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A CYTOGENETIC STUDY OF SOME RADIUM DIAL-PAINTERS AND THEIR PROGENY*

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and Jip Kim**

Abstract

The ingestion of radium by women employed in painting watch dials with luminous paint in the early decades of this century has produced a human population group undergoing continuous internal radiation exposure. In the course of long-term surveillance of members of this group by Argonne National Laboratory, an incidental observation has been that a number of their progeny exhibit various abnormalities which might stem from genetic transmission.

Cytogenetic methodology now permits the direct observation of numerical and morphological abnormalities in human blood cell chromosomes. Association of chromosomal aberrations with various congenital anomalies, with previous external radiation exposure, and with some forms of leukemia which are also increased in incidence following radiation exposure has been reported.

It was considered of interest to determine, first, whether any cytogenetic abnormalities were present in the blood cells of persons exposed to long-term internal irradiation from radium; and, second, whether any cytogenetic evidence could be found for a possible relationship between a significant maternal body-burden of radium and anomalies in the progeny.

In an initial study, two dial-painters and their progeny, and the progeny of two other dial-painters were examined. One of the dial-painters studied had developed an osteogenic sarcoma. Abnormalities among the progeny included mongolism, cerebral palsy, dwarfism, coarctation of the aorta, multiple unilateral anomalies, omphalocele, multiple miscarriages and familial recurrent infections. Pedigrees, estimates of radium body-burdens and cumulative critical organ radiation dosages, and the nature and frequency of chromosome aberrations observed, are presented in detail.

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RADIUM IN HUMAN TEETH: A QUANTITATIVE AUTORADIOGRAPHIC STUDY*

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This study of radium in human teeth was undertaken to determine the distribution of this radioelement in the dental tissues many years after medical or occupational exposure. Dudley has suggested that the total body content of a person contaminated with radium could be estimated from the radium content of a single tooth, and it appears from his measurements that the uncertainty involved in such an estimate is not much greater than a factor of two.(1) It would be most remarkable if the radium content of a tooth should give a representative measure of the radium content of the entire skeleton, for it has been shown that the radium content of equivalent bone samples (i.e., one gram) may vary as much as a factor of ten.(2) It is of interest to determine whether this observed correlation in teeth is fortuitous or is a metabolically significant observation.

Methods and Materials

Teeth from three radium cases were studied.

Case 03-473: (Dial-painter, female)

A former dial-painter who had painted for two years when she was 19 to 21 years old. An impacted mandibular 3rd molar was removed at age 55, following removal of a bone sequestrum from the left mandible six months before. Her total-body radium content was determined at this time by whole-body counting to be 1.2 μc Ra^{226}.(3)

Case 03-201: (Radium acquired therapeutically; female)

No precise information is available about the source of this woman's radium; we have assumed that it was acquired therapeutically about 35 years ago. An impacted mandibular 3rd molar was removed at age 52; no bone is available. The total radium content of this woman was determined at this time by whole-body counting to be 3.0 μc Ra^{226}.(3)

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Case 03-998: (Dial-painter, female)

This woman painted watch dials for a six-year period (1917 to 1923) when she was 27 to 33 years old. Her death occurred in 1925, at age 35; the autopsy report stated "severe anemia, with purpura, petechiae, buccal sepsis, early jaw necrosis and red bone marrow." The mandible, with 10 teeth, and a portion of the femur were obtained from a museum jar in which they had been stored dry. Although early estimates of the total radium content of this patient ranged from 90 to 180 μc,[4] recent studies of these bone samples indicate that the terminal content was in the range of 5 to 20 μc Ra^{226}, in addition to an equal amount of the shorter-lived Ra^{228}, which had been present originally.[5] Two teeth, the left canine and the left 2nd molar, were studied autoradiographically, while all ten were measured to determine their Ra^{226} content.

Each tooth included in this study was sealed, individually, within a glass vial and the gamma-ray spectrum of each recorded immediately and again a month later. From these two measurements, the total Ra^{226} content and the radon retention of each tooth was determined.

