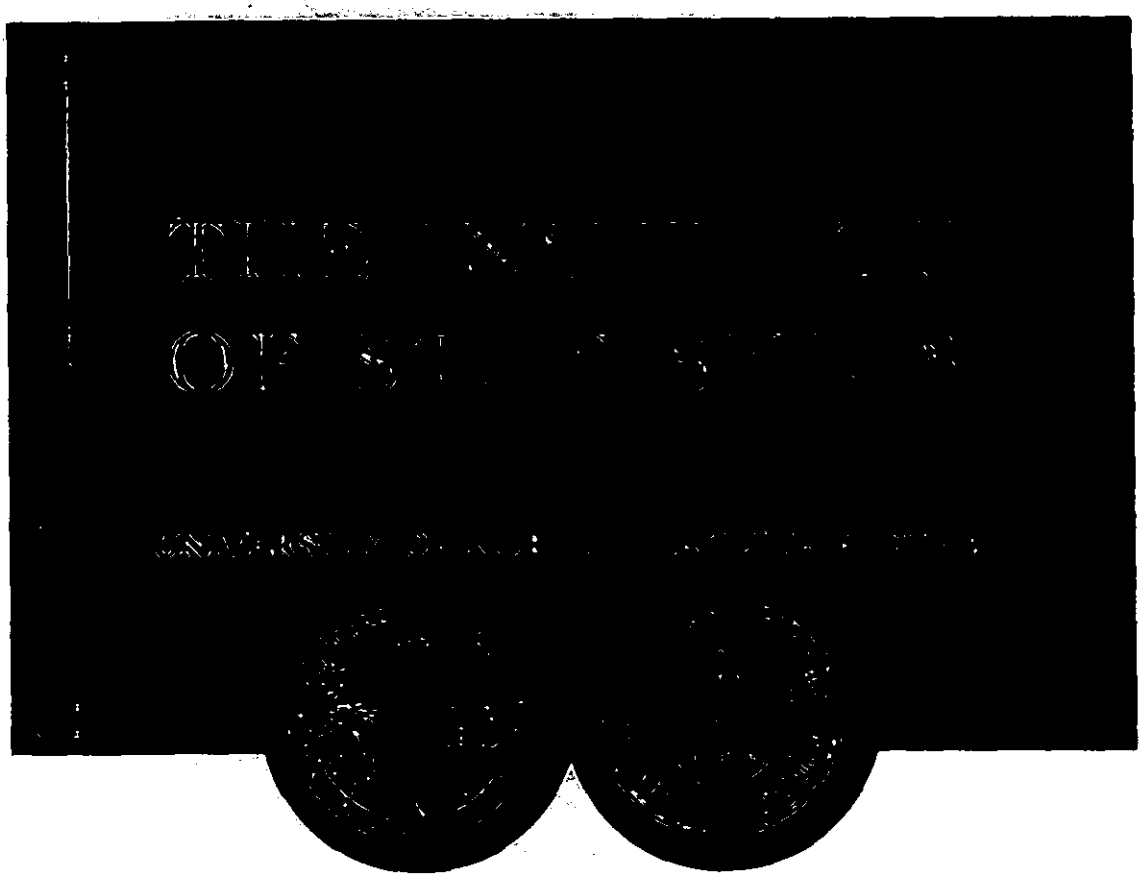

RISKS FROM UNDERGROUND PETROLEUM TANKS: REVIEW AND MODELING FRAMEWORK FOR DECISION-RELATED RISK ASSESSMENT

by

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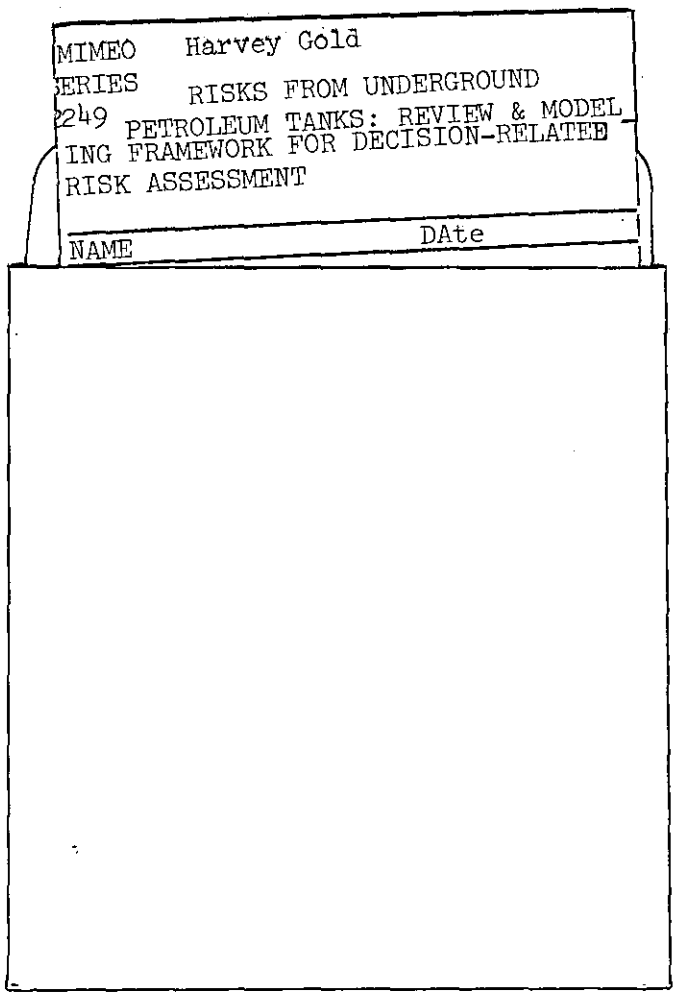
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RISKS FROM UNDERGROUND PETROLEUM TANKS – REVIEW AND MODELING FRAMEWORK FOR DECISION-RELATED RISK ASSESSMENT

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1. INTRODUCTION

The *specific* focus of this review is on the evaluation and management of health risks related to the contamination of groundwater from leaking underground petroleum storage tanks. More generally, this example is used to illustrate the complexity of environmental risk management, and to indicate needed interplay between knowledge and expertise from a variety of different disciplines.

A brief statement of the specific problem is that leaking underground tanks, in most cases designed to store petroleum fuels, are a major source of groundwater contamination. In North Carolina, for example, during the period of 1988-1989, 75% of the groundwater contamination incidents were due to leaking underground storage tanks, most of these involving petroleum products. Taylor (1989) quotes an EPA estimate that puts the number of underground tanks used to store petroleum and other hazardous substances between 2.5 and 3 million nationwide. He also quotes surveys which indicate that "up to 30% of the existing tanks leak."[1] The proportion of such tanks that are leaking is unfortunately subject to considerable uncertainty; Kostecki and Calabrese (1989) put the proportion at "up to" 60% . The likelihood of an existing tank leaking increases, of course, as the tank gets older. The overwhelming majority of these leaks involve petroleum fuels of some type.

When petroleum materials are introduced to the soil, they travel downward, eventually reaching the saturated or groundwater zone. The materials may subsequently be discovered to be contaminating well water (Figure 1). The petroleum components of most concern are benzene, ethyl-benzene, toluene and the xylenes (m-, o-, and p-). These are sometimes collectively referred to as the BTEX compounds. The compound of greatest concern from a health perspective is benzene, which has been shown to be a human carcinogen (see the report of Oak Ridge Nat'l Lab., 1989). The health risks discussed in this report will focus on the BTEX compounds, and in particular, on benzene.

Unfortunately, in many cases, by the time the leak has been discovered, the groundwater is already contaminated, and cleanup – if it is at all possible – is costly, uncertain, and takes many years. It has been argued by Bauman (1989), that in some cases it is doubtful if the cleanup can be completed before the offending materials would have been degraded by naturally occurring bacteria.

Evaluation of the health risk associated with a given leak is often subject to considerable uncertainty. A partial list of the uncertainties includes uncertainty as to: amount, spatial distribution and timing of the leak; rate of flow first through the unsaturated zone and then through the groundwater zone; amount, duration and type of groundwater use, which leads to human exposure; the toxicological dose-response relationship. In addition, there are uncertainties connected with the

[1] Unfortunately, Taylor neither cites the source nor explains what "up to 30%" means.

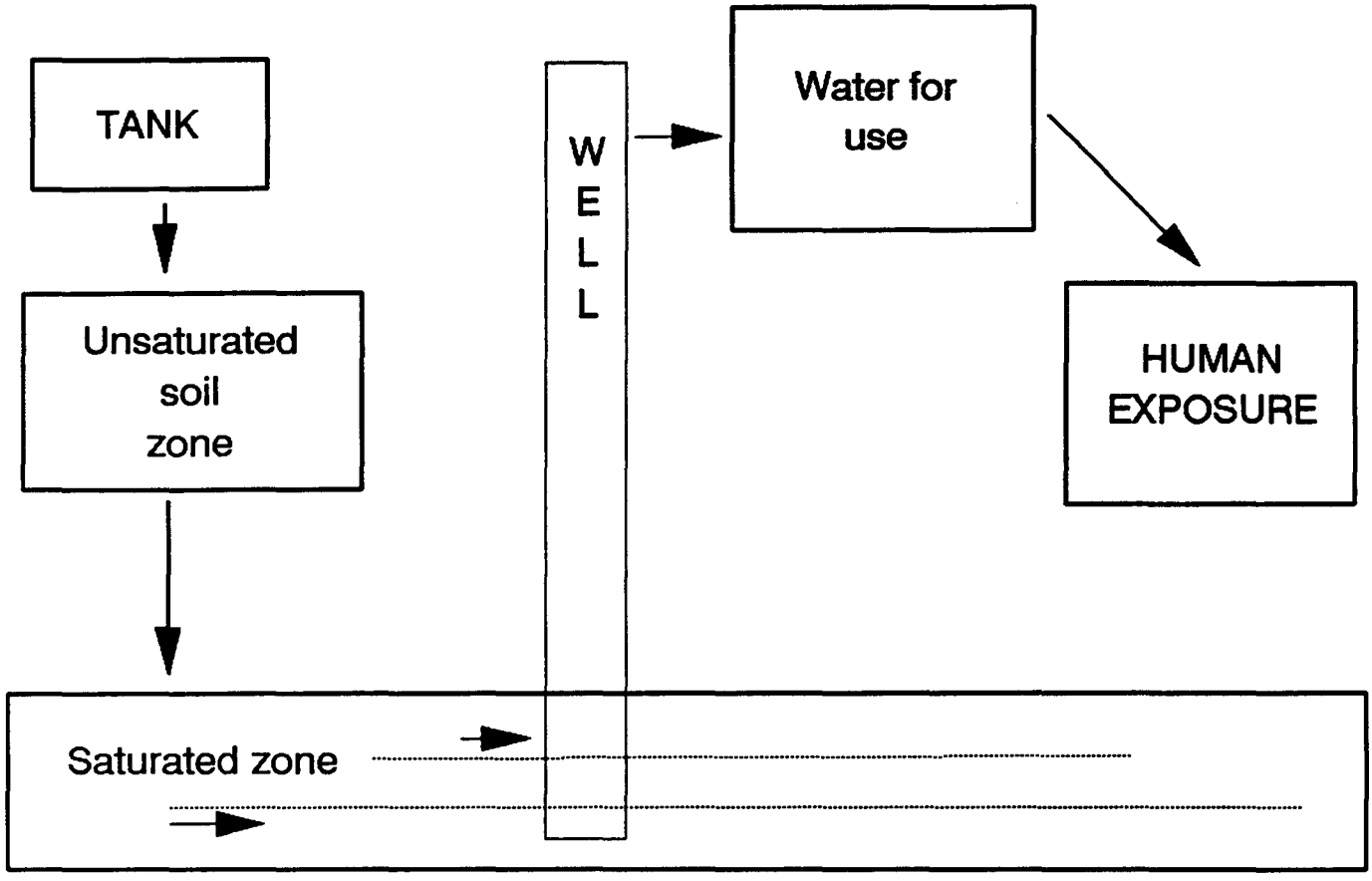

Figure 1. Flow diagram for petroleum pollutants from leaking storage tank.

efficacy and cost of remediation methods, as well as with evaluation of the health risks associated with those methods.

The cost of remediation of a given site may run into the hundreds of thousands of dollars. This certainly warrants a careful consideration of the uncertainties surrounding the remediation decision so as to ensure, as best as we are able, that the money is being spent wisely. Even more pressing is that policies that mandate certain standards and procedures involve expenditure of billions of dollars nationwide. Critical questions are:

- Are the money and other resources being used as effectively as possible, given the uncertainties?
- Could these resources, or a portion of them, be more effective in protecting public health and the environment if used elsewhere – or, alternatively, are we not spending enough on this problem?
- What new information (which is used to *reduce* uncertainty) might most effectively increase the quality of decisions on these issues.

This report is intended to develop a framework for probabilistic risk assessment applied to this problem, and for using such an assessment as a basis for decision making, within a decision analytic framework. We begin by describing, in general terms, the physical/biological system suggested by Figure 1, and considering the approaches used to model each of the subsystems and processes. In doing so, we highlight factors which are candidates for major sources of uncertainty in the health risk evaluation. We then describe the idea of probabilistic risk assessment in general terms, and examine how the approaches might usefully be applied to the LST (*l*eaking *s*torage *t*ank) problem. It becomes necessary to carefully examine the concept of *uncertainty*, how to formulate it in different contexts, and how to combine uncertainties that are traceable to variability in the receptor population, to lack of knowledge of parameter values or to lack of knowledge of underlying mechanisms. In considering how best to use information to deal with the uncertainties, it is necessary to examine approaches for combining information that arises from statistical data sets, from models of underlying physical and biological processes, and from subjective expert evaluation.

The physical system diagramed in Figure 1 is expressed as an aggregated component diagram in Figure 2. The diagram shows three inputs: the petroleum itself, precipitation (instrumental in carrying pollutant to the saturated zone), and groundwater flow into the area of contamination. The

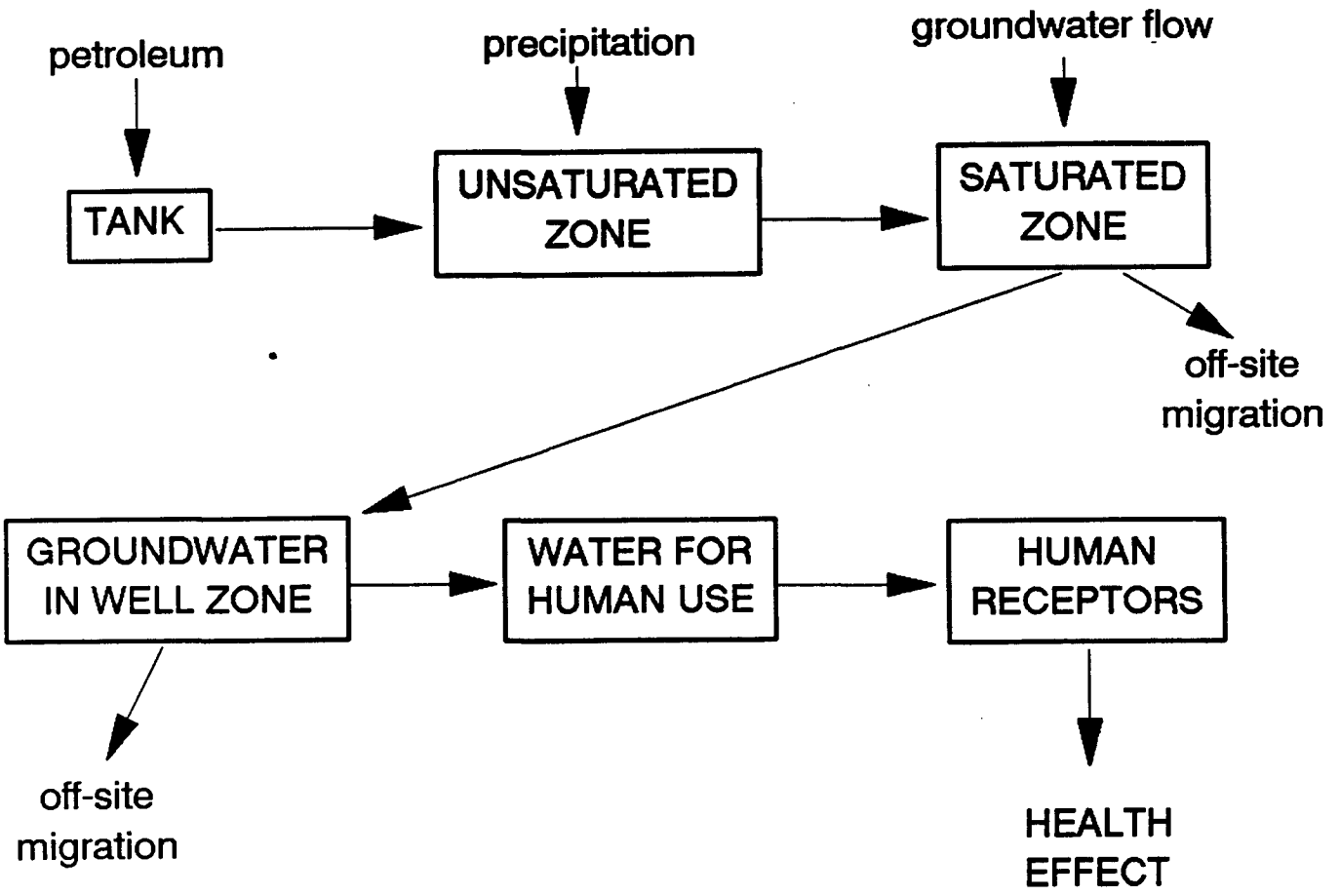

Figure 2. Aggregated component diagram for LUST risk assessment.

outputs *of interest* are the health effects, principally cancer initiations, traceable to the petroleum constituents.

