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ACTIVITY RATIOS OF THORIUM DAUGHTERS IN VIVO[*]

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ABSTRACT

A computerized method of least squares has been used to analyze the ^{228}Ac and ^{212}Pb-^{212}Bi and daughter γ-ray spectra obtained in vivo from 133 former workers at a thorium refinery. In addition, the exhalation rate of ^{220}Rn was determined for each subject and expressed as pCi of emanating ^{224}Ra. This value was added to the ^{212}Pb value determined from the γ-ray measurements to obtain the total ^{224}Ra present, and the ratio of ^{224}Ra to ^{228}Ac was calculated. Values of the ratio ranged from 0.52 ± 0.32 to 2.1 ± 1.7, with a weighted mean of 0.92 ± 0.17. However, it appears that the ratio observed in a given case is characteristic for that case alone; the computed mean value may not be meaningful. The least squares fitting procedure and the overall calibration of the counting system were validated by measurements of ^{224}Ra in the lungs of one subject postmortem, compared with results obtained from the same subject in vivo.

DISCLAIMER

Introduction

In our studies of the health effects of thorium exposure on workers, most of the internal dosimetry is based on external measurements of body radioactivity _in vivo_. These measurements determine, through γ-ray spectrometry, the body content of ^{212}Pb-^{212}Bi and daughters, and through breath collection, the amount of ^{220}Rn exhaled [6]. The latter measurement reveals the amount of ^{224}Ra that can be considered to be freely emanating, and we assume that the ^{212}Pb is in equilibrium with the non-emanating ^{224}Ra. The emanating and non-emanating parts of the ^{224}Ra are summed to give the total body content.

Unfortunately, this method establishes only a lower limit for the body contents of ^{228}Th, ^{228}Ra, and ^{232}Th. If, however, enough γ-ray activity (more than about 0.1 nCi) from thorium daughters is present _in vivo_, the ^{228}Ac activity can be determined and, therefore, if we assume equilibrium, we also determine the ^{228}Ra body content. Consequently, the ratio of ^{224}Ra to ^{228}Ra can be established.

Determination of the ^{232}Th content can only be made postmortem via radiochemical analyses. When enough cases are analyzed to establish the $^{228}Ra/^{232}Th$ ratio, we will apply this factor to the results of analyses _in vivo_. Since, however, many fewer cases will be available for examination postmortem than _in vivo_, the $^{228}Ra/^{232}Th$ ratio is critical. If we find that this ratio varies significantly from subject to subject, we will attempt to determine the relationship of the $^{224}Ra/^{228}Ra$ ratio to the $^{228}Ra/^{232}Th$ ratio. From this relationship, then, we can still estimate the amount of ^{232}Th present _in vivo_.

Method

Gamma-ray spectra were collected with large (290 mm x 100 mm) NaI(Tl)

crystals positioned above and below the thorax of each subject lying supine on a flat bed. The spectra were analyzed by a computer-based method of least squares in which the observed spectrum (after background subtraction) was treated as a linear combination of standard spectra stored in a computer library. The program, named "GASP", was developed at AERE Harwell [4] and has been adapted for use at Argonne. The advantage of this program is that it uses all the information in the observed spectrum, including scattered as well as primary γ-ray counts.

Standard spectra of ^{40}K and ^{137}Cs were obtained from polyethylene bottles filled with water solutions of either isotope and arranged in anthropomorphic configurations. The standard spectra from the thorium chain were obtained by placing point sources of either ^{232}Th or ^{228}Th at many different positions in the "lung" region of a simple thorax phantom originally developed by Miller [2]. The phantom was composed of masonite ("presdwood") and contained intervening air spaces to represent the lower density of lung tissue. The spectra from ^{232}Th and ^{228}Th, each with its daughters in equilibrium, are shown in Fig. 1. Each spectrum was supplied as a standard to the fitting procedure. The amounts of ^{228}Ac and ^{212}Pb in the spectrum from a subject were computed as follows: to fit the region around 0.91 MeV (a ^{228}Ac γ ray), the program used the ^{232}Th spectrum. If the daughters of ^{228}Ac were not in equilibrium in vivo, then the region around 2.6 MeV (the ^{208}Tl γ ray, assumed to be in equilibrium with ^{212}Pb) contained more or fewer counts in the resulting fit than were observed in vivo. The program subtracted or added the appropriate amount of the ^{228}Th spectrum so as to obtain a good fit at 2.6 MeV, while still fitting the 0.91 MeV region. In practice, the entire observed spectrum from 0.3 to 2.8 MeV was used, until the best fit was obtained. Consequently, the activity of the ^{232}Th standard found by the

