ENVIRONMENTAL HEALTH CONSIDERATIONS

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I. Background

Man has used chemicals since the beginning of recorded history. Among the first were pigments used for decoration, followed by the development of metals for use as weapons, containers and religious decorations. With these chemicals, and others that followed, has come first the presence and later the recognition of disease entities associated with excessive exposure, whether from their manufacture, use, or disposal.

Toxicity from lead, one of the first of such recognized diseases, was initially described by a Greek physician in the second century B.C. Pliny in the first century A.D. described lung disease associated with the use of asbestos fibers to make fireproof tablecloths as "the disease of slaves." The potential political utility of chemical toxins was first recognized in the same period with the popularization of criminal poisonings.

Within our most recent decades we have been made acutely aware of the toxic potential of chemicals in our environment by such natural and man-made disasters as Yusho (1968), Seveso (1976), Bhopal (1984), and Lake Nyos (1986). Such disasters have added new terms to our toxicology lexicon - terms such as the Minamata Bay Disease (mercury poisoning), Yusho Disease (PCB poisoning) and "superfund sites" to name but three.

While disease association with large, well-defined chemical exposures at relatively high doses is often very clear cut, making such associations under other conditions may be extremely difficult. This inherent difficulty arises from a number of basic scientific difficulties which need to be discussed in order to put our limited human health data base into perspective. For a small group and a limited event, it may be clear which individuals received an exposure. However for very large groups, such as populations adjacent to chemical releases, it may not be clear that all individuals are exposed, let alone that they have exposures of equivalent magnitude. Thus, attempts to establish a relationship between a particular chemical exposure and any disease incidence in that population may be distorted by the inclusion of many individuals who were not, in fact, exposed. This effect is compounded by a second basic problem of defining cause-effect relationships in chemically induced illness, latency. Particularly for chemicals causing malignancy, either directly or as the result of indirect mechanisms such as the production of immunodeficiency, there may be a period of 20 years or longer between the exposure and the overt presentation of the disease. Thus exposed populations may need to be followed by medical surveillance for extended periods in order to ascertain a cause-effect relationship. In practice, cause-effect associations are often made retrospectively during the process of investigating clusters of disease.

Once there is evidence of a cause-effect relationship between a chemical and a particular disease, it becomes necessary to define the relationship between the amount of exposure (or dose) and either the frequency or severity of the resulting disease process. This process is hampered by the technical and practical difficulties of quantitating exposures. The scenarios of concern may involve either acute or chronic chemical exposures. However, for neither case is there usually relevant data which would allow, using modeling, even a crude estimate of total exposure. Sampling and analysis, if done at all, are usually done at discrete times and locations. Extrapolation to other sites and locations is difficult and problematic. Even when frequent or continuous monitoring data is available, such as in the occasional occupational setting, actual penetration into the body depends on such factors as age, sex, respiratory rate and volume, temperature, skin permeability and surface exposure, and chemical concentration in air or water. Recent attention has been directed at more individual estimates of exposure via the monitoring of urine or blood concentrations of chemicals or their biological degradation products or the use of personal exposure monitors.

Quantifying a dose-response relationship is further complicated by a well-recognized and accepted variability in individual response. All individuals do not respond in an identical manner to any particular chemical exposure, assuming that the exposure is not uniformly fatal. The relationship of exposure to response can often be roughly depicted by a sigmoid curve (Figure 1). Dose response relationships may also be confounded by the presence of other relevant variables and background. That is, we must distinguish the effects of a given chemical from similar or identical effects that may derive from other chemicals in the environment as well as from the frequency of the particular effect which may occur in a totally unexposed population. All of these effects contribute to the uncertainty that often surrounds both the qualitative and quantitative associations of a chemical with a disease.

With this background, what is the origin of the data on which health decisions are based in chemical exposure incidents? The limited data which does exist for most chemicals derives from three sources: animal experiments, occupational exposure data, and data from prior accidents.

For most chemicals in common commerce, animal toxicity data exists. Such data usually consists of the results of experiments designed to determine lethal dose (i.e., LD50, LD90 etc.) and experiments designed to determine long-term toxicity where small doses are administered in the diet for months to years. Most such data is accrued from rodent experiments. Clearly, there are major difficulties in using animal toxicity data to predict human toxicity. There are numerous well-recognized examples of the dramatic non-concordance of such data. Furthermore, the conditions of the usual animal experiments described above rarely mimic the more usual human exposure scenario where moderate but usually sublethal doses are encountered for relatively brief periods of time.