Figure 3 shows an *influence diagram* perspective, which will be used to guide the modeling of probabilistic relations. Each of the rounded boxes in this diagram represents a random variable or vector of random variables. We may have some knowledge about each of these variables[2], but lack completely definitive information. We may express our knowledge (or uncertainty) about their values through the use of probability distributions. An arrow into a random variable implies that the variable at the head of the arrow is stochastically dependent upon the variable at the tail. That is, any knowledge of the variable at the tail will affect the probability distribution assigned to the variable at the head of the arrow.

As indicated in the lower right of the diagram, management decisions will be made on the basis of projected effects on cost as well as on the health effects. Monetary costs associated with health effects are treated separately from non-monetary considerations.

In addition to random variables, the diagram contains a rectangle with squared edges, which represents the decision taken as to remediation actions. As shown, this decision influences both the total monetary costs and the health effects by means of effect on the concentration of contaminants in the water supply.

2. DESCRIPTION OF THE PHYSICAL SYSTEM

Figures 2 and 3 suggest that descriptions of relevant characteristics of the system depend on a variety of disciplines:

Engineering - tendency of tanks to leak.

Hydrogeology - aquifer structure and movement of water and contaminants.

Demography and population behavior - pattern of expected urban/industrial development and of water use and consequent exposure to contaminants.

Toxicology - relation between individual exposure and health effects.

Public health - burden on health delivery systems and associated health care costs.

[2]Use of test information will be discussed later.

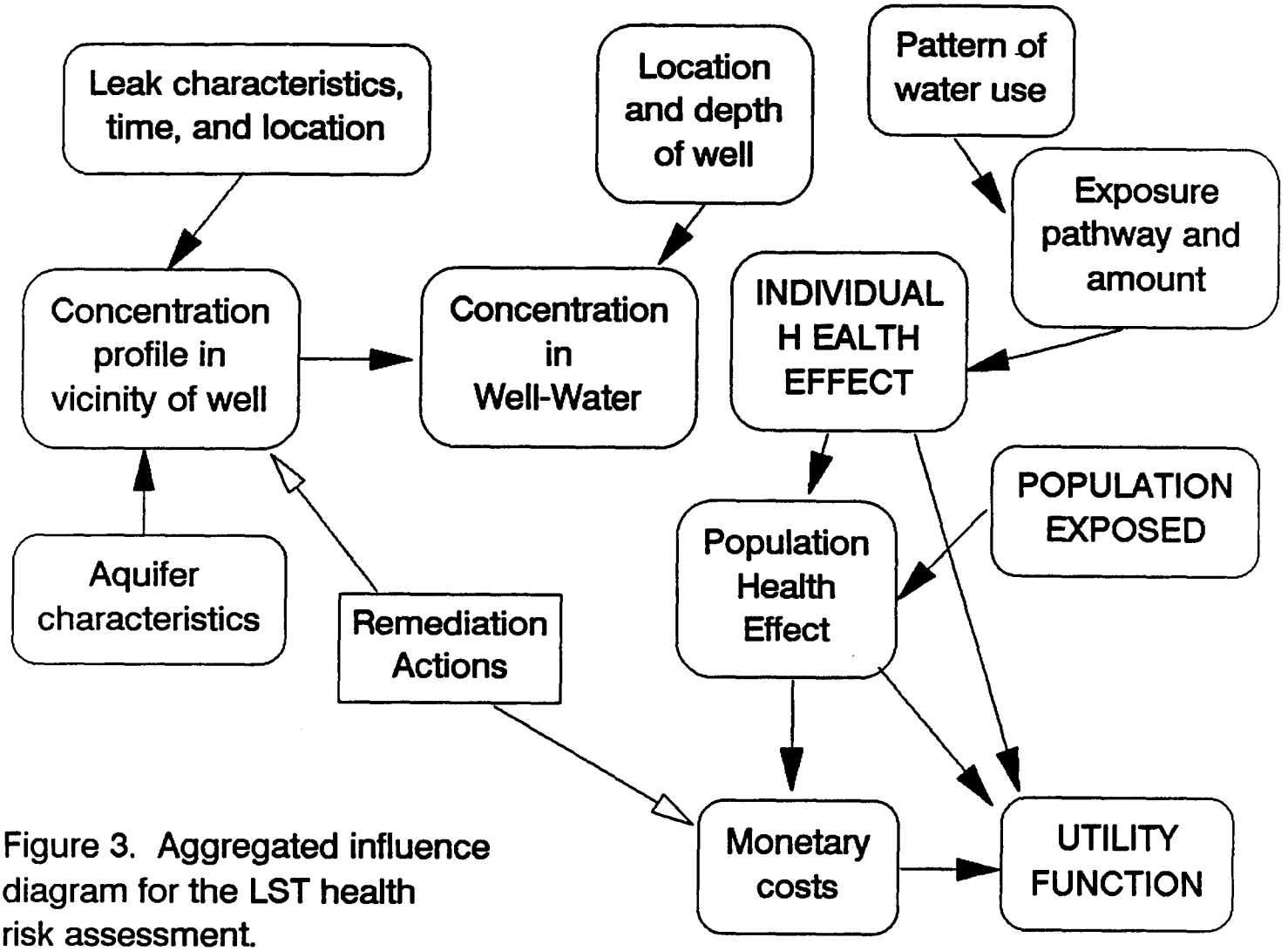

Figure 3. Aggregated influence diagram for the LST health risk assessment.

2.1. Tank failure and leakage.

Some relevant questions are:

- Where are leaks likely to occur (pipe connections, tank seams, top vs. bottom or side)?
- What is the likelihood of many small leaks vs. a few large ones?
- What are the likelihoods of various types of leaks as function of time and age of tank?

The answers to these questions will depend upon tank construction, soil redox potential and pH, moisture conditions. The answers are important for two reasons. First, in making risk based "run/replace" decisions in individual situations. Second, for the consideration of risk from an actual or suspected leak, the position and type of leak is important in determining the amount and spatial distribution of material leaked from the tank. Since amount and distribution of the leaked material is not readily observable with accuracy, consideration of these likelihoods is valuable input for formation of *prior* probability distributions which can increase the power and usefulness of test observations.

O'Brien (1988) discusses the construction of detailed fault-tree analysis conducted by EPA, which should be helpful in addressing these questions. Figures given by Haney (1989) indicate that of 174 cases in Arizona for which cause of leak was identified, 54% were associated with the piping (mainly loose seals and faulty installation), 36% were associated with tank failure (mainly corrosion), and about 10% were due to spills or overflows.

2.2. Migration and distribution through the unsaturated soil zone.

Normally, the non-gaseous fluid component of soil is aqueous. Non-aqueous liquids are foreign to the normal soil environment. Petroleum introduced into the soil from the tank enters the soil as *nonaqueous phase liquid (NAPL).*

As the petroleum enters the soil it tends to migrate downward through the unsaturated soil zone, under the combined influence of gravitational and capillary forces. In migrating through the soil pores, the NAPL will tend to displace loosely held pore water in the larger pores (but not the more tightly held water which wets the soil particles), and also to become sorbed to soil particles. The qualitative pattern of migration will depend upon: a) density of the NAPL; b) quantity and rate of introduction of the NAPL (large "instantaneous" spill *vs.* slow leak); and c) the soil pore structure (see, for example, Domenico and Schwartz, 1990; Dragun, 1988; Farmer, 1983). The following discussion will be limited to light hydrocarbons (density less than water) released over a period of time from a leak.

The pattern will depend upon the existence of soil *macro*pores or channels, which will allow the NAPL to migrate downward. If they are available, the liquid will flow downward primarily through the macropores, possibly in a dendritic pattern (Figure 4), as long as sufficient liquid is available to maintain a continuous flow. As Farmer (1983) points out, however, when further source material is no longer available, the stream looses continuity and forms into discontinuous droplets, or "blobs", with insufficient energy to deform so as to pass through adjacent smaller pores (see Mayer and Miller, 1992 for a discussion of dependence of this phenomenon on pore characteristics). This mechanism appears to be far more important in retaining hydrocarbons than other mechanisms such as sorption. Dragun (1988) points out that this *residual saturation* can remain in the soil in this state "for years". For small leaks taking place over a short period of time, all of the material will be converted into residual saturation. For somewhat larger quantities, the material will continue downward until encountering the capillary fringe. From there it may continue downward through larger pores not filled with water, and also spread laterally under the influence of capillary forces, until it is converted into residual saturation. It is interesting that the lateral spread of NAPL near the top of the capillary fringe is expected to be faster than near the groundwater level because *relative* permeability is less near the groundwater level. Still larger amounts of oil will form a "pancake" layer at the top of the water table; as the amount of material increases, the capillary fringe will be collapsed, and the groundwater level will be depressed under its weight (Figure 4).

In the absence of macropores, the NAPL will begin to spread laterally, saturating an oval shaped volume of soil, until it finds macropores (or creates a network of macropores), at which time relatively rapid downward migration will occur. This pattern is shown in Figure 5.

Lateral migration of the "pancake" will in general be in the direction of the hydrostatic head gradient. The rate of migration will be slowed by the capillary water, but will continue until a discharge area is reached or until all of the NAPL is converted to residual saturation or becomes dissolved in the groundwater.

Fluctuations in the water table have a substantial effect in allowing the floating NAPL in the "pancake layer" to come into contact with previously uncontaminated soil. As pointed out by Farmer (1983) and also by Domenico and Schwartz (1990), fluctuations either up or down will lead to transfer of material from the liquid mobile phase to that trapped as residual saturation. Fluctuations in the water table would also be expected to increase the amount dissolved in the ground water.

While the residual saturation can remain in undisturbed soil indefinitely, a portion (but not all) can be displaced downward by infiltrated percolating water (Farmer 1983).

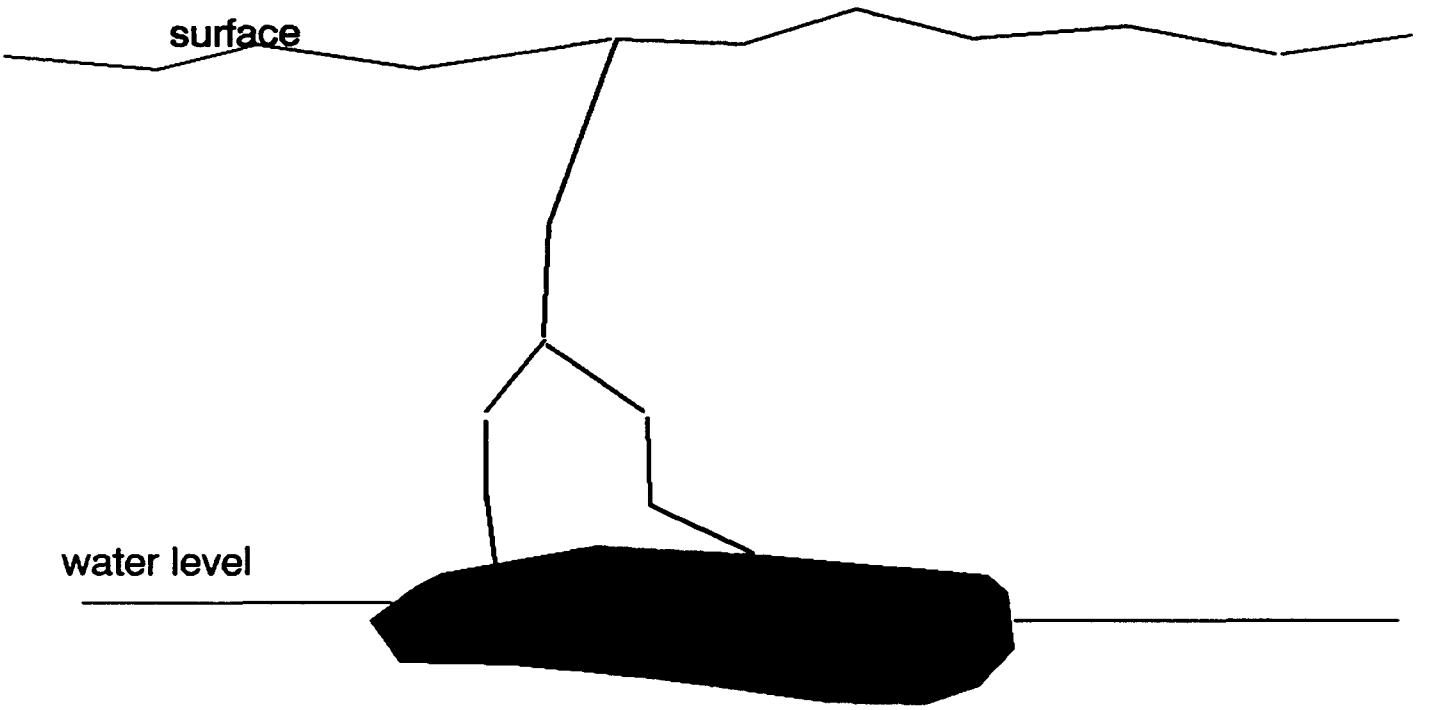

Figure 4. Light hydrocarbon pattern from slow leak into soil macropores. (Adapted from Dragun 1988).

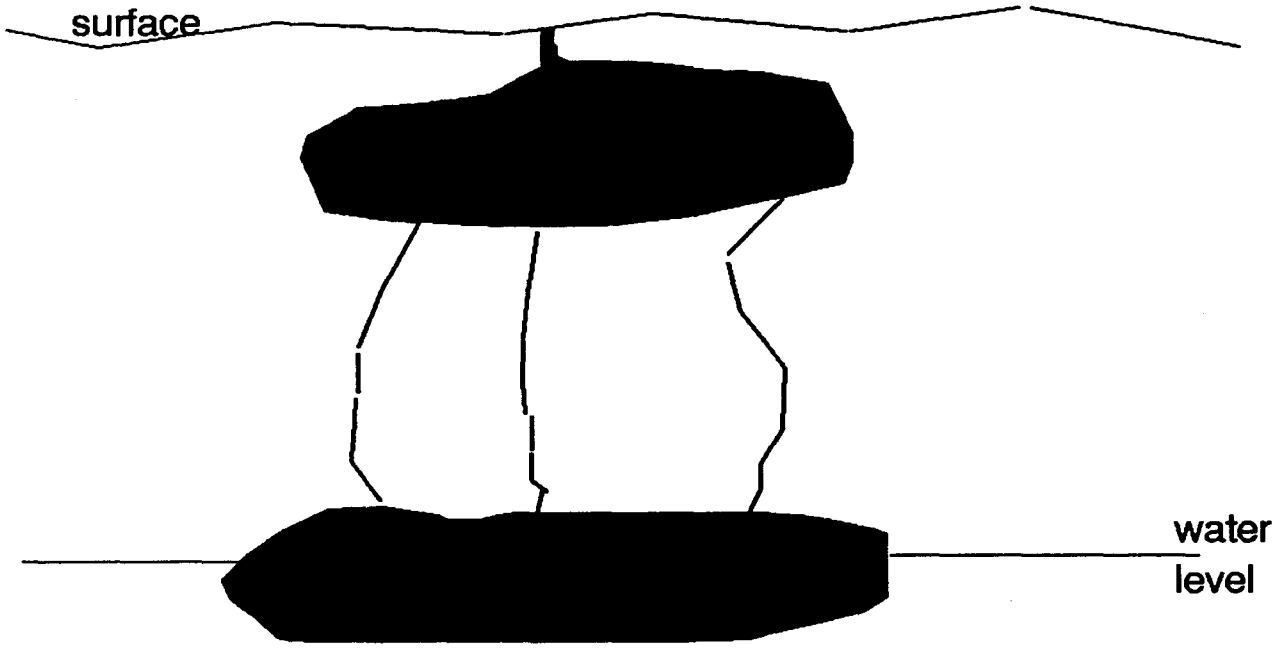

Fig. 5. Light bulk hydrocarbon pattern from slow leak into micropores. (Adapted from Dragun, 1988)

2.3. Dissolution of Petroleum Hydrocarbons into the groundwater.

Hydrocarbons are only sparingly soluble in water. While this might at first be regarded as a helpful circumstance, in fact it is the reverse for two reasons. First, even very small quantities of certain petroleum components will render water undrinkable either because of toxic effects or because of taste and odor. Second, the sparse solubility contributes to the persistence of petroleum contamination, once it is introduced to the soil environment.

Petroleum hydrocarbons may be introduced to the groundwater in several ways, depending upon the state of the hydrocarbon:

- Free NAPL.

This material may reach the groundwater slowly enough to go directly into solution in the groundwater. If a layer of free product is formed on top of the groundwater, then this material will dissolve from the NPAL-water interface. Farmer (1983) points out that since groundwater flow is associated with very little vertical mixing, downward dispersion relies primarily on diffusion. As a result, groundwater contamination would be expected to be greatest near the interface and to decrease downward.

- PH trapped in the vadose zone as residual saturation.

For hydrocarbons trapped as residual saturation in the vadose zone, the primary pathway is through displacement and dissolution by infiltrating precipitation, although this pathway might make limited contribution in urban situations, where the surface is paved.

A second pathway involves fluctuations in the water table. As the water table rises, this material is brought into direct contact with the water. As the water level fluctuates, material present as a floating pancake layer will be swept (up or down) through the soil and contribute residual saturation to previously unsaturated soil. The portion of the residual saturation trapped in soil pores below the water table would seem to be directly available for solubilization by groundwater flowing past. Dissolution would seem to be favored by the relatively high degree of surface area and by maintenance of high potential gradient between the trapped and adsorbed material and the aqueous phase by reason of the groundwater flow. Complications may arise, however, due to heterogeneity in the pore structure, and the possibility that the groundwater might flow *around* pores in which the hydrocarbon is trapped (Anderson, Johnson and Pankow, 1992).

