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METHOD AND DEVICE FOR TEST OF BIOLOGICAL FUNCTION

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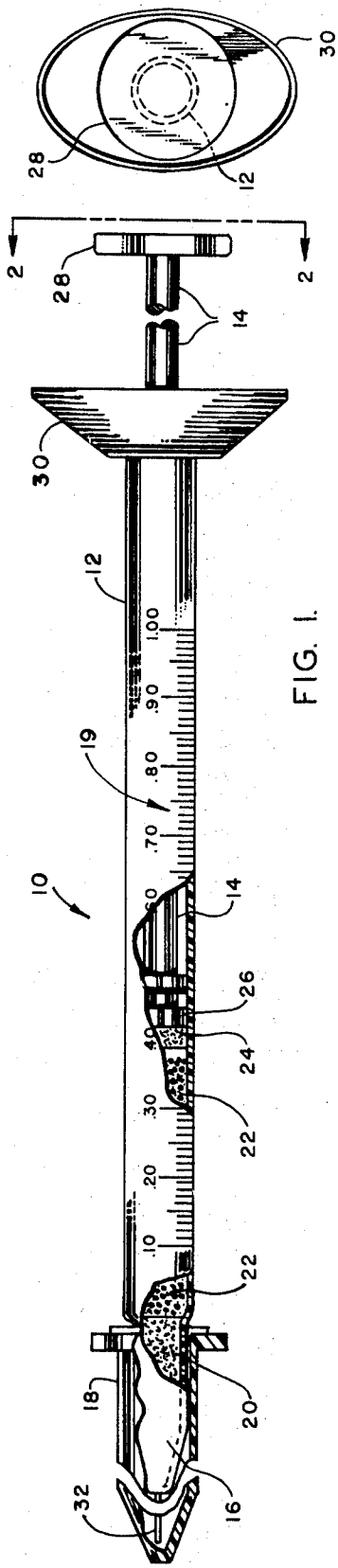


FIG. 2.

FIG. 1.

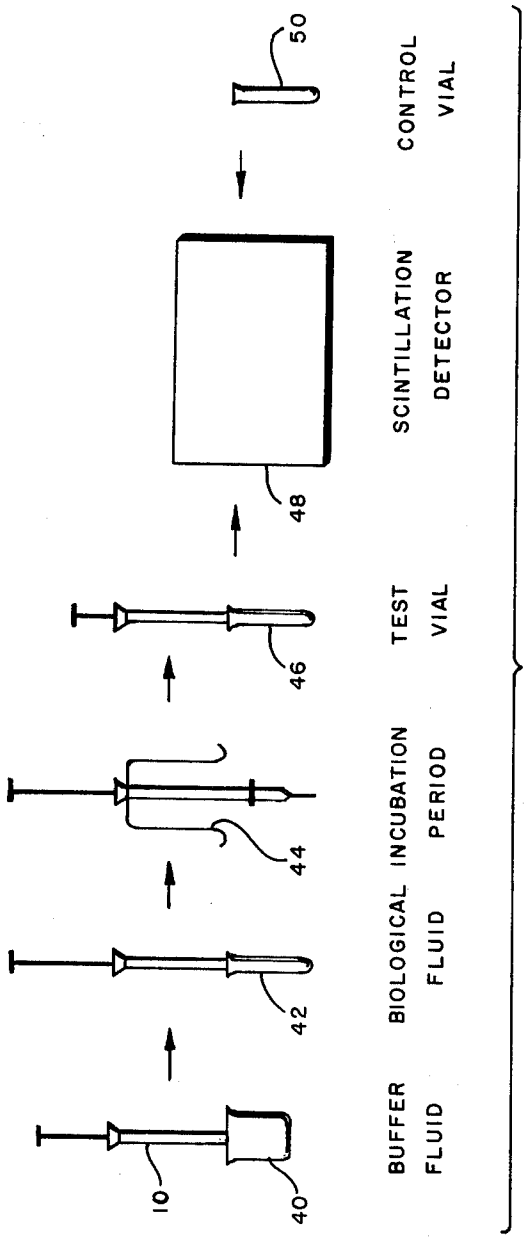


FIG. 3.

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METHOD AND DEVICE FOR TEST OF BIOLOGICAL FUNCTION

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ABSTRACT OF THE DISCLOSURE

Method and syringe for performing a test of the thyroid function, the syringe having a pair of filters with a mass of ion exchange resin granules between the filters, the granules being tagged with triiodothyronine, labelled with a radioactive iodine, I^{131}. The filter at the inlet of the syringe is treated with sodium citrate which acts as a catalyst in the ion exchange between the granules and serum or other biological fluid which is caused to ascend by suction through the filter and into contact with the granules following ascension by a buffer fluid.

BACKGROUND OF THE INVENTION

The present invention relates to a medical test method and device for performing the method, and more particularly to a syringe-like instrument adapted for performing a test for evaluation of the thyroid function.

