

April 30, 1968

P. NUMEROF ET AL

3,380,888

TEST UNITS

Original Filed March 31, 1961

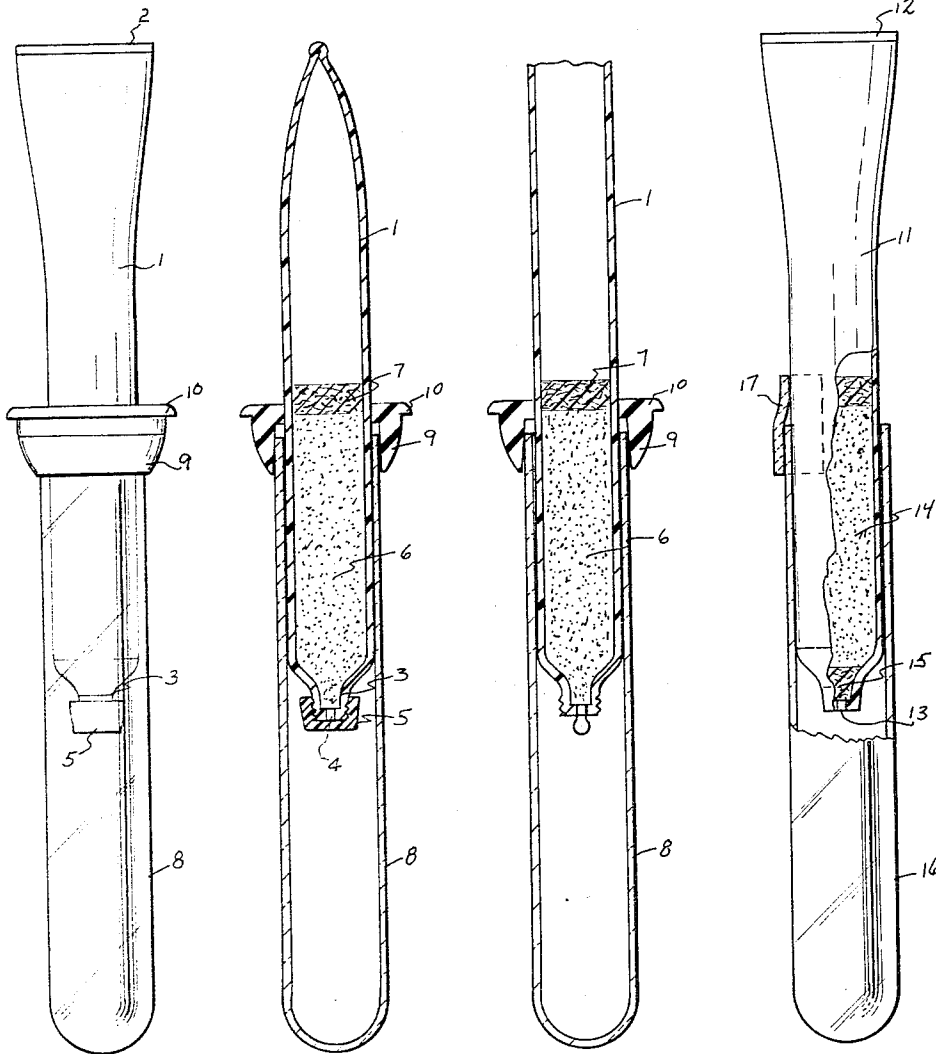


FIG-1

FIG-2

FIG-3

FIG-4

INVENTORS

PAUL NUMEROF  
ELLIOTT R. MORGAN

By *Lawrence S. Levinson*  
Attorney

1

3,380,888

## TEST UNITS

Paul Numerof, Highland Park, N.J., and Elliott R. Morgan, Ballston Lake, N.Y., assignors, by mesne assignments, to E. R. Squibb & Sons, Inc., New York, N.Y., a corporation of Delaware

Original application Mar. 31, 1961, Ser. No. 102,347.

Divided and this application Nov. 18, 1963, Ser. No. 330,218

8 Claims. (Cl. 167—84.5)

This application is a division of our application, Ser. No. 102,347, filed Mar. 31, 1961, and now abandoned, which in turn is a continuation of our application, Ser. No. 672,712, filed July 18, 1957, and now abandoned.

This invention relates to a method of determining the ratio of organically-bound iodine to total radioactive iodine in a biological fluid sample.

