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Retrospective Internal Radiation Exposure Assessment In Occupational Epidemiology

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INTRODUCTION

The National Institute for Occupational Safety and Health of the United States Department of Health and Human Services is currently conducting epidemiologic studies of workers at U.S. Department of Energy facilities. One goal of these studies is to evaluate the health risk associated with exposure to sources of external and internal ionizing radiation. While exposure to external sources of radiation can be estimated from careful evaluation of personal dosimeter data, the reconstruction of exposure due to internally deposited radioactivity is more challenging. This is in part due to the existence of monitoring programs that were designed more to demonstrate compliance with regulations rather than provide accurate exposure assessments. Attributes of past internal monitoring programs that challenge accurate exposure assessment include: 1) incomplete characterization of the workplace source term; 2) a lack of timely and sensitive bioassay measurements; and 3) the presence of missing and censored data. In spite of these limitations, many facilities have collected a large amount of worker and workplace monitoring information that, if evaluated using a systematic approach, can be used to evaluate internal exposure while minimizing misclassification. Based on available data, the exposure assessment could be either qualitative or quantitative in nature.

TYPES OF INFORMATION USEFUL IN EXPOSURE ASSESSMENT

Ideally, it would be desirable to collect sufficient information on each individual so that the internal radiation dose delivered to each organ could be evaluated. In retrospective internal exposure assessments, however, this is a challenging effort. In many cases, shortfalls in the characterization of the workplace exposure conditions and the lack of sufficient bioassay data dictate that an estimate of exposure be used as a surrogate for internal dose. In these situations, it may be possible to develop an ordinal classification of exposure based on parameters related to exposure such as monitoring status, job classification and duration of employment. When sufficient bioassay data do exist, however, it may be possible to quantitatively estimate internal doses and to classify these individuals into a number of categories for subsequent dose response analysis.

As indicated in Table 1, there are a variety of available sources of information for assessing internal exposures.

Table 1
Examples of Information Useful for Internal Exposure Assessment

C Routine Bioassay Measurements	C Aerosol Characteristics (i.e., Solubility and Particle Size)
C Bioassay Measurement Procedures	C Employee Work History
C Incident and Special Bioassay Measurements	C Process Descriptions
C Breathing Zone Air Samples	C Incident and Accident Reports
C General Area Air Samples	C Medical Records

Stewart et al. have previously published a strategy for the collection of exposure information to supplement air and personnel monitoring results (1). For many of the DOE cohorts presently under study, extensive databases of air and personnel monitoring exist. Since the bioassay results represent a direct measurement of systemic

excretion and/or deposition, they are typically considered the best indicators of exposure. Because of the high potential for misinterpretation, however, special care must be used in the collection, evaluation and use of this information in an internal exposure assessment. The following sections describe some of the key elements that must be considered when evaluating internal exposure monitoring data. Examples are provided for these key elements in relation to an exposure assessment at a uranium processing facility.

EVALUATION OF THE BIOASSAY AND AIR MONITORING PROGRAM

It is not only important to collect all available bioassay and air monitoring information, but it is equally important to obtain detailed information on the historical design basis of the monitoring program. This includes the collection of any technical basis documents, the rationale for participant selection, standard operating procedures and standard reports. Only with this background information can the bioassay results be interpreted properly. One key area that must be evaluated is the historical detection limits for the monitoring techniques employed and an indication of their relative accuracy and precision. A review of the analytical techniques used over time should be conducted to determine historical changes in the detection limits. For example, at uranium facilities the implementation of kinetic phosphorescence analysis (KPA) in the late 1970s and early 1980s lowered the detection limit for uranium in urine by about a factor of 25 over the previously used flourophotometric method. In fact, the KPA method was sufficiently sensitive to detect the trace quantities of uranium in urine from natural sources. This fact must be considered when evaluating reported positive results.

