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Description of a Radium-containing Applicator Suitable for Treating the Nasopharynx, along with a Brief Review of the Essentials of Radioactive Transformations and the Biological Effects of Exposure to the Rays Emitted by this Applicator.

By

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The applicator has been designed to make effectual radiation of lymphoid tissue in the nasopharynx as simple a procedure as possible, with a minimum injury to normal contiguous tissues.

With each copy of this paper is furnished an empty, i.e., non-radium-containing applicator designed for use with radon. Its size, shape and construction can be seen at a glance. The instrument consists of a handle approximately 15 cm. long, which is screwed into a tubular head. The chamber containing the radon is 15 mm. long and 1.5 mm. in diameter. The wall thickness is .3 mm. The applicator can easily be introduced through the nose into the nasopharynx. Let it be kept in mind that this sample applicator is not identical with the one recommended for use in the Air Corps of the Army. The sample is made of brass while the Army applicators will be made of monel metal, which is more durable. The wall thickness of the radium containing chamber of the Army applicator is 0.3 mm instead of 1.0 mm., as in the sample. This change was made to permit the use of more Beta Rays and thereby shorten the time of the applications. Note that by this change in wall thickness the outside diameter is reduced, making it easier to pass along the floor of the nose into the nasopharynx. Finally, the handle of the radium applicator is solidly attached to the tube and not removable, as in the sample. This is important for two reasons: first, there is no danger of accidental separation of the two parts of the instrument, and second, the danger of loss of strength by leakage is minimized and, with careful handling, it might be said entirely removed.

Dosage*

The radium nasal applicator is to all intents and purposes a constant source of radiation. When its physical and biological dosage is once obtained, barring breakage, it can be counted on to give the same dosage indefinitely -- from month to month and from year to year. As a matter of fact, it does depreciate, going down at a constant rate which leads to half value in sixteen hundred years.

While radium, as X-ray, is measured by its ionizing effect on air it is not practical to state in ionization units the amount of dosage. It is essential to record the size and shape of the applicator, the amount of radium in milligrams, the duration of the application in seconds or minutes, the character of the screening, i.e., the material and its thickness (in the case of the nasal applicator .3 mm. of monel metal), and, when possible, the actual size of the volume to be radiated (in this case, the nasopharynx).

Each applicator is designed to contain 50 mg. of radium. Two applicators may be used at the same time, one through each nostril.

ENCLOSURE (A) (12)-Sheet 1

They may be separated by the use of adhesive tape attached to the ends of the handles and to the skin on opposite sides of the face.

It has been empirically determined that a dosage of one gram twenty seconds with a single applicator is sufficient to destroy lymphoid tissue and not to injure the mucous membrane of one side of the nasopharynx. This often must be repeated twice, at four-week intervals An applicator containing one gram of radium is twenty times as strong as one containing fifty milligrams. Therefore, to obtain a dosage equivalent to one gram twenty seconds the duration of the application should be twenty times as long, or four hundred second, i.e., six minutes and forty seconds. For notation on the treatment sheet, it is only necessary to give the amount of radium and the duration of the application. Where both applicators are used simultaneously it should be so stated.

Should the applicator contain an appreciably smaller or greater amount of radium than fifty milligrams (one or two milligrams either way will make no difference) the time will have to be increased or decreased to approximately the desired dosage of one gram twenty seconds with each applicator. For example, if the applicator contains only forty milligrams the strength will be only one-twenty-fifth of a gram and the time should be increased to five hundred seconds or eight minutes and twenty seconds.

Accessory Arrangements

An alarm timeclock to control the duration of treatment.

A table in a separate room where the patient can lie comfortably during the treatment.

A heavy lead cylinder twenty cm. hight, with a central opening large enough to hold two applicators. From the top down this should be about fifteen cm. deep. A lining tube of glass or brass may be fitted into the cylinder and kept filled with alcohol. No top is necessary. The walls of the lead cylinder should be 25 mm. thick, which would make the diameter 50 mm., plus the diameter of the central opening, which would be approximately one cm.

The purpose of the lead carrying cylinder is to absorb all of the Beta rays and approximately ninety-three per cent of the Gamma rays emitted by the applicator. It is for the protection of the person giving the treatment and his assistants. The alcohol is used to sterilize the applicator. Lead is the cheapest effectual material available for the carrying cylinder and this is due to its high density.