Likewise the occupational data, while having the advantage of being human, also suffers from the dissimilarity of the "design" with the usual exposure encountered as

part of a hazardous materials incident. That is, the data generally relates to the prevalence of a particular disease (e.g., cancer) in a worker population after many years of exposure to relatively low levels of chemical.

Finally, data from prior "accidents" with a chemical are often the most revealing in that the scenario is likely to be similar. Unfortunately, little of this data exists, or at least little is retrievable on an acute basis. Very few publications in the public health or medical literature provide systematic health data on victims of accidental chemical exposures. Generally this data is not collected in a usable format the time of the incident and even when collected is rarely published in an available format. There is an urgent need for the development of reporting data bases of health information from chemical exposure incidents - data bases which could readily be accessed by subsequent health care providers faced with similar exposures.

One proposal which might lead to easier reporting of health effects and which would produce data of great potential value in planning for hazardous materials disasters involves the simple categorization of chemical injuries into the following six categories: 1) no medical care required, 2) field first aid only, 3) emergency department or clinic care needed, 4) hospitalization required, 5) intensive or special care required, and 6) death. Such a system, while crude in terms of specific health information, provides precisely the information needed by health planners involved in the formulation of a chemical disaster response plan.

Given a relationship between a chemical and specific human toxic effects, it could be helpful to be able to calculate the risk of injury for any particular of exposure. Such calculations are termed risk analysis. As it is unlikely that sufficient human data exist to directly determine this risk over a range of exposures, these estimates must be calculated assuming a specific model of the quantitative dose-response relationship. The model often selected because of its known fit to much human and animal data is the probit model. This model assumes individual thresholds to response - that is, there is a dose below which an individual will not respond with the adverse effect - and that the distribution of these thresholds is gaussian when plotted against the log of exposure. Other models have also been proposed and used, particularly for low dose exposure to known human carcinogens, where it is often assumed that no threshold or safe exposure level may exist. The primary use of such models has been to predict cancer risk in populations exposed to human carcinogens. It should be remembered that all such models are designed for predictive use in large populations and have a high potential error when used on a small group.

II. Mechanisms of Toxic Injury

In a very general way chemicals can affect human tissues in three broad ways: structural damage to the tissue, interference with cell function, or alteration of genetic material within the cell. Any given chemical may act by more than one mechanism. It should also be noted that hazardous materials may also provide symptoms in the absence of any demonstrable evidence of tissue injury. Such psychogenic

symptoms may be both physical and psychological in nature and may impose a major stress on health resources at the time of a major disaster.

Structural damage to cells is usually the result of direct exposure of the tissue to the chemical at relatively high concentration. Such effects are well exemplified by the tissue destructive effects of strong acids and alkalis - capable of causing major injury when dermal, mucosal or ocular tissue are exposed for even brief periods of time. Similar effects may occur in the lung following the inhalation of corrosive gases such as chlorine.

Undoubtedly the most common general mechanism of toxicity involves the effect of chemicals on cellular function. Such effects can occur by a myriad of different routes which may lead to altered cell function, cell death, or cellular alteration. Effects on specific cell types may in turn lead to organ death or dysfunction. Well known examples of such injury would include the effects of chlorinated solvents such as carbon tetrachloride on the liver and the effect of the herbicide paraquat on the lung. Many other well- studied toxins have been shown to produce their clinical effect by way of specific changes induced within the cell. Chemicals known to be teratogenic - that is those which produce abnormalities in offspring if exposure occurs during fetal development - also work by altering the normal development of early cell types.

A relatively few chemicals are known to alter the genetic material in cells. Such chemicals are said to be mutagenic. Changes in the genetic make-up of cells can lead to abnormalities in offspring. Direct mutagenesis is also thought to be one of several mechanisms which may produce malignancy. Examples of chemicals in this last category would include the common solvent benzene and benz(a)pyrene. Radiation is also known to be mutagenic.

For some chemicals, toxicity is, in part, dependent on changes produced in the chemical by the body. That is, the chemical itself may be relatively non-toxic but the body is capable of converting the chemical into a much more potent toxin. This phenomenon is termed metabolic activation. For most chemicals, however, the body will convert these chemicals into less toxin and more water soluble products as part of the body's normal elimination processes.

Finally, we need to distinguish between the effects of a chemical following acute and chronic exposures. For many but not all chemicals, chronic (months to years) exposure will lead to some accumulation of the chemical or its metabolic products in body tissues. Some chemicals are eliminated from the body so rapidly that no significant accumulation occurs. The nature of exposure (acute versus chronic) is an important consideration in assessing toxic potential. For some toxins, particularly those where exposures tend to be low (e.g., environmental exposure to PCB's or dioxins), toxicity may only occur after prolonged exposure resulting in significant body burdens of toxin. For many chemicals the pattern of clinical toxic effects is different following acute and chronic exposures.