The detection limit of the bioassay monitoring technique and the frequency of bioassay sampling determine the minimum level of internal exposure that can be detected. Given these two values, and applying standard metabolic models, it is possible to calculate the amount of dose that a worker could have received and gone undetected. This value is typically called missed dose or minimum detectable dose (MDD). An example of the minimum detectable dose for the inhalation intake of natural uranium as a function of monitoring frequency for solubility classes W and Y is provided in Figure 1. The detection limit used in this example of 0.005 mg U / L of urine is typical of the capability of the fluorophotometry techniques used in the 1960s and 70s.

As can be seen in Figure 1, the minimum detectable internal dose for a given bioassay monitoring program can vary over three orders of magnitude. In this example, a worker who was exposed to solubility class Y uranium and monitored on a yearly basis could have had an undetected intake that resulted in a dose exceeding 100 mSv. It is evident that such a monitoring program would be of little use in estimating the internal exposure to a cohort. On the other hand, a worker who was exposed to class W uranium and participated in a 30 day sampling program would have a minimum detectable dose of substantially less than 1 mSv. A program with this sensitivity could be useful in estimating the internal exposures of a cohort.

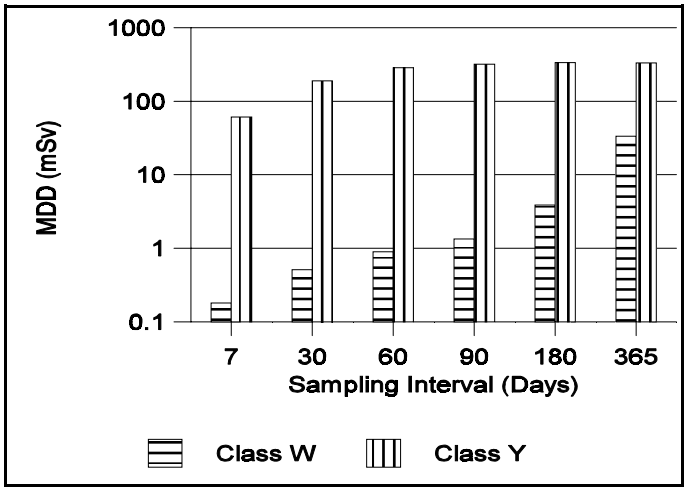

Figure 1. Minimum detectable committed effective dose equivalent for an acute inhalation intake of natural uranium.

EVALUATION OF DOSES TO INDIVIDUAL ORGANS

In the example provided above, the minimum detectable dose was calculated as the effective dose equivalent projected to be delivered over 50 years. This value, referred to as the committed effective dose equivalent (CEDE), is defined as:

$$H_{E,50} = \sum_t w_t H_{T,50}$$

where: w_t = the weighting factor for the irradiated tissue; and
$H_{T,50}$ = the dose equivalent delivered to the tissue over 50 years (2).

The CEDE is the current basis for limiting the risk of cancer and genetic effects to workers. While the CEDE is appropriate for radiation protection purposes, it is not applicable to an epidemiologic study due to the use tissue weighting factors and integration of dose over 50 years. The weighting factor applied in the calculation of CEDE is used to normalize the risk of developing cancer for an individual organ to that of an exposure to whole body penetrating radiation. In this way, the differential radiosensitivity of the individual organs is taken into account. For an epidemiologic analysis, the actual dose delivered to an organ must be integrated over the exposure period without the application of weighting factors. Given an intake of radioactive material, the dose delivered to an individual organ can vary considerably depending on the metabolic behavior of the radionuclide. As an example, Table 2 compares the internal doses delivered to selected organs from inhalation of solubility class Y natural uranium at various time periods post-intake.