The teeth studied autoradiographically were first embedded in methyl methacrylate and then cut into longitudinal sections 150 or 200 microns thick. To facilitate subsequent comparison with the autoradiographs, microradiographs were taken of each section (17.5 kv x rays, Eastman Kodak spectroscopic plates 649-0). Three different autoradiographs were then made from each section:

1) An appropriate exposure (3 to 120 days) on an alpha-track plate to produce an autoradiograph from which alpha-track counts could be made to determine the microscopic radium concentrations.

2) A long exposure (1-4 months) on a beta-sensitive plate to produce a visible image of the radium distribution in the tooth.

3) A stripping-film autoradiograph (2-month exposure) to yield high-resolution localization of the radium deposits within the tooth.

The radium concentrations found in various portions of the teeth were evaluated by counting the number of tracks per unit area in the autoradiographs. These counts were expressed as radium concentrations per gram of calcium, using an average alpha particle range of 6.3 mg/cm^2, radon retention values of 40% for the bone sections and 75% for the tooth sections, and calcium concentrations of 24.4%, 27%, and 36% by weight, respectively, for bone, dentin and enamel.[6]

Results

The radium content of each tooth studied in detail and of all ten teeth from Case 03-998 are tabulated in Table 26. For comparison with the skeleton (10^3 g Ca) the radium content of each tooth is expressed in terms of grams of calcium by assuming that the calcium content of a tooth is 28% by weight. This comparison is made in Table 27.

Table 26

Gamma-ray measurements of teeth from radium cases

Case	Tooth	Total activity, pc Ra^{226}	Weight, g	$\frac{pc}{g}$	$\frac{pc}{g\ Ca}$	Radon retention _in vitro_, %
03-473	Mandibular 3rd molar	2100	1.20	1750	6150	75
03-201	Mandibular 3rd molar	1510	1.45	1040	3730	44
03-998	Right canine	859 ± 8	1.022	840	3000	76
	Left canine	1318 ± 12	1.013	1300	4640	71
	Right lateral incisor	570 ± 7	0.477	1190	4250	75
	Left lateral incisor	595 ± 6	0.317	1880	6680	59
	Right first premolar	659 ± 8	0.799	825	2960	70
	Left first premolar	519 ± 7	0.715	725	2600	54
	Right second premolar	485 ± 4	0.398	1220	4360	62
	Left second premolar	711 ± 8	0.932	765	2710	66
	Right second molar	1623 ± 11	1.939	840	3000	68
	Left second molar	1614 ± 12	1.970	820	2930	60
03-998	Total	8953	9.582	935	3300	

Table 27

Comparison of the specific activity of the teeth and the skeleton

Case	Specific activity		Ratio: tooth/skeleton
	Tooth pc/g Ca	Skeleton pc/g Ca	
03-473	6150	1200	5.1
03-201	3730	3200	1.2
03-998 (10 teeth)	3300	(10000)*	(0.3)*

*Based on a body content of $10\mu c$.

The significance of these measurements will be discussed below.

Case 03-473: (Exposure at age 19 to 21 years)

The autoradiographs of the sections from this tooth indicate that dentin was being formed at the time of exposure to radium (Figure 45b). On the microradiograph (Figure 45a) cross hatching is employed to indicate the portion of the dentin which has given rise to this autoradiographic image. The dark lines in the autoradiograph, adjacent to a grey band, are interpreted to indicate that the original exposure to radium was at a high concentration for a short time, but that over the rest of the exposure period the intake was at a lower level.

When the tooth section is exposed to the autoradiographic plate for a longer period (Figure 45c), it is evident that radium is present in other portions of the tooth. In addition to the deposit in the forming dentin, deposits in the following locations are visible:

1) immediately under the surface of the enamel,
2) in the dentin which was formed before the exposure to radium,
3) in the dentin formed after the exposure to radium.

The radium concentrations measured in this tooth are tabulated in Table 28. The distribution in the pre-existing dentin, observed to decrease with depth, is shown in graphical form in Figure 46. This graph shows, in addition, the maximum hotspots and the average diffuse level observed in the small bone sample, and the magnitude of the concentration under the enamel surface.