A third mechanism, which has been shown to make a surprisingly large contribution, is vaporization and migration in the gas phase through the unsaturated zone (Mendoza and McAlary 1990; see also the discussion in Domenico and Schwartz 1990, p. 604).

2.4. Modeling the movement of Petroleum Hydrocarbons in the Soil

The nature of the physical and chemical mechanisms that govern the process of transport of petroleum hydrocarbons (PH's) through the unsaturated zone to the groundwater, and migration within the saturated zone are well understood, and a number of attempts to model these processes have been reported. A number of difficulties, however, interfere with attempts to model the process, including the large number of parameters needed and the high degree of site-specific idiosyncracy. These problems will be discussed later in this section, after discussing the way in which the physical mechanisms may be reflected in mathematical models.

2.4.1. *Modeling the Migration of Pollutant through the Unsaturated Zone.*

Bonazountas (1988) distinguishes between models based on a "traditional" differential equation formulation ("TDE" models) and compartmental models. The model of Abriola and Pinder (1985a and b) is an example of the TDE type of model. It represents each phase as a continuum. Within each phase, classical microscopic mass balance laws of continuum mechanics are used, and volume averaging techniques are used for describing behavior in a porous medium. Bonazountas discusses some of the drawbacks of TDE models, which include limitation on the number and type of processes that can be conveniently considered, difficulty of experimental verification, and difficulty of numerical solution. In addition, heterogeneity of the soil is extremely difficult to handle within the TDE framework, requiring use of spatially varying parameter values. Randomly placed discontinuities, such as macropores, present even more formidable difficulties.

The POSSM model (Brown and Silvers, 1986; Shields and Brown, 1989) is an example of a compartmental model. The soil column is divided into layers, each layer being treated as a compartment, governed by an overall balance equation,

$$\text{change} = \text{inflow} - \text{outflow} - \text{transformation/degradation}.$$

Parameters relating to moisture inflow and outflow are empirically determined, while transformation/degradation process are modeled as partial differential equations describing chemical migration and fate in the soil. Parameters of these are assumed uniform within each compartment.

Bonazountas (1988) lists a number of well documented models for dynamics of contaminant transport, including models which deal with the unsaturated zone. It seems clear, however, in the light of the difficulties noted above, that models at any reasonable and feasible level of detail cannot be expected to yield precise descriptions of the dynamics of flow and distribution of PH's in the vadose zone. It seems far more realistic to make do with an imprecise prediction, to evaluate the degree of imprecision, and, within the paradigm of decision analysis, to estimate the value, in a given situation, of trying to make the prediction more precise.

Another approach to modeling contaminant distribution in the vadose zone is discussed by Dragun (1988), who presents approximate formulas for the volume of soil needed to immobilize a given volume of hydrocarbon and for maximum depth of penetration. If one can assume that the distribution has reached equilibrium or steady state, such a description may be just what is needed to estimate the "source strength" for resupplying the groundwater with solute.

2.4.2. *Modeling the dissolution of Petroleum Hydrocarbons into the aqueous phase.*

Dissolution of soluble components of PH into the aqueous phase will take place either at the PH-water interface or, in the vadose zone, at the vapor phase-aqueous phase interface. Dissolution at the petroleum-water interface is discussed in detail by Pfannkuch (1984). He points out that four processes must be considered:

(1) diffusion of material dissolved in the NAPL phase to the interface (whether the NAPL is present as bulk material, say, floating on the groundwater surface, or as separated globules held as residual saturation);

(2) the dissolution reaction, in which molecules are released from the petroleum phase to the aqueous phase;

(3) diffusive transport of the material from the interface into the water;

(4) advective transport of water to the petroleum interface.

For a given interface, the rate of exchange may be empirically determined as a mass-exchange rate, k_m, which has units of amount transferred per unit time per unit of contact area. Pfannkuch cites separate sets of experiments which differ widely in the resulting values of k_m. Results appear to depend on whether the experiments are run in a porous medium or using free contact surfaces. If the experiments involve free contact surfaces, results appear to depend upon whether the phases are stagnant or flowing, and if flowing, how fast. Moreover, in applying the results to dissolution of hydrocarbons from petroleum trapped as residual saturation, the petroleum-water contact area is not easily determined.

Pfannkuch points out however that some degree of simplification may arise, since at the groundwater flow regimes normally encountered, the process is dominated by the equilibrium solubility, which presumably may be gauged by measures such as K_{ow}, the octanol-water partition coefficient. The problem of dependence on a largely unknown contact area remains, however.

Mendoza and McAlary (1990) have pointed out that for more volatile substances, the process of dissolution from the vapor phase may be important. Their simulation model for dissolution of trichloroethylene required the use of a number of context-dependent parameters, with regard to which the domain was assumed to be homogeneous:

bulk water content (unsaturated zone)

porosity (saturated and unsaturated zones)

effective diffusion coefficient (saturated and unsaturated zones)

longitudinal and transverse diffusivity (both zones)

retardation factors (both zones)

water table diffusion thickness.

It should be noted that Mendoza and McAlary do not appear to offer their model as a basis for prediction or description in specific cases, but rather as a basis for demonstrating that this often neglected process has the potential of being very important.

2.4.3. *Modeling migration in the groundwater.*

Principles governing migration of dissolved materials in groundwater, and their mathematical description, are discussed in detail by Domenico and Schwartz (1990). At least two processes must be considered: advection and dispersion, although some authors appear to include sorption and the resulting chromatographic effect (see below) as an important contributing factor (e.g., Fried, Munster and Zilliox, 1980).

Normally, advection is the dominant process. In this process, the dissolved material is simply carried with the moving water, at the same velocity as the water. Flow of the solute would then be described in terms of movement of a "plug" of uniform concentration.

Mathematically, in one dimension, the flux of a particular solute through a volume of porous medium, is given by

$$J = vCn,$$

where n is the porosity of the medium, C is concentration of the solute, and v is linear velocity of the

water through the pores. Velocity, v, is generally described using Darcy's equation. The form suggested by Domenico and Schwartz includes a correction for *effective* porosity n_e,

$$v = -\frac{K}{n_e}\frac{\partial h}{\partial l},$$

where K is hydraulic conductivity, and $\partial h/\partial l$ is the hydraulic gradient.

If advection were the only dispersive process, the boundary between contaminated water and uncontaminated water would be sharp. This boundary is made fuzzy by the process of diffusion. This process is responsible for a widening of the solute plume in the horizontal and vertical directions, and also for presence of solute in advance of the front predicted by pure advection. Fundamentally, the process of diffusion is caused by the random motion of solute molecules being superimposed on the moving frame of the solution. The random motion of the individual molecules leads to the net movement of molecules from regions of higher concentration to regions of lower concentration – that is, to net movement down the concentration gradient.

Classically, in one dimension, solute mass flux in a liquid medium is given by Fick's law,

$$J = -D\frac{\partial C}{\partial x},$$

where D is the "diffusion coefficient", whose magnitude depends upon mobility of the individual molecules in the solvent medium. In three dimensions, this becomes,

$$\mathbf{J} = -D \text{ grad } (C).$$

In a porous medium, the situation is considerably more complex. Two corrections are called for. First, as for the case of advective movement, we must correct for the fact that movement only takes place in the pores. Second, as demonstrated by Whitaker (1967), a correction is needed because in the irregular geometry of the porous medium, collision of solute molecules with pore walls hinders free diffusion. Whitaker refers to this as a *tortuosity* effect. The tortuosity effect, based on the "microscopic" phenomenon of molecular collision with pore walls, must then be averaged over a macroscopic volume in order to arrive at a description of solute movement in terms of observable phenomena. The result, as discussed by Domenico and Schwartz, is that in practice, models must rely on empirically determined *bulk* or *effective* diffusion coefficients.

An effect which may serve to selectively retard the movement of organic materials is the tendency to partition between the dissolved phase and organic material on the soil particle surfaces.

The extent to which a given chemical will be retarded will depend upon its relative solubility in water and the organic phase (which is related to the octanol/water partition coefficient), and on the soil organic content. As Dragun (1988) points out, the most common method for expressing the distribution between soil surface and water phase is the equilibrium ratio, $K_d = C_s/C_e$, where C_s and C_e are concentrations at the soil surface (per unit wt. of soil) and in the water phase, respectively. Experimentally it is found that variation between of K_d for a given chemical between soils can be reduced by normalizing for soil organic matter or soil organic carbon,

$$K_{om} = \frac{K_m}{om} \quad \text{and} \quad K_{oc} = \frac{K_c}{oc},$$

where *om* and *oc* are soil organic content and soil carbon content, respectively. Dragun presents experimentally determined values of these parameters for a variety of organic chemicals. Dragun (1988) and Domenico and Schwartz (1990) present mathematical formulations which relate the degree of retardation to soil porosity and the value of K_d. The approximate nature of such calculations is, however, highlighted by Dragun's statement that the equation "has been used successfully to estimate the velocity of organic chemicals, such as PCBs, dioxin and pesticides within a factor of two to three in relatively unstratified soils". The retardation may lead to a separation of constituents of the oil product. The mechanism is similar to that which underlies the analytical method of chromatography, and is thought to lead to a significant separation of oil constituents (e.g., Fried et al., 1980).

2.4.4. *Uncertainty and Variability in the Transport Process.*

As pointed out above, considerable difficulty surrounds any attempt to apply such models to the dynamic description of specific sites. To begin with, the system consists of four distinct phases and interfaces between them: solid (soil), aqueous, vapor, and NAPL. The modeling of even an idealized system requires specification of a large number of parameters describing the soil, the hydrocarbon, and their interaction (see, for example, Abriola and Pinder, 1985b). For realistic systems, modeling is made more complex by vertical non-uniformity as well as lateral heterogeneity of the soil. The soil structure is sufficiently complex, so as to be almost idiosyncratic, and, as pointed out by Hillel (1989), impossible to duplicate in the laboratory. Moreover, the petroleum is a complex mixture of well over a hundred compounds, and the composition of the NAPL will vary in both space and time due to varying rates of volatilization and dissolution, varying rates of chemical and biological degradation, and chromatographic separation.

In recent years, a number of workers have begun to address these problems through the construction of stochastic models (Kiefer, 1993; Zhang et al., 1993; McLaughlin et al., 1993). The question of using probability distributions (the result of such stochastic models) as a basis for management and decision making has been explicitly considered in a hydrogeologic context in a series of articles by Freeze and co-workers (Freeze et al., 1990; Massmann et al., 1991). An advantage of explicitly considering the uncertainties, and describing them with probability distributions, is that one can then design measurement and monitoring procedures that give the most valuable information for a specified level of effort. This point is elaborated on in detail by Freeze et al. (1992; see also Beven, 1993).

2.5. Biological Degradation.

A number of processes operate in the soil and groundwater environment to remove or degrade petroleum hydrocarbons. Chief among these is biodegradation. When petroleum hydrocarbons are introduced to a soil environment, there will generally be marked stimulation of microbial activity, as naturally occurring microorganisms use the organic compounds as an energy source. The oxidation process must, of course, be coupled with reduction of oxygen or other electron source, leading to the alteration of the soil redox potential. The stimulation of this degradative process as a remediation procedure will generally require resupplying the soil environment with oxygen as well as with other nutrients.

The process of biodegradation of organic chemicals in the soil is reviewed by Dragun (1988). Becker (1992) reviews biodegradation of gasoline components with particular reference to use of iron(III) as an electron acceptor.

The operation of these processes has lead to the assertion that motor fuels must be regarded as "nonpersistent" contaminants of soil (Bauman, 1989). Other research (for example, Barbaro et al., 1992) does not lead to so optimistic a conclusion. In any case, biodegradation of hydrocarbons is not an unmitigated blessing. While toxicity of the hydrocarbons may be reduced, the metabolic processes (see description of pathways in Dragun, 1988) produce products which may make use of the water undesirable because of odor or taste. Moreover, as discussed in detail by Schwille (1976), the reducing conditions induced lead to larger undesirable inorganic content, to persistence of organic substances causing unpleasant odors and tastes, and to an environment more congenial to the persistence of pathogenic and also nitrate reducing bacteria. These conditions would seem to argue for the artificial supply of oxygen.

Within reasonable ranges of concentration, the biodegradation of many organic chemicals seems to follow first-order kinetics (Dragun, 1988).

$$-\frac{dC}{dt} = kC,$$

where C is concentration. The problem in modeling biodegradation in a contaminated aquifer is that k depends upon a variety of factors, including:

- size and composition of the microorganism population;
- inhibitory effect of other chemicals present;
- acidity of the soil;
- oxygen concentration and the redox potential.

Each of the factors in this list is itself changed by the process. Growth of the microbial population, in particular, is generally described by the Monod hyperbolic rate law,

$$V = \frac{V_{\max} C}{K + C},$$

where V is the specific growth rate of the microorganism population, C is concentration of the organic material, and concentration of oxygen (or other electron acceptor) is implicitly assumed constant. A more general expression was used by Schafer and Kinzelbach (1992), assuming supplied oxygen to be the only electron acceptor,

$$V = V_{\max} \frac{C_{\mathrm{DOP}}}{K_a + C_{\mathrm{DOP}}} \frac{C_{\mathrm{DO}}}{K_b + C_{\mathrm{DO}}},$$

where DOP and DO stand for dissolved organic pollutant and dissolved oxygen, respectively.

Because of the difficulties involved, it is not uncommon to see models, such as that of Schafer and Kinzelbach, which are models of idealized prototype systems, intended for development of understanding of relevant relationships, rather for direct prediction and management of individual leak sites. Some recent models have been developed with incorporate both transport and biodegradation processes (for example, Dhawan et al., 1993).

2.6. Concentration of contaminant in well-water.

Concentration of contaminant in water entering the well will depend upon depth and length of the well screen, the vertical and horizontal concentration distributions of contaminant and the relative

flow velocity distribution over the length of the well screen. An exact solution to this problem is computationally formidable. A simplification (API, 1992) is to average the concentrations over a set of equally spaced vertical intervals.

3. TOXICOKINETICS: ABSORPTION OF THE "BTEX" COMPOUNDS

Following the sequence indicated in Figure 2, the next topic for discussion would seem to be an examination of patterns of water use, so that we might evaluate the ways in which water use leads to exposure to the volatile organic compounds of petroleum. However, in order to understand the relevance of various possible exposure pathways, it is necessary to understand how the substances are absorbed into the body. The severity of exposure to a toxicant may be measured in terms of the concentration in water or air, together with the duration of exposure and such parameters as breathing rate or volume of water ingested. The actual dose received by the body is also determined by the rate of penetration through the stomach and intestinal membranes for ingestion, through the lung for inhalation or through the skin for dermal absorption.

The general principles of the mechanisms by which toxic materials are absorbed and distributed through the body are discussed by Guthrie and Hodgson (1987a). They discuss four physical mechanisms whereby substances can cross membranes to enter the body:

- *Passive diffusion* which depends primarily on the miscibility of the xenobiotic with membrane lipid;
- *Filtration* by which small molecules may pass selectively through membrane pores;
- *Facilitated* and *active transport*, which depend upon special carrier mechanisms;
- *Endocytosis*, in which the membrane flows around the xenobiotic, "capturing" it.

For the compounds we are discussing, passive diffusion is likely to be the dominant mechanism. The rate of diffusion of a solute from dilute solution across a membrane can generally be approximated by the linear relation of Fick's law,

$$J = K\Delta C,$$

where J is the net flux across the membrane (mass/time per unit area), ΔC is the concentration difference across the membrane (mass per unit volume) and K is a proportionality constant (*permeability constant*) with dimensions of volume per unit time per unit area. In computing toxicant uptake, it is generally assumed that ΔC is equal to the concentration in the exposing medium (say, water or air). The total absorbed dose received during any period of time can be expressed as

$$D = J \times A \times T,$$

where A is membrane area and T is exposure time. Taking ΔC to be C, the concentration of the toxicant, we can then calculate the absorbed dose as

$$D = K \times C \times A \times T.$$

Ideally, one might hope to determine the permeability of a particular type of membrane from laboratory measurements, and perhaps to evaluate A from general physiological considerations. Then, using the exposure assessments discussed above to evaluate C and T, we would be able to estimate the total dose received. Indeed, such procedures are followed only in the case of estimation of dose from dermal absorption. The difficulties of estimating membrane permeability as well as area, and even exposure time to the relevant membranes, have lead to the practice instead of using empirically determined absorption efficiencies, as discussed below.

Note that the discussion in this section deals only with estimations of absorption from contaminated water. Other considerations are brought into play when considering ingestion of contaminated soil (deliberate or accidental) or dermal absorption from contaminated soil. These routes may be of importance in considering risks to children, or to workers involved in remediation.

3.1. Ingestion.

Until a few years ago, ingestion was thought to be the principle route of entry for contaminants in water. For a given compound, the absorbed dose is easily expressed, as

$$D_O = E_O \times C_W \times V_O,$$

where D_O is the absorbed oral dose, E_O is absorption efficiency, C_W the concentration in the water, and V_O the volume consumed. The BTEX compounds are generally accepted as being easily absorbed through the gastrointestinal tract. Shehata, for example, (1985) assumes 100% absorption for benzene, toluene and xylene, based on earlier EPA documents. Similarly, Jo et al. (1990) assume 100% absorption for ingested chloroform.

3.2. Inhalation.

In order for a volatile water contaminant to be absorbed through inhalation, it must first be volatilized. Conditions for volatilization include elevated temperature and running the water in such a way as to provide large surface area from which volatile material can escape. Cooking provides conditions of elevated temperature, as does use of hot water from the tap. Toilets customarily use water in such a way as to provide large surface area. Other uses provide both conditions – washing

machines and especially showers. As discussed below, bathroom environments provide confined spaces combined with conditions which lead to volatilization.