More important even than the lead is distance in reducing radiation The varies in intensity inversely with the square of the distance. At a distance of a foot or two the radiation from the nasal applicator can be considered as if from a point source. For example, at one foot the radiation is 1x 1 - 1, and we can call this intensity unity. At ten feet, 10 x 10 - 100, and the intensity is reduced to 1/100 of what it is at one foot. At twenty feet, 20 x 20 - 400, and the intensity is reduced to 1/400 of what it is at one foot.

When treatments are given the personnel should be at some distance away. When not in use the applicators in the cylinder should be stored in a safe place, as the radium is valuable.

A small hand truck should be available to carry the radium applicators in the load cylinders. During the treatment this can be kept next to the treatment table. When in storage the space should be large enough to take the truck and the container.

Local anesthetizing is rarely necessary and when necessary should be revealed by the preliminary nasopharyngoscopy.

As a lubricant, Boro-glycerine is most convenient. It can be washed off in a stream of water after each application.

Alcohol is a convenient means of sterilizing. Heat must never be used.

No one should ever touch the radium carrying tube at the end of the applicator. If this is done repeatedly, radiation changes may effect the skin of the fingers.

With this particular applicator, where there is so much Beta radiation, the wearing of rubber gloves should be helpful.

Protection to the Personnel Using Radium Applicator

If the precautions outlined are followed, there is no danger to the hands or fingers. The applicator should always be held at the end of the handle and away from the body. The placing of the applicator should be done rapidly and when treatment is completed the applicator should go back into the cylinder.

Over-radiation of the entire body daily for months will produce a drop in the white blood count. This is mainly in the lymphoid cells. One-tenth of an r. of Gamma radiation per diem is without any accumulative effect. Actually, in treating fifty patients a day and every day, if the precautions indicated are followed, the body would not be exposed to anything like this safe dose - probably not more than 1/100 r. per diem. There may be variations in tolerance - and it should be a routine practice to make a complete cell count of the blood in every doctor and nurse employed in these treatments. Counts might be made every two months. Individuals who at the onset, show a low white count should be excluded from the work.

Checking the Apparatus:

Radium itself is unstable and when radium is used it is in the form of a salt. For permanent radium applicators the insoluble sulfate is the best salt to use because in the event of a break there is much less danger of a loss. It should be kept in mind, however, that the applicator should always be handled as a delicate instrument.

On rare occasions a tube containing radium develops a microscopic fracture which can't be seen but which, nevertheless, allows radon,

the gas which is formed from radium, to escape. As will be explained later, if this occurs there is a loss of strength in the applicator. A simple method of determing whether such a break has occurred is by the use of a small inexpensive Alpha ray electroscope. If the applicator is put in the ionization chamber of such an electroscope and left for a few minutes and then removed, there should be no change in the functioning of the electroscope. However, if radon is escaping the electroscope will be radio-active and cannot be charged for several hours. If this method of determing ionization or some other simple device is employed, the tube should be tested about once a week.

Sources of Radium

Widely distributed in the earth's crust and waters, radium occurs in almost infinitesimal quantities. It is found in recoverable amounts in uranium-bearing ores, which are themselves rare, mixed with other minerals. Most minerals containing uranium are low-grade and not commercially valuable so far as the radium is concerned. Ores rich in uranium are exceedingly rare. The richest deposits so far uncovered have been in the Belgian Congo and in the Great Bear Lake region of Canada. Even when an ore consists of a pure uranium salt the proportion of radium to uranium is only one to four million. The popular movie, "Madame Curie", presents a very good picture of the general plan and difficulties encountered in separating radium from its ores. Since its first extraction by the Curies in 1898, there has been extracted perhaps as much as one thousand grams of radium. Most of this is in medical use, a considerable amount have been used in manufacturing luminous paints, and a modest amount employed for research in the physical laboratories.

General Facts

Radium's atomic weight is 226. It is an element and a metal.

It combines with acids to make stable salts, of which the commonest are the chloride, the bromide and the sulfate. The first two are soluble and suitable for use in radon plants. The last, the sulfate, is best adapted for medical radium preparations.

