occurred in only three of six animals given 200 mg/kg; however, the remaining three subsequently lost their hair after 250 mg/kg. A single dose of 300 mg/kg was lethal to two guinea-pigs. Two features of particular interest appeared in the studies of guinea-pigs. The dose of cyclophosphamide required to produce loss of hair was more than five times the effective dose in sheep, and at least three times the minimal lethal dose in the dog and rabbit. Susceptibility to loss of hair in the guinea-pig was apparently related to skin pigmentation. Multi-coloured guinea-pigs suffered the greatest loss of hair in those areas of the skin which were black and which produced black hair.

Studies now in progress using other antitumour agents will demonstrate the usefulness of these model systems as predictors of drugs producing alopecia and as tools for studying means of preventing iatrogenic alopecia.

These data have been presented in part at the autumn 1968 meeting of the American Society for Pharmacology and Experimental Therapeutics and published in abstract form[1]. We thank Mr Philip Marshall and Mrs Gayle Holland for their assistance. This work was supported by the US National Cancer Institute.

ELTON R. HOMAN

National Cancer Institute,
National Institutes of Health,
Bethesda, Maryland 20014.

ROBERT P. ZENDZIAN
WILLIAM M. BUSEY

Hazleton Laboratories, Inc.,
P.O. Box 30,
Falls Church, Virginia 22046.

DAVID P. RALL

National Cancer Institute,
National Institutes of Health,
Bethesda, Maryland 20014.

Received December 24, 1968.

[1] Homan, E. R., Zendzian, R. P., and Busey, W. M., *The Pharmacologist*, **10**, 172 (1968).

Long Term Retention of Radium in Man

THE late biological effects of skeletally deposited radium in man have long been used as a basis for setting maximum permissible body contents of both radium itself and other long lived bone-seeking radio-elements such as plutonium[1]. Knowledge of the retention pattern is a fundamental requirement in the relation of the body content of radium at the time of observation of a bone neoplasm to the amount of radium initially in the blood. Much effort is being devoted to a determination of this, chiefly in the United States[1-3] where a number of persons who received radium by injection or occupationally have been studied at intervals for many years. These people have radium-226 contents in the approximate range 0·02–2·0 μCi, levels which are easily measured by whole body gamma ray spectrometry. Only relatively few measurements have been made, however, and the accuracy of the estimated biological elimination rate for an individual is poor. Keane and Evans[2] reported an average biological half life of 28 ± 8 yr for a group of twenty subjects, 30–40 yr after acquisition, while Miller and Finkel[3] found an average of 15 yr (range 9·6–21·7 yr) for the biological half life in eight patients for the period 19–33 yr after injection.

In addition to its importance from the point of view of radiological protection, the late elimination rate of radium (or any alkaline earth) is of interest in the study of the physiology of bone, especially if data are available on the initial retention and plasma concentration. For example, experimental data of this kind can be compared with the predictions of Marshall's theory of alkaline earth metabolism[4].

Since 1957 measurements have been made intermittently of the body radioactivity of a healthy man then aged 52 who has been the voluntary subject of a number of experiments involving administration of trace amounts of radio-nuclides[5-8]. This man was exposed occupationally to radium-226 in September 1940 and our measurements show that a small burden remains at the present time. All the available data have been analysed in an attempt to determine a value for the biological half life over the period 17–28 yr after intake. Results have already been published[7] of the short term (60 days) retention and plasma concentration following an injection at the age of 60 of 11·4-day radium-223.

A total of sixty-one observations of the retained radon fraction of the body content of radium-226 was available. Each estimate was obtained from an analysis by the method of least squares of the gamma ray spectrum of the subject's body radioactivity, over the approximate energy range 0·75–1·7 MeV. Statistical standard errors were computed and these ranged from about $\pm 1{\cdot}5$ nCi in 1957 to $\pm 0{\cdot}5$ nCi in 1966 and subsequently. The improvement was the result of the introduction of more sensitive measuring equipment. A non-linear least squares fit to a single exponential term was made, each point being weighted by the inverse of the computed variance. A half life of $7{\cdot}9 \pm 1{\cdot}3$ yr was obtained, with an intercept (mid-September 1940) of 25 ± 3 nCi.

Because the gamma ray spectral analysis programme used an iterative procedure to find the "best" fit there was some smoothing of the statistical variations and this resulted in an optimistic value for the standard error. A value for the half life was therefore determined using the arithmetic averages for the individual years, each point being weighted by the inverse of the variance calculated from the spread of the points. This analysis gave a value for the half life of $9{\cdot}0 \pm 1{\cdot}8$ yr, and an intercept of 19 ± 7 nCi. The data used are set out in Table 1.

Table 1

Year	Number of observations	Mean time from intake (years)	Average RaB–C content, nCi	Standard error, nCi
1957	3	16·85	5·2	0·9
1958	2	17·91	5·9	1·1
1959	2	19·06	5·5	1·1
1960	2	19·76	2·85	1·1
1961	3	20·93	4·25	1·1
1962–3	8	21·85	3·07	0·37
1964–5	18	24·78	2·98	0·21
1966	10	25·74	2·19	0·23
1967	7	26·70	2·67	0·24
1968	6	27·80	2·35	0·41

It can be seen that much greater weight is being given to the values for the years 1965–67. From the methods of analysis it is considered that the higher value for the half life is the more reliable one; although it is lower than the averages found by the American groups[2,3] it is similar to the lowest value reported by Miller and Finkel[3]. The early retention data for radium-223 (ref. 7) and the late retention data for radium-226 in the same subject are consistent with the predictions of Marshall's theory[4]. A detailed discussion of this will appear elsewhere.

J. RUNDO

Health Physics and Medical Division,
AERE, Harwell,
Berkshire.

Received January 9, 1969.

[1] Evans, R. D., *Brit. J. Radiol.*, **39**, 881 (1966).
[2] Keane, A., and Evans, R. D., *Mass. Inst. Technol. Rep.*, 952–5 (II), *S*–1 to *S*–10 (1968).
[3] Miller, C. E., and Finkel, A. J., *Amer. J. Roentgenol. Rad. Ther. Nucl. Med.*, **103**, 871 (1968).
[4] Marshall, J. H., *J. Theoret. Biol.*, **6**, 386 (1964).
[5] Bishop, M., Harrison, G. E., Raymond, W. H. A., Sutton, A., and Rundo, J., *Intern. J. Radiat. Biol.*, **2**, 125 (1960).
[6] Rundo, J., and Lillegraven, A. L., *Brit. J. Radiol.*, **39**, 676 (1966).
[7] Harrison, G. E., Carr, T. E. F., and Sutton, A., *Intern. J. Radiat. Biol.*, **13**, 235 (1967).
[8] Rundo, J., *Intern. J. Radiat. Biol.*, **13**, 301 (1967).