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Evaluating the Industrial Hazards of New Chemicals

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Evaluating the Industrial Hazards of New Chemicals

In prescribing safe handling procedures for new compounds and old compounds in new uses, sound toxicological information is combined with knowledge of proposed use conditions

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CHEMICAL MATERIALS and chemical formulations are becoming more and more available to the consuming public and are playing an important role in our industrial and domestic lives. When misused, many chemicals are hazardous because they are capable of producing deleterious and sometimes serious physiological effects—they are toxic.

Toxicity

It is of particular importance to realize that toxicity is a property of matter. It is a physiological property which defines the capacity of a chemical to do harm or produce injury to a living organism by other than mechanical means. Chemical and physical properties are established by well known laboratory methods. Likewise, toxicological properties may be defined by conducting animal experiments in the laboratory. Toxicity entails a definite dimension, that of quantity or amount. On this basis, then, any chemical is more or less toxic, dependent upon amount. In a broader sense, everything is toxic. How much is toxic? Too much! Consider oxygen, a natural constituent of the air we breathe. We inhale enormous amounts of oxygen. It is essential for life. Is it toxic? It is, specifically so. Too much oxygen administered to the premature infant is capable of rendering him blind, a specific physiological reaction.

How about arsenic? When we think of arsenic we think of poison. Very small amounts are capable of producing serious systemic injury. On the other hand, arsenic, in therapeutic doses, is beneficial. It is used medicinally in treating several diseases. Toxicity is a property and possesses quantitive aspects.

Everyone has some concept of poison. We think of red warning labels, the skull and crossbones, and other devices designed to indicate that a material is harmful. A poison may be considered as a substance possessing a certain high degree of toxicity.

Toxicology is the science that treats of poisonous or toxic substances. We handle such materials in our industrial and domestic lives. We experiment with them. We produce them in large quantities. We package them, transport them, and sell them. In many cases, recommend them to the consuming public for specific uses. We may even eat them. Why then are we not in trouble on many counts? The answer is simply, because we do not get *too much*. It is the job of the industrial toxicologist to define what *too much* is, and to prescribe limitations of use so that normal, recommended use does not result in *too much*.

From a toxicological viewpoint, we must consider all types of exposure and the subsequent effects on the living organism. A material is toxic if it renders living cells incapable of performing their normal function. Chemical injury may be local or systemic. Local injury is the result of direct contact with tissue. The skin may be burned or the eye may be injured to the extent that vision may be impaired. The respiratory tract and lungs may be injured as a result of inhaling toxic vapors, fumes, dusts, or mists. These are all examples of direct chemical contact with tissues, and the toxicological reactions may be slight or severe. A material cannot produce internal or systemic injury unless it gains entry into the blood stream. In order to gain entry, a material must contact tissue, be absorbed by it, and subsequently be taken into the systemic circulation. Common routes of entry are through the intact skin, through the gastrointestinal mucosa and through lung tissue. Once in the blood stream, a toxicant may elicit general effects, but more than likely the critical injury will be localized in specific tissues or organs.

Degrees of Hazard

The extent of the injury produced by a material may depend upon several factors such as physical state, concentration, and duration of exposure. At this point, we must introduce another basic concept, that of hazard. Hazard treats of the probability or likelihood that a substance will cause harm. In evaluating hazard, toxicity is but one factor. Others are chemical and physical properties, warning properties such as odor and pain, use, and type and number of customers.

Two liquid materials may possess the same degree of high toxicity upon acute inhalation of vapors. One material may be odorless, colorless, and nonirritating to the eyes and nose. The other may have a pungent or disagreeable odor in minute concentration or be an eye or respiratory irritant. By comparison, the material with the warning properties presents a lesser degree of hazard. Its presence can be detected in time to avert injury. In another case, a material used by technical personnel as a chemical intermediate presents much less of a hazard than if it were offered to

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the consuming public as a cosmetic. The hazard in the latter case is increased on two counts—the probability of contact is increased and the customer is unassuming.

Evaluating Chemical Materials

In evaluating the toxicity of a chemical, the toxicologist has several devices at hand. To start with, there may be records of human experience available. This is particularly true for older chemicals such as caustic, kerosine, and others. Medical records through the years bear out the harmful effects of caustic materials if allowed to contact the eye or if inadvertently swallowed. Less notorious chemicals have found their way into the technical literature which is readily available to the enterprising toxicologist. In the fast moving field of chemistry, however, we are frequently confronted with evaluating the toxicity of new substances, perhaps never having been made or tested before. These materials must be taken into the laboratory and subjected to animal experimentation.

In the area of animal testing, the horizons are essentially unlimited. The toxicologist may do quick, limited, range-finding studies or he may conduct long-term chronic exposure experiments. His criteria may involve only a single gross observation or they may require meticulous histological preparation of tissues and subsequent microscopic examination. Pharmacological techniques may be employed to explore mechanism of action. In some cases, testing may be on human subjects.

