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CURRENT STATUS OF CURIUM INHALATION EXPOSURES IN HUMANS

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ABSTRACT

The maximum permissible amount of alpha-emitting curium in the human body ranges from 0.01 to 1 millimicrogram. Inhalation presents the greatest occupational risk. Since curium has but recently become available in quantities approaching a gram, its metabolism is known almost solely by analogy with plutonium and closely related elements.

An incident is described concerning a curium accelerator target aerosolized by explosion. Management of the spill, sampling, particle sizing, and medical findings are presented. Seven of the 27 persons present showed low levels of curium excretion. The data from this incident were compared with those from three other inhalation exposures to curium compounds at this Laboratory.

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Curium is not found in nature, being a man-made element--number 96--resulting from the neutron bombardment of other synthetic elements in a high-flux atomic pile. Thirteen curium isotopes have been reported; all are radioactive, with a range of half lives from 64 minutes to greater than 40 million years. Two of the isotopes, numbers 242 and 244, are of topical interest today. Proposals have been advanced for using multigram amounts of curium-242 for power packages in satellites and in terrestrial remote unmanned weather stations and navigation buoys. Somewhat less than a dozen grams has been synthesized. Curium-244 is of interest primarily as a research tool in the synthesis of new elements. Less than 1 gram has been produced. Both isotopes are alpha-particle emitters. As you will recall, alpha particles cannot penetrate even a piece of paper; they can affect tissue only when emitted within the body.

The toxicity of curium is complex and not completely understood. Because of their short half lives (162 days and 18 years), it is the radiation damage, not the chemical toxicity, that is important for these isotopes. Fundamentally their alpha particles passing through tissue deposit enormous amounts of energy as ionization along their tracks. Peroxides and other undesirable compounds are formed, and as a result, the basic cellular structure formed of complex organic molecules can be radically altered. Genetic material is especially sensitive to radiation-induced changes that cannot be repaired but are passed on as observable effects. Thus the ionization from a single alpha particle may be amplified in the living system to do a great amount of damage.

Much of the arithmetic of curium toxicity is based on the classic radium exposures of 43 years ago. We owe to these exposures most of our knowledge on relation of harmful effects to the amount of alpha-particle emission in human bone.[1] As you know, additional studies since that time have been carried on by numerous workers with practically all the radioelements, in an effort to relate their uptake, localization, and excretion to radiation dose, and thence to their toxicity for humans. Particularly for the bone-seeking elements such as curium, plutonium, and all the rare earth and transuranic elements, the radium data are crucial in relating exposure level to predicted risk.[1,2]

Deliberations of national and international bodies have been published on radioisotope toxicity, based on such considerations. Handbook 69 of the National Bureau of Standards presents the maximum permissible occupational limits for various radioactive materials in the body. For curium-242 the amount comes out to 15 micromicrograms. This is equivalent to a single spherical particle with a diameter less than one-fifth that of a red blood cell.

Of the several routes into the body, the inhalation route is considered the most dangerous. For many substances inhalation of suitably sized particles approximates an intravenous injection. For other insoluble materials in aerosols, the lung retains most of the deposit and lung or pulmonary lymph nodes get most of the radiation dose.[2, 3, 4] One of the problems remaining in the study of curium metabolism is the solubility of the various curium compounds in the body fluids after inhalation. It does not always follow the rules of simple solution chemistry. As you know, deposition of inhaled material in the alveoli depends on particle size, particle density, rate of respiration, and other factors. Subsequent translocation and hence the radiation dose depend on particle size, concentration, and chemical form of the element; the problem is extremely complex.[5] Plutonium oxide, for example, remains in the lung except for a small percentage of the smallest particles, which are carried in solution or in colloidal form by way of the blood stream to the rest of the body, especially to bone. On the other hand, inhaled plutonium nitrate approximates an intravenous injection. An excellent review of the industrial toxicology and physiology of plutonium has recently been prepared by Langham.[2] Much is known about curium chemistry that permits us to reason about its metabolism by analogy with these other elements about which much more is known. However, actual determination of the fate of a particular curium compound after inhalation is still a problem that must be answered by experiment.

