TWO HUNDRED SEVENTY-SIX MEDICALLY USEFUL RADIOISOTOPES

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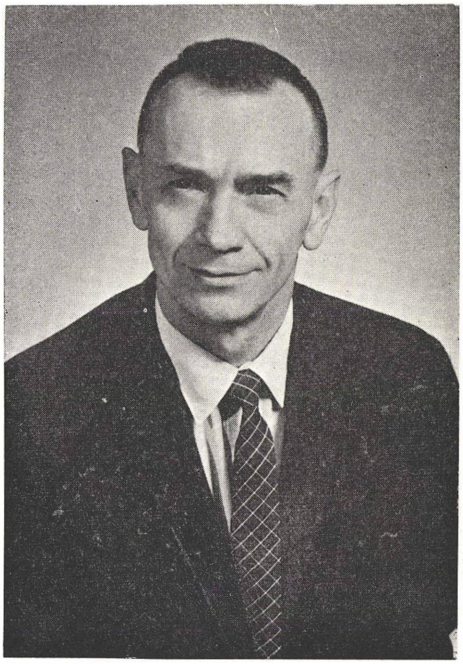

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There are still some physicians (hopefully none in Japan) who think that nuclear medicine is the diagnosis of thyroid disease with "Iodine Atomic Cocktails." Just before World War II some therapeutic physicians might have said that all nuclear medicine was the application of radiophosphorus to the treatment of blood disorders; but radicsodium was probably the first isotope to be used after the invention of the cyclotron with the idea of a medical application. This was Hamilton's work in Berkeley, California soon after the development of the cyclotron in Berkeley, carbon-11 and carbon-14 were being specifically manufactured with a biochemical application clearly envisaged by Kamen. The radiosodium investigations have at least a tenuous historical connection with the work that was done during the middle 1920's in Boston by Weiss, Blumgart, and Yens on adsorbing some radon onto a sodium chloride solution and injecting it into the human body for the study of circulation time. Probably even before the Boston workers, a group of European physicians, Christiansen, Lomholt, and Hevesy were using labeled bismuth preparations in the study of syphilis therapy.

Most of the hisrory of nuclear medicine can be traced back to one of two sources: either the "tracer" development by Hevesy just before World War I or to the very diversified attempts to apply radium to medical therapy during the first decade of the twentieth century. Almost everything that we are now attempting with radioisotopes (direct iniection, intracavitary therapy, seeds, wafers, balloons) was attempted before World War I with radium. These investigations did not fail, they just were not overwhelmingly successful. Much of the lack of success was because the biochemistry of

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radium was so different from that of elements ordinarily present in the normal metabolic behavior of the human body.

The dependence upon radium early during the century is understandable because it was the only isotope (or rather group of isotopes) that was reasonably available. After the cyclotron was developed, many other isotopes became available. So much was already known about the biochemistry of iodine that its isotopes began to replace all other isotopes to physicians who were thinking of metabolic processes.

During the 1930's the first production of a radioactive isotope of iodine did not result in the production of iodine-131. It was not until somebody got the idea that in a cyclotron it would be possible to make an entirely different isotope (which would then decay to become an iodine radioisotope) that iodine-131 became the important radioiodine. In 1937 Irving Ariel had considerable difficulty in getting a $300 grant so that the University of Rochester cyclotron could produce some tellurium-131 for physiological studies of iodine metabolism. Twenty-seven years ago the Rochester physicians thought that there might be a diagnostic, maybe even a therapeutic, potentiality to radioiodine.

