THE ADDITIVITY OF RADIONUCLIDE AND CHEMICAL RISK ESTIMATES IN PERFORMANCE EVALUATION OF MIXED-WASTE SITES

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ABSTRACT

Methods for assessing radioactive waste sites that contain chemical constituents are in the formative stages. In evaluating these sites, a key concern will be the hazard to personnel involved in cleanup work and to the general population. This paper focuses on what we have learned from pathway analysis and risk assessment about providing a combined estimate of risk from exposure to both chemicals and radionuclides. Quantitative radiation risk assessment involves a high degree of uncertainty. Chemical risk assessment generally does not provide quantitative results. Thus, it is not currently possible to develop a useful, quantitative combined risk assessment for mixed-waste sites.

INTRODUCTION

In radionuclide risk assessment, it is assumed that the dose is sufficiently low that only stochastic effects (those that occur by chance) need be considered. Stochastic effects are, mainly, cancer and genetic responses. No threshold (dose below which health effects are not observed) is assumed.

Conventional toxicological methods have been used to establish "safe" levels of exposure for chemicals presumed to have a threshold (doses below which significant nonstochastic effects such as death or severe injury are unlikely to occur). These methods cannot be used to establish safe exposure levels for chemicals that are suspected carcinogens or mutagens, because the doses are far below toxicological thresholds. As in radiation protection, chemical risk assessment involves mathematical models to extrapolate the probability of effects at relatively high exposure levels to lower levels where the actual health effect cannot be detected, either through epidemiological or experimental techniques.

With the advent of decontamination programs and cleanup of various mixed-waste sites throughout the United States, there is interest in combining risk estimates for radionuclides and those for chemicals to reflect total risk. Risk assessment evaluates known effects of radiation or chemicals on exposed individuals and populations and estimates probable effects of additional exposure. Radiation risk assessment is currently more advanced than chemical risk assessment; we will describe why.

BACKGROUND

Obtaining a reasonable risk estimate is a complicated web of equations, analytical techniques, and models. We will divide the process into several fundamental steps for clarity: hazard identification, dose-response assessment, exposure assessment, and risk characterization (NRC, 1983).

Hazard Identification

More information has been accumulated on the health effects of radiation than on any other environmental contaminant. Although there is disagreement on the effects of low radiation doses, higher doses represent a clear, measurable concern. In contrast, the likelihood of a chemical being a carcinogen is based on judgment. Initial qualitative weight-of-evidence statements are based on information about likely exposure and possible toxicity to humans (Anderson, 1983). There is no simple method or criterion to determine if a chemical is a human health hazard.

The U.S. Environmental Protection Agency (EPA) classification system for carcinogens is adapted from the International Agency for Research on Cancer (IARC) approach for judging the weight of evidence for human and animal data (EPA, 1986). The IARC Group 1 chemicals correspond to the EPA Group A (Table 1), which includes those shown to be carcinogens in humans. IARC Groups 2A, 2B, and 3 correspond to EPA Groups B, C, and D, respectively. EPA has a fifth group that includes chemicals shown to be noncarcinogens in humans.

IARC selects chemicals for evaluation based mainly on: known or suspected (derived from human, animal, or other laboratory data) human carcinogenicity. The selection is highly biased, and the group of over 500 compounds evaluated cannot be compared to a random sample of all chemicals.

Table 1. International Agency for Research on Cancer (IARC) and U.S. Environmental Protection Agency (EPA) classification system for carcinogenicity in humans.

IARC	EPA	Description
Group 1	Group A	Carcinogen in humans
Group 2A	Group B	Probable carcinogen in humans
Group 2B	Group C	Possible carcinogen in humans
Group 3	Group D	Not classifiable as carcinogen
	Group E	Evidence of noncarcinogenicity

Every year, over 400,000 new organic compounds are synthesized worldwide. Over 1,000 of these compounds will eventually be in use and will be disposed of in mixed-waste sites (Woo et al., 1985). Few of these new products can be adequately tested for carcinogenicity. Human data (case reports or epidemiological studies) are available for only a limited number of compounds (Saracci, 1981).