The status of the thyroid function has been shown to be related to the affinity of certain blood serum proteins for thyroxine (T4) and triiodothyronine (T3), and to the degree of saturation of the available serum binding sites. In "The Journal of Nuclear Medicine," 3:41, January 1962, there is reported a simplified test of thyroid function by John F. Scholer, M.D., in an article entitled, "A Simple Measure of Thyroid-Binding by Plasma: A Test of Thyroid Function" (pp. 41–46), which consists essentially of labelling a granular resin with T3 labelled with I^{131}, incubating the plasma to be tested with small portions of the labelled resin, determining the amount of radioactive label leaving the resin to go into the plasma and comparing it with a standard or control. The result of the test, which is referred to as the Thyro Binding Index (TBI), is expressed as the ratio of the net radioactive count of the unknown divided by the net radioactive count of a known euthyroid standard. In the case of a hypothyroid patient, the number of available binding sites is greater; so the TBI is higher, and vice versa in a hyperthyroid situation. The test has been clinically correlated and has the advantages that it is essentially unaffected by the presence of iodine and there is no exposure of the patient to radiation. However, a variety of clean volumetric pipettes are required and the utmost care must be exercised in cleaning them. Also, the control and the test samples must be subjected to an incubation period with tumbling agitation during which time and temperature are critical, particularly if the period is less than two hours.

It is, therefore, an object of the present invention to refine further the aforementioned method by providing a simple and economical device and method of using the same which obviates the need for the pipettes and tumbling agitator and reduces considerably the time required for incubation with a wider temperature latitude.

To accomplish the aforementioned objective, the present invention contemplates a syringe-like instrument or device which contains granules of an ion exchange resin labelled with T3 which is labelled with I^{131}, manipulation of the device to cause ascension by suction through the resin of a buffer, followed by the biological fluid being tested, for effecting ion exchange between the fluid and the resin. The resultant fluid is analyzed.

BRIEF DESCRIPTION OF THE DRAWING

Other objects, advantages and features of the invention will become better understood by reference to the following detailed description when considered in connection with the accompanying drawings wherein:

FIG. 1 is a view illustrating the syringe-like instrument of the present invention, with parts broken away to show the relationship thereof;

FIG. 2 is a detail view taken generally along line 2—2 to show the form of the enlargements on the instrument of FIG. 1 for manipulating the same; and

FIG. 3 is a schematic diagram illustrating the method of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to the drawings in which like reference characters designate like or corresponding parts, there is shown in FIG. 1 a syringe-like instrument or device designated generally by reference numeral **10** and comprising a tubular body **12**, a plunger **14**, a tip **16** and a protective cap **18**, all of a suitable material, such as plastic or the like, body **12** being transparent and provided with indicia or markings **19** for a purpose later appearing. Tip **16** is filled with a porous barrier **20**, for example a sponge or cotton, which is treated with sodium citrate and acts as a filter for fluids. Adjacent to, and inwardly of, filter **20** is a mass of resin granules **22** extending to a filter **24** which may take the form of a small sponge or wad of cotton or other porous barrier. Usually disposed adjacent filter **24** is a piston **26** secured to the inner end of plunger **14**, the outer end of the plunger being provided with a circular enlargement **28**. The end of body **12** is also provided with an elongated enlargement **30**, which enlargements (see FIG. 2) are adapted to be manipulated for holding the instrument and moving piston **26** to draw in fluids or expel them. If desired, tip **16** may be provided with a hypodermic needle **32**.

The granules **22** may be of any suitable ion exchange resin material, for example the Dow Chemical Company formulation known as Dowex 21K, or the Rohm and Haas Company resin designated IRA 400, which is treated with potassium perchlorate and calcium chloride and is adjusted to a pH of 5.2 to provide a strongly basic ion exchange resin in the chloride form. The resin granules **22** preferably have a particle size from 18–35 mesh of the U.S. Standard Sieve series and are also treated so as to be labelled or tagged with T3, which is labelled with a radioactive iodine I^{131}. The amount of resin granules in each device **10** is about 0.2 gram ± 0.05 gram which has no more than one microcurie of radioactivity.

A thyroid function test method employing the syringe **10** is schematically illustrated in FIG. 3. To perform the test, the bottom of piston **26** is set at the .40 mark and the needle **32** (or tip **116** if there is no needle) is placed in a buffer or reaction fluid comprised of trisma maleate (hydroxymethyl aminomethane maleic anhydride