The dose absorbed through respiration may be expressed as (see, for example, Shehata, 1985),

$$D_r = E_r \times C_a \times V_r \times T$$

where E_r is the efficiency of absorption through the lung, C_a is concentration in the air respired, V_r is the volume of air respired, generally expressed as volume of air per unit time, and T is duration of exposure. Shehata quotes EPA documents indicating 50% absorption for benzene, 93% for toluene and 64% for xylene. Clearly we might expect some degree of individual variability in these figures. Such variations might conceivably be related to age and health state, as well as inherent, i.e., genetic differences.

With respect to V_r, the respiration rate, Shehata quotes National Academy of Sciences estimates of 8 m^3/day for children and 20 for adults. This number too is easily seen to be subject not only to uncertainty, but also to very broad individual differences depending on age and health state, and temporal differences depending upon degree of physical activity.

3.3. *Dermal Absorption.*

In the case of oral and respiratory absorption, the xenobiotic is absorbed across a membrane "designed" for efficient absorption. Skin, on the other hand is normally thought of as a barrier. Several routes however, are available for penetration, including movement through hair follicles and sweat ducts, as well diffusion through the stratum corneum (Guthrie and Hodgson, 1987a). Under normal conditions, Guthrie and Hodgson point out that direct movement through the stratum corneum is the dominant pathway for lipid soluble xenobiotics. However, skin lesions will enhance absorption.

Direct measurement of penetration efficiency is, for the most part, based on work with experimental animals. However, there are substantial differences in the penetration efficiency for different animals, and it is far from clear what animals are the most appropriate models for humans; indeed, it may depend upon the type of substance. Data quoted by Guthrie and Hodsgon for permeability to benzoic acid and acetylsalacylic acid show permeability for pigs, rats and humans to be substantially below that of mice. Other data indicate very wide variations depending upon anatomic site. Measurements quoted for permeability to hydrocortisone show permeability for the scrotum to be 42 times that of the forearm, while permeability for the foot is only 14% of the forearm.

A number of other factors are relevant. Guthrie and Hodgson point out that detergents can markedly increase penetration. Penetration is also increased by high temperatures. Finally, while many measurements of skin penetration for hydrocarbons have been made with the pure liquid hydrocarbon, absorption from dilute aqueous solution has been found to be much higher than from pure liquid, on a per unit concentration basis (Brown et al., 1984). All of these factors are relevant to the estimation of absorbed dose from domestic showers or baths.

Some authors have attempted to estimate the level of dermal absorption for volatile organic compounds directly from Fick's law in the form,

$$D_d = K_d \times C_w \times A \times T,$$

where K_d is the dermal permeability constant and A is the body area exposed. Brown et al. (1984) used literature values for K_d determined for toluene, ethylbenzene and xylene from direct exposure of a human hand to dilute aqueous solutions. Assumptions about body area exposure were: 80% for adult bathing; 75% for infant bathing; and 90% for children swimming. With these assumptions, they estimated the dermally absorbed dose for low concentrations of ethylbenzene and toluene to be about two to three times that from ingestion for adults who spend 15 min. per day bathing, about equal to the ingested dose for infants bathed for 15 min. per day, and about 10 times the ingested dose for children who spend 1 hr. per day swimming.

Brown et al. point out that a number of factors were neglected in these calculations. Some of the factors discussed are,

- *Temperature.* Increased temperatures will enhance absorption, so that amount absorbed during bathing is likely to be underestimated.
- *Skin condition.* Insults to the stratum corneum (sunburn, cuts, wounds, abrasions, skin disease) will increase absorption.
- *Anatomical region.* Permeability coefficients were based on measurements of hand absorption. Brown et al. cite studies indicating that the hand epidermis has lower permeability than many other regions of the body (Guthrie and Hodgson above also discuss these results).
- *Soaps and detergents* will substantially increase penetration.
- *Other routes of entry.* Brown, et al. cite other studies to indicate that other tissues which may be exposed during bathing or swimming – such as tissues of the mouth, nose and ear cavities – are especially permeable to lipophilic substances in aqueous solution.

Other authors have attempted to develop models from fundamental principles of mass transfer, that will predict skin permeability to specific compounds, using the compound's octanol-water partition coefficient and molecular weight (McKone and Howd, 1992).

Because of the difficulties in estimating dermal absorption based on the use of Fick's law, it is interesting to look at an experiment conducted by Jo, et al. (1990a), who tried to determine the relative proportions of chloroform absorbed in showering through inhalation vs. dermal absorption. Subjects were asked to shower normally, and separately to "shower" while clothed in rubber clothes and boots to avoid dermal contact. Relative degree of chloroform absorption was evaluated from concentrations of chloroform in the breaths of the subjects. The results indicated that the dose received by dermal absorption was approximately equal to that received through inhalation.

4. POPULATION DEVELOPMENT, LAND USE, AND CATEGORIES OF WATER USE.

It is not possible to define the risks associated with a given level of water contamination without first specifying the size and type of the population that will be using the water, together with the type and amount of use. Clearly, if the water isn't used, there is no risk. Moreover, if the argument of Baumann (1989) is accepted, that petroleum contamination is non-persistent, one may conclude that if the aquifer will not be used for an extended period of time, say 30 to 50 years, there is little risk from petroleum hydrocarbons.

If water that is currently being used from the aquifer is threatened by the petroleum contamination, then it will usually be possible, through monitoring and computational projections, to estimate the population exposure to toxic contaminants. However, in evaluating the risks associated with alternative courses of action as regards the contamination, possible *future* uses become relevant.

In considering the influence of land and water use on risk management and remediation decisions, one may take one of several alternative courses of action, which include:

- base decisions on current land use;
- base decisions on best estimate of future land use;
- base decisions on the assumption of the most sensitive use (see, for example, Kirkwood, 1985);
- base decisions on an evaluation of the suitability and probability distribution over the set of possible future uses (as might be done in a Bayesian risk analysis);
- regulate, so that land uses involving more than some threshold level of risk are proscribed.

Figure 6, based in part on the land use listing of Saft (1990) is intended to illustrate the kinds of land use and development patterns that might influence exposure and risk.

Estimates of the relative likelihoods and desirability of various types and densities of use for a particular parcel of land over a thirty year period must, of course, be regarded as highly uncertain and speculative. Among the factors that might influence relative likelihood of various alternative types of development are (see Saft, 1990):

- The demographic and economic description of the community.
- Historical and anticipated trends in the demography and economy of the community.
- Historical and anticipated trends in the demography and economy of the larger region.
- Topography of the site, which may determine the feasibility of various types of uses.
- Availability of similar type of property (e. g., lakeside property in an area in which there is much *vs.* little lakeside acreage).
- Existence of other development in the area which may be incompatible with certain uses (e.g., residential vs. industrial) or might lead to zoning restrictions.

It is clear that specific projections about use type and intensity for a given area of land are not usually to be relied upon. In keeping with the spirit of probabilistic risk assessment (see below), we would be interested not in specific projections, but in estimates of relative likelihoods. In particular, the seriousness of prohibiting a particular use, as measured by the *expected cost* of such a prohibition, would depend on the probability of that use in the absence of the prohibition.

Such estimates would of necessity have to rely heavily upon expert judgment, and would have to address the question of reliability of expert judgment and disagreement between experts.

5. EXPOSURE FROM WATER USE – EMPIRICAL INVESTIGATIONS

In 1977, the Safe Drinking Water Committee of the National Academy of Sciences recommended using a figure of 2 L/d for adult water consumption in estimating health risks associated with drinking water (National Academy of Sciences 1977). This figure was chosen as a relatively safe upper bound, and has been widely used. More recently, two types of results point to the need to revise risk assessments based on these figures. First, is the analysis by Roseberry and Burmaster (1992) of earlier reported data indicating that for the subjects studied, while mean total water intake may be about 2 L/d, *tap* water intake averaged only about 1.1 L/d. The remainder was water intrinsic in purchased foods. Second, are numerous findings that inhalation and dermal absorption may be as important or more important exposure pathways than ingestion.

RESIDENTIAL	Private homes; Apartments Mobile homes; Nursing homes	Drinking, Showering, Cooking
COMMERCIAL	Offices; Retail stores and malls Hotels; Restaurants	Drinking water, Restaurant use; Shower facilities
PUBLIC SERVICE	Government: Museums; Libraries Churches; Prisons; Hospitals	
RECREATIONAL	Health clubs; Sports facilities, stadiums; theaters; amusement parks	
INDUSTRIAL	Factories; Distribution centers; Warehouses; Research centers	Personal - drinking, showering, meals. Inudstrial Process - steam and vapor inhalation
AGRICULTURAL	Field Crops; Truck Crops; Poultry; Other Livestock	Personal use (empolyees) drinking, showering, meals

Figure 6. Illustrative breakdown of possible land uses and associated health-related water use (adapted from Saft, 1990).

5.1. Water consumption.

Roseberry and Burmaster (1992) report a re-analysis of data originally analyzed by Ershow and Cantor (1989). The analyses are based on an intensive Nationwide Food Consumption Survey, conducted by the U. S. Dept. of Agriculture during the period 1977-1978. Following Ershow and Cantor, water consumption was divided into two categories: (i) tap water intake, which includes direct consumption and water added to food during preparation; and (2) "intrinsic" water – water intrinsic in foods as purchased, including water added during commercial preparation. After dividing the data into age groups ($0-1$; $1-11$; $11-20$; $20-65$; over 65), Roseberry and Burmaster found that the data fit very well to lognormal distributions (R^2 values all in excess of 0.95). Median values for total intake and tap water intake are shown in Table 1. Of possible interest for our purposes, are figures presented by Ershow and Cantor indicating the fraction of tap water consumed directly or in the preparation of reconstituted juices and noncarbonated drinks. Assuming that at least for age groups above 1 year, this water is not heated, while other tapwater (used in coffee, tea, and other foods) is heated before use, one may expect a difference in the concentration of VOC's in the water as consumed. Table 1 includes the average fraction of water consumed without heating, based on this assumption.

Table 1. Estimated Median Values for Water Intake (taken from Roseberry and Burmaster, 1992) in L/d.

Age Group	total	tap	percent tap not heated
0 – 1	1.074	0.267	–
1 – 11	1.316	0.620	78.4
11 – 20	1.790	0.786	75.0
20 – 65	1.926	1.126	51.8
over 65	1.965	1.198	53.0

It seems reasonable that for risk estimation associated with contaminated well water, it is the tap water figure which is relevant. While the median value for tap water consumption is considerably less than the 2 L/d used by the NAS, larger values occur with non-negligible frequency; the 97.5 percentile for the over 65 group was 3.044 L/d. Roseberry and Burmaster report means and standard deviations for the lognormal distributions, as well as estimated quantiles.

5.2. Routes of exposure from tap water.

Shehata (1985) has pointed out that tap water provides an example of how a single source of contamination can contribute to all potential exposure routes – ingestion, inhalation and dermal absorption. It is clear that water used for preparation of beverages, especially cold beverages, contributes to ingestion. Water used for cooking and preparation of hot beverages may have lost some or most of its VOC content, which, however, contributes to contamination of indoor air. Other household contributions to VOC concentration in indoor air may come from:

- dishwashers and clothes washers;
- general kitchen use and cleaning;
- toilets;
- showers and baths.

Showers and baths provide especially "good" opportunities for inhalation exposure, since the subject is in close contact with hot water in a relatively confined space. Moreover, the individual will usually spend some time in the bathroom after the air has been loaded with volatiles by the shower or bath. Similarly, the toilet can make a smaller, yet significant, contribution to the bathroom air. Showers and baths also provide excellent opportunity for dermal exposure and absorption.

A few authors have estimated the relative importance of the three types of exposure to water contaminants. Shehata (1985) considered specifically the problem of gasoline contaminated water, and made estimates for the compounds benzene, toluene and xylene. Computations were made separately for children and adults, and were based on the assumption of a total house volume of 450 m^3, a bathroom volume of 11 m^3, showering or bath time of 15 minutes, and water consumption rate of 1 L/d for children and 2 L/d for adults. In estimating the volatilization characteristics, literature values for chlorobenzene were used because of similarity of Henry's Law constants. In computing the relative contribution of oral, inhalation and dermal exposure, Shehata added estimates of amounts that might be normally ingested with food[3], and for ambient air concentrations, which were taken to differ between urban and rural locations. Computations were made for water concentration ranging from 0 to 50 mg/L.

Shehata presents the most detailed results for exposure of children to benzene. Dermal absorption is negligible. When food and ambient air sources are subtracted from Shehata's results, so

[3]Shehata used the National Academy of Sciences estimate of consumption of benzene from food sources of 250 μg for adults and 207 μg for children.

as to focus on the contribution of the contaminated water, the results indicate that in summer, the exposure is approximately 20% from inhalation, 79% from ingestion and only about 1% from dermal absorption. In winter, inhalation exposure is substantially increased, so that it makes up about 30% of the total. Toluene and xylene have much greater dermal absorption rates, and therefore dermal absorption is calculated to be a make a much greater contribution, as shown in Table 2.

Table 2. Approximate percent relative contribution of exposure routes to a child's body burden from tap water (Rural location, summer). Taken from Shehata, 1985.

	Inhalation	Oral	Dermal
benzene	20	79	1
toluene	22	45	32
xylene	21	62	18

Considering all pathways, Shehata computed the concentration for each compound needed to reach the EPA recommended maximum body burden. Table 3 summarizes some of the results.

Table 3. Water Concentrations to Achieve EPA's Total Long Term Body Burden, in mg/L. (from Shehata, 1985).

	child	adult
benzene	0.0	0.08
toluene	0.15	0.12
xylene	0.4	0.9

These figures might be compared with the North Carolina standards for drinking water in mg/L: benzene – 0.001; toluene – 1.0; xylene – 0.4 (NC, 1989).

Other authors have examined importance of inhalation and dermal exposure to other types of VOC's in tap water. McKone (1987), in an investigation particularly of the inhalation pathway, used a more detailed model than that of Shehata, and also considered ranges for relevant variables. He estimated 24-hr. profiles for air concentration in the shower stall itself, in the bathroom and in the rest of the household for seven compounds: carbon tetrachloride, chloroform, ethylene dibromide, dibromochloropropane, trichloroethane, tetrachloroethylene and trichloroethylene. These compounds were selected because they had been detected in California water supplies. McKone's calculations give a range of the ratio of inhalation uptake of VOC's to ingestion intake of about 1.5 to 6. He quotes other studies indicating ratios of 1 and 2.6.

Jo et al. (1990a and b) report a series experiments in which they separated dermal from inhalation absorption of chloroform in showers, and concluded that they contribute about equally. They cite other studies indicating that dermal absorption of VOC's can be substantial, and a simulation study indicating that dermal absorption, inhalation and ingestion can be expected to contribute about equally for several VOC's.

Most of the investigations concerning exposure to VOC's from tap water refer to residential use. As Figure 6 indicates, however, there may be significant opportunity for exposure in the work place, and also in public facilities. Of course, oral exposure through drinking will have the same dependence on water concentration regardless of where the water is consumed; and dermal exposure in the shower should be about the same wherever the shower is taken. Based on residential calculations and measurements, we might expect buildup in the air in public restrooms, as well as in communal shower facilities. Andelman (1985) cites data on trichloroethylene (TCE) concentrations in the ladies room of a municipal building during the lunch hour (12:20 PM). Inhalation exposure to workers resulting from industrial uses of water has not, apparently been widely researched.

6. TOXICOKINETICS AND THE DOSE-RESPONSE RELATIONSHIP.

Toxic effects of chemicals are commonly divided into (Levi, 1987):

- Acute effects, traceable to a single exposure or a few exposures and observable within a few days after exposure. These include, in particular, interference with the nervous system and with oxidative phosphorylation.

- Chronic toxicity refers to longer term effects. Types of chronic toxicity discussed by Levi are:

  carcinogenesis

  mutagenesis - hereditary changes in the genetic information stored in DNA

  teratogenesis - malformation of developing fetuses

  organ toxicity - to liver, kidney or to the lungs

  behavioral effects

The BTEX compounds have been implicated in a wide variety of toxic responses. Of particular interest from a risk standpoint is chronic toxicity, and, in particular, carcinogenic activity. Of the BTEX compounds, benzene is thought to be a potent carcinogen. It is also the one in highest concentration in most petroleum fuels. In addition, it is one of the most extensively studied of the chemical carcinogens. For these reasons, after a discussion of some general principles, we will focus most explicitly on benzene.

6.1. General Discussion

Once a toxicant crosses the boundary and enters the body, several process occur. First, the material enters the blood stream, where it can be distributed to remote parts of the body. Second, the compound can be acted upon by enzyme systems. As described by Hodgson (1987), there are typically two phases to this metabolic activity. The first phase introduces a polar functional group into the molecule. This sets the stage for a second phase which results in highly water soluble compounds, which can be excreted. Although this is generally thought of as a detoxification process, it may happen that metabolic intermediates are either more or less toxic than the original. Indeed for some toxicants, it is a metabolic intermediate which is the source of the toxicological response. This metabolic activity can occur at any point along the distribution pathway, beginning with the membrane through which the toxicant gains entry. Third, either the initial compound or an intermediate can give rise to the toxicological response. Again, this can occur at any point beginning with the point of entry of the toxicant. In particular, if it is a metabolic product which produces the response, the tissue affected may be the tissue which contains the enzymes that form the product. Finally, the toxicant or its metabolic products may be eliminated from the body - usually through the kidney or with the bile, depending upon molecular weight and solubility, or through the lungs for very volatile materials (see, for example, Guthrie and Hodgson, 1987b).

To summarize, the processes that need to be taken into account, once the toxicant has entered the body include: distribution; metabolic conversion; the toxic response itself; elimination.

Consideration of each of these processes is important for the qualitative as well as quantitative understanding of the patterns of toxic response from different toxicants.