Table 2 shows 13 chemicals and 5 industrial processes classified as human carcinogens. Except for the three drugs, exposure is occupational (Saracci, 1981). Tables 3 and 4 show chemicals from IARC Groups 2 and 3; their carcinogenicity is debatable.

Table 2. Chemicals and industrial processes carcinogenic for humans (Group 1).[a]

- 4-Aminobiphenyl
- Arsenic and certain arsenic compounds
- Asbestos
- Manufacture of auramine
- Benzene
- N, N-bis (2-chloroethyl) - 2-naphthyl-amine (chlornaphazine)
- Bis (chloromethyl) ether and chloromethyl methyl ether
- Chromium and certain chromium compounds
- Diethylstilbestrol
- Underground hematite mining
- Manufacture of isopropyl alcohol by the strong acid process
- Melphalan
- Mustard gas
- 2-Naphthylamine
- Nickel refining
- Soots, tars, and mineral oils
- Vinyl chloride

[a]Adapted from Saracci, 1981.

Table 3. Chemicals which are probably carcinogenic to humans (Group 2).[a]

Subgroup A — Higher Degree of Human Evidence

- Aflatoxins
- Cadmium and certain cadmium compounds
- Chlorambucil
- Cyclophosphamide
- Nickel and certain nickel compounds
- Tris (1-aziridinyl) phosphone sulphide (thiotepa)

Subgroup B — Lower Degree of Human Evidence

- Acrylonitrile
- Amitrole (aminotriazole)
- Auramine
- Beryllium and certain beryllium compounds
- Carbon tetrachloride
- Dimethyl carbamoyl chloride
- Dimethyl sulfate
- Ethylene oxide
- Iron dextran complex
- Oxymetholone
- Phenacetin
- Polychlorinated biphenyls

[a]Adapted from Saracci, 1981.

Table 4. Chemicals not classified as carcinogens in humans (Group 3).[a]

- Chloramphenicol
- Chlordane/heptachlor
- Chloroprene
- Dichlorodiphenyltrichloroethane (DDT)
- Dieldrin
- Epichlorohydrin
- Hematite
- Hexachlorocyclohexane (technical-grade HCH/lindane)
- Isoniazid
- Isopropyl oils
- Lead and certain lead compounds
- Phenobarbitone
- N-Phenyl-2-naphthylamine
- Phenytoin
- Reserpine
- Styrene
- Trichloroethylene
- Tris (aziridinyl)-1-para-benzoquinone (triaziquone)

[a]Adapted from Saracci, 1981.

Dose-Response Assessment

Risk estimates for low-level radiation are determined by studying large population groups that have been exposed to high radiation doses. These include the Hiroshima and Nagasaki bomb survivors, patients who were medically exposed, and occupationally exposed populations. Several scientific committees reviewed these data and estimated the risk from exposure to low doses. Figure 1 shows a typical radiation dose-response relationship. There is considerable evidence to support a linear relationship between dose and risk, although a linear-quadratic model is supported by some studies (for example, BEIR, 1980). Even with the large data base for radiation risk assessment, there is disagreement between models because of the large uncertainty associated with the exact shape of the dose-response curves at low doses (100 μSv to 5 mSv).