Mme. Curie, by electrolysis of a fused salt, obtained pure radium which oxidizes rapidly. It melts at 700° C.

While sold in milligrams of pure radium it is not measured by a scale but by the amount of Gamma Rays emitted. A standard preparation of pure radium chloride containing 21.99 milligrams of radium chloride was prepared by Mme. Curie in 1912. The Bureau of Standards in Washington has one of the numerous subsidiary standards. A Gamma ray electroscope is employed in comparing the strength of an unknown preparation with the standard preparation.

Radio-activity is the process of spontaneously omitting rays.

Radio-active transformation is the name applied to the changes which occur in radio-active materials.

Kinds of Radiation from Radium

Rays or particles of matter are discharged from atoms undergoing radio-active transformation. These rays or particles in the case of radium, in equilibrium with its products, are of three kinds:

1. The Alpha particles are positively charged helium atoms. They carry most of the energy of radiation, have initial speeds of from 9,000 to 20,000 miles per second, and they weigh about eighteen hundred times as much as the Beta rays. Even those with highest speeds are absorbed by a few centimeters of air, a thin sheet of paper or glass and, of course, completely by all metal covers. They are not, therefore, to be considered in connection with the nasal applicator.

2. The Beta rays are true particles, negatively charged ions which are ejected from the atoms at speeds varying from 20,000 to 186,000 miles per second. They are almost completely absorbed by two centimeters of tissue. Under the heading of "Filters" their availability will be further considered.

3. The Gamma rays have no electrical charge and have the speed of light, 186,000 miles per second. Under modern physical conceptions, just as in the case of light, they have to be considered particles (quanta) traveling in wave forms. They have a very high capacity of traversing matter opaque to ordinary light and are identical with X-rays produced at voltages from 400,000 to 3,000,000.

Radio-active Transformations

Practically all spontaneously radio-active substances belong either to the uranium or thorium groups of elements. Artificial radio-activity in almost any element can now be produced by bombardment with neutrons. The discovery of the neutron has materially changed the idea as to the construction of the atom.

We need only to consider the uranium family of which radium is a member. This group of elements starts with Uranium I, atomic weight 238, and ends with lead, atom weight 206. Note that the atomic weight decreases. This is at the rate of four for each transformation - exactly the weight of an Alpha particle (helium atom). When lead is reached, also known as Radium G, stability is attained and there is no further transformation. Some of the group only give off Beta and Gamma rays. In this case, the new atom is called an isotope of that from which it is derived and has the same atomic weight but different chemical properties and is a true element.

Omitting from consideration the isotope, the uranium series consists of:

A. Uranium I, weight 238, which by sponstaneous transformation decreases to one-half in 4,670,000,000 years.

B. Uranium II, weight 234, whose half value is 2,000,000 years.

C. Ionium, weight 230, whose half value is 69,000 years.

D. Radium, weight 226, half value 1,600 years.

E. Radon, weight 222, half value 3.85 days.

F. Radium A, weight 218, half value 3 minutes.

G. Radium B and Radium C, weight 214, half value 26.8 minutes and 19.7 minutes, respectively.

H. Radium F, Polonium, weight 210, half value 136.3 days, and finally lead, weight 206.

All these elements are solids with the exception of radon, which is a gas.

A feeble Beta and Gamma radiation is given off by the isotopes of Uranium II and by the isotopes of Polonium.

The effectual Beta and Gamma rays from a radium-containing tube, are from Radium B and C.

Omitting from consideration the predecessors of Radium and the descedants of Radium B and C, there remains only Radium, Radon and Radium B and C of importance in the nasal applicator.

All three types of rays, Alpha, Beta and Gamma, have the property of ionizing gases. If their energies are measured by their ionizing power in small volumes of gas, the Alpha rays are ten thousand, the Beta rays one hundred, and the Gamma rays are one. This is a rough approximation. If the energy of each is measured by complete absorbtion, the Alpha rays carry 88.8%, the Beta rays 4.5%, and the Gamma rays 6.7% of the total energy.