It could be argued that the overwhelming emphasis on radioiodine has tended to restrict our thinking of nuclear medicine to thyroid physiology. Most of our medical gamma-ray instrumentation is built around the iodine-131 energy. It might also be argued that iodine-131 made nuclear medicine popular, for radioiodine was immediately significant both diagnostically and therapeutically. However, the important point of the first University of Rochester experiments is that the radioiodine was a part of a decay scheme of tellurium to iodine to zenon. But this is not really a simple parent to daughter to stable decay (P→D→S). Except for the naturally occuring radioisotope transmutations, it is one of the most complex of schemes. Two parent isotopes are formed ${}_{52}\mathrm{Te}^{131}$ and its isomer ${}_{52}\mathrm{Te}^{131\mathrm{m}}$. One parent is also the daughter of the other parent and both parents decay to ${}_{53}\mathrm{I}^{131}$, but this isotope in turn can decay in three ways. Either it decays to stable ${}_{54}\mathrm{Xe}^{131}$ or it decays to a granddaughter ${}_{54}\mathrm{Xe}^{131\mathrm{m}}$ or to ${}_{54}\mathrm{Xe}^{131\mathrm{mm}}$. One of the granddaughter isotopes has so short a half-life (nanoseconds) that it can easily be considered a part of the iodine-131 decay. The other has a 12-day half-life. Fortunately, however, it is in so small proportion (0.7%) that it is of negligible amount unless the iodine-131 metabolism is studied over a period of weeks to months.

The same complex mode of decay is true of almost half the isotopes that are available to physicians. It is hard to say what is and what is not important. Sodium, for example, is obviously an important element in the body. The body contains a lot of sodium, but only one kind is stable (by our tentative and somewhat unstable "stability"). Six kinds of sodium are radioactive with half-lives ranging from half a second to 2.6 years. We cannot say that any one isotope of sodium is more important than any other except, perhaps, in so far as we can measure and conceive of a metabolic usefulness of the isotope itself.

The human body is a walking leather bag full of isotopes. We can say that there is more oxygen, for examqle, than there is magnesium and therefore by magnitude oxygen is more important than magnesium. Or, instead of using magnitude, we could use "diagnostic usefulness" as a criterion. We know a little bit of how iodine is transported through the body and what it seems to accomplish. We do not know so much about antimony; therefore, we can say that iodine is more "diagnostically useful" than antimony. There is only one stable kind of iodine: iodine-127. But there are 22 different isotopes of iodine. They do not all have equal diagnostic potentialities. Many of the isotopes of indine have half-lives too short to be diagnostically measurable. Some of the radioisotopes of iodine have similar characteristics, but the half-life, or the energy, or the ease of production, makes one more diagnostically desirable than another. Three particular isotopes of iodine have very particular values. Iodine-125, for example, hae a low gamma energy. Iodine-131 has a medium gamma energy and iodine-132 has a high gamma energy. Most of our instruments for gamma measurement are built around the iodine-131 energy level; therefore, these are by historical accident the ordinary instruments. If iodine-125 is used special instruments are highly desirable. If iodine-132 is used a shielding problem arises with almost any instrument.

The half -lives can make a big difference in medicine. Iodine-131 has a half-life of a little more than a week. This can easily be considered the medium length for hospital and clinical use because it is what we are accustomed to. In comparison iodine-125 has a long half-life and iodine-132 a short half-life. With the measuring equipment now available, we can do sample counting of iodine-131 with a dose of microcuries given to the patient. If we do sample counting with iodine-125 it takes about a tenth of the amount and with iodine-132 about a third. If our intention is to do scanning (as we now think of scanning) then it takes many microcuries of iodine-131. Scanning is very superficial with iodine-125. Our instruments are not quite fast enough yet to do good scanning with iodine-132. At the present time we do not do therapy with iodine-125. We use millicuries of iodine-131. It would take many millicuries to accomplish the same task with iodine-132. Even though the various isotopes of iodine will have a similar pharmacology in the body, the results of a measurement, the technique of studying metabolism, and even the instrumentation might be decidly different with each of the isoropes.

There are 1338 isotopes now listed; however, this number changes with publication of physics journals. By the time you read this there will probably be 1400 or even more. If we stop at the January 1961 listing of all isotopes and consider this as "absolutely correct" (it is incorrect, but we have to stop someplace), the large number of 1338 isotopes is entirely too much for a physician to contemplate. Some of the isotopes are either stable or have a very short or very long half-life. If we accept as "medically potential" only those isotopes that are radioactive, without alpha rays, with a half-life between one day and a hundred years (with exceptions), we are left with 276 artificially-produced radioactive isotopes. If we add the restriction that a detailed knowledge of pharmacology must be available, there are many fewer. If we relax the restriction on the many radioisotopes that have much longer or shorter half-lives, there would be many more than 276.

