American Journal of Public Health
and THE NATION'S HEALTH

Volume XXIII October, 1933 Number 10

Radium Poisoning
A Review of Present Knowledge

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IN some circles victims of radium poisoning are regarded as curiosities, and the view advanced that careful studies of the cases—particularly such fundamental studies as the distribution of radium in the system—are of secondary importance. This view arises from the fact that most of the reported cases arose from uninformed carelessness in one occupation, luminous watch and instrument dial painting, in which protective measures have now been taken.[1, 2]

The view is untenable, however, for three reasons (1) Careful study of the distribution of radium in victims can contribute to knowledge of bone architecture and to the investigation of analogous heavy-element poisoning cases, such as lead and arsenic. Study of the anemias involved has already led to major contributions by Martland. (2) New cases will continue to appear because some physicians are still experimenting with radium solutions for therapeutic uses; because radium solutions are still peddled by the nostrum vendors, who realize splendid profits therefrom; and because radium "activators" for the treatment of drinking water—some of which are dangerous—are still sold in large numbers to a gullible public. (3) Thus far every case of radium poisoning has been fatal, but there is no *a priori* reason for believing that a satisfactory cure will never be found.

Cases of true radium poisoning arise where the victim has taken radium into the body, by mouth or by injection, in which case a fraction of the radium taken remains permanently in the body, and the radiation which it continually emits produces the effects described as radium poisoning. It must be emphasized that the modern use of radium in the treatment of cancer usually involves an entirely different mode of use of radium, and cannot result in true radium poisoning. Since only the penetrating gamma radiation of a radium product is utilized, the radium never enters the patient's system, and the exposure is of definite, limited duration. Over-doses of gamma rays will produce pernicious anemia and myeloid leukemia as late as 4 years after a massive exposure,[3] but these

* Read at the Fourth Annual Meeting of the Western Branch, American Public Health Association, in Pasadena, Calif., May 30, 1933.

effects are to be regarded as radiation burns rather than as true radium poisoning.

Each of the 40 known radioactive elements has a definite rate of spontaneous disintegration which cannot be altered by invoking extremes of temperature or pressure, or by chemical combination. When an atom of radium explodes it emits an alpha ray, a high-energy, doubly-charged helium nucleus, which will traverse a few hundredths of a millimeter of living matter, and is only brought to rest by expending its energy in ionizing about 100,000 atoms. Gamma rays, similar in nature to X-rays, are also emitted.

The exploding radium atom loses mass, electrical charge, and energy in the emitted alpha and gamma rays. The residue is an atom of radon, a heavy, inert, radioactive gas, which can be observed in the air expired by a victim of radium poisoning.

Half of any given quantity of radon decomposes in 3.8 days, the so-called "half-period." Radon is the principal active agent in the water from radioactive springs and drinking water activators, but its short half-period shows that bottled water will become practically free from radon in about 3 weeks.

Radium, because of its relatively long half-period of 1,600 years, cannot disintegrate rapidly enough to be appreciably reduced in amount during the lifetime of a person. Hence radium, once fixed in the bones of a victim of radium poisoning, holds its deadly alpha ray bombardment of the bone structure and of the blood producing centers at a nearly constant rate.

Radium decomposes into radon. Radon, in turn, decomposes into an element called radium A, and this in turn into radium B, radium C, radium C″, radium D, radium E, and radium F (polonium), which disintegrates into lead, the stable end-product of this decay series. In the gamma ray treatment of cancer, the gamma ray of radium C is principally employed.

Radium is chemically quite similar to barium, hence also to calcium. Efforts to remove radium from the body of a victim of radium poisoning must therefore involve mobilization of the calcium, and must borrow heavily from the body of knowledge which is calcium therapy.

In cases of radium poisoning, at least one other radioactive element is of major importance, because it has been widely used in luminous paint and in radioactive nostrums. It is called mesothorium-1, is a beta ray emitter with a half period of 6.7 years, and, like radium, gives birth to a long chain of radioactive substances, one of them gaseous (thoron), five of them alpha ray emitters, four more beta ray emitters, and has lead as its stable end-product.

As in the case of the radium series, the presence of these radioactive decay products multiplies, in proportion to the number of alpha ray products, the destructive effects which could be produced by radium or mesothorium-1 alone.

The term radium is used in this paper as a convenient abbreviation of the long list of radioactive elements which accompany it, and the effects of mesothorium-1 or of radiothorium are the same.

MODES OF ENTRANCE OF RADIUM INTO THE BODY

It is now possible to distinguish between radium water and "activated" water. The former contains actual radium salts (usually the chloride) which, because of the long half-period of radium may be regarded as permanently radioactive. The radium spring waters, and "activated" waters from emanators and other devices are merely radon water, that is, they contain the short lived radioactive gas radon, which, like all other gases, dissolves in liquids

to a limited extent. These waters go dead in a few weeks unless they are continually reactivated.