The toxic response is generally thought of as taking place through some set of biochemical interactions at the molecular level. The probability of such interactions will depend upon the concentration of the toxic substance at the *cellular* level. Figure 7 illustrates the relationship. In particular it becomes understandable that the pattern of response may depend upon the path of entry and the route that the substance takes before being mixed with the general blood supply. This is further illustrated by Figure 8 from a publication of Environ Corp. (1986). An understanding of the contribution of each of these processes also makes it clear that differences between species in intermediate metabolism may lead to differences in susceptibility to particular toxicants.

When authors refer to the "dose-response" relation, it is not always clear which type of dose is being discussed. It is, however, the exposure dose that can be most easily measured. Moreover, unless the range of actions being considered includes medical intervention, it is the exposure dose that we can do something about. It follows that the relation between exposure and whole animal response is the dose-response relation of particular interest.

6.2. Types of evidence for establishing relation between dose and response.

One can think of four types of scientific evidence for helping to determine the dose-response relation for a given toxicant.

6.2.1. *Epidemiologic evidence.*

The first, and most direct, is epidemiologic evidence, based on observation of the effects of exposure of humans to the suspected toxicant. Such studies might involve:

- relating the incidence of water, air, or soil pollution to the occurrence in the exposed population of some measured response.
- correlation of effect with exposure in some occupation, such as in mining, or in an industry using a suspected toxicant.
- measurement of effects in a population exposed as a result of some accident, such as in Seveso, Italy or in Bhopal.

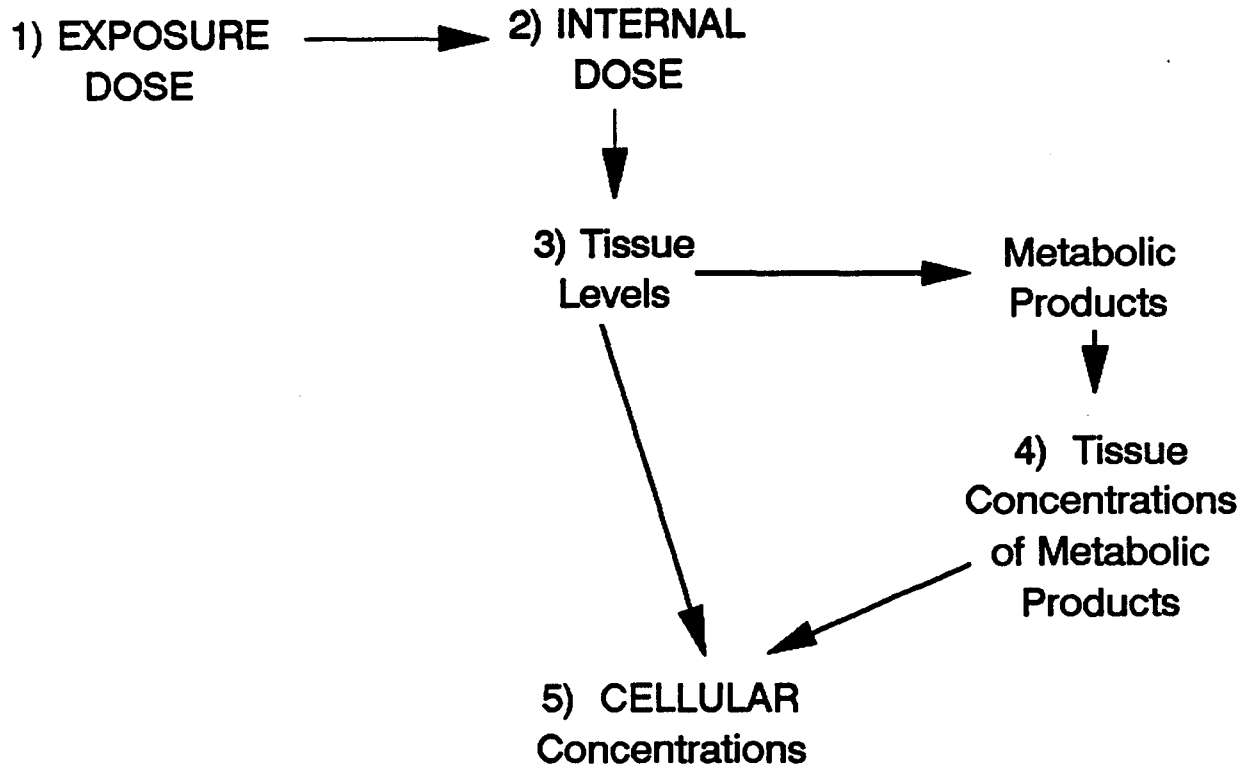

Figure 7. Relation between "dose" at different levels.

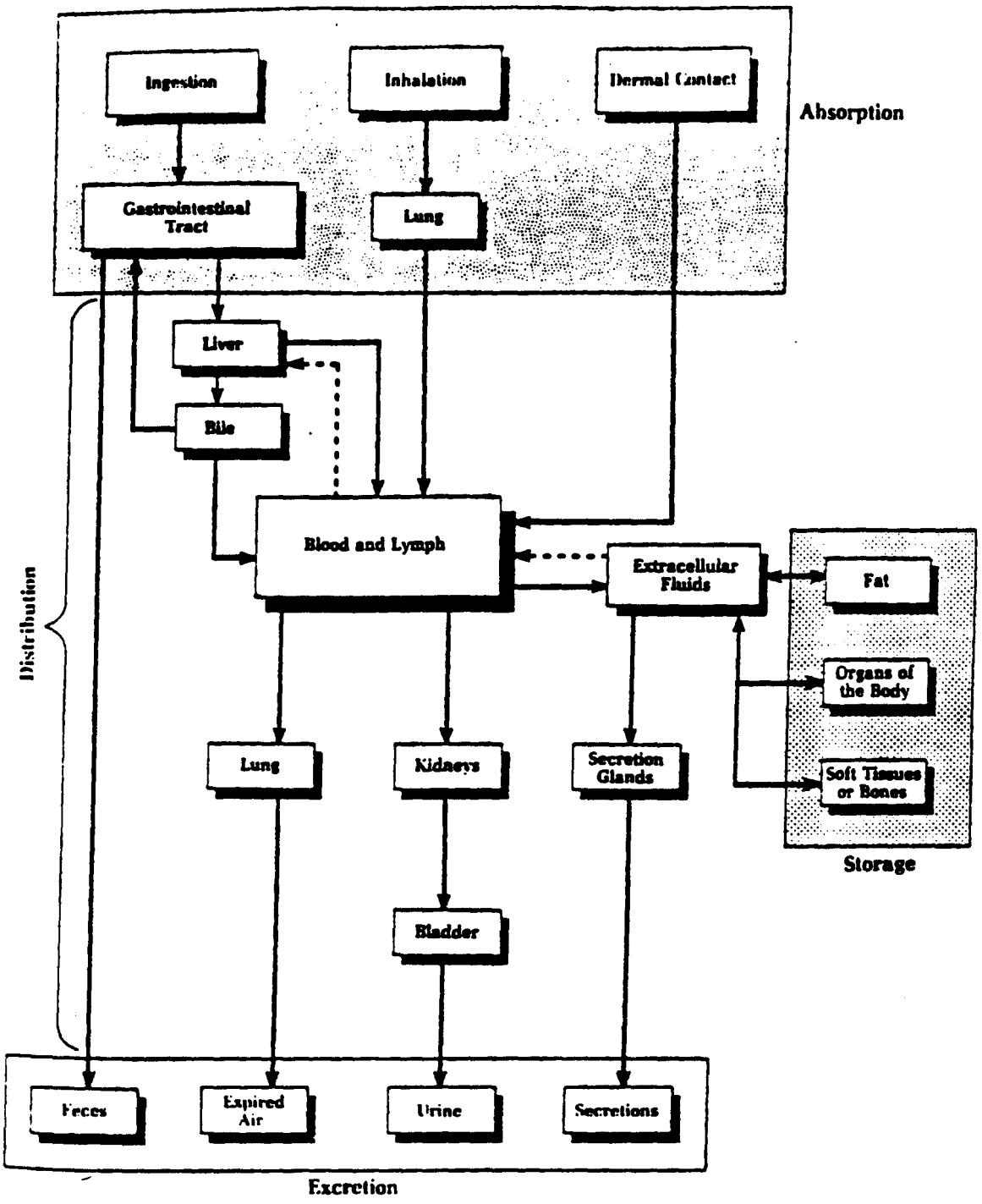

Figure 8. Fate of chemical toxicants in the body (from ENVIRON Corp., 1986)

Cohrssen and Covello (1989) list the following conditions, which make epidemiologic investigation suitable:

- high exposure (e.g., smoking or high levels in water, soil or air)
- unusual health effects (e.g., rare forms of cancer)
- clear symptoms and linkage between the effect and causal agent

These are conditions which lift the effect being studied above background noise.

Failure to satisfy these conditions compromises the definitiveness of epidemiologic data. Other serious limitations are absence of experimental control, and inability often to account for multiple sources of exposure, or for the confounding effects of exposure to multiple toxins. Moreover, the actual dose received by any individual can usually only be estimated.

6.2.2. *Laboratory animal dose-response studies.*

In the simplest type of animal study, laboratory animals are exposed to the suspected toxicant, and the incidence of response (no. of animals exhibiting the toxic response) is plotted as a function of exposure level, resulting in a "dose-response curve". In the simplest studies, the "response" might be death of the animal. Other types of experiments involve killing the animals at a fixed time, and observing the incidence of tumors of various types. Such curves are usually re-scaled before use in estimating human risk, so that dose is put in terms of amount per unit of body weight. Unfortunately, use of such data to estimate human risk suffers from a number of serious drawbacks. The two most serious are:

- Extrapolation to low doses.

For application to human risk, we are often interested in quantifying responses which may occur in very low numbers in the population. Many EPA or OSHA regulations are geared to levels and effects that occur in the range of one in every thousand to one in every million exposed persons. It is not usually feasible to conduct experiments for a sufficient length of time and in sufficient numbers to give meaningful statistical data at such levels. The answer of course is to use much higher levels of toxicant, which produce much greater frequencies of effects. We then extrapolate *beyond the range of the data*, to low doses, with no evidence that the observed relation continues to hold. Traditionally, the extrapolation used has been linear, passing through the origin – that is, zero effect at zero concentration. This will be in error if the mechanism itself is nonlinear, or worse yet, if different mechanisms operate at different

levels. For example, there is a large repertoire of biochemical toxification and detoxification mechanisms (Hodgson, 1987) which in some cases may operate so as to prevent any toxic effect from being exhibited until a certain threshold is reached.

- Interspecies extrapolation

This problem is, if anything, more serious, because of differences between animal species. Relevant differences include rate of absorption by different pathways and existence or absence (or differences in the activity) of relevant metabolic pathways. In the case of benzene, for example, observed responses in experimental animals include cancers in organs, such as the Zymbal gland, which humans do not have.

6.2.3. *Biochemical Response*

This type of animal experiment is based on prior evidence that specific metabolic intermediates are involved the process of disease production. The reasoning might be that the level of toxic response is then related to the rate at which the supposed toxic metabolites are produced. The experiments then involve the measurement of these rates either *in vivo* or in tissue preparations.

6.2.4. *Physiologically Based PharmacoKinetic (PBPK) models.*

Such models are be based on the formulation of a detailed chain involving absorption and distribution of the parent xenobiotic through the body, mechanisms and rates of production of toxic intermediates, and the mechanism of toxic action. Such models are becoming increasingly useful in helping to guide both the use of results from epidemiologic and animal studies, and the design of new experiments by identifying critical informational needs.

6.3. Benzene Pharmacokinetics and Toxicology

6.3.1. *Toxic Effects of Benzene.*

A publication prepared by Oak Ridge National Laboratories (1989) summarizes the health effects of benzene, and extensively reviews the related literature. Very high doses of benzene, either orally or by inhalation, are lethal. Acute effects at somewhat lower doses include drowsiness, headache and dizziness. Among the longer term toxic effects that have been attributed to benzene are damage to the hematopoietic (blood forming) system, damage to the immune system, effects on the

reproductive system, interference with embryo development, and carcinogenicity. Figure 9 (Figure 1.1 from Oak Ridge Nat'l. Lab., 1989) gives an idea of the ranges in which various effects have been observed.

The carcinogenic effects of benzene have been the subject of several recent reviews (Cox, 1991; Goldstein, 1989; Oak Ridge Nat'l. Lab., 1989; Mehlman, 1989). A variety of cancer types have been found to be caused by benzene in experimental animals (Maltoni, et al., 1989). They are to some extent species and even strain specific. In humans, however, the primary carcinogenic effect associated with benzene appears, on the basis of statistical epidemiologic evidence, to be leukemia. According to the analysis of epidemiologic data performed by Lamm et al. (1989), only one specific form of leukemia, called acute myaloid leukemia (AML) has been consistently observed to be associated with benzene exposure. Nevertheless, it seems to be not uncommon for analyses of epidemiologic studies to fail to make this distinction, and to be based on all forms of leukemia. A relevant distinguishing characteristic of AML (compared with many other forms of cancer) is a relatively short interval between exposure and death. In cases where this interval can be established, it is found to be typically less than 10 years (Lamm et al., 1989).

The mechanism of benzene carcinogenesis is not known exactly. It is established, however, that the active carcinogenic substance is not benzene, but a metabolite of benzene. Initial metabolism occurs in the liver, while the ultimate carcinogens may be formed by reaction within the bone marrow (Cox, 1991). A proposed metabolic scheme is shown in Figure 10 (from Henderson, et al. 1989). The compounds that are implicated in the toxic responses are phenol, hydroquinone, catechol and muconaldehyde. Detoxification pathways are the paths leading to phenyl mecapturic acid, and the formation of glucuronide or sulfate conjugates. While muconaldehyde is implicated in the toxic response, muconic acid is a detoxification product. One result of this complex metabolic network is that the toxification and detoxification pathways may be thought of as competing with each other, so that the relation between exposure dose and response is unlikely to be simple (Parodi, et al. 1989).

6.4. Quantifying the Risk – The Dose-Response Relation.

Before discussing the specific relation between dose and response, it is necessary to discuss what we will mean by each of these terms.

6.4.1. *Quantifying the Dose.*

In discussing acute toxic effects, specification of the dose is unambiguous, especially if the entire dose is experienced at a single time. Administered dose in chronic toxicity experiments with

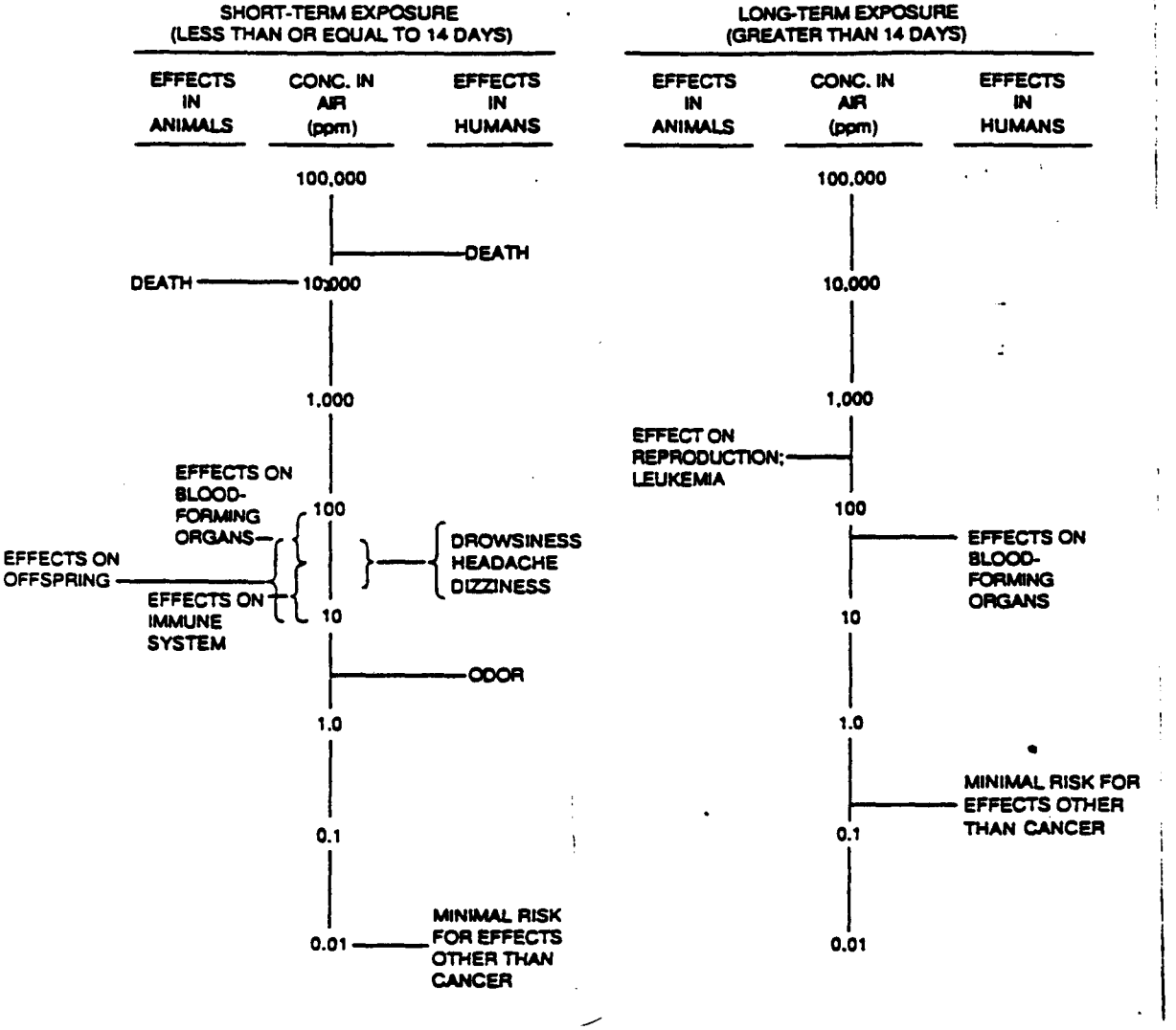

FIGURE 9. HEALTH EFFECTS FROM BREATHING BENZENE
FROM OAK RIDGE NAT'L LAB., 1989)