To use radioisotopes to their fullest advantage, most physicians (especially those interested in nuclear medicine) will have to know at least that there are multiple modes of decay. Figure 1 shows a system for thinking about the decay of isotopes. Some are very simple decay modes from a parent to a stable. Some are more complex and decay through a daughter. Sometimes there are two parent isotopes and sometimes one of the parents besides being a parent is also a daughter of the other parent.

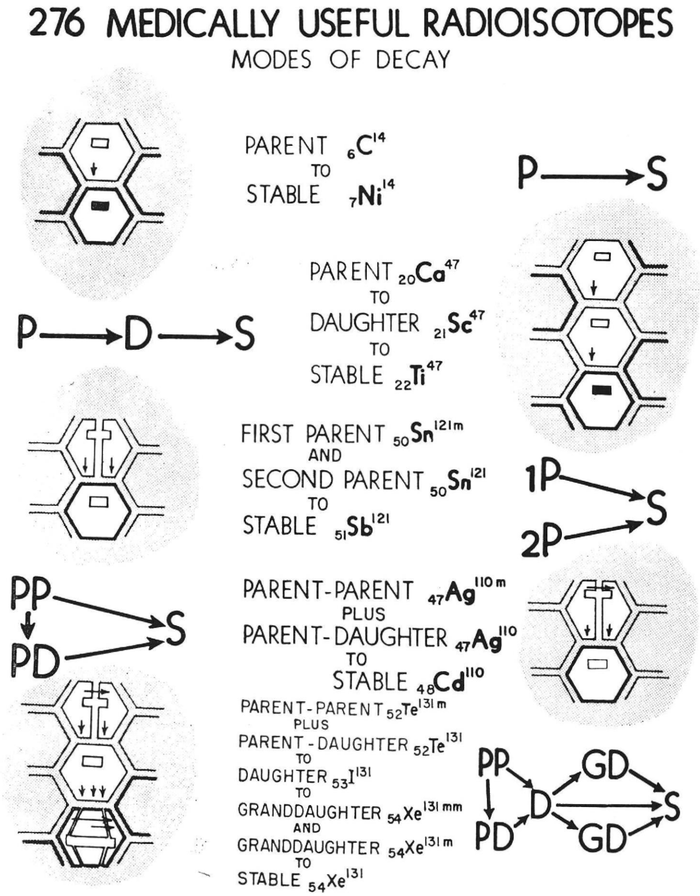

Fig. 1.

We also have to know something about the decay scheme. Carbon-14, for example, gives off a low-energy electron to become a stable nitrogen-14. Some isotopes give off a high-energy electron. Some give off a positron; some give off a beta ray followed by a gamma ray; some decay with electron capture and (for all practical purposes) can be considered pure gamma emitters. Some isotopes, like iodine-131, may give off any of a number of different-energy beta rays and each of these may be followed by one or even more than one different-energy gamma rays. The scheme of the decay is a fingerprint of the isotope. It is also a method for classifying the various kinds of radioactive isotopes.

In addition to the mode of decay and the decay scheme, the fact that there are so many varities of possibilities of decay makes it necessary for the physician to know something about the potential isotope that might be involved. Some parent isotopes with a very long half-life may have daughter isotopes with long or short half-lives. The short half-life daughter probably will not participate in the metabolism of the parent, but a long half-life daughter may be even more important pharmacologically than the parent, and the daughter may or may not be more important from the standpoint of its radiation dosage.

The subject of nuclear medicine, which started out with such a simple idea to make it possible to see the pharmacology of an element in action, has retained only of its features. It is no longer a simple study, but it is still possible to see the elements in action. There are now well over 100 separate techniques for using radioisotopes in clinical medicine. In some situation the techniques are useful because they are far simpler than a purely chemical technique; in others the diagnostic procedure cannot be done without a radioactive isotope. Like all other procedures in every other field of medicine, a lot must be understood before even the simplest procedure can become practical. Presumably the purpose of the Japanese Journal of Nuclear Medicine is to make this very complex information available to Japanese physicians. Throughout the world all medical scientists (not just Japanese scientists) hope that the journal will be a success.

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