radioisotopes in the medical laboratory

Rapid progress has been made in a branch of medical work which uses radioactivity without involving the patient. Known as "in vitro" — or test tube — procedures, they are valuable because of their simplicity and may be of great advantage in developing countries.
This brief review is by Dr. H. Belcher, of the Division of Life Sciences.

It is now thirty years since an artificial radioisotope of iodine was first used in clinical medicine to investigate the functional state of the thyroid gland. Since that time, radioactive tracer techniques have become firmly established as part of routine medical practice, to the point that medical radioisotope laboratories exist in most major hospitals and medical institutions throughout the world.

In radioactive tracer techniques the fate of a substance of interest in the system under investigation is followed by introducing a small quantity of the substance labelled with a suitable radioisotope and following what happens to it by recording the radiation emitted at various stages.

The tracer techniques used in clinical medicine fall into two main categories. In the first are scintigraphic techniques to provide an actual picture of the various organs of the body and thus to locate tumours, cysts and other lesions; these techniques depend on the administration of labelled substances that are taken up by the organs or tissues of interest and the subsequent mapping of the distribution of radioactivity. In the second are techniques for the investigation of various aspects of the composition of the body and the functional state of its organs and tissues; these involve observations on the uptake, turnover and excretion of labelled substances in the body. They may be based on direct radioactivity measurements on the patient or on measurements made of blood or other samples.

Both these types of technique involve the administration of radioactive materials to the patient and, like X-ray examinations result in his exposure to certain amounts of radiation. Whilst the associated radiation hazards may be quite negligible, the patient must still attend the clinic to receive the radioactive dose and also, in most cases, to undergo the necessary measurements.

A Symposium on "*In vitro* procedures with radioisotopes in clinical medicine and research" recently held at Agency Headquarters has focussed attention on a third group of techniques in which no radioactive material is given to the patient, the necessary procedures being carried out entirely *in vitro* (i.e. in the test tube) on samples of blood, urine or body tissues. These techniques involve no radiation exposure to the patient; indeed, they do not require his direct participation at all and may well be carried out at some central laboratory on samples sent in from a wide area. They are thus particularly suitable for use in regions where local facilities are limited or where field studies have to be undertaken. Progress in these techniques has been especially rapid during the last few years and their present scope may be judged from some of the procedures discussed at the Symposium.

In one group of procedures, small samples of body tissues which can readily be obtained by minor surgery, or of blood, are incubated *in vitro* with a labelled substance and the way in which this substance is metabolized by the tissue is followed. Such investigations can be valuable in the diagnosis of cancer, diseases associated with inherited enzyme deficiencies and various other conditions.

Epidemics and immunization

Another group of procedures make use of radioisotopes to investigate the immunity of populations to infectious diseases. The immunity of an individual to a given infection may depend on the existence of specific antibodies in his blood which can combine with and so render harmless the infecting organisms or the toxic substances which they produce. In the control of outbreaks of such diseases as cholera and plague, it is important to know the extent to which the threatened population is immune in order to determine whether mass immunization is necessary. The classical methods used to examine blood for antibodies against given organisms require rather large samples of blood and are inconvenient to use on large numbers of subjects. Results indicate that it may be possible to develop tests based on the use of labelled bacteria or bacterial toxins which require only a few drops of blood and which can be easily carried out on a large number of subjects when an outbreak of a disease occurs.

One of the first *in vitro* radioisotope procedures to be used in clinical medicine was in fact a test of thyroid function and was based on the observation that if a small amount of a thyroid hormone labelled with a radioisotope of iodine is added to a sample of a patients' blood the amount of the labelled hormone incorporated with the red cells depends on the functional state of his thyroid. The test was first described in 1957 and since that time has undergone considerable refinement. It is now widely used for "screening" patients suspected of having thyroid disease.

The investigation of patients with endocrine disorders requires estimations of the levels of various hormones in their blood, urine and body tissues. The classical bioassay methods for the estimation of hormones are elaborate and expensive; and *in vitro* radioisotope techniques are being increasingly used for this purpose. One group of procedures, particularly used for the estimation of the corticosteroids is based on the general method known as derivative analysis, in which the substance of interest is made to react with a labelled reagent which is added in excess to the reaction mixture. The amount of the substance of interest present in the sample can then be inferred from the amount of radioisotopic label incorporated into the resulting compound, or derivative. The method itself has been known since 1946, but its application to the estimation of hormones is more recent.