In one incident in our Laboratories, two persons were exposed to curium-242. Curium oxide somehow escaped from a glove box during routine manipulations, and was inhaled in small amount. The radioisotope was detectible in the urine of each individual for more than 9 months afterward, although calculations indicated that much less than the permissible amount was inhaled. A few months later, in a second glove box incident, a single individual was exposed to curium-242 again--this time to the highly soluble curium citrate, but again by inhalation. Radioactivity was found in the urine in decreasing amounts during the ensuing 3 months. Again the data indicated an exposure well below permissible levels. Excretion data from these individuals are summarized in Table I. A typical excretion curve is shown in Fig. 1.

Several other accidents have occurred under conditions where a probability of spill was anticipated; respiratory protective equipment was properly applied beforehand and exposures were presumed nil or nearly so. There has been no clinical laboratory follow-up on the personnel involved in these instances. However, routine assay of urine for alpha radioactivity is being done on all those potentially exposed to curium in their daily work, and can be expected to reveal any cumulative exposures before permissible levels are reached.

Table I

Particle sizing on the curium-244 oxide airborne in the Hilac spill

Size range--diameter (microns)	% of 799 particles counted
0.4 - 1.5	0.2
0.13 - 0.26	6.4
0.07 - 0.129	11.7
0.027 - 0.06	15.9
<0.027 -	65.8

The arithmetic mean activity per particle was < 17 disintegrations per minute.

Method from Leary and Fitzgibbon (Ref. 7).

A year ago, about 150 micrograms of curium-244 oxide was accidentally dispersed by explosion into a fairly large building. Many details of this event have been published.[7] The airborne curium was characterized (by particle size measurements) as potentially serious. The maximum diameter was found to be about 1.5 μ; 81% by count was less than 0.06μ (Table I). The very small particle size was judged not due to the mechanics of the rupture, but rather to the particular techniques of preparing the target (electrodeposition in "ionic wind" from droplets of solution to a catching surface). Less than a third of this building and its innumerable pieces of equipment escaped contamination. The cleanup job required 50 man months of effort. From air sampling, an educated guess of the quantity inhaled by one of the cases (A. G.) was 0.1 to 1.0 μC. Fortunately, later analysis of excretion data indicated he somehow got considerably less than this amount (see below). The actual retained radioactivity was well below permissible levels.

This curium oxide aerosol was water-soluble, the chemists tell us. One would expect it might be handled by the lung more like plutonium nitrate than plutonium oxide. Of the deposition sites other than lung, bone and liver should be prominent. Essentially complete retention of the bone-deposited material throughout lifetime can be predicted.

Twenty-seven persons were in the building at the time of the dispersion. An initial evaluation of the incident was made on the basis of history of exposure, nose swipes, rapid survey of the first 24-hour urine specimen for alpha radioactivity, and complete blood count. These studies indicated that all exposures were either small or negligible by comparison with damaging amounts. No therapy was indicated. However, there was some uncertainty as to the amount that might remain in the lungs. There was also the opportunity to gain information on excretion versus retained amount that may be of use in the future.