METABOLIC SCHEME FOR BENZENE

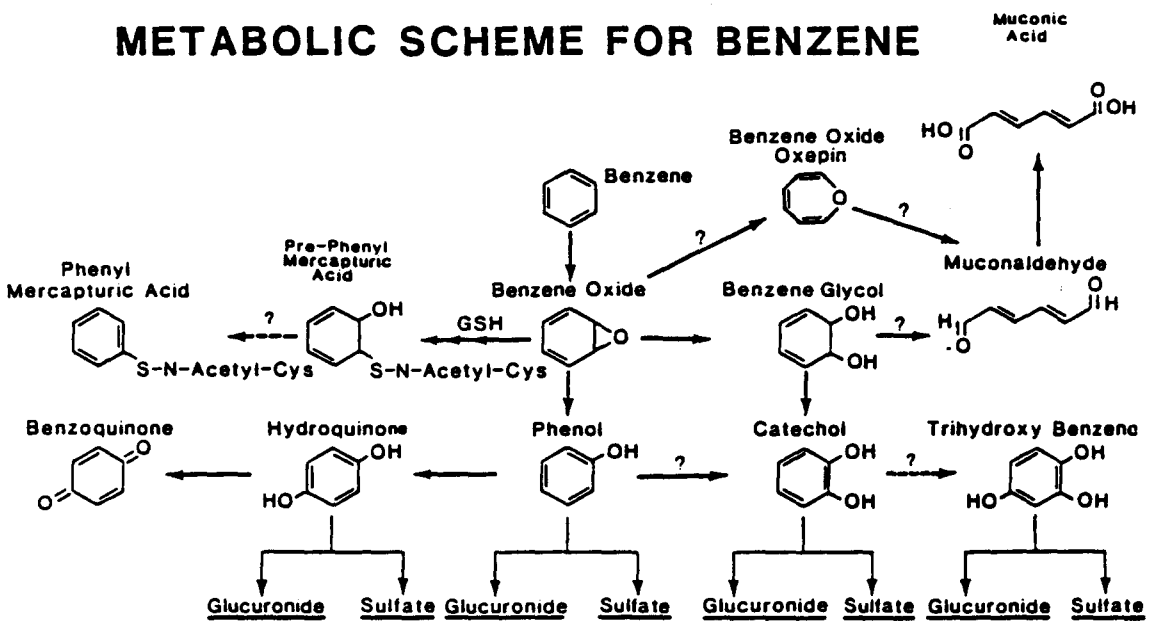

FIGURE 10. FROM HENDERSON, ET AL., 1989

animals may also be unambiguously defined in terms of an exposure protocol over a period of time. Human exposure, on the other hand is likely to be intermittent, with levels that vary with time. The usual solution to this is to express dose in terms of cumulative total amount. For example, in discussing ingestion, the dose rate may be expressed as mg per kg of body weight per day. This would then be multiplied by the period of time over which exposure takes place. If the exposure pathway is through inhalation, the dose rate might be assumed to be proportional to the concentration of toxicant in the air, and so might be expressed in terms of ppm. Cumulative dose would then be expressed as ppm x time.

This presents a problem, of course, if the exposure is through more than one medium. The usual way of handling multi-media exposure would be to multiply each by an assumed absorption rate (see above discussion on absorption), and so convert each to an effective internal dose. If it can then be assumed that the absorption and distribution is sufficiently rapid so that the effect is independent of absorption pathway (as seems to be the case for benzene), these doses can simply be added.

Basing the dose-response relation entirely on cumulative dose, however, requires the assumption that dosing rate does not matter. That is, for example, that intermittent high exposures have the same effect as lower constant exposure, as long as the average exposure rate is the same. This assumption is questionable in general for carcinogenesis (Kodell et al., 1987) and, in particular, for benzene (Henderson et al. 1989; Cox, 1991). The reasons are complex. They are related partly to the saturation of the metabolic pathways discussed above, and to the suppression of survival of leukemic cells by higher concentrations of benzene (Cox, 1991).

6.4.2. *Quantifying the Response*

A number of quantitative measures of risk have been proposed (see, for example, Cohrssen and Covello, 1989; Hallenbeck and Cunningham, 1986).

- *Excess Individual Lifetime Risk.* The probability that an individual will develop the disease in question during his or her lifetime is assumed to be a function of exposure to the toxicant, $P(\text{disease}) = f(\text{exposure})$. In most cases, there is assumed to be some background risk, say P_0, so that $P(\text{disease})$ becomes $P = P_0 + \Delta P$. In this formulation, it is usual to model ΔP as a function of exposure.

- *Population Risk.* In any population, one may expect some number of cases in a given time period, often one year. This expectation might be obtained as the product of the

probability for a single individual times the population size. Clearly, the individual probability used must be scaled to the same time period. As for the individual risk, we may express this expected number as $< N > = < N_o > + < \Delta N >$, where ΔN is now a function of the level of exposure of the population. Often the conversion between the quantities individual risk and population risk is based on the assumption (often unstated) of a linear dose-response relationship.

- *Relative Risk (RR)*. This is the ratio of risk in the exposed vs. unexposed population,

$$\text{RR} = \frac{\text{proportion of cases in exposed group}}{\text{proportion in unexposed group}}.$$

Clearly, this may be modeled as a function of exposure level.

- *Standardized Morbidity Ratio, (SMR).* It is often not possible to obtain reliable estimates for an "unexposed group". On the other hand, it is usually possible to obtain statistics for the general population, which leads to the use of the SMR measure,

$$\text{SMR} = \frac{\text{incidence rate in exposed group}}{\text{incidence in general population}}$$

- *Odds-Ratio (OR).* Whereas the probability of a "win" might be thought of as the proportion of individuals in a groups who "win", the *odds* might be interpreted as the ratio of winners to losers. Formally, the odds would be the ratio. $P/(1-P)$. If P_e is then the probability of mortality in an exposed group and P_c is probability of mortality in a control group, the odds-ratio would be,

$$OR = \frac{P_e/(1-P_e)}{P_c/(1-P_c)}$$

This is a convenient measure to use in the context of logistic regression (Kleinbaum et al., 1982), and was used by Rinsky et al. (1987) and Brett et al. (1989) to study benzene carcinogenicity (see discussion below).

In the above measures, the comparison group would generally not simply be the general population, but a sub-population matched with the exposed group with respect to variables that may

influence susceptibility, such as age, health status, and possibly sex. Other measures which have been discussed are perhaps a bit more subtle,

- *Loss of life expectancy.* This can be applied on an individual or a population level. Instead of counting deaths, however, we count number of years of life expectancy lost. As a basis for prioritizing action, this places higher priority on hazards that affect younger people.

- *Averaged utility of life.* Most diseases not only decrease life expectancy, but also diminish the quality of life before death. A number of authors have argued that such considerations should enter into the setting of environmental priorities, and have proposed scales for doing so (see, for example, Keeney and von Winterfeldt, 1991; Mauskopf and French, 1991).

Nearly all discussions in the literature related to environmental carcinogens, are based on measures involving number of deaths.

6.5. Epidemiologic Risk Assessment Studies for Benzene

Epidemiologic studies on the risk of Leukemia due to benzene exposure have been mostly based on occupational exposures. Four such studies are extensively reviewed and compared by Brett et al. (1989). These are (see Brett et al for references to the original work):

- A study of Goodyear workers exposed to benzene in the manufacture of rubber hydrochloride (Pliofilm) at three facilities in Ohio (reported by R. A. Rinsky and co-workers; see Rinsky, 1989 for a brief review of this study). Exposures for three groups of workers were during the period of 1940 through 1965. The total cohort consisted of 1165 white males. Vital status was followed for at least 15 years. Exposure was measured in terms of cumulative dose of inhaled benzene, in units of ppm-years (see discussion above).

- A study of 594 Dow Chemical workers employed between 1940 and 1973 (reported by M. G. Ott and co-workers), and an additional group of 956 exposed between1940 and 1982 (reported by G. G. Bond and co-workers).

- An investigation of 34 shoe manufacturing workers admitted to a hematology department of a medical school in Istanbul, Turkey during the period from 1967 to 1975 (reported by M. Aksoy). The total number of workers in such facilities was estimated to be 28,500. Based on examination of these 34, the leukemia rate in the group of shoe manufacturing workers was estimated to be significantly higher than that of the general population.

- A study of 4602 male chemical workers exposed to benzene between 1946 and 1976 (reported by O. Wong).

The primary difficulty with each of these sets of data is the absence of reliable quantitative information on exposure level. On this basis, while the data used by Rinsky is far from unambiguous, Brett et al. conclude that it is the only set of data appropriate for quantitative estimation of dose-response curves.

However, even for this set of data, there has not been agreement on how to estimate the exposure levels. According to the account of Brett et al. (1989), benzene monitoring data for the three locations were extremely sparse, and, for much of the period, were completely missing. On the basis of the existing data, estimates were made for benzene level in individual work areas. The estimates made on the basis of data from one plant were used for another plant employing the same type of process, and these levels were assumed constant during the period of the study. In another analysis of the same data, also reviewed by Brett et al., K. C. Crump and B. C. Allen, instead of assuming exposure levels to be constant, assumed the relation of the measured concentration to the recommended occupational standard to be constant. It follows that the assumed exposure levels would be assumed to have changed as these standards changed. This latter supposition is in closer agreement with other evidence based on the hematological effects of benzene (Kippen et al., 1989). Brett et al. also discuss other data analysis refinements made by Crump and Allen. As Brett et al. discuss, the Crump and Allen estimates lead to the assumption of greater exposures than does the original analysis of Rinsky, so that the risk estimates are lower (see below).

6.6. Dose-Response Relations, based on the Epidemiologic Data

A number of dose-response relations have been used as a basis for extrapolating from one exposure level to another. Several are discussed by Brett et al. (1989).

6.6.1. *Linear Model*

The simplest is the linear equation,

$$P = P_0 + \beta x,$$

where P_0 is the "background" rate of death from leukemia, in the absence of benzene exposure, and x is the cumulative lifetime exposure. Linear extrapolation generally been regarded as providing a "conservative" estimate of risk. That is to say, it is considered to overestimate rather than underestimate the true added probability of mortality. Clearly, the estimate of β will depend upon assumptions that lead to the estimate of exposure for the observed group. To the extent that either this value or the value of P_0 is uncertain, the risk estimate will also be uncertain.

6.6.2. *One-Hit and Multi-Stage Models*

The one-hit model is based on the supposition that a cancer is initiated by a single "hit" of a receptor site by a tumorogenic agent. It leads (see Gaylor, 1988, for a brief review) to an expression of the type,

$$P(d) = 1 - e^{(-\gamma d)}.$$

When the background probability is taken into account, the equation for the *total* risk at dose level d becomes,

$$P(d) = P_0 + (1 - P_0)[1 - e^{-\beta d}],$$

where the second term on the right is the excess risk due to the carcinogen. Brett et al. (1989) review risk assessments of White et al (1982) based on the Rinsky data, and using the one-hit model.

The one-hit model has the appeal of a model which appears to be based on mechanistic reasoning. Unfortunately, this is misleading for at least two reasons. The first is that it is pretty well established that the development of a cancer is a multi-step process. Second, the active carcinogenic substance is not benzene, but consists of a mixture of metabolic products (see discussion above). Another point is that at the level of β values that apply, the equation is very nearly linear, so it is hard to see what the advantage might might be for using a more complex model.

6.6.3. *The Odds-Ratio Model*

The analysis of Rinsky et al. (1987) was based on a "case-control" methodology, in which observed cases are compared with controls matched on variables such as date of birth and date of entering Pliofilm work. This leads to an odds-ratio model of the general form (Kleinbaum et al., 1982)

$$OR = e^{\sum \beta_i x_i},$$

which is fit by logistic regression. Possible predictor variables considered were cumulative exposure, in ppm-yrs, duration of exposure and average exposure rate. Cumulative exposure was by far the strongest predictor. They arrived at the expression,

$$OR = e^{0.0126x},$$

where x is the exposure in ppm-yrs.

6.6.4. *Numerical Results*

Brett et al argue that of the available sets of data, that used by Rinsky et al. provide the most reliable basis for risk analysis. Rinsky et al. (1987) divided the 1165 workers in their study into four groups according to cumulative exposure. Table 4, drawn from Rinsky et al. shows some of the relevant raw data.

Table 4. Observed deaths from leukemia in 1165 workers. Data extracted from Table 2 of Rinsky et al., 1987.

exposure (ppm-yr)	observed deaths	SMR	95% C. I.
0.001-40	2	109	12-394
40-200	2	322	36-1165
200-400	2	1186	133-4285
>400	3	6637	1334-19,393

The small number of actually observed cases leads to very broad confidence intervals for the SMR values. These values were used as a basis for determining the β value in the odds-ratio equation

quoted above. However, while the data might be consistent with the exponential form (derived from logistic regression), it would seem equally consistent with the assumption of a threshold value somewhere in the vicinity of 40 ppm-yr.

Brett et al. (1989) recalculated the risks based on the data of Rinsky et al., using the constant exposure estimates originally used by Rinsky et al., and also using the alternative assumption of Crump and Allen that exposure levels were approximately constant as a proportion of the prevailing standard. Since the prevailing standards had been lowered several times, and since exposure levels measured in the 1950's, 60's and 70's were extrapolated backward to the 1940's, this meant that the Crump and Allen exposure estimates were higher than those used by Rinsky et al. The results, some of which are summarized in Table 5, show a substantial difference in the risk estimates based on the two different sets of assumptions.

Table 5. Expected excess Deaths per 1000 persons due to benzene exposure from the Pliofilm worker data, as calculated by Brett et al. (1989), based on the data of Rinsky et al. (1987). Nos. in parenthesis show 95% confidence intervals.

Exposure Assumptions	Cumulative Exposure 45 ppm-yr.	450 ppm-yr.
Rinsky et al.	6.4 (1.2-14.7)	819 (26.4-991)
Crump and Allen	0.7 (0.1-1.3)	11.0 (1.4-30.9)

As seen in Table 5, the two types of exposure assumptions lead to very different estimates. However, in each case, the 95% confidence intervals are more than an order of magnitude wide; the C.I.'s for the different exposure assumptions overlap!

The results shown in Tables 4 and 5 indicate the large uncertainties due to the small number of cases observed, and also due to uncertainty about the actual exposures. Some additional sources of uncertainties are discussed below.

6.6.5. *Additional Sources of Uncertainty*

Some additional sources of uncertainty that might add to the "noisiness" of the data are:

- Population variability; that is, we might be dealing with a population in which, for a given exposure level, each individual may have a different probability of contracting leukemia. If the population is indeed heterogeneous in this respect, then given the relatively small numbers in the study, the sub-populations with different sensitivities might not be equally represented at different exposure levels.
- Uncertainty in the exposure levels, which were not necessarily held constant.
- Effect of exposure in other activities. The employee records apparently indicate the amount of time spent in the Pliofilm operation. Not taken into account was the exposure the employee might have received to benzene or *to other chemicals* while engaged in other activities.
- Exposure is determined purely from inhalation, whereas the actual process might have involved occasional direct contact leading to dermal absorption.
- The numbers shown in Table 5, are based entirely on cumulative exposure estimates, whereas there is evidence that the time course of exposures is important (Bailer and Hoel, 1989; Cox, 1991).

This discussion has been based largely on the review of Brett et al. (1989). Other discussions which highlight the sources of uncertainty involved in estimates of risk due to benzene exposure are in papers by Lamm et al. (1989) and by Byrd and Barfield (1989). Of addtional interest are several reports in the statistical literature, directed at making risk estimates in the face of various types of measurement uncertainty (for example, Carroll, Gail and Lubin, 1993; Satten and Kupper, 1993).

6.7. Pharmacokinetic (PBPK) Modeling for Benzene

Several recent articles report on physiologically based pharmacokinetic modes for benzene (Bois and Paxman, 1992; Medinsky et al., 1989; Spear et al., 1991; Spitzer et al., 1989; Travis et al., 1990). In such models, the body is typically divided into several compartments, with each compartment usually representing an organ or group of organs. Rates of metabolite production (usually limited to reaction in the liver) and exchange between organs are described in terms of physiological and biochemical parameters.

The approach can be illustrated by the model of Medinsky et al. (1989), which is shown in Figure 11. Metabolism is modeled using a scheme somewhat simplified from that of Figure 10, and is based on standard enzyme kinetic formulations. Exchange between the compartments is modeled in terms of physiological parameters including blood flow, membrane permeability, ventilation rate, etc.

Such models are increasingly effective in understanding the rates at which benzene and, in particular, the putative carcinogenic metabolites are distributed through the body. They help to understand how the concentrations of these metabolites *at the target tissues* depend upon level of exposure, exposure pathway and the time pattern of exposure. They also help to understand the observed differences in sensitivity of different types of experimental animals, and thereby to understand how animal experiments may be more rationally extrapolated to humans (for example, Cox and Ricci, 1992).

It should be borne in mind that neither the knowledge of the appropriate biochemical/physiological pathways nor knowledge of the parameter values is precise. Spear et al. (1991) have analyzed the effect of parameter uncertainty on predictions of PBPK models. They used uniform or log-uniform distributions for parameter values, based on three different sets reported in the literature. These distributions were then used as input to Monte Carlo simulations. The authors note that "the largest vs. the smallest values of total metabolite produced in any of the three vector sets differed by a factor of four." That seems not too bad in comparison with the error ranges discussed above for the epidemiologic studies.