fitting routine was taken as the amount of ^{228}Ac present in vivo, and the algebraic sum of the activities of the ^{232}Th and ^{228}Th standards was taken as the amount of ^{212}Pb present in vivo. If the fitted amounts of ^{232}Th or ^{228}Th were not statistically significant (i.e., values less than their associated errors), the case was rejected. Finally, as mentioned above, the emanating ^{224}Ra content was added to the ^{212}Pb content to obtain the total ^{224}Ra, and the ratio of ^{224}Ra to ^{228}Ac was computed.

The fitted spectrum and the observed data from case L-1167 are shown in Fig. 2. The validity of the fitting procedure was determined by analyses postmortem of the amount of thorium in one patient (L-1521), to be discussed below, and also by the observation that the mean potassium content of this group of subjects was determined to be 0.20 ± 0.03 % of body mass, and the mean ^{137}Cs/K ratio was 7.9 ± 3.9 pCi/g. The former value is that for "reference man" [1], and the latter is typical of that observed for other groups of subjects at other laboratories [3,5].

Results

When the procedure was applied to the spectra obtained from the 134 individuals who contained more than 0.1 nCi ^{212}Pb in the thorax (the maximum content observed was 2.9 ± 0.1 nCi), fitted values of the ^{224}Ra/^{228}Ac ratio ranged from 0.52 ± 0.32 to 2.1 ± 1.7, with a weighted mean of 0.92 ± 0.17. The variance ratio was 0.64 and the value of χ^2 was 15.4, indicating that a single population was sampled. The distribution of values of the ratio is shown in Fig. 3. Thus, it appears that on the average, some ^{224}Ra was being excreted, following its production from ^{228}Th.

One feature of the data is that over one-third of the values exceed 1.0, although only five of them exceed 1.0 by more than one standard deviation.

The weighted mean for those values (45) exceeding 1.0 is 1.09 ± 0.22. Although this value is not significantly different from the mean for all cases, we will look carefully at work histories vs. observed $^{224}Ra/^{228}Ac$ ratios to investigate the possibilities that exposures to ^{228}Ra or to ^{228}Th (enriched relative to ^{232}Th) took place.

Several cases for whom repeat measurements are available show decreases in thorax content of ^{212}Pb with half-times of a few years, but the majority of these cases, extending across all ranges of the $^{224}Ra/^{228}Ac$ ratio, show little or no decrease in thorax content over periods of three to five years. A few cases actually show increases in thorax content of ^{212}Pb over the period of repeat measurements, and one even shows a concomitant increase in the $^{224}Ra/^{228}Ac$ ratio, suggestive of the growth of ^{228}Th in vivo from an exposure to ^{228}Ra.

At the other end of the ratio scale, 38 cases had values below 0.8, suggestive of prior exposure to freshly separated thorium; at the time of measurement in vivo, the ^{228}Th activity may have decreased and not as yet been replenished by growth from newly formed ^{228}Ra. Again, a careful consideration of work history and time elapsed between exposure and measurement will be required. These low values could equally well be due to loss of ^{224}Ra in vivo.

As shown in Fig. 4, extreme values of the $^{224}Ra/^{228}Ac$ ratio (less than 0.8 or greater than 1.20) are associated with lower amounts of radioactivity in the thorax and so are less reliable.