III. Clinical Toxicity

Exposure to chemicals may occur by a variety of routes following a chemical release (Figure II). Once exposed, chemicals can enter the body by a variety of routes. the most common routes in hazardous materials exposures are inhalation and dermal absorption. Occasionally accidents may lead to entry via ingestion, injection injury, or even absorption through the eye. Often multiple entry routes of exposure occur in the same victim. Once into the body, chemicals enter the circulation and reach all organs in the body to varying degrees. Which organs will exhibit significant damage is chemical dependent. Prediction of which organs will be target organs is problematic for any chemical and must be either empirically observed or extrapolated from chemical similarities to other chemicals whose toxicity is known. To some degree the target organs in an individual with a specific exposure are also individual specific. That is, while a specific chemical may be known to produce symptoms of brain, liver and kidney damage in humans, not all individuals, given a specific dose, will respond with the same pattern of injury - some may have evidence of brain damage alone while others may show only evidence of liver damage. The precise reasons for this variability of response are generally not known.

Inhalation represents the most common route of exposure to hazardous materials. Significant physical contact with a solid or liquid chemical which might lead to extensive dermal contact or ingestion is generally limited to those in very close proximity to an event. However, the airborne spread of a chemical as a true gas, mist, dust or fog may be quite extensive, leading to the potential exposure of large populations located some distance from the initial event. Such exposures may involve both dermal and ocular exposures to the chemical as well as inhalation, although the latter route almost always accounts for the overwhelming quantitative portion of the exposure.

The nature and degree of pulmonary injury from an inhalation exposure depends on many factors including: the chemical(s) involved and their concentrations, particle size if not a true gas, duration of exposure, temperature, respiratory rate and route of inhalation (oral or nasal) and any preexisting respiratory disease. Unless overwhelmed or bypassed by oral breathing, the upper respiratory tract is relatively efficient at removing large particles such as fogs and dusts. Smaller particles and true gases, however, may penetrate deep into the respiratory tract leading to more diffuse and generally more severe injury.

Absorption through the skin occurs with most chemicals, although for many it is a relatively slow process. Some chemicals, however, such as lipid soluble solvents, may be absorbed quite readily through the skin. It must also be remembered that in many hazardous materials events, individuals in close proximity to the site may suffer significant damage to the skin from physical trauma or burns. these injuries may negate the effectiveness of the skin as a barrier and may result in enhanced absorption of chemicals.

Direct ingestion of chemicals is uncommon in hazardous materials events although explosions and splashes may result in modest oral exposures. The possibility exists of large scale exposures via ingestion of domestic water systems which have

become contaminated by chemical run-off or ground water leaching caused by spills or releases. While many chemicals may have odors or tastes which will warn of their presence at very low concentrations, others may not. It may be necessary to rely on chemical analysis of suspect water supplies to confirm their freedom from chemical contamination. Fairly modest levels of chemicals in domestic water systems may lead to significant exposure because of relatively large volumes of water to which the average citizen is exposed and because of the high efficiency of absorption which occurs with most chemicals in the gastrointestinal tract. Exposure may also occur from the consumption of contaminated food supplies. While this is unlikely to be a major hazard for most chemical releases, some toxins such as radioactive strontium or PCB's may concentrate in the food chain.

Finally, an uncommon but potentially devastating route of exposure is the injection injury. Chemical is literally blasted into the tissue as the result of its release under high pressure in close proximity to the victim. Such injuries may result from explosions, ruptures or malfunctions of high pressure equipment. Injection of many chemicals in this manner leads to severe tissue injuries not infrequently resulting ultimately in the loss of the body part.

As mentioned above, chemicals are capable of damaging virtually any organ system in the body. The specific target organs will depend on the organs in which a particular chemical concentrates and the sensitivities of the particular tissues in that organ to damage. Not all chemicals damage all tissues. At sufficiently low concentrations, no tissues will be damaged by most chemicals.

Table 1 provides examples of chemicals known to cause injury to specific body tissues. These are examples and are by no means the only chemicals known to injure these tissues. These are examples and are by no means the only chemicals known to injure these tissues. Information of this type is extremely valuable to health care providers in determining what medical problems need to be anticipated following exposure to chemicals. It may prevent the unnecessary cost of needlessly monitoring organ systems which are not damaged by the chemical in question. In the case of a large disaster with multiple victims, it may also alert the medical system, allowing it to anticipate the resources which may be needed. Thus, if the chemical were chlorine gas, it could be anticipated that extensive pulmonary support resources would be needed.