Table 2
Percentage of Committed Dose Equivalent Delivered at Various Times After Acute Inhalation of Class Y Natural Uranium

	1 yr	5 yr	10 yr	20 yr	50 yr
Lung	20.1	58.3	70.8	80.6	100
Bone Surfaces	1.7	12.6	30.7	63.0	100
Kidney	11.7	43.3	70.0	91.7	100
Red Marrow	2.1	13.9	32.2	61.1	100

It is evident from examination of Table 2 that the use of a 50 year integration period would overestimate doses to organs of cohort members who experienced intakes less than 50 years in the past. Because of this, only individual organ doses that are integrated over the actual period following exposure for a cohort member should be computed. Also, it can be seen that the temporal distribution of dose varies considerably among the individual organs. It should be emphasized that the estimation of dose becomes more uncertain for those organs that are not the primary deposition site. In the example provided above, an evaluation of *in vivo* measurements of uranium deposited in the lung could provide a fairly good estimate of lung exposure whereas the dose to the other organs must be inferred from metabolic models.

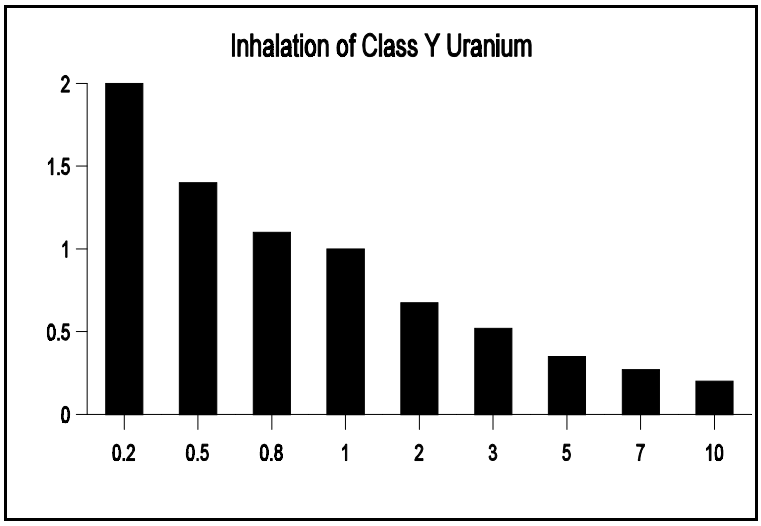

Figure 2. Relative lung dose as a function of particle size. (values normalized to 1um AMAD)

CHARACTERIZATION OF EXPOSURE CONDITIONS

To interpret any bioassay or air monitoring results, it is necessary to understand the historical radiological exposure conditions. Since in most cases workers were exposed through inhalation, the aerosol particle size distribution and solubility of the material in the lung must be understood. Internal doses can vary widely as a function of these two parameters. Figures 2 and 3 provide examples of the differences in the first year dose delivered to the lung per unit intake of uranium as a function of particle size and solubility classes. The values reported in Figure 2 were

calculated using the standard parameters of the ICRP 30 lung model and are normalized to the committed dose delivered by a 1 Fm aerosol (2). As can be seen, the dose delivered to the lung can vary significantly depending on the activity median aerodynamic diameter (AMAD) of the exposure aerosol. For the larger particles, the delivered dose can be overestimated by up to a factor of five whereas submicron aerosols will deliver up to twice as much dose per unit activity intake as a 1 Fm AMAD particle.

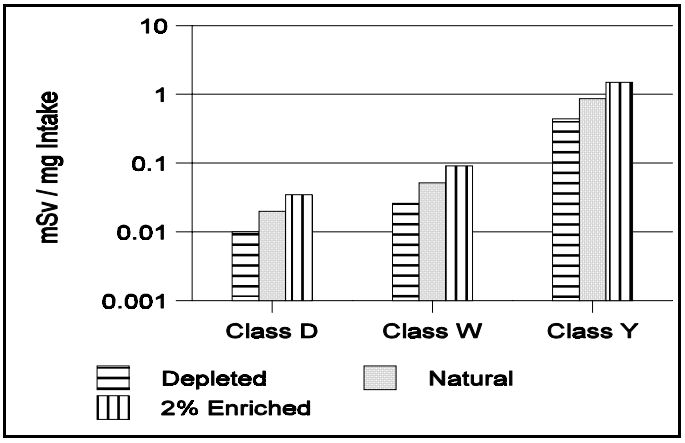

Figure 3. Dose per mg inhalation intake of different solubility classes and degrees of enrichment.