Validation of this method and determination of the $^{228}Ra/^{232}Th$ ratio depends on analyses of tissue samples postmortem. To date, samples are available from only four patients, only one of whom had also been examined in vivo. Results from this case (L-1521) postmortem confirmed the results

in vivo, which had given a ^{224}Ra/^{228}Ac ratio of 0.88 ± 0.14. The lungs and thoracic lymph nodes obtained at autopsy were placed in a reproducible geometry under one of the NaI(Tl) crystals used for measurements in vivo and their γ-ray spectra were recorded beginning 12 hours postmortem and continuing almost daily for four weeks. The data shown in Fig. 5 are the ratios of counts in the 2.61-MeV band (^{208}Tl) to those in the 0.91-MeV band (^{228}Ac), and the smooth curve is a fit to the growth of ^{224}Ra, predicting a ^{224}Ra/^{228}Ac ratio extrapolated to the time of death of 0.83 ± 0.03, in agreement with that observed in vivo. This comparison rests on the assumption that the ratios of ^{208}Tl to ^{212}Pb and ^{212}Pb to ^{224}Ra were the same at death as during the measurements in vivo, if not actually equal to 1.0 (allowing for branching ratios and ^{220}Rn exhalation).

Following these measurements, the lungs and lymph nodes were placed in the simple thorax phantom and the ^{208}Tl γ rays were counted with the same procedures used in vivo. The resulting net count rate was 14.6 ± 0.6 cpm, which when corrected for the ^{224}Ra/^{228}Ac activity ratio of 0.83 at death equals 12.1 ± 0.7 cpm. The counting rate observed in vivo was 12.2 ± 1.3 cpm. Final validation of the calibration factors for measurements in vivo will depend on the radiochemical analyses of the lung and lymph node thorium contents, which are currently in progress.

Many difficulties are inherent in the process of analyzing thorium daughters in vivo via γ-ray spectrometry, such as low counting rates and therefore poor statistics, the effects of variations in physique among subjects, and, as appears from the values of the ^{224}Ra/^{228}Ac ratio we have observed, variability in the metabolism of thorium daughters in vivo. At this point we conclude that the value of the ratio observed is probably representative of that given individual alone; a computed mean value for a

group of subjects may have little or no meaning. Nevertheless, it does appear that analyses of this parameter along with work histories, exposure records, smoking habits, and other parameters in our data base on the thorium workers will shed some light on the metabolic behavior of thorium daughters following inhalation of thorium.

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Figure Captions

1. The γ-ray spectra of ^{232}Th and ^{228}Th, each in equilibrium with its daughters, normalized at the 2.61-MeV peak of ^{208}Tl.

2. Data observed in vivo (circles) and least squares fit (smooth curve) for case L-1167.

3. Histogram of the values for ^{224}Ra/^{228}Ac for 134 former thorium workers.

4. Mean thoracic counting rates (left-hand scale) and contents of ^{212}Pb (right-hand scale) for each group of ^{224}Ra/^{228}Ac ratios shown in Fig. 3.

5. Growth postmortem of ^{224}Ra in the lungs and thoracic lymph nodes of case L-1521.

^{212}Pb (^{224}Ra)

^{228}Ac (^{228}Ra)

^{232}Th + daughters

^{228}Ac (^{228}Ra)

^{208}Tl (^{212}Bi)

^{228}Th + daughters

Net CPM per 10 keV

γ-ray energy, MeV

^{228}Ac	2.78 ± 0.08	nCi
^{212}Pb	2.60 ± 0.11	nCi
^{137}Cs	1.18 ± 0.20	nCi
^{214}Bi	0.59 ± 0.06	nCi
K	163.4 ± 2.8	g

γ-ray energy, MeV

Net CPM per 10 keV

Ratio of ^{224}Ra to ^{228}Ac

Mean thorax content of ^{212}Pb, nCi

Ratio of ^{224}Ra to ^{228}Ac

Mean CPM at 2.62 MeV over thorax