented as necessary by experiments on animals and analytic testing.

Actual surveys in the industrial workplace are usually a responsibility of the industrial hygienist. Chemicals in the workplace may be hazardous as a result of their explosive, flammable, oxidizing, or toxic properties. Toxic hazards may be a function of the physical form as well as the chemical structure. This is especially true in confined spaces. For example, a dust mask provides little or no protection against hazards from toxic gases.

The hazard—the likelihood of injury—in a given occupational exposure depends on three factors: the nature of the environmental stress (see Section 4), the intensity of exposure, and the duration of exposure (7). The intensity of exposure to environmental chemicals (concentration) is determined by direct or indirect methods considered satisfactory for the substance(s) in question. Direct methods for sampling the atmosphere include such diverse means as colorimetric tubes of varying sensitivity and infrared analyzers. Indirect methods involve capture of the sample in a special syringe, evacuated can, sampling pump, or other suitable device, plus subsequent analysis by gas chromatography or other appropriate means. Figure 1a shows a personal sampling pump useful for detection of a variety of contaminants. An introduction into modern industrial hygiene should consider the basic concepts (8), available methods (9), and analytic procedures recommended for specific industrial chemicals (10).

The third step is evaluation of the various analyses and related data to provide a rational, cost-effective basis for control. The basic strategies are outlined in Fig. 2 (7). Ideally, deleterious substances should be removed from the environment to below the level of impairment; if this is not feasible, the worker must be protected from the environment by appropriate clothing, respirators, or other equipment.

In a few cases the only feasible solution may be abandonment. The potent carcinogen β-naphthylamine has not been manufactured in this country since 1962. New or complex situations

Figure 1.1 (a) Personal air sampler pump (Du Pont P-4000) designed to be clipped to the worker's belt, with filter media clipped to shirt collar and connected to pump by flexible tubing. The pump automatically compensates for pressure drop across filter media and may be programmed to shut off after any period of operation between 15 min. and 8 hours. (b) Inside of air sampler pump.

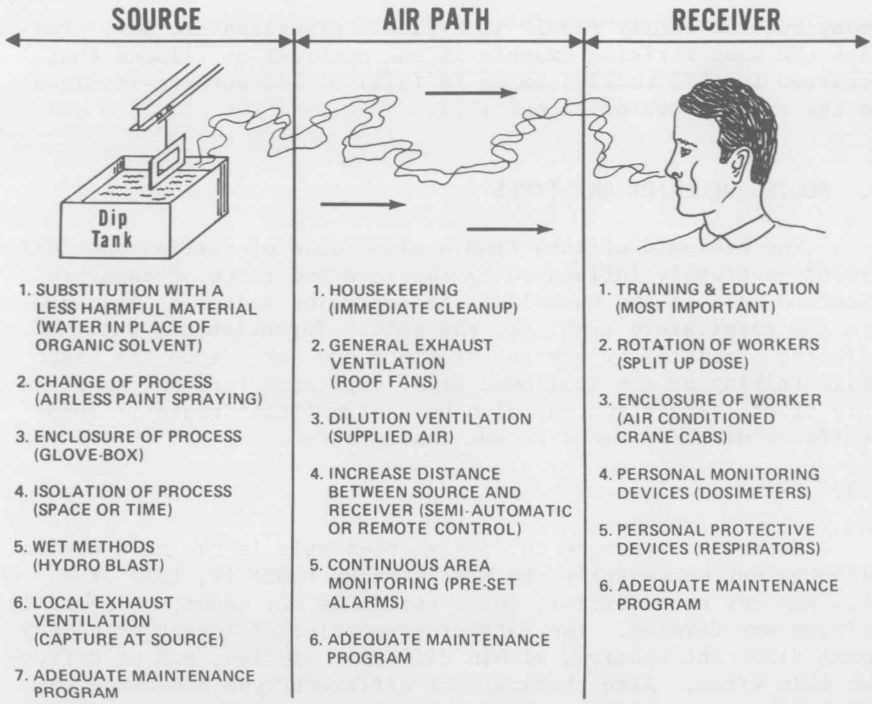

Figure 1.2 Generalized diagram of methods of hazard control. Reprinted with permission from J. B. Olishifski and F. E. McElroy, Fundamentals of Industrial Hygiene, copyright 1971 and 1979 by National Safety Council, Chicago, IL 60611.

may require integration of various inputs—typically, industrial hygiene surveys, experimental research on animals, and medical record data. Records of acute injuries, general medical problems that might be aggravated by work-related factors, and chronic disease may all be pertinent to occupational medical records.