A. Numerically, ingestion has been far more important than injection in producing victims of radium poisoning. Public [4] and professional [5] attention has been well focused on the tragic and horrible death of E. M. B. and several of his friends as a result of their drinking the radium water nostrum "Radithor." [4, 5] For the first few months after taking radium into the body there is a sensation of well-being and general physical improvement. Soon, however, the deadly alpha ray bombardment of the blood producing centers begins to be felt, and death follows in a year or more, depending on the total quantity of radium fixed in the system. Protection of the public from these nostrums is mainly a matter of public health education and legislation.

B. Although the greatest number of victims came out of the luminous watch dial industry, this source has been quite well stopped by the introduction of machinery and of protective measures where hand work is still necessary. From the war period until the end of 1924 an average of some 350 persons, mostly women, were employed in hand painting luminous numerals and hands on watches, clocks, airplane instruments, etc. Due to labor turnover probably about 800 people worked long enough to endanger their lives. In painting the numerals on a fine watch, for example, an effort to duplicate the shaded script numeral of a professional penman was made. The 2, 3, 6 and 8 were hardest to make correctly, for the fine lines which contrast with the heavy strokes in these numerals were usually too broad, even with the use of the finest, clipped brushes. To rectify these too broad parts, the brush was cleaned and then drawn along the line like an eraser to remove the excess paint. For wiping and tipping the brush the workers found that either a cloth or their fingers were too harsh, but by wiping the brush clean between their lips the proper erasing point could be obtained. This led to the so-called practice of "tipping" or pointing the brush in the lips. In some plants the brush was also tipped before painting a numeral. The paint so wiped off the brush was swallowed.

The luminous paint is a mixture of a gum binder, zinc sulphide, and enough radium, mesothorium-1, or radiothorium to give the required fluorescence. The mixture is about 1 part of radioactive material in 40,000 of paint.[6] Depending on their skill, the workers tipped the brush from 1 to 15 times per dial, and painted 250 to 300 dials per day. A worker who licked 1 mg. of paint from her brush 4 times per dial, 300 dials per day, 5 days per week, would therefore ingest about 4,000 micrograms of radium in 6 months. When fixed in the bones, as little as 2 micrograms of radium has been fatal. Only rapid elimination of ingested radium, mainly in the feces, prevented prompt death.

C. Radium solutions have been used by some physicians in treatment of such ailments as gout, arthritis, cancer and leukemia. A fraction of the radium is deposited in the erythrocyte and leukocyte producing areas, and irritates these parts, with the result that there is an increase of both red and white blood corpuscles, and an apparent improvement in health. A period of overstimulation and then one of exhaustion may follow in which there is marked leukopenia and regenerative anemia, followed by fatal terminal infections. Apart from these effects on the blood forming apparatus, radioactivity has never been proved to be a specific therapeutic agent in internal medicine.[7, 8, 9]

D. Those who, in hospitals, chemical or physical laboratories, or mines, handle radium solutions, make up radon

needles, or otherwise come in contact with radioactive dust or radon contaminated air, have been victims of fatal anemia in which radioactive substances were introduced through their lungs.[7, 10]

E. Fortunately, most of the radium "activators" sold for treating drinking water contain far less radium than their vendors claim.[31] So far as I know, no deaths have been traced to these devices; but in spite of years of trial, there is no controlled clinical evidence that this radon water is beneficial.[11] Those activators in which the water comes in contact with the radioactive source become dangerous when this material is appreciably dissolved in the water,[10] for here one would be drinking radium water—not radon water. The better grade of "activators" will produce a radon concentration of 0.01 microcurie * per liter in water in 1 day, or 0.15 microcurie per liter in 1 month. As normally used, the water will have a radon concentration of about 0.1 microcurie of radon per liter, and also 0.0001 microgram of radium per liter.

EXIT OF RADIUM FROM THE BODY

The normal body throws off a large percentage of any radioactive material taken into it.

Where radon is breathed in, it remains in the blood only about 3 hours.[10, 12, 13] Where radon water is drunk, the gas is carried by the blood to the lungs, where it passes out by diffusion and is soon lost from the body in breathing.[14] The equilibrium distribution ratio (Henry's law constant) between blood and air at body temperature is between 0.42 and 0.31 to 1 by volumetric concentration.[15, 16] During the few hours that radon is in the blood, about 1 or 2 per cent of it decays into the solid radioactive product radium A, some of which is deposited permanently in the system and continues in the radioactive decay series until, after emitting 4 alpha and 4 beta particles per original atom of radon, it eventually becomes lead.