7. SOME CALCULATIONS ON THE RISK OF AML FROM BENZENE IN HOUSEHOLD WATER

In this section, we attempt to combine the epidemiologic conclusions of Rinsky et al. (1987) with the exposure calculations of Shehata (1985) to estimate the risk associated with low levels of benzene in drinking water. We start with the odds ratio equation of Rinsky et al.,

$$\mathrm{OR}(d) = e^{0.0126d},$$

where d is the cumulative dose expressed in terms of ppm-yrs. In order to combine this with doses through other pathways, it is necessary to put dose in terms of absolute amounts, say mg. Assuming a temperature of $22^{o}C$ and 1 atmosphere of pressure, we can calculate that at 1 ppm, one cubic meter of air contains 3.225 mg. of benzene. In order to calculate the cumulative exposure associated with 1 ppm in the air for one year, we need to make certain assumptions concerning the length of the working day, number of days per year, respiration rate, and absorption rate. We assume,

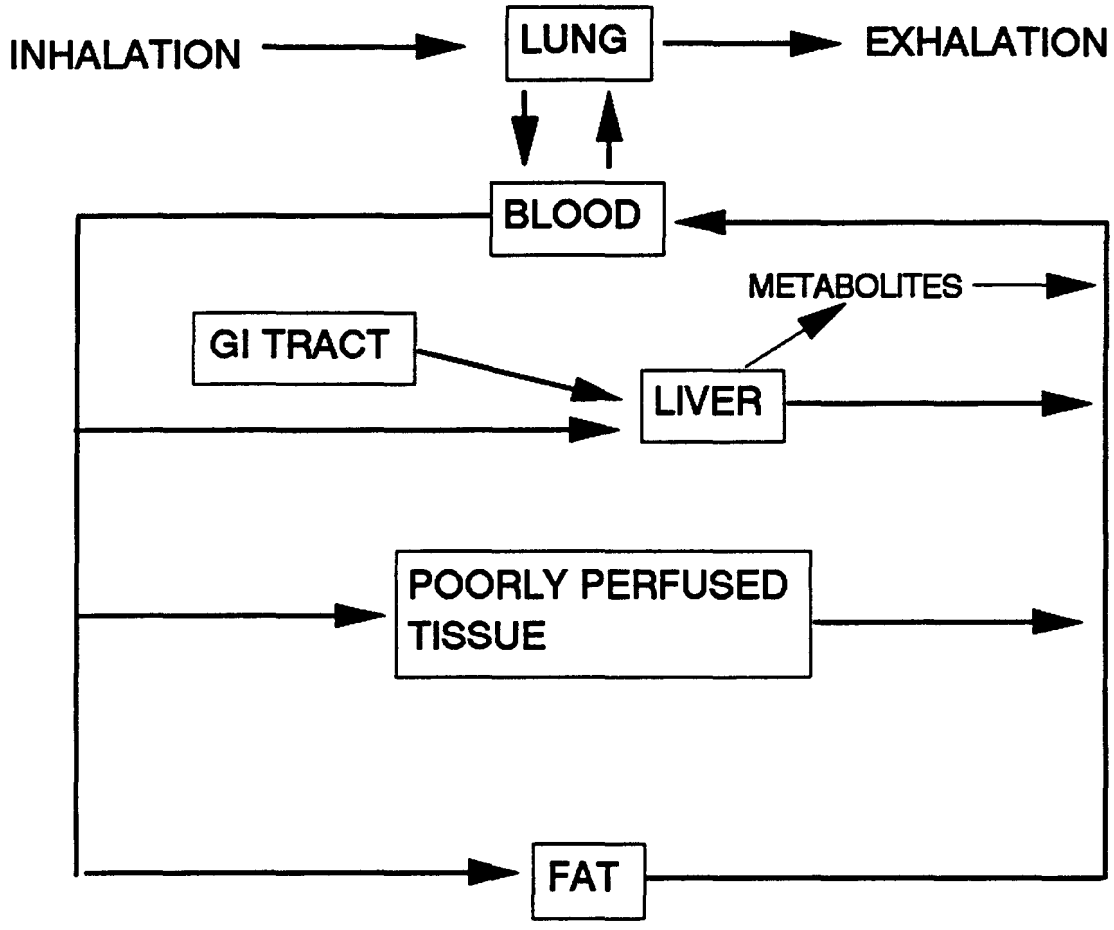

FIG. 11. Physiological Model for Benzene. Adapted from Medinsky et al., 1989

length of working day	= 8 hours
days worked per year	= 250
respiration rate	= 20 cu. meters per day
absorption rate	= 0.5

With these assumptions, 1 ppm-yr. is equivalent to absorption of 2687.5 mg. of benzene. Expressing dose in terms of cumulative mg. exposure, the equation for odds ratio becomes,

$$\mathrm{OR} = e^{4.69 \times 10^{-6} d}.$$

The *excess* probability due to benzene exposure can be obtained from the defining equation for OR. Solving for $P(d)$,

$$P(d) = \frac{\mathrm{OR} \cdot P_o}{\mathrm{OR} \cdot P_o - P_o + 1},$$

with *excess* probability, $P_e = P - P_o$. Using these relationships and the value of P_o from Rinsky et al. of 0.002318, one can compute P_e as a function of cumulative dose.

The next step is to relate concentration of benzene in water to the cumulative dose. To do this, we use the exposure estimates of Shehata (1985) discussed above. This involves estimating absorption through ingestion, inhalation and dermal absorption. Shehata included calculations for rural as well as urban households for which there may be a background ambient concentration of benzene in the air. Using the figures for rural household, the daily dose rate is approximately proportional to water concentration. Shehata also included a figure for benzene ingestion in foods, but it seems reasonable that this would be part of the background figure for P_o. The result is a figure of approximately 5.115 mg. of benzene absorbed per day per mg of benzene per liter of water.

Consistent with usual EPA practice, we have assumed exposure over a lifetime of 70 years. The result is a curve of P_e vs. benzene concentration, which is very nearly linear for low concentrations of benzene,

$$P_e \simeq 0.00146c,$$

where c is expressed in mg./L. This amounts to an estimate of one to two excess deaths per million of

exposed population at 1 ppb (0.001 mg/L) in the water, which is the current North Carolina standard for benzene, or about 7 per million at the EPA standard of 5 ppb.

8. A BRIEF REVIEW OF RISK ASSESSMENT THEORY

Risk assessment as a field is fairly new. Both fundamental theoretical and methodological underpinnings are still under development. The book by Cohrssen and Covello (1989) is a good introduction to concepts. Hallenbeck and Cunningham (1986) is a more applied introduction focusing on methodology. For those wishing to become oriented to the work in risk assessment, perusing the pages of the journal *Risk Analysis* is a good idea.

In this brief review, we adopt a decision analytic perspective (Gold, 1992), which stems from the view that the reason for any assessment or analysis of risk is to provide a basis for making a decision concerning the acceptance of the risk or the adoption of measures to reduce it or to avoid it. In order to proceed from this point of view, it is necessary to introduce some of the notation and terminology of decision analysis.

8.1. Components of a decision.

The essential components of a *decision* about the system might be listed as follows (Gold, 1989):

- A set of decision alternatives $\{d\}$.
- A set of possible outcomes (consequences, resulting scenarios, ...), $\{c\}$
- A value or utility function, which assigns a relative degree of desirability to each outcome, $c \rightarrow v$
- A probability distribution over the set $\{c\}$, or, equivalently, a probability distribution over the values for v. Note that this probability distribution depends on choice of d. We can not choose the outcome c; *through the choice of d, we choose a probability distribution on $\{c\}$.*
- Criterion for determining which probability distribution is best?

  We can define a value or utility function U in such a way that it becomes reasonable to order the desirability of probability distributions based on the associated expected value $\mathcal{E}(U)$.

- The final ingredient in the process is some way of handling new information. There are basically two things we want to do with information
  - determine in advance if it is likely to be worth the time, effort and cost of getting it; and
  - once we have it, use it to revise our probability distributions.

8.2. Hazard and Risk.

The literature on risk analysis often makes an important distinction between hazard and risk; although both of these terms specifically refer to possible bad or adverse outcomes. The term hazard refers to the *existence* of some danger. For example, a large rock in a body of water might be termed a boating hazard. It is not a risk, unless there are boats in the area. Moreover, the risk might be reduced or eliminated by creating some sort of boundary which keeps boats away. The rock would still be a hazard, however. In this same way, BTEX compounds in groundwater present a hazard. It is not a risk unless there is some chance that people will be be exposed to the water.

Using the above notation, *hazard* has been defined as the set of possible *bad* outcomes, or sometimes (Kaplan and Garrick, 1981) as the set of pairs,

$$H = \{(c_i, v_i)\}.$$

The *risk*, would be defined by adding the probability to obtain the set of triples,

$$R = \{(c_i, v_i, p_i)\}.$$

Given the mapping $c \rightarrow v$, this notation is somewhat redundant. The essential point, however, is that without the element of uncertainty, the concept of risk is undefined. A disaster which will occur for certain is not a risk. Moreover, we have not defined the risk until we have evaluated the uncertainties.

8.3. Decision Analytic Extension

If this set of triples (or of ordered pairs, (v_i, p_i)), focusing on adverse consequences, defines the risk, the decision analytic perspective extends the framework in two ways.

- First, it extends the framework to include good as well as bad outcomes, since we are often in the situation of asking, "is the risk worth taking?"

- Second, it adds consideration of a criterion for telling when one probability distribution is better than another.

Of course, there are no good outcomes that come to mind that are associated with groundwater contamination. On the other hand, if one considers the possibility of petroleum contamination of groundwater to be a risk incurred in the use of petroleum products, few would argue against the proposition that the benefits in modern civilization are worth incurring *some* such risk. The level of risk might be thought of as characterized by:

- a probability distribution over levels of contamination; high risks being characterized by a distribution with higher probabilities being assigned to higher levels of contamination.
- the value function, which allows one to balance a particular probability distribution against cost of prevention or cleanup or other remediation procedure.

8.4. Expressing the risk: "Deterministic" vs. "Probabilistic" risk assessments.

For the LST problem the set of events $\{c_i\}$ can be defined either in terms of levels of groundwater pollution or in terms of the toxic response. Defining the set of events in terms of levels of pollution is considerably easier, but is very far removed from the value function. That is, in order to define the mapping $c \rightarrow v$, we *must* consider the toxic response.

As indicated in the introduction to the section on toxicology of the BTEX compounds, the way in which the toxic response is expressed is not uniquely determined. One possibility would be to estimate the expected number of deaths from AML due to benzene exposure, per million people exposed under some specified condition. This is a common way of expressing risk, and was used in our discussion in the previous section.

Two related measures are: the number of excess deaths expected in a *given* population, and the excess probability incurred by a single individual actually exposed. One can argue that these are the real questions of interest (see discussion below on values). Converting expected no. per million, say, to either of these other measures would appear to be a simple task. If N is population size, we just take expected no. per million and multiply by $N \times 10^{-6}$. For the probability associated with a single individual, we just take $N = 1$.

Again, these are common practices, but there are some problems that relate both to uncertainty and to variability. Let's begin by defining some notation. Let $\mathcal{N}_M(x)$ be the number of cases per million people exposed to a specific exposure regime x[4]. It is important to note that this is a relative frequency, not a probability. We are generally rather uncertain as to its value, and we may describe that uncertainty in terms of a probability distribution. That probability distribution will have an expectation, say, $E_M(x)$, which is most often used as the best estimate of $\mathcal{N}_M(x)$.

More generally, in a specific instance we are usually unsure as to the exposure level x. Indeed, even if we can say quantitatively and precisely how the toxicant is distributed in space and time, it will be clear that there will be variations in exposure within the population. Therefore, the exposure of a given population in a specific instance will be defined by a frequency (*not* a probability!) distribution. Of course, we rarely will know that frequency distribution precisely. It could be any one of a number of possible frequency distributions. Some of these will be considered to be more likely than others. In other words, we will have a probability distribution defined over a family of possible frequency distributions. Most often, the tendency will be to pick the *expected* frequency distribution (that is, the expectation of the probability distribution) and use it as if it were *the* frequency distribution, neglecting the uncertainties[5]. The relation is diagramed in Figure 12. Of course, if the dose-response relation is linear, then the value of $\mathcal{N}_M$ will depend only on the average exposure, say $\bar{x}$, and will be insensitive to the specifics of the the distribution.

Another problem is that all people are not likely to be equally susceptible. That is, we are likely to be able to divide our population into a number of sub-populations, each of which would have a different value for $\mathcal{N}_M$ for any exposure regime x (if we could make the measurement). This number might depend upon age, health status, lifestyle, exposures to other substances, and certain genetic characteristics. Since the development of a cancer is generally perceived to be a random process at the cellular level (Moolgavkar 1991, has a good discussion), it makes sense to associate a probability of cancer development with a particular individual, which could be viewed as a quantitative measure of

[4] In this discussion, the exposure regime x will refer to the time trajectory of exposure by all routes (ingestion, inhalation and dermal). In order to make the points about interplay of frequency and probability in this section, we will assume that the x-space is well ordered. For benzene exposure, this seems to be reasonable, but may not be so in general.

[5] The frequency distribution is often treated as if it were a probability distribution. Uncertainties about it might then be referred to as *second order* probabilities. This is an unfortunate use of the concept of higher order probability and arises, in my view, from the confusion of probability with frequency.

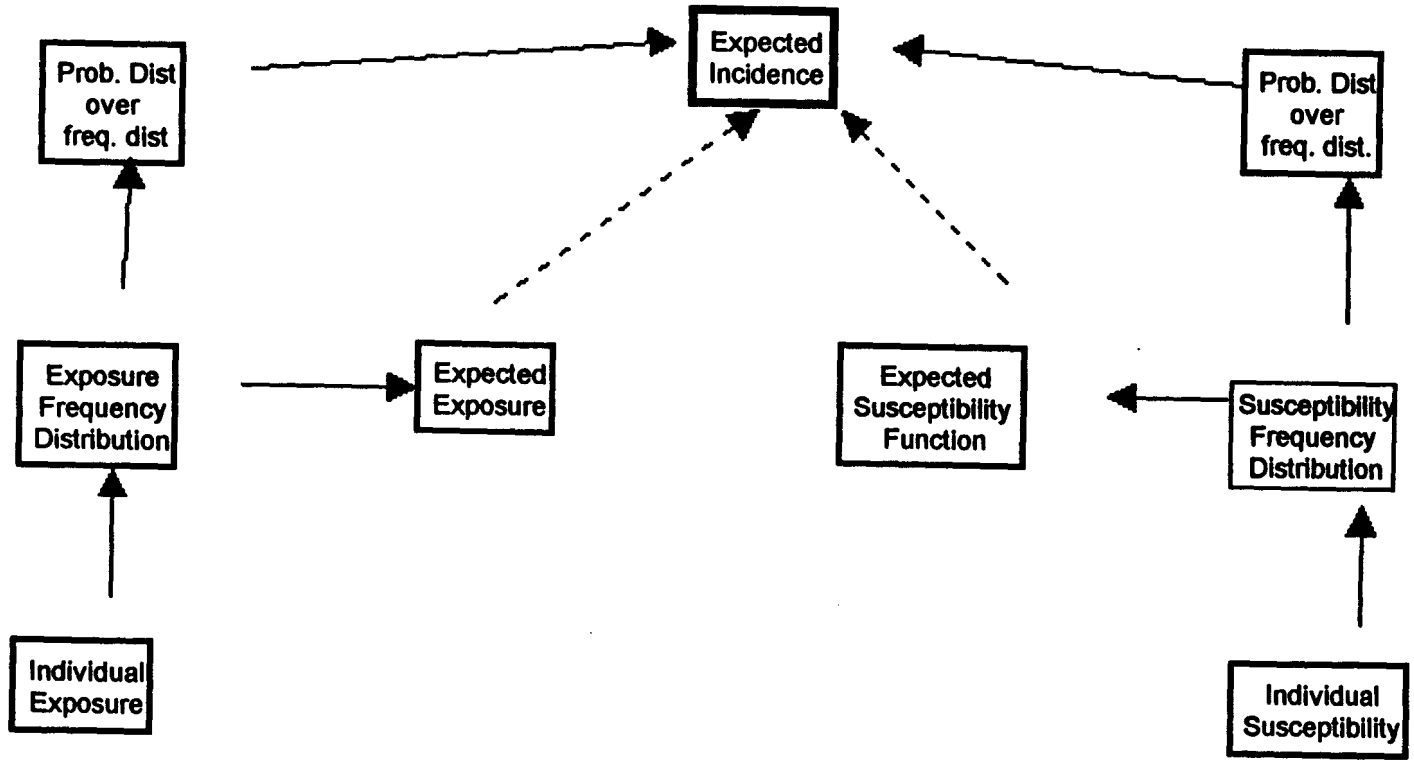

Figure 12. Interplay between frequencies and probabilities.

that individual's susceptibility. This would presumably be an increasing function of exposure x. The preceding argument makes it plausible, then, that the overall population would be characterized by a frequency distribution of such susceptibility (i.e., probability) functions. As for the case of the exposure variable x, we are not likely to know what that distribution is; rather, we would have a probability distribution over a family of frequency distributions. For an individual selected at random from the population, ***with no knowledge of the variables specific to that individual***, the probability function would be estimated from $E\left(N_M(x)\right)$.

The literature of risk analysis makes a distinction between "probabilistic risk analysis" (PRA) and "non-probabilistic" risk analysis. "Non-probabilistic risk analysis" is based on best estimates, and may include some indication of error in the form of confidence intervals or standard errors. The work reviewed above on benzene is an example. Papers published under the heading, "probabilistic risk analysis", often seek to explicitly model the uncertainties and their propagation, though often the distinction between frequency and probability is not clearly drawn. Some interesting references on methodology and applications of probabilistic risk assessment are Bogen and Spear (1987), Feagans and Biller (1981), Fiksel and Rosenfield (1982), Iman and Helton (1991), Kaplan (1991), Linnerooth-Bayer and Wahlstrom (1991). McKone and Bogen (1992) present an interesting case study for tetrachloroethylene contamination of groundwater.