He begins with an evaluation of the problem. He learns what the material is and how it is to be used. He then devises laboratory experiments to simulate use-conditions. The importance of problem evaluation must be emphasized. All factors must be brought into focus and the approach placed in the proper perspective lest we spin our wheels and perhaps jeopardize the health and safety of our employees or detain the development of a new product. The toxicologist solicits the understanding and cooperation of everyone concerned in this matter. He wishes to know all chemical and physical properties of a material, what stage of development it's in, in what form or concentration it is to be used, and how it is to be handled. It is important to define the problem. If it's a legal problem, will it involve FDA, a State Household Poisons Act, or will someone be sued? Perhaps one is simply comparing several compounds of equal efficacy to determine which is the most favorable from a toxicological viewpoint. Certain handling problems may require very limited laboratory investigation, to determine effects of direct skin or eye contact.

Armed with this information, the toxicologist is ready to conduct laboratory experiments. The data obtained reveal, for example, the type and extent of injury which might be expected from direct eye contact with a chemical. Injury might be very slight, or severe, severe to the extent of resulting in permanent impairment of vision. The effect of washing is particularly important to note for it indicates how rapidly the material reacts with the eye tissue. It is not uncommon for the toxicologist to encounter a chemical that is essentially harmless if leisurely washed from the eye, which if allowed to remain, would produce loss of vision. Some chemicals, of course, are capable of exerting extensive injury almost immediately upon contact. Such materials are particularly hazardous and for their handling, the toxicologist must prescribe tight fitting chemical workers goggles whenever the likelihood of eye contact exists.

It is necessary to study the effect materials may have when they contact the skin. Several reactions may occur as a result of chemical contact with the skin. A common reaction is a chemical burn characterized by necrosis or denaturation which usually is followed by a scab formation and scarring.

Many chemicals produce skin irritation of a minor degree. Effective organic solvents frequently cause such a response, sometimes referred to as eczema.

Some chemicals have the ability to penetrate intact skin. They are absorbed through the skin, into the systemic circulation, and in many cases, very small amounts may rapidly produce serious internal injury, even death.

Some chemicals are so-called skin sensitizers. They are capable of producing an allergic, edematous, contact-type dermatitis in humans. Skin may become sensitized as a result of a single massive exposure or to contact with minute amounts of material over a long period of time.

Careful interpretation of skin irritation data, along with the knowledge of physical and chemical properties, permits the toxicologist to evaluate hazard and in turn prescribe precautionary measures to be observed for safe handling in research, production, or use.

The toxicological effects of vapors, gases, fumes, or dusts are determined in the laboratory by actually exposing animals in fume chambers. From such studies the toxicologist gains information regarding no-effect levels as well as those levels which produce systemic injury of various types and degrees.

It is not unusual to conduct metabolic studies on animals. In some cases, it is advantageous to know what becomes of a chemical during the process of metabolism. The toxicologist can frequently establish that a material is rendered innocuous and efficiently eliminated by various excretory mechanisms. The effects of chemicals, when taken by mouth, are observed in the laboratory by feeding graded amounts to animals. The dose which proves lethal to 50% of the animals fed is used as a measure of relative acute toxicity. This amount is known as the LD_{50}.

Chronic feeding studies are conducted to determine the effect of ingesting small amounts of materials over extended periods of time. This procedure allows the toxicologist to establish no-effect levels as well as levels which elicit toxic signs and symptoms. This information is useful in evaluating a chemical for use as a food additive, for establishing residue tolerances for agricultural chemicals, and in evaluation of industrial hazards.

Basically, the toxicologist will assume that if a given material elicits a specific effect in test animals it is probable that it will do likewise in man. The seriousness of this effect will guide his choice of safety factors. In this regard, the experience of the toxicologist is invaluable.

Using Toxicological Information

As an example of how toxicological information is used, it is of particular interest to follow the thinking of the toxicologist in evaluating the appropriateness of a solvent material for a rather specific use. The term "bucket solvent" refers to an organic chemical used in small containers for the manual cleaning of metal parts, floors, and all sorts of objects. The containers may be buckets, cans. or small tanks, and the usual quantities of the solvent range from several quarts to several gallons. We have probably all used "bucket solvents" in our own homes.

This example is chosen because of its obvious universal use, and because normal use assumes gross exposure to the liquid and vapors. For such use, the toxicologist would prescribe the ideal solvent—a colorless, odorless, nonflammable, nonirritating, nontoxic material posing no handling hazard whatsoever. No such organic chemical exists. It is recognized that many different substances may be used for miscellaneous cleaning purposes. The factors of cost, flammability, cleaning performance, and volatility tend to limit the choice to certain aromatic hydrocarbons, benzene, toluene, and xylene, to certain petroleum fractions such as Stoddard solvent and to the chlorinated aliphatic hydrocarbons, carbon tetrachloride, tetrachloroethylene, trichloroethylene, methylene chloride, and 1,1,1-trichloroethane. These solvents are all readily available for use.