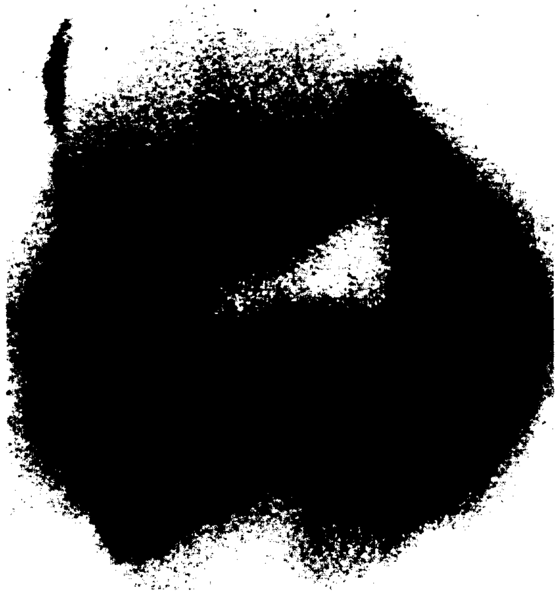
Table 28

Radium concentrations measured in bones and teeth

Case	Number and type of deposition	Bone pc/g Ca	Dentin pc/g Ca	Enamel pc/g Ca
03-473	Hotspots	13,500	84,000 22,000	-
	Diffuse	740	380-1250	900
03-201	Hotspots	-	404,000	-
	Diffuse	(1500 ± 750)	210-3030	1700
03-998	Hotspots	88,700	63,000	-
	Diffuse	1,880	300-17,200	880

(a)

(b)



(c)

Figure 45

A 200-micron thick section cut from the mandibular third molar of Case 03-473. a) A microradiograph; b) an autoradiograph exposed for one month; and c) an autoradiograph exposed for four months. The outline of the autoradiographic darkening of (b) has been indicated on the microradiograph (a) with cross hatching.

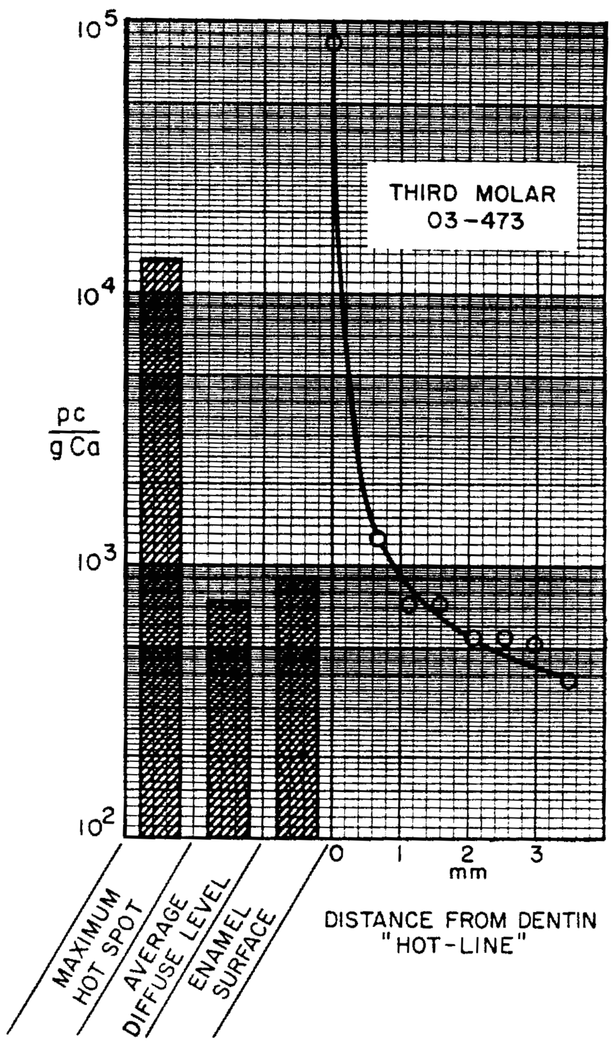


Figure 46

Comparison of the radium concentrations observed in the bone and tooth of Case 03-473. The maximum hotspot and the average diffuse level measured in the bone, and the enamel surface concentration are shown as histograms; the radium concentration in the dentin is plotted as a function of the distance from the dentin hot-line.

Case 03-201: (Exposure during late teens?)

