EDITORIAL

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Radioactive Isotopes in Medicine

Modern theory postulates an atom that consists of a central, heavy, positively-charged nucleus, surrounded by a zone of negatively-charged electrons. The nucleus itself contains two kinds of particles of approximately equal mass, the protons, which carry the positive charge, and the uncharged neutrons. Each element has its own atomic number, which specifies the number of protons in the nucleus and also the number of orbital electrons in every atom of that element, since the atoms as a whole have no charge.

The existence of isotopes of an element is due to the variation that can occur in the number of neutrons in the nuclei of its atoms. For example, carbon, of atomic number 6, has isotopes whose atoms contain 4, 5, 6, 7 and 8 neutrons in their nuclei in addition to 6 protons and which are called C₁₀, C₁₁, C₁₂, C₁₃ and C₁₄ respectively.

Should the combination of protons and neutrons in any particular nucleus be unstable, there tends to be a readjustment and one or more particles may be emitted, together with energy in the form of gamma rays, while the atom assumes a more stable form. This disintegration with emission of energy and return to a more stable form of nucleus is called radioactivity.

Many elements occur in nature as a mixture of isotopes, but few are radioactive and these are found in appreciable quantity only in the well-known uranium and thorium series. Today, however, the cyclotron furnishes us with rapidly moving protons, deuterons and alpha particles, while, like the atomic pile, it also provides a source of neutrons. Any of these particles may, under certain circumstances, enter the nucleus of an

atom and render it unstable. In this way, artificial radioactivity is produced. For all practical purposes, these artificial radioactive isotopes act chemically exactly as do their normal counterparts but, in addition, they have the property of radioactivity.

Each has its own constant spectrum of radiations and decays in a constant manner. The activity of an isotope falls to half its initial value in a time called the half-life. This half-life may vary very widely among different isotopes. The unit of activity is the curie (defined as 3.7×10^{10} disintegrations per second) and the fractions of this unit with which we usually deal are called millicuries and microcuries.

The greatest contribution that radioisotopes have made to the advancement of human knowledge in medicine has been due to their use in investigation as 'tracer' substances. An element which is known to take part in the process of metabolism to be investigated is 'tagged' by the addition of a small quantity of its radioactive analogue and its movements can thereafter be followed by means of a suitable detecting instrument, usually one of the forms of Geiger counter. Notable advances, for example, have been made by such means in the study of the uptake, distribution and excretion of many elements, in the determination of the permeability of the phase boundaries of the body and in the examination of the life history of red blood corpuscles.

These procedures, however, belong rather to the research laboratory and it is the more clinical applications of radioisotopes that we wish particularly to discuss; those in which use is made of the radiation to investigate and treat disease.

Frontispiece.—Some years ago the patient sustained a penetrating wound of the sclera. The present lesion appears to be an arteriovenous anastomosis spreading outward from the choroid. Note the conjunctival vessels running across the deeper lesion. From the First International Exhibition of Medical Photography (by kind permission).

By their very nature, these materials, particularly in the high activities demanded by their use for therapeutic purposes, are dangerous to patient and doctor alike and they should be used only by those who have a sound knowledge of the physics of radiation and the biological effect of ionizing radiations in man. The problems of protection from radiation, disposal of excreta and general prevention of contamination can be solved only with the aid of a properly equipped physics department. In general, the longer the half-life the greater the danger, and the injudicious use of such agents, especially in young patients, may produce effects which are no less unpleasant because they are delayed.

The thyroid gland's avidity for iodine has provided the basis for a great volume of work with Iodine 131 designed to clarify our knowledge of thyroid metabolism and help us to distinguish the normal from the abnormal. An extension of the technique, using a shielded Geiger counter, has made it possible to measure the anatomical extent of the iodine-containing tissues and thus provide a useful diagnostic aid in cases of retrosternal masses of doubtful origin. Still further, much work has been done on the I131 uptake in thyroid carcinoma and it has been found that a small proportion of such tumours do, in fact, compare with the normal gland in the way they take up iodine. Metastases may behave in the same way, but if they do not, some may be induced to do so by first removing all the normal thyroid tissue so as to encourage the metastases to take over thyroid function.