When radium is taken into the system it behaves in a manner similar to lead, being carried in the blood until it is either deposited as colloidal matter, principally in the bones, marrow, spleen, liver and lungs, or is excreted. After taking a soluble radium salt by mouth a much greater fraction is eliminated in the first 4 days than if it is received by intravenous injection.[14] Thereafter the rate of elimination of radium is quite independent of the mode of entrance. According to the individual, from 2 to 35 per cent of the radium received by mouth remains in the system more than 5 days after ingestion,[14, 17] while 55 to 65 per cent received by intravenous injection remains more than 5 days.[14] By the 10th day after taking radium, the rate of elimination is below 1 per cent of the quantity remaining in the system. Several years after taking radium the rate of elimination is down to 0.002 to 0.005 per cent per day.[17] At this low rate it would require about 45 years to eliminate half the radium in the system.

About 90 per cent of the radium eliminated is excreted in the feces, the remaining 10 per cent in the urine.[14, 17] No radium is eliminated through the skin, as has been demonstrated by heavy sweating of a subject following an intravenous injection of 100 micrograms of radium.[18] Although no radium can be exhaled in the breath, some radon does leave the system in this way, thereby relieving the body of the severe alpha particle bombardment from the decay products of radon. The fraction of the radon expired varies between the extreme limits of 2 and 40 per cent [17, 19] of the total amount of radon produced in the body by the decay of radium.

* When radioactive equilibrium is present one curie of radon is associated with each gram of radium. Micro- = one millionth.

Efforts have been made to speed up the normal rate of elimination of radium. Martland [7] tried without results to mobilize the radium deposits by intravenous injections of rapidly oxidizing colloidal solutions and by exposure of the body to ultra-violet light.

Aub found that a temporary acidosis, induced by the use of ammonium chloride, converted insoluble calcium and lead salts into soluble salts and expedited their excretion, particularly if the subject was on a low calcium diet. Following the original work of MacCallum and Voegthin, and later of Collip, Aub [20] found that the injection of parathormone mobilized calcium and lead. Because the chemistry of calcium and radium is somewhat similar, Flinn and Seidlin [21] inferred that advantage could be taken of this knowledge of calcium metabolism to speed up the normal elimination of radium. In 1929, 3 patients were each given parathormone every other day for a month, the dosage beginning at 10 units and working gradually up to 40 units per day. After a 2 weeks' rest, the treatments were continued, with 40 to 50 units injected every other day for 2 weeks. The 3 patients originally carried about 10, 20, and 40 micrograms of radium respectively; each patient lost about half of her radium during the treatment, gained weight and improved in general condition. One has since died of a brain tumor, the other 2 are still alive, but not in good health. Later, Flinn [22] reported that 20 drops of viosterol given 3 times a day considerably hastened the elimination of radium. The mobilization of radium through calcium therapy seems at present to hold the only rational hope for the treatment of radium poisoning.

SYMPTOMS

In September, 1924, Dr. Theodore Blum, a New York dentist, reported [23] his belief that a case of osteomyelitis of the mandible and maxilla, in a dial painter, which appeared similar to phosphorus necrosis, was in reality due to the action of radioactive substances taken into the mouth. The failure of the jaw to heal after the extraction of teeth, and the development of necrosis and osteomyelitis of the jaw is not only the condition which led to the first identification of radium poisoning, but remains today one of the first symptoms noticed in new cases.

The same symptoms are exhibited by victims of radioactive water nostrums [5] and by dial painters.[7] Symptoms may fail to appear until several years after the ingestion of radium has been discontinued. These facts lend weight to the belief that the jaw and mouth are slightly less resistant to radioactive bombardment than are other parts. Gingivitis, buccal infection, bone necrosis and osteomyelitis, low blood pressure, and regenerative anemias resembling true pernicious anemia are the most common symptoms of radium poisoning. X-ray examination will often disclose sharply circumscribed, nearly circular areas of rarefaction in the skull.[21] Particularly in the cases which have long resisted the alpha ray bombardment of radioactivity, radiation osteitis and osteogenic sarcoma, often accompanied by slow-healing, spontaneous fractures, are quite generally present.[24]

The occurrence of pregnancy is possible in victims of radium poisoning. The administration of ether anesthesia to victims of radium poisoning has been fatal in 3 cases.

For a more detailed discussion of the symptomatology of radium poisoning the reader should consult the excellent papers of Martland [7, 24-28] and his coworkers.

Here it will suffice to point out that in cases where a radium history is suspected, the physician need never remain in doubt as to the presence of radium poisoning. Regardless of the presence

or absence of pathologic symptoms, the physicist offers at least 6 unambiguous physical laboratory tests for radium poisoning in living persons, only 2 of which (2 and 3 below) demand the presence of the patient in the laboratory.