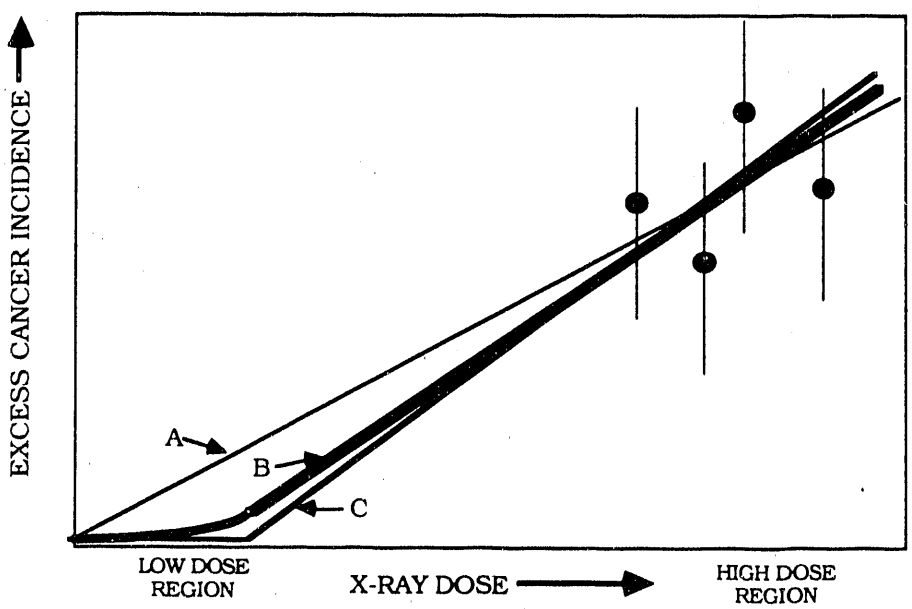

Figure 1. Radiation dose-response extrapolation (adapted from Hall, 1984). A = Linear extrapolation model, B = linear quadratic extrapolation model, C = threshold response model.

Other dose-response models have been developed. For example, the U.S. Department of Energy (DOE) combined absolute and relative risk models from BEIR (1980) to estimate health effects from the Chernobyl accident (Goldman et al., 1987). Using recent data on organ sensitivity

and dose response, they provided three estimates of the risk range: an upper, a best (central), and a lower estimate. The bottom of the range for each is zero.

Dose-response assessment for chemicals usually involves extrapolation from high exposures (of experimental animals, or exposures in epidemiological studies) to the lower human exposure levels expected in the environment. Unfortunately, the data are extremely limited and, most importantly, good epidemiological data are lacking, particularly for newly developed chemicals. These data are not likely to become available because of current emphasis on safety and worker protection. Also, actual dose is not usually measured for chemicals, and complex, poorly understood factors can modify the effect by orders of magnitude.

If data are available at doses equivalent to environmental exposures, the curve that best fits should be used (EPA, 1986). Most often there is no biological justification to support the choice of model to describe actual chemical risk. The model recommended by EPA for risk extrapolation to low levels is the linear nonthreshold model of Crump (1981). This model is not used to establish actual risks but to set reasonable upper bounds. Generally, no attempt is made to pinpoint risks within the broad bounds defined at the upper limit by a dose-response model and, at the lower limit, near-zero (EPA, 1986).

Exposure Assessment

Personnel are routinely monitored for radiation by personal dosimetry, bioassay, and whole-body counting. In contrast, no one approach to assess chemical exposure is appropriate for all cases (Albert, 1985).

Each waste site has a unique physical setting and chemical profile. Extensive monitoring data are generally available only for certain pollutants, pesticides, and a few heavy metals (Nisbet, 1981). Carcinogenic responses to chemicals may differ with exposure pathway (ingestion, inhalation, absorption), term of exposure (chronic or acute), and metabolism. Inside the body a chemical may be translocated to a particular organ, stored, activated to a carcinogenic form, or excreted. Thus, it is unlikely that two assessments of exposure to the same chemical will be identical (OSTP, 1985).

Another complicating factor is the assignment of separate responsibilities within government for environmental monitoring (air, water, and waste sites), food, drugs, consumer products, and the workplace. In each area, specialized estimating techniques, data sources, and

expertise have been developed. Each federal agency tends to focus on those aspects of exposure that are relevant to the laws it administers (OSTP, 1985), and there is little coordination among government agencies.

For the 18 most frequently observed chemical contaminants at 929 chemical storage facilities, only arsenic has both a drinking-water and human-health standard. Only seven others have either drinking-water standards (lead, manganese, chromium, mercury) or human-health criteria (trichloroethylene, tetrachloroethylene, benzene). Clearly, much more information is required for standard setting and risk assessment.

Many chemicals can be detected in the body: lead in blood, cadmium in urine, and polychloride biphenyl compounds (PCB) in serum are well-accepted indices of exposure. Unfortunately, the number of chemicals that can be detected is small compared to the number and types of chemicals released. Furthermore, bioassays indicate only that the chemical is present in the body and not the amount.