The detection and localization of brain tumours have been attempted, using I131 in diiodo-fluorescein. In spite of confident claims, however, we feel that, as yet, the best that the method has to offer is confirmatory evidence in a small proportion of cases. Phosphorus 32 has been used for the same purpose and undoubtedly localizes in brain tumours, but is only suitable for use if a craniotomy is to be performed, since its radiations do not penetrate the skull.

Sodium 24 has been used in the measurement of circulation time and in the localization of the placenta. The labelling of red blood cells with P32 to measure the volume of circulating blood has

enabled this to be done more accurately than by any other method.

Turning now to the therapeutic uses of radio-isotopes, we may examine them under several headings.

As a Replacement for Interstitial Radium and Radon

The use of such materials as Cobalt 60 and Tantalum 182 in the form of beads, wire or foil offers greater flexibility than the established techniques using radium and radon. There is an advantage, too, on the score of cheapness, but no great improvement in results is to be expected.

As Surface and Intracavitary irradiators

Co60 or Ta182 as mesh or foil may prove worthwhile as gamma ray surface applicators. P32 solution in blotting paper or more elegantly and uniformly incorporated in thin flexible sheets of polythene has a distinct advantage in cheapness and convenience as a beta ray applicator and may find a wide field of usefulness in the treatment of superficial lesions of skin and mucosa.

Peritoneal spread of carcinoma may be treated by injecting into the peritoneal space a colloidal suspension of Gold 198. The particles in the suspension must, of course, be large enough to ensure that little absorption takes place through the membrane. Reports indicate that regression of small superficial tumours and suppression of the formation of ascitic fluid may be expected, and it may be that this will prove a valuable palliative procedure.

Superficial carcinomata of the bladder and tumours in other hollow viscera have been treated by introducing a rubber bag and then filling it with a solution of a suitable radioactive salt. Co60, Na24 and Bromine 82 have been used in this way. The treatment time is short, discomfort is not great and the early results satisfactory.

By Direct Infiltration of Tumours

A tumour is infiltrated with a volume of a colloidal suspension of suitable activity. Au198 has been principally used in this way, remaining in the tumour long enough to provide a very great number of effective point sources of radiation.

By Selective Localization

It was at first thought that physiological localization of radioactive elements in the body might be of value in the treatment of disseminated and inaccessible cancer. Results have fallen far short of expectation, however, principally because, with the exception of iodine and phosphorus, the ratio of uptake in tumour to that in normal tissue has been too small. To deliver an effective dose to the tumour under these circumstances usually means an exposure of the whole body to far too much radiation.

The treatment of disorders of the thyroid gland by radioiodine has been practised for some years. The results in hyperthyroidism, particularly where there is no cardiac disability, are good and the method provides a substitute for surgery and deep X-ray therapy where these are not available or sometimes where they have failed. It is generally agreed, however, that in young patients the method is best avoided, at least for the present.

The thyroid carcinomata that take up iodine well are usually well-differentiated adenocarcinomata showing colloid formation. This is by no means always so, however, and any disseminated carcinoma, however anaplastic, deserves a trial to test its iodine-concentrating powers. The best method of treatment would appear to be by a single large dose and as much as 250 millicuries may sometimes be given by mouth with no ill effects save lassitude and perhaps nausea for a day or so.

The uptake of P_{32} in a tissue depends principally on its rate of growth. High concentrations are therefore likely to be found in red marrow and in rapidly growing tumours. A combination of rapid growth and sensitivity to radiation selects a tumour as suitable for treatment by P_{32} . Such properties are possessed by the leukaemias, lymphosarcomata and anaplastic carcinomata and, in these cases, radiophosphorus provides a good alternative to deep X-ray therapy and appears to be superior to most chemotherapeutic agents. In only one disease, polycythaemia rubra vera, has P_{32} yet established itself as the treatment of choice and here, intravenous injection of 5 millicuries, followed four to six weeks later by a further 3 or 4 millicuries, often produces a remission which may last several years.

The application of radioactive isotopes to the field of therapy is as yet in its infancy. Experience gained up to the present has shown that none of the techniques discussed in this paper is yet of sufficient value to warrant the abandonment of established surgical or radiotherapeutic methods. What advantages there are lie in ease of application generally, and specifically in some small groups of patients for whom orthodox methods have little or nothing to offer.

In short, these substances have yet to find their true place in therapy. This, we think, will come about only when there is a clear understanding of the chemistry and metabolism, not merely of tissues as a whole, but within the cell itself.

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