THE PRINCIPLES AND APPLICATIONS OF RADIOACTIVE TRACERS TO THE MEDICAL AND BIOLOGICAL SCIENCES

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The fundamental postulate upon which rests the value of the artificial radioelements as tracers is the fact that the radioactive isotope of a stable element differs only in its property of radioactivity. The chemical and physiological properties of the two forms of the element, or compound, into which a radioactive element may be incorporated, are identical so long as the radiations from the radioactive isotopes are not sufficiently intense to produce physiological changes. In general, this limiting factor can be avoided in most tracer studies since the amounts of radioactive material required for studies of this character are too small to produce any chemical or physiological changes by the action of their radiations.

Three general technics have been developed for the use of radioactive isotopes as tracers in the biological and medical sciences: First, the assimilation of the administered radioelement, or labelled compound, its distribution in the tissues, conversion into other compound by the body, and finally its elimination may be followed quantitatively by direct measurement of the radioactivity of the samples of tissues after the removal from the body. Second, the selective accumulation of the radioactive isotopes of a number of elements and compounds may be observed in the organs and tissues of the intact animal or human subject by measurement of the radioactivity of these structures in situ. Third, the correlation between the distribution of the radioactive element or compound in the tissues to their microscopic anatomy may be studied by the aid of photographic films. This last mentioned technic is usually defined as radioautography.

The first named technic is the most widely employed and is applicable to all the radio-elements. The radioactive material may be given either as a simple inorganic compound, or may be incorporated into a complex organic molecule. For example, radio-sodium is usually administered as sodium chloride, radio-phosphorous as disodium phosphate, radio-iodine as sodium iodide, etc. The distribution of labelled elements or compounds in the body may be followed as the total content of the administered radioactive material in the various organs, tissues and excreta. For example, the rates of conversion of administered radioelements to various complex compounds by the physiological processes of the body may be observed. Illustrative of this point is the synthesis of hemoglobin from iron, of phospholipids, nucleic acids, and nucleo-proteins from inorganic phosphates, and of thyroxin from iodine. In studies of this character, the compound is isolated from the tissues and its radioactivity is compared with the total amount of radio-element originally administered. Complex organic compounds may be labelled for tracer studies by the inclusion of radioactive atoms in the molecules. For example, thiamin (vitamin B_1) has been tagged by synthesizing it from radio-sulfur. The labelled thiamin is then administered and its fate in the body followed by measuring the distribution of radioactivity from the radio-sulfur in the tissues, body fluids and excreta. By this procedure its conversion in the body into other compounds may be observed. The comparatively recent availability of the 5,000 year radioisotopes of carbon, C^{14}, has made it possible to label amino acids, carbohydrates, drugs, hormones, vitamins, etc., to study their metabolic pathways and fate in the body.

A second general technic makes use of the ability of many artificial radioelements to emit penetrating gamma rays which can pass through many centimeters of tissue without serious attenuation and which can thus be measured at some distance from the site of origin. The presence of the accumulated radio-element in the particular organ or tissue under study is detected by placing a suitable measuring

device, such as a Geiger counter tube, over it and measuring the intensity of the gamma rays emitted from the radioactive atoms which have been stored selectively in the tissue. The application of this second major type of tracer technic is illustrated in the study of the iodine metabolism of the thyroid gland in normal and goitrous human subjects. The selective deposition of the administered radio-iodine by the thyroid is determined by placing a Geiger counter tube over the neck and measuring the intensity of the gamma rays emitted from the radio-iodine accumulated in the thyroid tissue. Since by this method the necessity of removing tissue for determination of its radioactivity is eliminated, it offers two distinct advantages. First, it enables the observer to follow the ebb and flow of the labelled element or compound in the same human subject or animal for a considerable period of time. The results thus obtained give a continuous record of the fate of the accumulated radioactive atoms or molecules. Secondly, it makes possible in vivo tracer studies in normal human subjects.

The third technic makes use of the photographic action of the radiations from artificial radio-elements, by means of which the distribution of the administered labelled elements or compounds in tissues may be investigated. Thin sections of the radioactive tissues are placed against photographic films. After an interval of time sufficient for adequate exposure, the film is removed and developed. The sections are stained, and each section with its corresponding piece of developed film (radio-autograph) is examined under the microscope. The areas of darkening in the film correspond to the regions of the tissues in which the greatest deposition of the radio-element has taken place. Thus a correlation between the deposition of the labelled element or compound and the histological structure of the tissue can be established.