Radio-active Equilibrium

Beta and Gamma rays are given off invaribly together. Only Radium B and C, very short-lived products, produce these rays. When Radium is sealed in a tube it begins to form Radon, and the Radon Radiums B and C. These products begin also to disintegrate, rapidly at first and then slower. It takes approximately thirty days for the radium tube to reach equilibrium, i.e., the point of maximum Radiums B and C content. When once attained it is, for our purposes, constant.

When Radon is sealed in a tube it reaches equilibrium in four hours and then begins to decrease at the rate of about one-sixth every day. There is no Radon and no Radiums B and C after about thirty days.

A milligram of Radium contains millions of atoms but only few undergo transformation in a unit of time. This rate is perfectly uniform and cannot be changed by any of the physical agents known at

this time.

Much higher concentrations of Radon are possible than in the case of Radium. In the same volume, at least forty times as active preparations are possible. The Radon is measured in the same way as Radium: A Curie of radon has the same energy as a gram of Radium and the same applies to fractions such as milligrams and millicuries.

What Happens when Radiation is Absorbed?

If the material traversed is thick enough there is complete absorption of all three types of rays. If an atom is pictured as composed of a central nucleus and orbital electrons (the nucleus containing protons, electrons and neutrons) it is simpler to visualize. Each proton carries one positive charge and each electron (Beta ray) one negative charge. A neutron is composed of a proton and an electron and has no charge. An Alpha ray may strike an atom, lose some of its energy, and release enormous electrons. Such electrons act as Beta rays do. Very infrequently, an Alpha ray strikes an atom solidly and causes it to lose a proton. This is artificial radio-transformation. It was first observed by Rutherford in the transformation of oxygen into nitrogen. With Lawrence's Cyclotron and the development of Neutrons this has been accomplished for many elements. The Alpha ray finally loses all its energy.

Beta rays, which are definite particles, also produce secondary electrons and characteristic X-rays. They act on the orbital electrons of the substance through which they pass and have most irregular paths, bounding from atom to atom. They vary in their energies and speeds-- the higher the energy the more the effect.

Gamma rays, as visible to light and X-rays, are impenderable, but are also absorbed and scattered. In passing through tissues they release electrons from atoms and also characteristic X-rays. Some of the observed pheonomena are only explainable on the wave theory, while others demand the particle (quanta assumption) to be the understood. The manner of their action and their nature is still in doubt and had been argued pro and con since the time of Isaac Newton. It would seem that Gamma rays, like X-rays and like ordinary visible light, are particles of matter and proceed in the form of waves -- the higher the energy in the particle the shorter the wave length. In the production of X-rays the length of the wave is proportional to the voltage applied to the tube. One can, therefore, speak of Gamma waves of certain wave lengths as rays due to certain voltages.

The wave lengths can be estimated by the crystal defraction spectroscopic appearance and by the absorption methods.

Effect of Covers on Radium Preparation

As already pointed out, screening, or filtration, markedly changes the amount and character of the radiation used in treatments. For various reasons, mainly, however, controlled by the aim to limit the dosage to the tissue to be treated, it is advantageous to use different screens for different purposes.

With a homogenious radiation, i.e., in the case of Gamma rays, all of the same wavelength, or, in the case of Beta rays with the same speed or energy in any material the absorption is exponential, i.e., in a unit of thickness of the absorbed, there is the same percentage of absorption.

The Beta and Gamma rays from Radium are not homogenious but are in bands. When analyzed they are not in a continous spectrum as is the case with X-rays. When considering Radium one speaks of soft and hard Gamma and Beta rays. The soft rays are more easily absorbed and have a higher coefficient of absorption than the hard rays. As a consequence, the total radiation drops rapidly with the first thin filter and only becomes exponential when the radiation becomes homogenious from the disappearance of the softer rays.

The absorption capacity of a filter is proportional to its density. To absorb all the Beta rays only about .5mm. of platinum, gold or tungsten is required, one mm. for lead or silver, two mm. for brass or monel metal, 10 mm. for aluminum, and twenty mm. for water and animal and human tissues, with the exception of bone which is about ten mm. Even when all the primary Beta radiation is absorbed there is a secondary Beta and Gamma radiation from the filter. This is most penetrating from the metals of high density. It is not large from monel metal; it is constant from a fixed source as in the case of the nasal applicator and, for the treatment of the nasopharynx, does not require a secondary screen of lighter material ordinarily used in deep treatments.