The assumption as to the age at which this woman received radium is verified by the autoradiographs of the tooth sections. A narrow line of darkening, 50-250 microns wide, is present in the autoradiograph (not illustrated) of the dentin between the pulp cavity and the enamel. Since the 3rd molar has completed its crown formation and started root formation by age 17 (95th percentile),[7] it is likely that this girl was in her late teens when she received radium. The narrow line of darkening, actually resolvable into two narrow lines, suggests that she received two courses of treatment which lasted not more than a few months; the route of administration was probably intravenous.

The radium concentrations in this tooth are illustrated graphically in Figure 47. No bone was available for comparison; however, a diffuse

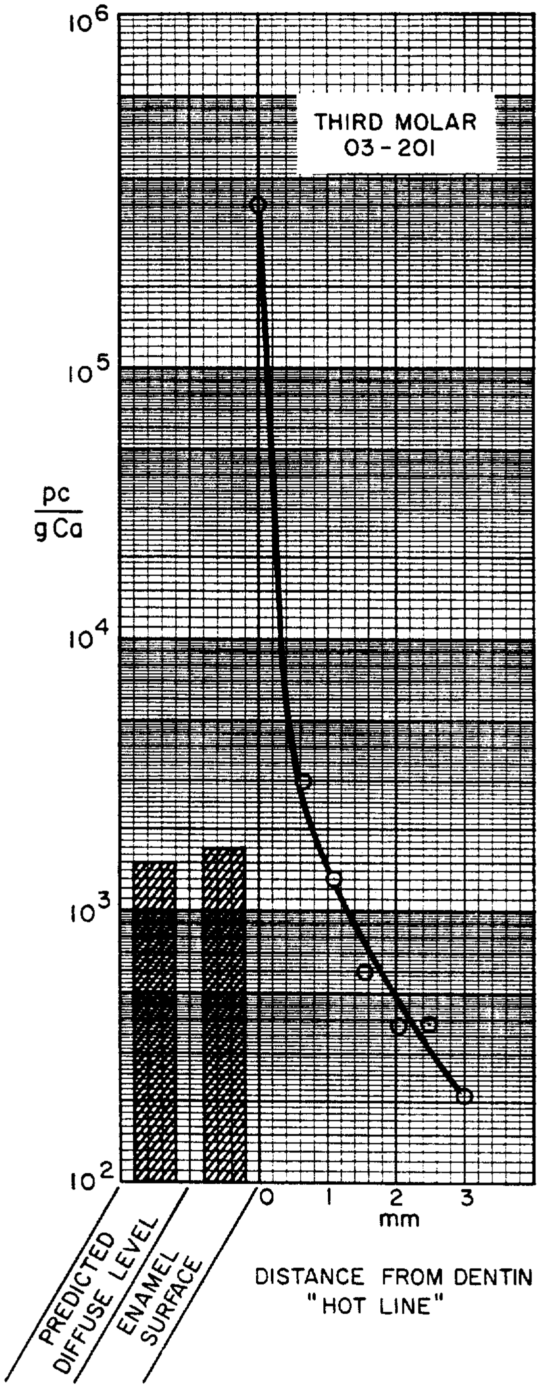


Figure 47

Comparison of the radium concentrations observed in the tooth of Case 03-201. A predicted diffuse level, as described in the text, is also shown for comparison.

distribution, predicted on the basis of the body content, is shown. This prediction is based on the observation that the diffuse level is approximately one half of the uniform label, i.e., that concentration obtained by dividing the skeletal radium content by the skeletal mass.[8]

Case 03-998: (Exposure over a six-year period, from age 27 to 33 years)

In spite of the age of this woman at exposure, dentin was being formed in the left second molar (Figure 48). In addition to the dentin deposit, a longer autoradiograph (Figure 48c) illustrates the same distributions listed for Case 03-473. In the canine tooth (Figure 49) no growth of dentin took place, so that the entire label was in the pre-existing dentin and the enamel surface. However, in both the molar and the canine tooth an intense deposit of radium is present in the outermost layer of the cementum which covers the roots. This deposit is equal in specific activity to that observed in the dentin, suggesting that this layer of cementum was probably formed during the exposure to radium. The measured specific activities are shown in graphical form in Figure 50.

A small disk of enamel, lying on the surface of the dentin between the two roots of the 2nd molar is visible in the microradiograph (Figure 48a). Enamel in this location is not unusual,[9] but it is mentioned here because it is highly radioactive, and thus is known to have been formed during this six-year period.