1. Rapid and very sensitive, is the ionization-chamber-electrometer test of expired air for the presence of radon or thoron.[7, 14, 19]

2. The gamma ray ionization-chamber-electrometer test for penetrating gamma radiation from the patient's body is widely used, and is best able to give a quantitative idea of the total amount of radioactive material contained in the system.[7, 17, 19]

3. The Geiger point-counter and the Geiger-Müller tube-counter are sensitive, low pressure, electrical instruments which discharge when a radiation passes through them. When connected to a vacuum tube amplifier and a radio loud speaker they register as clicks in the speaker the number of quanta of radiation effective in them. Such an instrument placed near a victim's body will show a noticeable response to gamma radiation from the patient.

4. A small fraction (*ca* 0.005 per cent daily) of the radium in a victim is eliminated daily in the feces. Sensitive emanation electroscope methods[17, 29] can be used for detecting radium in a solution of fecal ash. With proper apparatus, this method is extremely sensitive.

5. About one-ninth as much radium is eliminated daily in the urine as in the feces. Urine ash can also be tested by the emanation method.

6. Where a dentist has removed a tooth or a sequestrum from the jaw, radioactivity, if present, can easily be detected by at least 4 methods: the gamma ray ionization chamber, the Geiger or Geiger-Müller counters, the alpha ray emanation electroscope, or by self-photography due to the action of its beta and gamma rays on a photographic plate.[5, 26, 30]

DISTRIBUTION OF RADIUM IN SYSTEM

Radioactive material tends to be phagocyted into the bones, marrow, spleen and liver. Because of its bearing on other heavy-element poisoning cases, the study of the distribution of radium in a victim of poisoning can be of considerable value. These can be carried out with some precision, because radioactive quantitative analytical methods are over a million times as sensitive as ordinary inorganic analytical technic.

A total of from 2 to 180 micrograms of radium in the entire body has been measured in the fatal cases to date. Depending on the resistance of the individual's system, from 2 to 10 micrograms of radium, when fixed in the system, is a fatal dose.

The radioactive self-photographs of the bones of deceased victims show a lack of uniformity of distribution of radium.[26, 30, 32] In some cases two or three small areas will be brilliantly self-photographic, while the remainder of the bone will display only a moderate amount of fairly evenly distributed radiation. This irregularity of distribution is important as an independent fact, as well as a warning that an analysis of a fragment chosen at random may not be representative of the entire bone from which it came.

Post-mortem radium analyses have been made on individuals who acquired

TABLE I

	I	*II*	*III*
Vertebrae	100	100	100
Jaw	...	51	20
Femur	...	48	27
Tibia	...	30	...
Skull	...	18	...
Rib	...	...	11
Teeth	...	...	46
Heart	0.5	...	0.04
Brain	...	0.4	...
Stomach	0.0	...	...
Liver	65.0	0.5	0.06
Intestines	2.0	...	...
Spleen	8.4	0.9	0.05
Lungs	17.0	2.2	0.04
Kidneys	0.4	...	0.17

I. Diagnosis, Cancer of Uterus. One milligram radium injected Sept. 1, 1913. Autopsy held Dec. 17, 1913. The high radium content of the liver and other organs shows radium was still being fairly rapidly eliminated from the system.

II. Diagnosis, occupational poisoning, watch dial painter. Died Sept. 12, 1922. Body exhumed and autopsy held Oct. 15, 1927.

III. Diagnosis, poisoning from drinking radium water nostrum over a period of 5 years.

their radium by: (I) intravenous injection,[12] (II) dial painting,[30] (III) drinking radium water nostrums.[5] The original data have been recomputed and are presented in Table I in a form which shows the *relative concentration* of radium in the various bones and organs before ashing them for analysis. For reference purposes the concentration of radium in the vertebrae, measured in grams radium per gram of bone, is taken as 100.

SUMMARY

Radium poisoning results when a few micrograms of radium or other alpha ray emitting solid radioactive substance become fixed in the system. Its action is principally to destroy the blood producing centers, and to weaken the bones. Calcium therapy, following Aub's and Flinn's work seems the only hope of removing radium from a victim's system. Modes of entrance of radium include the ingestion or breathing of radioactive substances by watch dial painters, chemists and miners, drinking radium water nostrums, and intravenous or other injections of radium by physicians.

From 60 to 98 per cent of the radium taken into the system is eliminated, principally in the feces (90 per cent) and urine (10 per cent). Some radon is lost in the expired air; no radium is lost in perspiration. Necrosis of the jaw, osteogenic sarcoma, and regenerative anemia are among the most common symptoms of radium poisoning. At least 6 unambiguous physical laboratory tests are available for identifying radium poisoning.

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