It is quite certain that all the Beta rays from the applicator are absorbed by the tissues of the nasopharynx. On the other hand, the proportion of absorption of the Gamma rays is small. At a given distance of the tube from the walls of the nasopharynx the most intense radiation is from the axis perpendicular to the center of the tube, and much less at the ends. This is because of the inverse square law. The radium in the tube may be considered as a line of points.

The influence of filtration by monel metal is approximately as follows:

With .3 mm -	Beta rays	32%,	Gamma rays	70%
With .5 mm -	"	"	25%,	"	"	75%
With 1. mm -	"	"	3%,	"	"	97%
With 2. mm -	"	"	0%,	"	"	100%

This refers to the quality of the beam and not the total quantity of radiation.

The primary action of the radiation is directly on the atoms of the tissue and has already been described.

<u>Biological Effects of Radium</u>

Changes in living tissues and cells are directly proportional to the radiation absorbed. While this is true of a single exposure given in a short time, it may be modified very greatly by the reparative powers of tissues. A unit dose given at one sitting produces more

(12 - Sheet 8

effect than the same total dose in a period of a week with daily fractions being given each day. When the fractions are given at weekly intervals or a great many weeks, there may be neither macroscopic or microscopic changes demonstrable. All available evidence goes to show that the changes in tissues due to Gamma and Beta rays are identical, provided the amount of energy absorbed is identical and the time factor kept constant.

Not long after its discovery, some accidental burns occurred with those handling radium and these observations suggested its use as a therapeutic agent.

It was early observed that macroscopic changes occurred only after an interval of a number of days. This was termed the latent period. Microscopic changes can occur and be demonstrable even with small doses in a few hours. As the intensity and amount of dosage increases the latent period becomes shorter and shorter.

When dealing with normal tissues, it was soon recognized that they varied greatly in their ability to tolerate radiation. That the lymphoid tissues were injured by dosage that apparently had no effect on other tissues, was shown by Heinecke in 1904. This has been confirmed by every experimental study made since then and by countless clinical observations. Malignant, transformed cells were found to be less tolerant than the normal cells from which they are derived. It is this difference in tolerance which forms the basis for all irradiation therapy. What actually takes place is exceedingly complex and but very imperfectly understood. There are physico-chemical and chemical alterations immediately following the exposures. Whether these primary changes lead to the permanent changes, directly or indirectly, is unknown. There is abudant microscopic evidence of the final changes in growths and tissues, such as replacement by connective tissues of the parenchymal cells.

It is almost certain that the primary changes in a cell involves both nucleus and protoplasm. Which recovers first and what effect injury of one or the other may have on the other is not known. It is probably that the intracellular tissue is contributory to the changes. Edema is a constant change following radiation.

Bacteria, especially pathogenic ones, which cannot be destroyed in cultures, are destroyed by radiation of tissues in which they are located. This must be a secondary effect.

Cells definitely vary - depending on the stage they are in. They are most easily injured at the time of division and a very mild radiation may cause injury of the reproductive part of the cell alone.

Hyperplastic tissues are more easily injured than quiescent tissues.

The recovery period of the nasopharyngeal tissues, after a moderate radiation injury, takes about four weeks. It is because of this that the intervals between treatments has been fixed at this period.

The surroundings and physical conditions in all adenoids vary and exactly the same effects from a similar dosage cannot be expected in each case.

The aim of the treatment is to remove mechanical obstruction which prevents free ventilation through the Eustachian tubes, but perhaps more important is the relief of infection which cause hyperplasia of the lymphoid tissues and edema and swelling of the mucous membrane.

Biological dosage is a term applied to the dosage necessary to produce a desired effect. In this case, it might be called the adenoid dose. Filtration has marked effect in this connection, e.g., where a millimeter of brass, or its equivalent, monel metal, is employed this dose is two gram minutes on either side. If the filtration is reduced to .5 millimeters, the dosage becomes one gram forty seconds, and with the applicator we recommend .3 millimeters, one gram twenty seconds. The energy absorbed is approximately the same and, with the tissue we are dealing with, the results are nearly the same.