Maximum measured or estimated exposure concentration is used to obtain a "worst case" risk estimate. Although incorrect, the highest concentration present is used routinely to quantify risk. Adding upper bounds serves only to compound this conservatism, which stems from adopting the linear no-threshold model (and the need to extrapolate from animal data).

Risk Characterization

The results of exposure and dose-response assessments are combined to quantitatively estimate carcinogenic risk. For example, lifetime risk from 10 mGy whole-body irradiation is about 280 additional fatal cancers per million persons (BEIR, 1980). Based on the LOE model used for Chernobyl, 230 additional fatal cancers per million persons would be expected from exposure to 10 mGy (Goldman et al., 1987). For both estimates, the additional cancers from whole-body irradiation represent an increase of about 0.015%, well within the variability of natural cancer mortality. Even with the extensive data base, quantitative estimation of carcinogenic risk from low-dose, low linear energy transfer (LET) radiation is subject to numerous uncertainties (BEIR, 1980). Unlike sampling variation, these uncertainties cannot easily be summarized in probabilistic terms. Thus, there is more emphasis on the estimation method than on the estimate obtained.

For chemicals, no established procedure exists for making "most likely" or "best" estimates of risk within the range of uncertainty defined by upper and lower limits (EPA, 1986). Nevertheless, quantitative risk assessment has been applied to provide information for making policy decisions regarding public health. For example, by law EPA is required to list hazardous air pollutants and regulate sources as necessary. A potency index, defined as an upper-bound unit risk estimate and a qualitative weight-of-evidence statement, is given for each chemical (Anderson, 1983).

Table 5 shows unit risk estimates for chemicals that might present a hazard to humans in air. Most are also identified as probable or possible human carcinogens by IARC and EPA (Tables 2 and 3). The upper-bound unit risk is defined as the increased individual lifetime risk for a 70-kg individual, breathing air containing 1 $\mu g/m^3$ of chemical for a 70-yr life span. Exponents of the risk estimates range over a billionfold, from 10^{8} to 10^{-1}.

Table 5. Upper-bound unit risk estimates for suspected carcinogenic air pollutants.[a, b]

Chemical	Upper-Bound Unit Risk Estimates
Acrylonitrile	7×10^{-5}
Allyl chloride	5×10^{-6}
Arsenic	4×10^{-3}
Benzene	7×10^{-6}
Beryllium	6×10^{-4}
Diethylnitrosamine (DEN)	2×10^{-2}
Dimethylnitrosamine (DMN)	5×10^{-3}
Ethylene dibromide	6×10^{-5}
Ethylene dichloride	7×10^{-6}
Ethylene oxide	2×10^{-4}
Formaldehyde	5×10^{-5}
Manganese	4×10^{-4}
Nickel	6×10^{-4}
N-nitroso-N-ethylurea (NEU)	1×10^{-2}
N-nitroso-N-methylurea (NRU)	7×10^{-1}
Perchloroethylene	2×10^{-6}
Trichloroethylene	3×10^{-6}
Vinyl chloride	4×10^{-6}
Vinylidene chloride	4×10^{-5}

[a]Unit risk is excess lifetime risk associated with a 70-kg person breathing 1 $\mu g/m^3$ of chemical over a 70-yr life span.
[b]From Anderson, 1983.

Based on responses in humans, some chemicals with the best evidence for carcinogenicity have relatively low potencies (for example, vinyl chloride and benzene, with unit risks of 10^{-6}). Therefore, EPA emphasizes that numerical estimates should be accompanied by the various assumptions and uncertainties on which they are based. There is a tendency to use risk estimates and ignore the biomedical evidence, or to treat suspected carcinogens as if they were known to be human carcinogens. In some cases, upper-bound estimates have been treated as actual risk estimates, and uncertainty estimates have been ignored.

RISK ESTIMATION PROCEDURES

Combining risk estimates for different agents has been considered for some time. EPA recommends (EPA, 1986), and others concur, that the possibility of interaction among several chemical carcinogens can be ignored and the risks summed (EPA, 1986; Albert, 1985).