The difference in dose delivered to the lung is even more dependent on the solubility class of the material. As shown in Figure 3, the dose per unit intake of uranium can vary by over two orders of magnitudes depending on the solubility of the material and the degree of enrichment. If these parameters were not characterized during production operations, it may be possible to estimate them.

For example, if concomitant air and bioassay monitoring results are available, it may be possible to empirically determine the relative solubility of the material by examining the ratio of the urinary output to measured air concentrations. This approach requires that: 1) air samples representative of the breathing zone of workers are available; 2) that urine samples were colleted at the appropriate intervals for the solubility class; and 3) the monitored workers were representative of all members of the exposure group. If *in vivo* measurements and urinalysis were routinely performed, the ratio of lung content to urinary excretion can be used to estimate the solubility of material. Alternatively, an examination of production records may provide an indication of the chemical forms of the material processed.

EVALUATION OF MISSING AND CENSORED INFORMATION

In retrospective exposure assessment it is not uncommon to have gaps in the worker monitoring data. This may be due to incomplete monitoring programs for certain time periods or the loss of historical monitoring records. A workshop held at the National Institute for Occupational Safety and Health previously examined procedures for interpreting non-detectable and erroneous values in occupational radiation exposure records (3). When bioassay monitoring data are missing, a technique using nearby data has been proposed (4,5). While this technique was originally applied to external monitoring results, it may be equally applicable to chronic internal exposure scenarios. Due to inconsistent timing of sample collection following exposures and the exponential clearance patterns associated with most acute exposures, though, the use of this technique would be precluded.

At a number of facilities, bioassay measurements that were not determined to be statistically different from background were recorded as below the limit of detection (LOD). Although methods for determining the LOD varied over time and from site to site, this practice had the effect of biasing the distribution of measured values. At the NIOSH workshop, three methods were identified that attempt to correct for this bias (6, 7, 8). Two methods complete the distribution below the LOD by substituting the LOD/2 or the LOD/o2 for the censored value while the third method uses a maximum likelihood estimate based upon the assumption of a lognormal distribution.

If the workplace air monitoring program was well-documented, and it can be established that the data are representative of a worker's exposure, it could be used to replace missing data. This approach has several limitations which must be recognized and evaluated to determine its feasibility. For example, the purpose and the scope of area monitoring must be evaluated with regard to its intended use. The historical purposes for area sampling, e.g., compliance, hazard evaluation, control technology assessment, inherently limits its utility to derive exposure estimates for epidemiology. Sampling duration, sensitivity, specificity and purpose for sampling are all parameters that must be considered.

CONCLUSIONS

The interpretation of workplace monitoring results in retrospective internal radiation exposure assessment requires a thorough understanding of the historical workplace exposure conditions and the temporal changes in the monitoring programs employed. Based on a detailed review of the historical monitoring techniques and capabilities, it is possible to evaluate the minimum detectable dose associated with the monitoring programs over time. In situations where the minimum detectable internal dose is estimated to be large, the use of ordinal classification of exposures should be considered. Where minimum detectable doses are estimated to be small, quantitative estimates of internal dose may be possible.

A quantitative estimate of internal dose must consider the workplace exposure conditions. Two exposure parameters that have a large effect on internal dose are the particle size distribution of the aerosol and the solubility of the material in the lung. If these parameters were not characterized during production, efforts should be made to evaluate them from available worker and workplace monitoring data. Missing and/or censored data for chronic exposure scenarios can be addressed using one of several previously published techniques. To allow for an accurate assessment of risk, all organ doses used in epidemiologic analysis should be calculated for a worker's actual exposure period without the use of modifying factors that attempt to normalize risk.

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