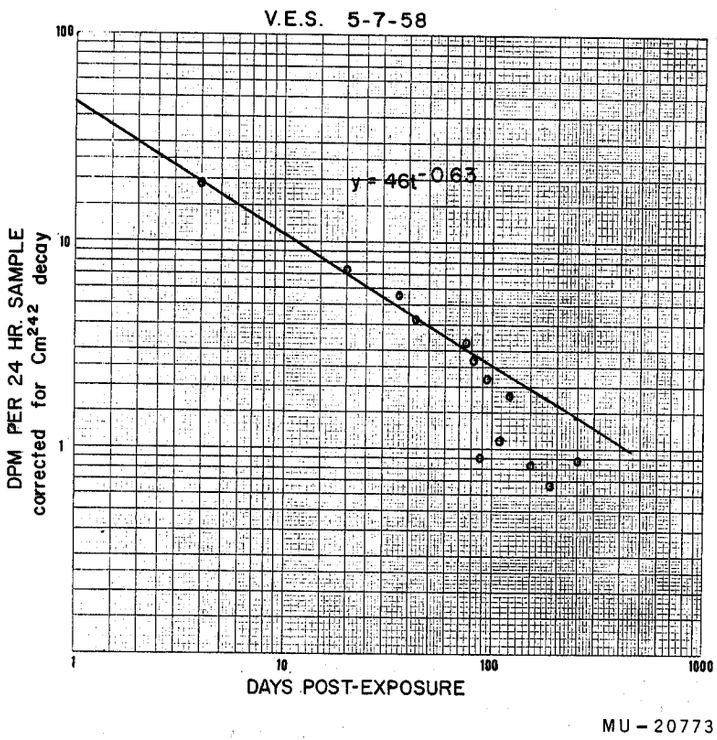

Fig. 1. A typical urinary excretion curve after inhalation of curium oxide in man.

Therefore, on seven individuals in whom there was detectible radioactivity we have since been obtaining urine and stool specimens for radioassays (Fig. 2). In three of these the levels were high enough initially so that a crude analysis of the declining excretion rate curve has been possible (Table II).

In six persons from all three incidents described here we have noted so far that urinary excretion declines, but at a decreasing rate, resulting in a power-function fit to the data with a mean slope of -0.53. That is, the logarithm of the amount excreted per day, when plotted against the logarithm of the number of days after the exposure, results in a straight line with a slope of -0.53 (Fig. 1). This is reasonably comparable to the excretion curve found by Langham for intravenous plutonium in humans, $Y = 0.002\,t^{-0.74}$.[3] Comparison of this limited excretion data from all incidents (Table II) tentatively suggests that inhaled curium oxide is indeed handled by the body in a manner similar to curium citrate and to soluble plutonium compounds.

Stool specimens are also being collected from the Hilac spill. Initially they indicated that some individuals had curium passing through the gastrointestinal tract, either from ingestion, or from swallowed material being brought up from the lungs. Analysis of fecal excretion curves and fecal-urinary ratios has been attempted. It is proving very difficult not only because the samples are close to background counting levels, as was feared, but also owing to variable amounts of natural alpha radioactivity in stool specimens, around 2 to 5 dpm per 25-hour specimen (Fig. 2). Interestingly enough, we have found little or nothing in the literature on natural levels of alpha emitters in stools.

We have mentioned the difficulties in predicting metabolic behavior of inhaled materials even when chemistry and particle size are known. A related problem that distresses the industrial physician is that of making a quantitative estimate of retained activity from excretion-curve analysis. Even for thoroughly studied situations such as human exposures to radium or intravenously administered plutonium there is great variability and uncertainty. For curium itself there are no data except for the preliminary experiments by Scott, Axelrod, and Hamilton in 1949 that found the excretion and distribution of curium in a few rats to be like that of americium;[8] hence, it is much like that of all the transuranium and rare earth elements.[9-12] Further data specifically on curium are being gathered by Dr. Durbin at Lawrence Radiation Laboratory. Emphasis will be on data from inhalation exposures.

But, let us examine the present basis for quantitative estimates of retained curium activity in humans. One knows from the data mentioned above that curium is distributed and excreted very much like americium, element 95. Their solution chemistry is also very similar. From experiments of Langham et al.[13] one knows that americium is excreted about twice as fast in rats as plutonium, element 94. From Langham's experiment with plutonium injected intravenously in humans, one has a curve relating injected dose to excretion rate[3,14] (Table II). There was considerable variability among the people from whom the mean excretion curve was constructed. Combining these facts into a quantitative statement regarding