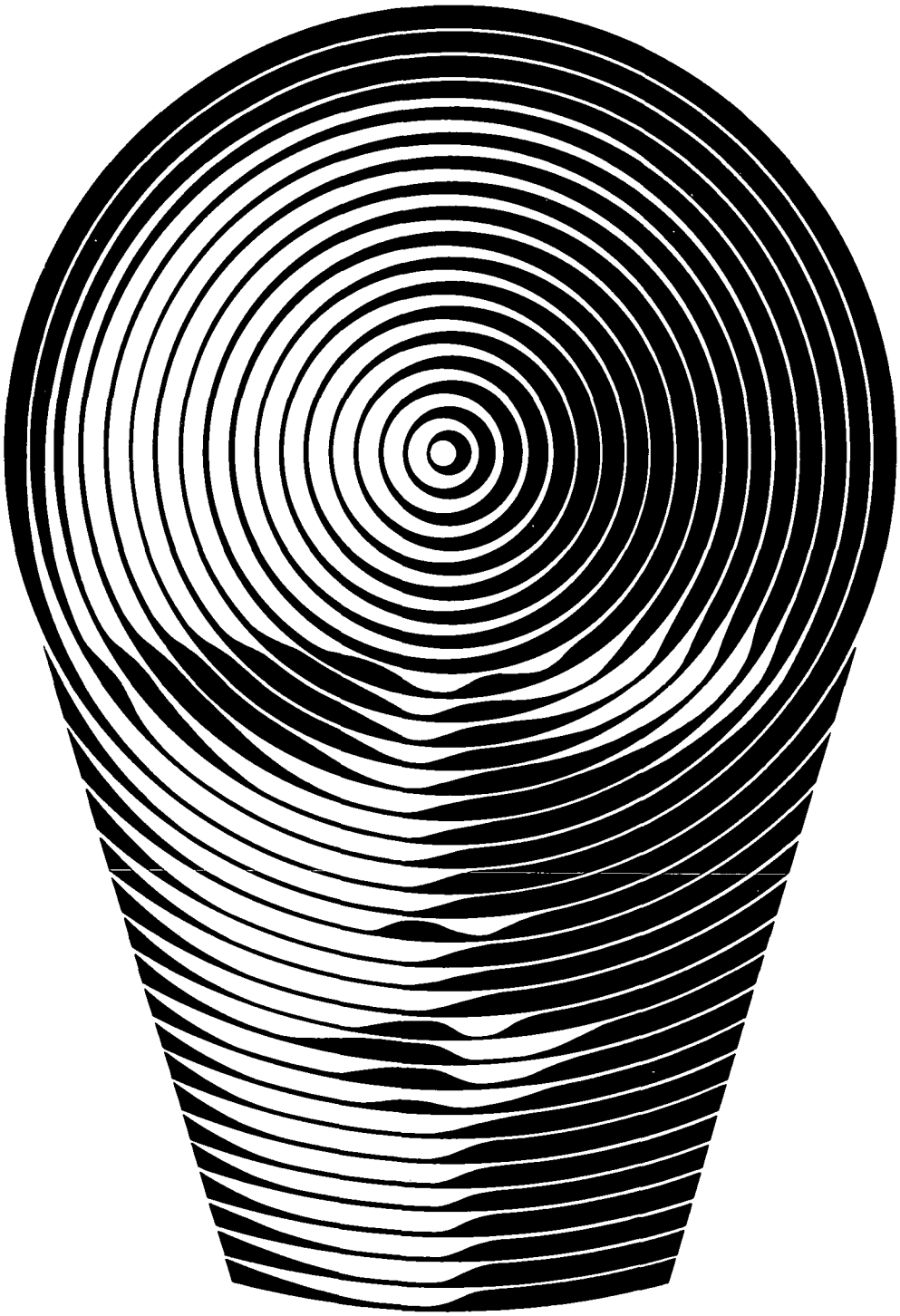
Other procedures are based on a method known as saturation analysis in which a small amount of the substance of interest labelled with a suitable radioisotope is first added to the sample; a protein, resin or other binding agent which binds the substance of interest is then added in quantity sufficient to bind some but not all of the substance present in the sample. The amount of this substance may then be inferred from the partition of the radioisotopic label between the bound and the free fractions.

Hormones and vitamins

Procedures based on saturation analysis are now widely used to estimate a variety of hormones and vitamins. The choice of binding agent depends on the nature of the substance to be estimated. For corticosteroids and other hormones, specific binding proteins are used. For vitamin B_{12}, the estimation of which is of value in the diagnosis of pernicious anaemia and other blood diseases, charcoal or ion-exchange resins may be used.

Very great progress has been made in recent years in the development of radioimmunoassay procedures. These procedures can also be regarded as based on saturation analysis, the binding agent being in this case an antiserum containing antibodies against the substance to be estimated. Radioimmunoassay was first used in 1960 for the estimation of insulin. Similar procedures have now been developed for glucagon, growth hormone and the other hormones of the pituitary gland, parathyroid hormone and many other protein and polypeptide hormones. These procedures permit a new approach to the study of endocrine disorders such as diabetes, acromegaly and dwarfism.

The great advantage of these procedures lies in their relative simplicity as compared with the corresponding classical methods and there can be no doubt that they will be even more widely used in future years, especially in the developing countries. Since the equipment which they require is already available in most medical radioisotope laboratories, they can readily be practised wherever such laboratories exist. On the other hand their correct use requires considerable training and experience. Moreover, their establishment on a sound basis still requires considerable effort in the intercomparison and standardization of techniques. The Agency is collaborating with the World Health Organization to satisfy these needs.



This symbol will be seen often in the coming year.
Designed by Victor Casarely it will be used in conjunction with UNESCO's International Education Year.
It represents "an abstract head of universal man illuminated by knowledge".