Several approaches have been suggested to estimate risks from combined exposure to different carcinogens (e.g., radiation and chemicals). In one system (NRC, 1983), carcinogens are ranked. Scores are assigned for number of species affected, number of histologically different types of neoplasms, spontaneous incidence of neoplasms, amount and duration of treatment required for a specified response, malignancy of induced tumors, and genotoxicity in a battery of short-term bioassays. These methods produce a variety of end points rather than a risk estimate.

Another approach to estimating combined risk relates mutagenicity of a chemical to the amount of radiation that would produce an equal effect. A "rem-equivalent" chemical dose (REC) produces genetic damage equal to that from 1 rem (10 mSv) chronic radiation exposure (Crow, 1973). The REC was introduced not to estimate risk but as a guide to set standards. Because there were accepted radiation standards, NRC hoped that chemical risks could be evaluated by comparing chemical effects to those from radiation. However, chemicals produce various biochemical effects that are different from those produced by radiation. Most radiation-induced mutations include chromosomal breakage; some chemicals induce point mutations and changes in DNA. Although radiation damage can be measured in tissues, that is not currently the case with chemicals. A newer method, discussed below, may provide valuable information in this area.

Molecular dosimetry, a step toward detecting and measuring chemicals in tissues, is based on the relationship among altered genetic material, DNA, and carcinogenesis. The presence of carcinogen-altered DNA or DNA adducts may indicate persistent damage at the molecular level from exposure to chemicals (EPA, 1986). DNA adducts have been measured in cells and tissues from people occupationally exposed to carcinogenic polycyclic aromatic hydrocarbons (Harris et al., 1987).

CONCLUSIONS

There is currently no rationale or mathematical justification for combining radiation and chemical risk estimates. The major gaps in risk assessment of mixed waste reflect limitations in the process of chemical risk assessment.

There is no simple method or criterion for determining whether a chemical is a human health hazard. Radiation risk assessment estimates actual harm that could occur under the conditions of exposure. Many chemicals produce a spectrum of lesions that is different from that produced by radiation. Often, carcinogenicity is assumed because a substance is related to a chemical class in which another substance is a known carcinogen. There is currently no easy way to directly measure the damage from exposure to chemicals in human cells.

The data base for chemicals is inadequate for establishing dose-response relationships in humans. The data most appropriate for estimating cancer risk are from epidemiological studies. Many investigators believe that no defensible epidemiological study has been made on potential health effects to residents near hazardous waste-disposal sites (Corn and Breysse, 1985). Nor have there been acceptable studies on genetic effects in offspring of adult females exposed to a chemical mutagen.

The concept of radiation dose allows extrapolations from one exposure condition to another that are impossible with chemicals. Radiation dose, regardless of its source, produces biological effects (cancer and genetic effects) proportional to that dose (with quantifible modifiers). This is not the case for chemical risk assessment.

Exposure assessment methods for various chemicals do not necessarily provide an equivalent result because of different chemical properties, behavior (persistence and reactivity) in the environment, and route of initial exposure. A large number of potential carcinogens are unlikely to occur in the environment in quantities such that humans would

be equally exposed to them all. If one agent dominates the calculated risk for an individual or population, other carcinogenic agents can be ignored until exposure to the dominant agent is reduced.

Radiation doses can be related to natural background; there is no easily measured background exposure for chemicals. Risk can be compared among chemicals, but a quantitative assessment is not possible. While the biological response to radiation generally follows well-defined physical and chemical processes at the molecular and cellular level, responses to chemicals often vary. Many chemical carcinogens require metabolic activation and the presence of cocarcinogens or tumor promoters to produce an effect.

Because epidemiological data are minimal, accurate evaluation of human risk from chemicals requires detailed exposure, dose, and response studies in the laboratory. Continued research in molecular dosimetry is essential. Although laboratory animal data can provide an approximation of chemical risk to humans, the expense, difficulty, and inaccuracy in extrapolating from animal data make this solution impractical. We must develop methods to rapidly screen chemicals and to understand the mechanisms and biochemical effects of carcinogens and mutagens. We must also develop models to simulate the interaction of chemicals with biological systems at the molecular level, especially in humans. Such investigations should lead to a statistically acceptable and scientifically sound procedure for chemical risk assessment and should result in an acceptable method for combining risks from radionuclides and chemicals.

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