(a)

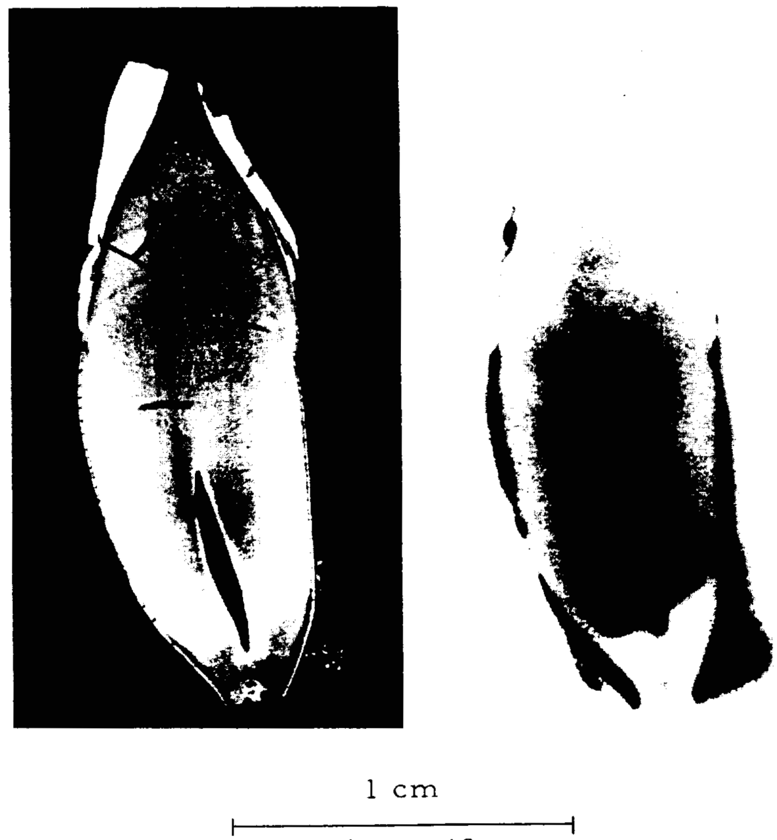
(b)

(c)

Figure 48

A 150-micron thick section cut from the left second molar of Case 03-998. a) A microradiograph, b) a seven-week autoradiograph, and c) a four-month autoradiograph.

5 mm



1 cm

Figure 49

A 150-micron thick section cut from the left canine tooth of Case 03-998. a) A microradiograph, and b) a four-month autoradiograph.

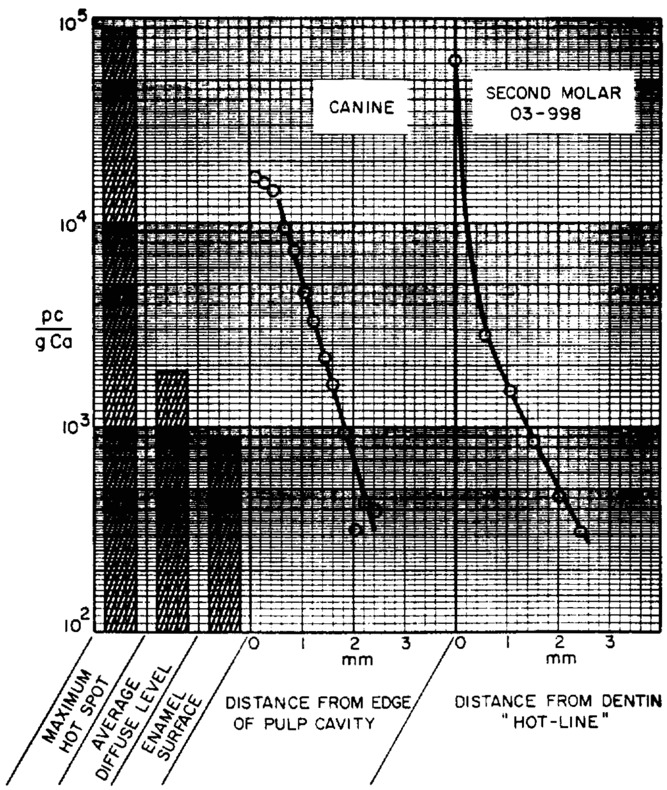


Figure 50

Comparison of the observed radium concentrations in the teeth of Case 03-998 with the concentrations in bone. The deposit in the dentin of the canine tooth was measured from the edge of the pulp cavity, while this distribution in the second molar was measured from the hot-line in the dentin.