Prior to this invention, it was known that thyroid function could be estimated by a test procedure involving a so-called "conversion ratio." This test measures the ability of the thyroid to convert a given amount of radioactive inorganic iodide (e.g., sodium iodide) to protein-bound radioactive iodine. To perform the test, a patient would receive an oral dose of radioactive iodine as sodium iodide and would later submit a sample of blood. A given volume of the plasma, say about five cc., would be tested for its total radioactive iodine content. This radioactivity would consist of iodine present as both free inorganic iodide and also as radioactive iodine organically bound to protein. After the total radioactive iodine content of the plasma has been determined, the radioactive inorganic iodide would then be removed and the residual radioactivity as organically-bound radioactive iodine would then be determined. This latter value, the protein-bound radioactivity, divided by the total radioactivity of the plasma, constitutes the "conversion ratio."

An object of this invention, therefore, is to provide a simple, economical method for the separation of the inorganic iodide from the organically-bound radioactive iodine in a plasma sample.

This object is achieved by using the test unit (and assembly) which comprises an elongated container, fabricated at least in part of deformable (preferably resilient) material, being closed at one end and having the other end adapted to provide a restricted opening, said container being partially filled with an ion exchanger.

The test unit (and assembly) is illustrated in the accompanying drawing, wherein:

FIGURE 1 is an elevational view of one embodiment of this invention;

FIGURE 2 is an axial cross-section thereof;

FIGURE 3 is an axial cross-section of the embodiment of FIGURE 1 after it has been prepared for use, illustrating the manner of using it;

FIGURE 4 is an elevational view (with part internal exposure) of another embodiment within the scope of this invention.

Considering FIGURE 1 of the drawing, the test unit of this invention comprises a tube 1 fabricated of deformable material (e.g., a resilient-walled tube of a material such as polyethylene plastic or rubber), sealed at one end 2 (e.g., by flattening the walls at the end and heat-sealing) and having a neck portion 3 at the other end. As shown, the neck is provided with a restricted opening 4 which is closed by a removable cap 5 (e.g., internally threaded to screw on the correspondingly-externally-threaded neck of the tube). Alternatively, the neck 3 is provided with a readily pierceable blind end, in which case no cap is required.

The tube is partially filled with an anion exchanger 6, such as an anion exchange resin as exemplified by Dowex

2

or IRA-400, which is retained in contact with the end of the tube having (or adapted to have) the restricted opening by a fluid-permeable barrier 7, as by wads of cotton, glass wool or other fluid-permeable material.

For ease of handling and to prevent contamination, the tube is assembled with an open-end container 8 as shown in the drawing. This container can be made of any material but preferably is transparent (e.g., of glass or transparent plastic). To assure a close fit between the tube and container and to prevent the undesired complete insertion of the tube into the container, a gasket 9 is preferably provided, which is frictionally retained on the tube, adapted to abut and removably fit over the open end of container 8, and having a flange 10 to facilitate handling.

Referring now to FIGURE 4, there is illustrated a modified test unit (and assembly) within the scope of this invention, which comprises a tube 11, of deformable material sealed at one end 12 and having an uncapped restricted opening 13 at the other end. The tube is partially filled with an anion exchanger 14 which is retained in contact with the restricted opening end of the tube. Desirably, a fluid-permeable plug 15, made of glass wool or other fluid-permeable material, is positioned between the anion exchange particles and the restricted opening to assure retention of the particles in the tube. The tube 11 nests in and is frictionally retained by an open-end container 16 as shown in the drawing. To prevent accidental removal or insertion of the tube prior to use, a strip of removable tape 17 can be provided, which is attached to a portion of the tube and an adjacent section of the wall of container 16.

For operation (in the embodiment shown in FIGURES 1, 2 and 3) the tube is removed from the container for removal of the cap or piercing of the blind end as by a needle, and the tube is repositioned in the container. [For operation of the embodiment shown in FIGURE 4, the tube need not be removed from the container.] The sealed end 2 or 12 is then opened, either by means of a knife or by cutting off the topmost part of the tube; and the plasma sample (the total radioactive iodine content of which had previously been counted) is poured into the open end of the tube (see FIGURE 3). Where the tube is formed of resilient-wall material, the walls of the end opened by cutting tend to spread apart and assume a circular shape, thereby facilitating pouring in the sample. The open end of the tube is then folded over and rolled down, thereby forcing substantially the entire liquid through the anion exchanger bed into the container 8 or 16. [To assure complete passage of the sample through the anion exchanger bed, the folded and rolled end of the tube is opened again, a washing liquid (e.g., water) poured in and the washing liquid forced through the anion exchanger bed in the same manner as the sample.] The inorganic iodide is adsorbed on the exchanger, whereas the organically-bound iodine passes therethrough and is received in the container. After the operation is complete, the tube is removed from the container, and the radioactivity of the contents of the container is measured. The ratio of this activity to the total radioactivity of the starting sample gives the "conversion ratio."