Let us consider the various hazards. What about ingestion? All of these solvents would be considered to have low acute oral toxicities; that is, their LD_{50} values are in the range of several grams per kilogram of body weight. There should be no problem from ingestion incidental to the use of solvents. There is little need to differentiate between common solvents in this regard, although there are significant differences between them. Harmful effects can result only from willful or accidental swallowing. Workmen have been known to drink solvents for the intoxicating effects and children have accidentally swallowed them. With all organic solvents, it is readily possible to swallow sufficient amounts to produce serious systemic injury, even death. All should be stored in clearly labeled, appropriate containers, not "coke bottles," and stored *out of reach of small children*. Workmen should be made to understand that solvents are not substitutes for ethyl alcohol.

What about eye irritation incidental to use of a "bucket solvent"? Here again, there is probably no real need to differentiate between them. They are all capable of producing local irritation, particularly to the conjunctiva, but prolonged or permanent effects are not likely. Owing to the unique character and importance of the eye, it is desirable to protect against all foreign substances. Minimal eye protection or safety glasses, if you wish, should certainly provide ample safety measure for most operations.

When it comes to skin contact, it is virtually impossible to find a substance which does not have some adverse effects. All of the effective organic solvents extract natural fats and render the skin dry in appearance and feeling. Repeated exposure may result in inflammation, scaling, fissuring, and some may even burn. Solvents such as xylene, and orthodichlorobenzene may produce an irritation upon relatively short contact. Some materials, particularly crude petroleum fractions, may cause acne-form dermatitis.

The recommendation for all "bucket solvents" is that measures be taken to avoid prolonged and repeated contact with the skin. It is recognized that short, infrequent contacts may not be harmful. For many solvents, there are gloves and protective garments which are sufficiently impervious to afford protection where excessive contact cannot be avoided.

A candidate for use as a "bucket solvent" must not have a high toxicity by absorption through the skin. It should be sufficiently low in toxicity that occasional contacts are not harmful, even though they may be extensive and somewhat prolonged. Some of these common materials with which we are concerned meet this qualification.

The hazard from vapor inhalation is the most important problem in the use of a "bucket solvent." Consider a bad actor, carbon tetrachloride. "Carbon tet" can be tolerated at a level ranging up to 25 p.p.m. in the atmosphere. One can expect minimal effects from single exposures to 50 to 300 p.p.m. and serious effects from exposures of $\frac{1}{2}$ hour to 8 hours at concentrations from 300 to 1000 p.p.m. This latter condition may well prove fatal and can be anticipated in the use of "carbon tet." Benzene and carbon disulfide generally fall into this same category.

At the other end of the gamut, we find 1,1,1-trichloroethane. It can be tolerated without effect for prolonged and repeated exposure at concentrations up to 500 p.p.m. Single exposures having minimal effects range from about 700 to 1000 p.p.m. Serious effects may be expected from exposures of $\frac{1}{2}$ hour to 8 hours at concentration of the order of 5000 p.p.m. Atmospheric concentrations exceeding 500 p.p.m. would be unlikely in the use of 1,1,1-trichloroethane as a "bucket solvent" where reasonable natural or artificial ventilation is present.

In the evaluation of hazards in the examples cited above, it is important to consider the toxicological consequences of overexposure, as well as the concentration which produces them. "Carbon tet" produces anesthesia and nausea as well as severe liver and kidney injury. 1,1,1-Trichloroethane, on the other hand, produces anesthesia, but is not likely to cause appreciable organic injury. If a workman were to be overcome from the vapors of "carbon tet," he might recover from the anesthesia but likely not from the organic injury. In a parallel case of 1,1,1-trichloroethane, about all he would need would be a few minutes in fresh air. His recovery, likely, would be complete and uneventful.

The other solvents, except for benzene, which is highly toxic, fall somewhere between carbon tetrachloride and 1,1,1-trichloroethane in suitability for use as a "bucket solvent."

Threshold Limits

On the subject of air-borne contaminants, published MACs—maximum allowable concentrations—are frequently misunderstood and misused. Most environmental measurements are concerned with the amount of material that is being breathed. This is a major industrial problem because one of the easies, ways to become overexposed to a chemical in a work environment is by inhalation. The acceptable exposure by inhalation in the case of vapors is usually expressed as parts per million by volume of air and particulate matter, such as mists and dusts, as milligrams per cubic meter. There are several ways of arriving at this value. It may be a result of careful toxicological evaluation with animals; it may represent measurements actually made in a work environment which was known to represent acceptable or barely acceptable exposures. In still another case, the MAC or Threshold Limit may have been chosen on the basis of similarity in chemical structure with an already established material. Sometimes the figure may have been chosen as one which would be necessary in order to avoid real systemic injury or, on the other hand, the control may be aimed at avoiding unpleasant or painful exposure. In some cases, safety factors are built into the control figure, while in other cases the figure may represent the actual concentration which barely avoids injury. There is no standardized procedure or method for arriving at a maximum allowable concentration.

If one is to compare toxicity of materials, he must not overlook differences in consequences of overexposure. Suppose that 100 p.p.m. of material "A" represents the control necessary to avoid headache or dizziness whereas the 200 p.p.m. required for control for chemical "B" is designed to avoid serious liver injury. The dangers of comparing the materials on the basis of suggested control figures become obvious. At best, MAC values serve only as guides for controlling environmental health hazards. If one always stays below the quoted figure, it is unlikely that injury will occur.

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