A major question is how to combine uncertainties that arise from various sources. A somewhat simplistically "conservative" practice has been simply to evaluate each contributing variable at the pessimistic boundary of its 95% confidence interval. The problem with using such a procedure is illustrated by the following example quoted from Paustenbach (1989):

> "For example, if an upper bound on on the intake of a chemical in drinking water were calculated assuming that the water is contaminated at the 95% percentile, and if a person drinks large quantities of water (the 95th percentile), and if he were physically small (the 5th percentile, then the upper bound is not a 95% upper bound, but rather a much higher confidence limit. The maximum level of confidence here is almost 100% (specifically, $[1-(0.05)^3] = 0.99875$)."

The difficulty here is a failure to separate the problem of determining the likelihood that something will happen from that of determining how bad it is if it does happen; that is, separating probability assessment from value determination. An approach based on a decision analytic paradigm would involve assessing probabilities in as neutral and objective fashion as possible, and then through a

separate consideration of values, to take action would would keep the probability of adverse effects acceptably low. The approach quoted by Paustenbach confounds the two by explicitly overestimating the probabilities of adverse consequences. It can be easily appreciated from the simple example quoted that such an approach may not offer an appropriate basis for comparing risky situations as to the seriousness of the risk, or establishing priorities for taking action.

An approach to combining uncertain information from different sources, which has been used in other contexts but does not seem to have been very much applied to risk analysis, is that of influence diagrams. Briefly, an influence diagram is a graphical representation of a network of probabilistic dependencies. In the diagram of Figure 3, for example, each of the variables in the boxes with rounded edges would be considered to be a random variable. The arrows indicate stochastic dependence. Heuristic procedures have been developed that make these diagrams useful tools for problem structuring and model development. The formalisms that accompany the diagram are based on a combination of graph theory and probability theory and lead to practical computational procedures. The methodology has developed almost simultaneously within the literature of decision analysis and of artificial intelligence, where it is more generally referred to under the heading of probabilistic belief networks. Useful descriptions of the methodology and theory, from different perspectives, may be found in Matheson and Howard (1984), Schacter (1986), Pearl (1988) and in articles contained in Oliver and Smith (1990). Use of influence diagrams to help integrate information from diverse sources is discussed by Gold et al. (1990).

9. VALUES AND ETHICAL ISSUES

The major adverse effect of petroleum contamination of ground water that has motivated most of our discussion, is the increased risk of cancer. For benzene, which is the compound of greatest concern, this means specifically increased risk of acute myaloid leukemia. Over and above the questions that have been discussed above, is the question, "How much money and effort is it worth for how much reduction in risk?" At one extreme, one might argue that any expenditure is worth the elimination of any individual source of cancer risk. This is the extreme currently built into federal food laws. Some of the problems with this viewpoint are easy to list:

- We don't *have* unlimited resources.
- There are numerous sources of cancer risk.
- There are numerous risks other than cancer risks that confront us.
- Resources spent on reduction of one type of risk are not available for reduction of other risks.

– Resources spent on risk reduction are not available for other types of expenditure that increase our well-being in other ways.

If the point of view cited above is not adopted, then there are a host of other questions that must be dealt with. What expenditure or public resources is it worth to save a given number of human lives? Should there be a linear relation between lives saved and expenditure of resources? Given the uncertainties discussed above, should the *expectation* of lives lost or saved be the only variable that dictates level of expenditure? Is it only loss of life, or is it also the condition of *being at risk* that people should be protected against? Should the risk per individual be lowered more for individuals who are part of a large group than for individuals who are part of a small groups (so as to achieve lowest possible number of loves lost)? Are all lives equally valuable? Should younger people be protected more than older – that is, should the variable of interest be number of *lives* or number of *years of life* lost? Or, should the variable of interest be overall *utility* of life, which would be some function of length of life and quality of life? This latter would mean that substances which reduce health, and therefore quality of life, would be permitted to compete for risk reduction resources, even though the effects were not lethal.

Other questions concern the "statistical" nature of public risk. A simple example might illustrate the question. Suppose situation X subjects 10 specific individuals to near certain death. Situation Y subjects 10,000 individuals each to a 0.001 probability of death, giving an expectation of 10. Which of these has higher priority? If the answer is situation X, then how high must the probability go in situation Y in order for it to be considered of equal priority? The problem becomes somewhat more subtle if we compare, for example, one situation in which 100 people are subject to a risk of 0.1, with a situation in which 10,000 people are exposed to a risk of 0.001.

Debates related to such questions appear regularly in the daily news. They involve placement of hazardous waste treatment facilities, expenditure on "superfund" site cleanup, regulation of pesticide use, workplace safety standards, etc., etc.

These are not scientific questions. They are questions of philosophy, of ethics and values. Their resolution, insofar as they involve public policy and public decisions, necessarily lies in the arena of politics. Nevertheless, the methods of scientific inquiry can contribute to the discussion. In particular, scientific approaches can:

- Help to *define* the ethical issues, so as to provide a basis for more productive discussion and negotiation;
- Help to develop valid methodology for determining what values people hold on public issues; that is, for determining what aspects of risk are important, and how important they are (see, for example, Slovic, 1987);
- Help to develop approaches to use this information as a basis for negotiation and for arriving at decisions that engender trust and that people recognize as fair.

Interesting discussion on these issues can be found (among other places) in: Cropper and Portney (1992), Graham and Vaupel (1981), Gregory, et al. (1991), Keeney (1984), Keller and Sarin (1988), Kunreuther, Linnerooth and Vaupel (1984), Mauskopf and French (1991). The article by Merkhofer and Keeney (1987) appears to document the somewhat unusual situation in which some of these issues were directly addressed as part of the public decision making process.

From a comparative risk perspective, Travis and Hester (1990) call into question the reasonableness of existing regulations. They examine leading sources of cancer risk from chemicals in the general environment, including indoor air, water and food. Using EPA methods, they estimate that the overall background risk of cancer from chemicals in the environment is likely to be in the range of 2.5×10^{-3}, which is a small percentage of all cancers. On this basis, they question the value of costly EPA efforts and regulations to reduce the risk from individual sources to the range of 10^{-7} to 10^{-5}. They suggest that it might be more cost effective to put resources into reduction of the background risk.

A related question is the appropriate role of legislation and administrative regulation in the public management of risks. This issue is reviewed by Rosenthal, Gray and Graham (1992).

10. SOME QUESTIONS TO BE ANSWERED

In the light of the preceding discussion, one can raise a series of types of questions related to risk assessment. These may deal with, for example:

- Individual contaminated sites;
- public risk and development of public risk management policy;
- Characterization of uncertainties in risk assessment and risk management;
- Needs for information (to reduce uncertainty).

10.1. Risk Evaluation For Individual Sites.

10.1.1. *Some Relevant Questions*

Some specific questions that might be posed in the examination of an individual contaminated site are:

- What are the groundwater contamination risks that it poses?
- Given current land and water uses, and population level, what are the health risks?
- Are there reasons other than health risk for remediation action? Possibilities might include esthetic considerations, effects on real estate value, etc.
- Can we separate out effects on "intrinsic" value of the site from value effects imposed by legal liability?
- What are the costs, risks, and likelihood of success of available alternative cleanup procedures?
- What is the range of other decision alternatives? Possibilities might include, for example: water treatment for residents in the area; piping in water from nearby aquifer; direct payment for loss of real estate value (see, for example, the discussion in Gregory et al., 1991).
- How do each of these questions impact decisions relative to installation of new storage facilities, or to decisions concerning replacement of existing facilities, when leakage has not yet occurred?

10.1.2. *Sources of Uncertainty.*

The answers to such questions rest on a number of physical, biological and sociological details about which there is a good deal of uncertainty. Relevant uncertainties may be divided into uncertainty about characteristics about the particular site, and uncertainty about more general relationships. Among uncertainties concerning characterization of a specific site are:

- The characteristics of the leak: where in the tank the leak (or leaks) occurred; amount and time course of the leakage.
- Detailed hydrogeologic characteristics of the affected area: including porosity, hydraulic conductivity, hydraulic gradient, and certain relevant characteristics which are virtually inherently random, such as pattern of macropores.

- The extent and pattern, at any given time, of time of the hydrocarbon plume; certain relevant characteristics of the plume are inherently random, such as the distribution of trapped hydrocarbon globules within the soil pores, and the pattern of water flow relative to those pores.
- The exact composition of the hydrocarbon plume; the spatial pattern of this composition will continually change due to dissolution of more soluble components, volatilization of more volatile ones, biodegradation and chromatographic separation.
- Exact pattern of future land development and water use.

Other uncertainties that affect the decision related to a given site are more generic, and less specific to the site itself. These include

- Patterns of individual water use and consequent exposure within homes or within commercial or industrial establishments.
- Absorption of toxicants as a function of exposure from inhalation, ingestion or dermal exposure.
- Level of toxic response as a function of exposure dose (cancer as well as other health effects).

Categories of uncertainty relative to decision variables include,

- Costs, effectiveness and exposure risks associated with alternative cleanup procedures.
- Feasibility and long term acceptability of other decision alternatives.
- Effects on real estate value.
- Outcome of possible proceedings involving legal liability.
- The individual esthetic values (and, in some cases, public image concern) of the individual decision maker.

Cutting across these uncertainties, which relate to characteristics of the physical world, is a different type of uncertainty: uncertainty as to what value structures and tradeoffs should be used as a basis for decision making, and the question of how this type of uncertainty should reasonably be combined with uncertainties as to "facts".

For each of these uncertainties, there is a two-fold problem. The first is characterizing the uncertainty in a way that is relevant to the specific decision problem in hand. The second is the

development of general methodology that can facilitate the characterization of the relevant uncertainties in specific cases.

10.1.3. *Computational Aids*

A wide variety of commercial and public domain computer packages have been developed in recent years to assist in various aspects of risk assessment. Many of these are exhibited at annual meetings of organizations like the Society for Risk Analysis, and brief descriptions of these are published (for example SRA 1991). Moskowitz et al. (1992) have in particular surveyed the use of computer packages designed to assist in decision making related to hazardous and radioactive site management; most of these are primarily concerned with modeling environmental fate and transport. Software packages are beginning to be available that facilitate characterization of uncertainties; two examples of such software packages are: SITES, a Contaminated Sites Risk Management System (Cohan et al. 1988); and the Risk Assessment Decision Support System (API, 1992).

10.2. Risk Evaluation From a Public Decision-Making Perspective.

10.2.1. *Some Relevant Questions.*

From the standpoint of public decision making and public policy formulation, say, for a State governmental body, some of the relevant questions are:

- What is the distribution of groundwater contamination risks posed within, say the State? How might one characterize that distribution, as well as the uncertainties relative to that distribution.
- Given current land and water use and population patterns, what are the health risks within the State posed by leaking storage tanks?
- How do these compare with other health risks and other sources of water contamination?
- State-wide, what are other reasons for concern (such as esthetic values, real estate values, tourism and state image)?
- To what extent do legal liabilities that are imposed by the State actually reflect the "value" associated with health effects, and economic use value?
- What are the aggregate costs and risks imposed by policies concerning cleanup procedures and standards?

- What are the aggregate costs and risks imposed by policies which admit utilization of other decision alternatives? (water treatment, piping, direct indemnification)?
- How should each of these questions impact public policy regarding regulation of new facilities, replacement requirements or, in general, the use of petroleum products (or, by extension, use of other hazardous materials).

10.3. Relation between Individual Site Management and Public Decision Making: The Role of Modeling Hierarchies.

The relation between individual and public decision making can be modeled in a hierarchical framework (Mesarovic et al., 1970). At least two types of hierarchy are relevant. First is a descriptive hierarchy (an abstraction hierarchy in the terminology of Mesarovic et al., 1970). That is, each of the factors or variables that characterize an individual contaminated site gives rise to a frequency distribution for that variable over the region affected by the policy decision. It is important to note that this is a frequency rather than a probability distribution; that is, it will tell us how often a certain condition (or combination of conditions) is encountered within the geographic area, say the State. The relevant characteristics of the region might be described in terms of some aggregate set of variables, or perhaps summary statistics.

A second type of hierarchy that is relevant relates to the decision making process. Use of a hierarchical decision framework recognizes that policy decisions taken at the State level are primarily designed to influence decisions which are made at the level of management of the individual sites of contamination. The book by Mesarovic et al. discusses basic concepts related to both types of hierarchy.

Both types of hierarchy are associated with a good deal of uncertainty. As relates to the descriptive hierarchy, uncertainty is introduced by incompleteness of the data (we do not have data on every square foot of the State) as well as by the inaccuracy of the data we do have. If the State level is described in terms of a frequency distribution, we are left with a probability distribution over the space of possible frequency distributions (see the discussion above on frequency vs. probability).

For the decision hierarchy, the situation is that we can never be certain of the impact of a policy level decision on the decisions taken at the management level. The common procedure is to predicate such decisions on their *most likely* impact. A more rational approach might be to consider the range of possible impacts, the likelihood of each, and the relative desirability of each.

Value considerations at the State level are also different from those at the individual level. At the State level, we deal with public values related to public health and economics, as well as with fairness and equity of policy decisions. These questions are surrounded by disagreement and controversy. Uncertainties therefore involve not only doubt about what is "right", but also the type and strength of public reaction to policy decision alternatives.

10.4. Information and Monitoring: The Value of Information.

10.4.1. *Categories of information needed.*

Each of the sources of uncertainty listed above indicates a need for information. Several types of information may be distinguished:

- ***Information which characterizes individual sites*** (or the collection of sites in the State). This would include hydrogeologic characteristics, population patterns and water use patterns. Hydrogeologic characteristics can, in principle, be determined by one-time surveys or measurements; they are not absolutely static, but are expected to change on a longer time scale than population and water use patterns. The latter may have to be re-determined from time to time.

- ***Information on the current state of the site*** (including status of tanks which may pose leakage hazards), on the extent and nature of plumes from tanks which have already leaked, on the chemical composition of the plume. Keeping such information current requires systematic monitoring and sampling procedures, which may pose special statistical problems (Cooper and Istok 1988a and 1988b; Istok and Cooper 1988; Maness 1993).

- ***Information which of itself is independent of the specific LST context.*** This would include, for example, patterns of behavior related to water use and other exposure routes, and physiological information related to chemical absorption and toxic response.

- ***Information, as well as judgments, on public values,*** as related to health or other value related issues (some approaches are reviewed for example in Pearce and Turner, 1990).

10.4.2. *Valuing Information from a Decision Analytic Perspective*

Given this broad array of types of information which are "needed", and given that obtaining such information requires intensive use of resources, and given limited resources, it seems clear that one cannot escape the need to set priorities. An approach to this problem is through "value-of-information" considerations taken from the field of decision analysis (see Howard 1977 for basic theoretical discussion; Freeze et al. 1992 for discussion in specific context of hydrogeologic decisions).

The basic concepts of information value can best be explained in terms of the decision analytic notation introduced in the section on risk assessment theory. In that section it is explained that, at least in principle, it is possible to define a utility function U with the property that the relative desirability of different decision alternatives d_i can be ordered according the resulting values of expected utility, $\mathcal{E}_i(U)$. The expectation $\mathcal{E}_i$ is taken with respect to the probability distributions relevant to decision d_i.

Within the paradigm of decision analysis the effect of information is entirely captured in terms of its ability to alter probability distributions held prior to receiving the information. The consequence of this alteration may or may not be to change the choice of decision alternative; that is, to change the decision. If it does change the decision, say from d_i to d_j, it is because under the altered probability distribution, $\mathcal{E}_j(U) > \mathcal{E}_i(U)$, whereas this was not true before. The strength of the desirability for changing the decision is a function of the increase in expected utility, $\mathcal{E}_j(U) - \mathcal{E}_i(U)$. We might label the increase, the "expected utility of the information", or *EUI*.

Different types of information will be associated with different expected utility. The *EUI* then becomes a rational basis for setting information gathering priorities. For any given type of information, we can, in principle, compare the *EUI* with the cost of getting the information in terms of time and resources. Most often it is possible to relate the utility $\mathcal{U}$ to a monetary value V, which allows one to directly compare the expected cost of obtaining some particular type of information with the expected *value* of that information.

From a more general perspective, the result of any analysis might be considered the generating of information. The usefulness or value of the analysis may indeed be discussed these same terms (Gold 1992). It follows from this perspective that ***the value of a risk analysis depends on its potential impact on risk management decisions.***

11. CONCLUDING REMARKS.

In order to evaluate the health risk due to any environmental contamination, it is necessary to take account of the entire chain (Figure 2), beginning with the normal utilization of the potential contaminant, release to the environment, exposure and production of the health-related effect. The various steps in the overall process have each been made the domain of a different scientific discipline. Furthermore, in spite of intensive study in each of the relevant disciplines, large uncertainties remain at almost every step in the chain. An area of study which cuts across the disciplinary boundaries deals with the questions of how to describe the uncertainties, how to obtain and use information to reduce them, and how to incorporate consideration of the remaining uncertainties into decisions related to the management of risk. Consideration of risk management at the societal level or at the level of the individual decision maker necessarily involves ethical and value questions, as well as questions related to risk perception.

The array of subject related and methodological disciplines that need to be brought to bear is clearly too broad for any single individual to be expert in all. The list of disciplinary areas includes biology, the geosciences, engineering, mathematical sciences and social science. The intent of this review has not been to treat any of these areas in depth, but to examine the types of information needed from each, as well as how that information relates to the overall risk analysis and management problem, and to develop some appreciation of the difficulties and uncertainties that arise in each area. An objective is that individuals who choose to specialize in one of the component areas will thereby better appreciate how that discipline relates to others and to the overall problem of risk analysis. Comprehensive efforts in risk analysis and risk management must clearly be highly interdisciplinary in nature.

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