It should also be noted that hazardous materials events may involve several chemicals. There is almost no data available on simultaneous human exposure to multiple chemicals. As a general rule the effects produced are assumed to be additive, although with some chemical combinations one might anticipate that synergistic effects could occur. This is a clear area where more research is urgently needed.

For large chemical releases, the potential hazard of secondary exposure via environmental contamination exists. This was mentioned above in the context of water pollution, but it may also occur if land surfaces are contaminated from

explosions or toxic clouds. Of particular risk under such circumstances are children who tend to have much greater exposures to soil contamination than do most adults.

IV. Prevention of Chemical injuries

There are four areas which can impact on the outcome of potential chemical injury: 1) measures to minimize exposure, 2) rapid and effective decontamination of victims, 3) rapid access to definitive medical care, and 4) advance planning.

Minimizing exposure can occur in a number of ways. Perhaps the most important is providing appropriate information for large populations in areas with potential exposure. While evacuations of such populations often would seem to be the appropriate solution, this is often not possible nor practical within the time contracts imposed by the spread of hazardous materials. For many chemicals, a safer alternative is to shelter-in-place such populations by providing information on closing off dwellings or workplaces until a cloud of toxic material has passed or dissipated. Either of these approaches require the ability to effectively communicate with this population. Minimizing the exposure of initial responders is also important, both to assure their safety, as well as to assure the effectiveness of their intervention. This requires recognizing the nature of the hazard, providing effective protective gear and hazard information for those in the danger zone and keeping non-essential personnel in a safe area.

TABLE 1. EXAMPLES OF CHEMICALS CAUSING SPECIFIC ORGAN INJURY

Organ	Chemical	Nature of Damage
1. Skin	mineral acids dioxins hydrocarbons	necrosis acne-like rash irritation
2. Eye	formaldehyde chlorine methyl alcohol	irritation burns blindness
3. Lung	asbestos chlorine organophosphate insecticide	fibrosis/cancer irritation/bronchitis pulmonary edema
4. Liver	carbon tetrachloride phosphorous	liver cell injury jaundice
5. Intestines	copper carbamate insecticides lead	vomiting diarrhea abdominal pains
6. Kidney	ethylene glycol diquat	kidney blockage kidney cell injury
7. Heart	carbon monoxide phosgene fluoride	irregular rhythm increased heart rate hypotension
8. Central Nervous System	hexachlorophene thallium carbon disulfide	seizures delirium coma
9. Peripheral nervous System	manganese hexane acrylonitrile	Parkinsonism -like condition muscle weakness loss of sensation
10. Blood	arsine benzene	anemia low white blood cell count malignancy
11. Immune System	dioxin/PCB's	immune deficiency

As discussed previously, one of the important variables in determining the amount of chemical to which one is exposed is the duration of exposure. For this reason, rapid and effective methods of removing the chemical (decontamination) from those exposed, particularly those with dermal or ocular exposures, can make the difference between minimal or serious injury. Clearly advance preparation and training of responders at all levels, together with the availability of appropriate equipment and supplies is necessary for this to occur.

Of equal importance is the rapid availability of definitive medical care, usually at a civilian hospital facility. Rapid access to care requires the ready availability of appropriate transport services, usually ambulances with crews trained in the handling of chemically contaminated patients. Hospital facilities must have access to staff trained in basic life support as well as specialty areas, most notably pulmonary medicine. The availability of intensive care services will be crucial for those few percent of victims who require this level of care. Hospital facilities must also be prepared to deal with chemically contaminated victims appropriately in order to avoid the further spread of toxins to staff or facilities.

Finally, as noted above, advance planning is crucial if injuries are to be minimized in a hazardous materials event. Planning must involve all participants in the response, particularly those with roles in the health delivery system. It is clear from many documented experiences that if involved units are not individually trained in their roles and not experienced in working together as an integrated response team, results, in terms of the prevention of morbidity and mortality, will be poor.

V. Summary

It is clear that chemical exposure in the context of hazardous material related events has the potential for major impacts on individual and public health. Optimal response to these events, when they occur, requires knowledge of the toxic effects to be anticipated from these chemicals under the conditions of the event, together with properly trained and equiped response units. In both the areas of toxicologic knowledge and of response capabilities, serious defects presently exist. Future efforts should be directed at improving the collection, organization and dissemination of information gained from hazardous materials events. There is also a serious need for improving integrated response capabilities, both within political jurisdictions and across jurisdictional lines.

VI. References

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