Comprehensive medical record data provide a basis for epidemiologic surveys. Epidemiology may be defined as "a method of reasoning about disease that deals with biological inferences derived from observations of disease phenomena in population groups" (11). A classic example is the recognition in 1973 that two and then three cases of angiosarcoma of the liver among a limited number of workers exposed to vinyl chloride was an unusually high rate of a rare form of cancer. Such inferences more often require statistical analysis. "Epidemic poisoning" is uncommon in the occupational health scene in the United States today but can easily result if hygienic practices are lax. Perhaps the most striking example is the outbreak of illness that occurred in 1974 to 1975 among 76 (57%) of 133 workers involved in the manufacture of kepone (12).

3. ROUTES OF ENTRY AND TYPES

The biologic effects from a given dose of foreign chemical are often greatly influenced by the rate and route of exposure (Section 1). In the workplace the two major routes of exposure are the respiratory tract and the skin. Ingestion may occur if airborne particles or aerosol droplets are taken into the mouth while talking or are swallowed after expulsion from the respiratory tract. Ingestion may also be a significant route if foodstuffs or drinking water become contaminated.

3.1. Skin

Cutaneous exposure to foreign chemicals is the most common although not necessarily the most serious route (4, 13). The skin may act as a barrier, local reactions may occur, or systemic effects may develop. The barrier properties of intact skin vary among different species, within different species, and at different skin sites. Also chemicals of different type penetrate the skin with varying ease; even for a given chemical, marked differences may result depending on the concentration of chemical and type of vehicle (if any) used in the application. Environmental factors such as temperature, relative humidity, and pressure can influence both local and systemic reactions.

3.1.1. Local Effects. The term "occupational dermatosis" includes all skin abnormalities of occupational origin; such skin alterations may include scaling, simple erythema, eczema, acne, pigmentation changes, neoplasia, granuloma, or ulcers. Approximately 75 to 80% of occupational dermatoses are of the inflammatory type classed as contact dermatitis or, more specifically, contact eczematous dermatitis (14). Most occupational dermatitis is caused by primary irritant chemicals; allergenic materials account for approximately 20% of occupational cases. Figure 3 shows a long-standing irritation complicated by secondary infection. The more common agents associated with selected industrial occupations are shown in Table 1.

3.1.2. Percutaneous Absorption. Chemicals may pass through the skin by transversing the epidermal cells or by entering through the follicles (Fig. 4). The majority of the skin surfaces consist of epidermis, which therefore is probably the more common

Figure 1.3. Chronic hand dermatitis due to the primary irritant effects of soaps and solvents in a man working as a "spotter" in the drycleaning industry. Note secondary bacterial infection with fissuring between the third and fourth fingers. Reprinted with permission from R. M. Adams, Occupational Contact Dermatitis, J. B. Lippincott Company, copyright 1969, Philadelphia, PA 19106.

pathway. Follicular absorption usually requires mechanical assistance such as massage.

Examples of industrial chemicals that readily pass through the skin are aniline and related aromatic amines, also undiluted solvents such as carbon tetrachloride, benzene, and dimethylsulfoxide. Percutaneous absorption of solvent vapors from the surrounding air in the work environment is considered generally insignificant. In tests with human volunteers, exposure of the total body surface (light permeable clothing) to 600 ppm of xylene vapor for 3.5 hours was found to correspond to an equally long inhalation at a concentration < 10 ppm (16). If the intact skin barrier is impaired or broken, for example, by defatting, mechanical injury, or disease, passage of a toxic agent may be greatly facilitated.

3.2. Inhalation

Gases and vapors as well as liquid and solid materials in the form of respirable particles may be inhaled. The dose actually received and retained or absorbed in the respiratory tract depends on a great variety of factors—basically, the

TABLE 1. SELECTED CHEMICAL CAUSES OF SKIN CHANGES[a]

Agent	Primary Irritants	Sensitizers	Action on the Skin (More Serious Changes in Other Organs May Result)	Typical Occupations, Processes, or Uses Where Exposure May Occur[b]
Acids				
Acetic	X		Dermatitis and ulcers	Manufacturing acetates, printing and dyeing, food preservative, solvent
Carbolic (phenol)	X		Irritation and erosion of skin	Disinfectant; manufacturing of disinfectant, dyes, pharmaceuticals, resins
Chromic (chromic trioxide)	X	X	Ulcers ("chrome holes") on skin, inflammation and perforation of nasal septum	Plating, metalworking, corrosion inhibitor
Hydrochloric	X		Irritation and ulceration of skin	Bleachers, picklers (metals), refiners (metals), chemical manufacturing
Hydrofluoric	X		Severe burning of skin, erosion, ulcers, formation of blisters	Fluorination processes, enamel manufacturing, etchers
Nitric	X		Severe skin burns and ulcers	Manufacturing of fertilizers, explosives, many organic chemicals; electroplaters, metal refiners