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Discussion

The autoradiographs of these teeth indicate that a significant quantity of radium has been deposited within the dental tissues. This observation is in agreement with the studies of the radium content of teeth from radium cases that have been made at MIT[1] and at Argonne.[10] These studies have shown that such teeth usually contain a radium-to-calcium ratio of the same order of magnitude as the skeleton; the MIT study suggested that the ratio

$$\frac{(\mathrm{Ra}/\mathrm{Ca})\ \text{tooth}}{(\mathrm{Ra}/\mathrm{Ca})\ \text{skeleton}} \simeq 0.3$$

with a range of 0.10 to 0.73.

On the basis of the present study this conclusion should be modified to apply only to teeth that were mature at the time of exposure. In those teeth which were still being formed when radium was present the above ratio may be as large as 5 to 1 (Table 27). The reason, of course, lies in the high uptake of the isotope in the forming dentin, as illustrated in Figure 45. Even in mature teeth a considerable range is to be expected, for the radium-to-calcium ratio of a given tooth will depend upon the ratio of dentin to enamel and the ratio of buried dentin to dentin adjacent to the pulp cavity in that tooth, and will be influenced by the amount of bone and cementum attached to the tooth when the measurement is made.

These observations give rise to the basic question: by what process does this isotope enter the dentin of a mature tooth, or the pre-existing dentin of a forming tooth? Could this be a manifestation of a long-term exchange process?

The ability of the dental tissues to acquire trace elements by an exchange process is well known. An autoradiograph of a tooth from a radium-dial painter which appears to illustrate this uptake has been published.[11] Previous to this the ability of pre-existing dentin to acquire lead from the blood supply had been described.[12] The most striking demonstration of this exchange capacity was provided by Sognnaes et al.,[13] who, using monkeys, described the uptake of P^{32} in the dental tissues at short time intervals after administration. Indeed, they showed that the P^{32} in the dentin decreases with depth in a manner similar to the approximately exponential decrease shown here for radium (Figures 46, 47 and 50).

Thus, it is evident that these isotopes can enter the teeth quickly and remain there for long periods, just as is the case in bone. It is paradoxical that, even after a 30-year residence in dentin, Ra^{226} should show a distribution in depth so similar to that of P^{32} at very short times. A deposition resulting from an exchange process, which operates rapidly enough to be seen in minutes, might be expected to be drastically altered after many years.

It is instructive to compare the magnitude of the dentin deposit with the equivalent deposition in bone, the so-called diffuse distribution. It is evident from Figure 46 that the dentin within 1 mm of the pulp cavity (or the edge of the pulp cavity at the time the radium was in the blood) contains as much, or more, radium per gram of calcium as is found in the diffuse distribution in bone. Further in depth the dentin contains less activity than the bone; in this respect it should be recalled that few regions in bone are more than a few hundred microns from the blood supply, while portions of the dentin may be 10 to 40 times this distance. In each tissue there exists a microscopic distribution system, the canaliculae in bone and the dentin tubules in the dentin. This distribution system could provide a rate-limiting step in the process of distributing these tracers in depth.

When the dentin tubules no longer transport fluids, such as is the case when they become filled with mineral deposits (sclerosis), exchange phenomena would no longer take place within the affected region. If the stoppage occurred before the radium were present, no uptake of the isotopic tracer would take place; note that this appears to have been the situation in the lower portion of the root of the canine tooth from 03-998 (Figure 49). If such occlusion occurred after the isotope had been deposited within the dentin, no further removal by exchange would take place.

Let us consider an alternative mechanism for the deposition of these isotopes within the dentin, namely, that they indicate a net gain of mineral in these regions. This implies that the dentin must be continually increasing in density. The sclerotic process, mentioned above, is an example of such an increase, and may account for a portion of the uptake of such tracers. Yet, the fact that all of the teeth examined in all of the studies mentioned have shown uptake of isotopic tracers, independent of the age of the teeth, strongly suggests that the bulk of this uptake must be due to long-term exchange and not to a gain of additional mineral.