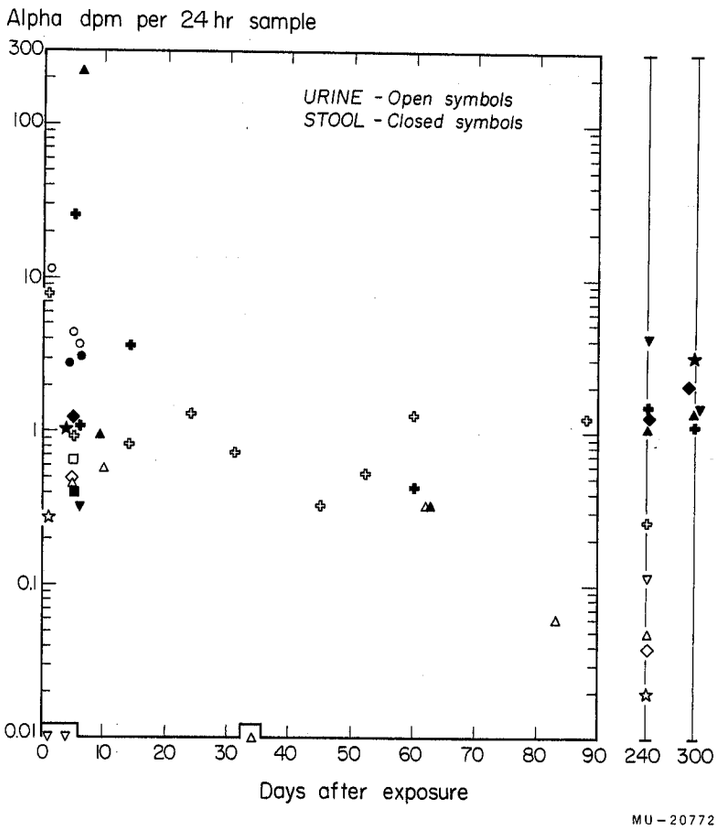

Fig. 2. Alpha radioactivity in urine and stool specimens of seven humans after inhalation of curium-244 oxide at the Hilac high-level spill.

Table II

A summary of excretion-curve analyses from the three separate incidents of inhalation exposure to curium described in the text.

Case	Isotope	Chemical form	dpm/24 hr
V. V.	Cm^{244}	CmO_2	$y = 7.8\ t^{-0.67}$
R. D.	Cm^{244}	CmO_2	$y = 1.2\ t^{-0.45}$
A. G.	Cm^{244}	CmO_2	$y = 11.2 t^{-0.62}$
V. E. S.	Cm^{242}	CmO_2	$y = 46\ t^{-0.63}$
N. V. C.	Cm^{242}	CmO_2	$y = 9.0\ t^{-0.32}$
K. M.	Cm^{242}	Cm Citrate	$y = 14.5 t^{-0.51}$
Langham I. V. Pu data in humans	Soluble Pu^{239}		$y = 0.002\ t^{-0.74}$

curium, as you see, would be risky enough even if it were intravenously injected. With the added complications of the inhalation route, it can be expected to give only a rough order-of-magnitude estimate. However, in circumstances where the calculated dose is a couple of orders of magnitude below permissible, as in these exposures, the analysis can be reassuring.

More accurate quantitative estimates of body burden can sometimes be achieved with the new technique of counting total gamma radioactivity in the whole intact human body with a whole-body counter. Unfortunately some of the more dangerous elements such as curium and plutonium are not suitable for such analysis except in very large amounts. Coincidence counting should improve the sensitivity of whole-body counters for both curium-242 and curium-244. Their gamma rays are weak and in small quantity, but the situation is somewhat better than for plutonium. We are planning to push toward the limit of detectability of curium in this way when the whole-body counter in Berkeley is completed. At present we must rely on excretion-curve analysis as a more sensitive method, and the only way to prove the presence of curium in amounts that are near the permissible burden.

The therapy indicated for a systemic curium burden of dangerous proportions is a chelating agent such as diethylene triamine pentaacetic acid (DTPA), known to exert a significant removal of bone-deposited americium and plutonium in humans.[15] It can also be predicted to do so for curium, though no treatment of a case of curium poisoning with chelating agents has been reported yet. Whether chelation is an appropriate treatment for a lung burden of a curium compound of uncertain solubility is a complex and still unanswered question.

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