(OCOCH:CHCO)

a buffer system with pH range adjusted with HCl or NaOH), anhydrous sodium acetate and sodium thiosulfate and held in a container **40**. The plunger **14** is then pulled out until the bottom of the piston is at the .60 mark which causes a column of buffer fluid to ascend by suction through the filter **20** and the resin granules **22**. After allowing a few seconds for the buffer fluid to find its level, the syringe is withdrawn and placed in the serum or other biological fluid to be tested, which may be contained in a test tube **42** or the like. The plunger is then

pulled out to set the bottom of the piston at the 1.00 cc. mark which causes the buffer fluid to ascend out of contact with the resin granules and a column of serum to ascend by suction through filter **20** and into contact with the granules. After a few seconds, the syringe is withdrawn and placed in a rack or other suitable support **44** and allowed to stand and incubate. In the passage of the buffer and biological fluids through filter **20**, some of the sodium citrate is taken up and acts as a catalyst in the ion exchange which takes place between the serum and the resin during the incubation period of about one-half hour, without rotation or shaking, at a temperature between 20° and 35° C. This compares favorably with the prior art method described in the aforementioned Journal of Nuclear Medicine article which requires tumbling or mixing for about one hour of incubation at 37° C., small variations in time and temperature being permitted when the incubation period is extended to about two hours.

Following the incubation period of thirty minutes ±five minutes, the plunger **14** is pressed firmly and the fluid contents of the syringe are expressed into a test vial **46**. The plunger is then withdrawn and moved to set the bottom of the piston **26** at the .50 mark, following which the syringe is placed in container **40** to withdraw buffer fluid therefrom and the bottom of the piston is moved to the 1.00 cc. mark. After a few seconds, the syringe is withdrawn and then placed in the test vial **46** and its fluid contents are expressed thereinto. The test vial is then placed in a well-type scintillation counter or other suitable detector **48** and the radioactivity is determined. Here again is an improvement over the prior art method. Since the resin granules are retained in the syringe, there is no need to spin down the resin or allow time for settling.

The radioactivity determination for the test fluid is compared with the radioactivity determination for a standard or control fluid kept in a sealed vial **50**. The control vial is made up at the same time as a batch of the syringes **10**, using the same radioactive iodine, and is packaged with the batch for use as a standard. In this way correction is made for radioactivity decay.

It is understood, of course, that the syringes and control vials are produced under quality controlled laboratory conditions to insure safety, reliability and reproducibility of results. The syringes may be economically mass produced of a plastic material for use only in one test and properly disposed of afterward.

What is claimed is:

1. A syringe device for tests of a biological function, comprising in combination:
- a tubular body having an inlet;
- first filter means in said body adjacent said inlet;
- second filter means in said body spaced inwardly from said first means;
- ion exchange material disposed between said first and second filter means; and
- a plunger extending into said tubular body from the end thereof remote from said inlet for drawing fluids into said tubular member through said first filter means and into contact with said ion exchange material, and for subsequently expelling the fluids through said inlet.

2. The device as defined in claim **1**, wherein:
- said ion exchange material comprises a strongly basic ion exchange resin in the form of granules tagged with triiodothyronine labelled with a radioactive iodine.

3. The device as defined in claim **2**, wherein:

- said resin is treated with potassium perchlorate and calcium chloride and has an adjusted pH of 5.2 and not more than one microcurie of radioactivity.

4. The device as defined in claim **2** wherein:
- said granules of resin have a particle size of 18–35 mesh.

5. A syringe-like device for tests of a biological function, comprising in combination:
- a tubular body having an inlet;
- first filter means in said body adjacent said inlet, said first filter means comprising a porous barrier of sponge- or cotton-like material treated with sodium citrate;
- second filter means in said body spaced inwardly from said first filter means; and
- ion exchange material disposed between said first and second filter means.

6. Method for test of a biological function, comprising the steps of:
- (a) ascending by suction a column of buffer fluid firts through a filter and then into cnotact with solid state ion exchange material;
- (b) ascending by suction said column of buffer fluid out of contact with said exchange material;
- (c) ascending by suction a column of biological fluid first through said filter and then into contact with said exchange material; and
- (d) effecting ion exchange between said material and said biological fluid.

7. The method as defined in claim **6** further characterized in that:
- said filter is treated with sodium citrate prior to passage of said fluids therethrough.

8. The method as defined in claim **7**, wherein:
- said buffer fluid comprises hydroxymethyl aminomethane maleic anhydride, anhydrous sodium acetate and sodium thiosulfate.

9. The method as defined in claim **6** further comprising the steps of:
- (a) causing said fluids to descend through said material and filter into a container;
- (b) ascending by suction another column of buffer fluid through said filter and into contact with said exchange material; and
- (c) causing said buffer fluid to descend through said material and said filter into said container.

10. The method as defined in claim **9**, further comprises the step of:
- (a) analyzing the resultant fluid in said container by a scintillation counter type of radioactivity detector.

References Cited

UNITED STATES PATENTS

3,376,114	4/1968	Eberle.
3,380,888	4/1968	Numerof et al.

OTHER REFERENCES

Sterling et al.: J. Clin. Endocrin, 21, 456–464 (1961).

Samuelson, O.: Ion Exchangers in Analytical Chemistry, John Wiley & Sons Inc., New York., 1953, pp. 65, 81, 93, 94, 238 relied on.

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