It can be concluded from this study that when Ra^{226} is present in the blood, it will be incorporated within the teeth. It will be deposited in those regions in which new mineral is being formed, and will, to a lesser extent, enter those portions of the mineral previously formed. In the pre-existing dentin this deposit decreases exponentially in magnitude with distance from the blood supply. In the enamel a deposit is present along the outer surface; if there is also a deposition in depth within the enamel it is much less intense, for it was not visible in the teeth studied here.

The processes described above may be expected to apply to the other members of the alkaline-earth family, namely calcium, strontium, and barium. Thus, mature teeth can, by virtue of their ability to acquire these elements by exchange processes, be expected to give a reliable indication of the amount of contamination of the entire skeleton following exposure to the radioactive forms of any of these elements.

It is of interest to note that the radium concentration in small samples of bone in which no appositional growth had taken place during the exposure to radium, and thus would contain only a diffuse label without any hotspots, would provide a valid method of estimating the radium content of the entire skeleton. The uncertainties inherent in extrapolating radium concentrations measured in small bone samples to the entire skeleton arise from the continual removal and replacement processes at work in normal bone. The teeth, in contrast, once their growth is finished, provide a stable environment in which isotopes acquired by long-term exchange processes remain undisturbed.

It is thus understandable why the observed gamma-ray measurements of the teeth correlate so well with the total skeletal content. It should also be evident that quantitative autoradiographic measurements of the teeth could yield even better estimates of the total skeletal content of an alkaline-earth isotope deposited within the skeleton.

The teeth in this study were acquired through the efforts of Drs. A. J. Finkel, C. E. Miller and L. D. Marinelli, of this Laboratory, and Dr. R. J. Hasterlik, of the Argonne Cancer Research Hospital.

References

1. R. D. Evans. Reliability of teeth as indicators of total-body Ra burden. Annual Progress Report, Radioactivity Center Massachusetts Institute of Technology (May 1960). pp. 5-12.

2. W. P. Norris, W. P. Speckman and P. F. Gustafson. Studies of the metabolism of radium in man. Am. J. Roentgenol. 73, 785-802 (1955).

3. C. E. Miller. Unpublished measurements, 1962.

4. H. S. Martland. Occupational poisoning in manufacture of luminous watch dials. J. Am. Med. Assoc. 92, 466-552 (1929).

5. R. E. Rowland. Detailed autoradiographic and microradiographic studies of bone from human radium cases. Argonne National Laboratory Radiological Physics Division Semiannual Report, January through June 1961. ANL-6398, pp. 5-23.

6. R. F. Sognnaes. Dental aspects of the structure and metabolism of mineralized tissues. In: Mineral Metabolism, I-B, (Ed. C. L. Comar and F. Bronner). Academic Press, New York, 1961, pp. 677-741.

7. S. M. Garn, A. B. Lewis and D. L. Polacheck. Variability of tooth formation in man. Science 128, 1510 (1958).

8. R. E. Rowland and J. H. Marshall. Radium in human bone: the dose to microscopic volumes of bone. Radiation Research 11, 299-313 (1959).

9. M. A. Rushton and B. E. Cooke. Oral Histopathology. Livingstone, Edinburgh, 1959. p. 24.

10. C. E. Miller and J. B. Corcoran. Estimation of radium body-content of exposed humans from the activity of extracted teeth. Argonne National Laboratory Radiological Physics Division Semiannual Report, January through June 1960. ANL-6199, pp. 68-70.

11. J. C. Aub, R. D. Evans, L. H. Hempelmann and H. S. Martland. The late effects of internally-deposited radioactive materials in man. Medicine 31, 221-329 (1952).

12. J. C. Aub, L. T. Fairhall, A. S. Minot and P. Rexonikoff. Lead poisoning. Medicine 4, 1-250 (1925).

13. R. F. Sognnaes, J. H. Shaw and R. Bogoroch. Radiotracer studies on bone, cementum, dentin and enamel of Rhesus monkeys. Am. J. Physiol. 180, 408-420 (1955).