The invention may be otherwise variously embodied within the scope of the appended claims.

What is claimed is:

1. A method of testing thyroid function which comprises administering an inorganic radioactive iodide to a patient, sampling the blood of said patient, measuring the total radioactivity of said sample, passing the sample through an open end of a thin resilient-walled integral tube having its other end apertured to provide a restricted opening and containing a column of particulate anion exchanger, capable of selectively adsorbing inorganic iodide

3

from a mixture thereof with organically bound iodine, positioned in said tube and extending from said apertured end part way towards the open end, whereby the inorganic iodide in said sample is adsorbed on the exchanger, folding the portion of the tube between the column and the open end of the tube to force substantially the entire sample through the tube, unfolding said portion, passing a washing liquid through the tube, refolding said portion of the tube to force substantially the entire washing liquid through said tube, collecting all substances which pass through the tube, and measuring the total radioactivity of said substances.

2. A method of testing thyroid function which comprises administering an inorganic radioactive iodide to a patient, sampling the blood of said patient, measuring the total radioactivity of said sample, passing the sample through an open end of a thin resilient-walled integral tube, said tube having its other end apertured to provide a restricted opening and containing a column of anion exchange resin, capable of selectively adsorbing inorganic iodide from a mixture thereof with organically bound iodine, positioned in said tube and extending from said apertured end part way towards the open end, whereby the inorganic iodide in said sample is adsorbed on the resin, into an open-end container extending over the end of the tube having the restricted opening for a portion of the length of the tube, folding the portion of the tube between the column and the open end of the tube to force substantially the entire sample through said tube and into said container, unfolding said portion, passing water through the tube into said container, refolding said portion of the tube to force substantially all the water through said tube into said container, removing said tube from said container, and measuring the radioactivity of said container and its contents.

3. A method for separating inorganic iodide from an aqueous mixture thereof with organically bound iodine, which comprises passing said mixture through an open end of a thin resilient-walled integral tube having its other end apertured to provide a restricted opening and containing a column of particulate anion exchanger, capable of selectively adsorbing inorganic iodide from a mixture thereof with organically bound iodine, positioned in said

4

tube and extending from said apertured end part way towards the open end, whereby the inorganic iodide in said sample is adsorbed on the exchanger, and folding the portion of the tube between the column and the open end of the tube to force substantially the entire mixture through the tube.

4. The method of claim 3, wherein said portion is then unfolded, a washing liquid is passed through the tube, said portion is refolded to force substantially the entire washing liquid through said tube, and all substances which pass through the tube are collected.

5. The method of claim 4, wherein the mixture is a human blood sample containing inorganic iodide and organically bound iodine.

6. A method for separating inorganic iodide from an aqueous mixture thereof with organically bound iodine, which comprises passing said mixture through an open end of a thin resilient-walled integral tube, said tube having its other end apertured to provide a restricted opening and containing a column of anion exchange resin, capable of selectively adsorbing inorganic iodide from a mixture thereof with organically bound iodine, positioned in said tube and extending from said apertured end part way towards the open end, whereby the inorganic iodide in said mixture is adsorbed on the resin, into an open-end container extending over the end of the tube having the restricted opening for a portion of the length of the tube, and folding the portion of the tube between the column and the open end of the tube to force substantially the entire mixture through said tube and into said container.

7. The method of claim 6, wherein said portion is then unfolded, a washing liquid is passed through the tube, and said portion is refolded to force substantially the entire washing liquid through said tube into said container.

8. The method of claim 7, wherein the mixture is a human blood sample containing inorganic iodide and organically bound iodine.

No references cited.

SAMIH N. ZAHARNA, *Primary Examiner*.

REUBEN FRIEDMAN, *Examiner*.