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BLOOD TEST

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6 Claims. (Cl. 23—230)

This invention relates to a new and useful means for detecting the presence of occult blood associated with body excreta.

The importance of occult blood detection in feces and urine, for example, as a means for assisting in the diagnosis of certain body disorders has long been recognized. Cancer of the gastro-intestinal tract to mention one of the common disorders of the body is an important and highly fatal disease, and its early detection, as by means of examination of the stools for the presence of blood is imperative in the interest of corrective surgery and other therapy.

However, desirable though such examinations may be in assisting in the early diagnosis of such and similar disorders, they are too frequently not made at all, or are made only after the later and more serious stages of the disease have set in. The reason for this lies frequently in the inconvenience associated with obtaining stool samples; most patients are averse to collecting a stool specimen and transporting it to a laboratory or to a doctor's office for an analysis, and generally it is only with hospitalized patients that such specimens are available.

The present methods for the determination of occult blood in such body excreta as feces and urine are based on color reactions which occur when such blood is contacted with a reagent such as ortho-tolidine, ortho-toluidine, benzidine the salts of these compounds and other well known blood detecting reagents as well as mixtures containing such materials. According to the presently practiced methods for determining the presence of occult blood, the feces must be first removed from the toilet bowl or bed pan with a tongue depressor or like object and placed upon a suitable surface so that conventional occult blood tests can be run. These tests are normally carried out by making a solution of the reagent or reagent mixture and dropping such solution onto the feces. The color shades and even the colors themselves, developed in the reagent under such circumstances, are difficult to evaluate against such a vari-colored background, and in the case of small amounts of blood in the feces, inaccuracies and false negatives are apt to result.

For a number of reasons then, the detection of occult blood by conventional methods is unsatisfactory, entailing not only difficulty in obtaining samples, but requiring technical skill and laboratory equipment for the performance of the test.

Accordingly, it is an important object of the present invention to provide a novel means for detecting the presence of occult blood readily and accurately.

Another object is to provide a simple, rapid and convenient method of detecting occult blood, which does not require laboratory skill or laboratory equipment.

A still further object is to provide a simple method for detecting occult blood in the feces and in the presence of urine.

The present invention is bottomed on the novel concept of utilizing an occult blood detecting device in the form of a reagent composition encased in a package or envelope formed of a permeable sheet material, which package or envelope when dropped into a toilet bowl, bed pan or the like containing feces and/or urine, is wetted, subsequently floats on the surface and acquires a characteristic color if the urine and/or feces contain occult blood.

The permeable sheet material which may suitably be of paper, not only serves as a container for the reagent mixture encased therein but functions as an essential functional component of my novel indicator device, in some way appearing also to provide a capillary network for the formation, adsorption and diffusion of the oxidized reagent; it also acts as a background against which color or absence of color can be ascertained.

The reagent mixture which I have found preferable in the practice of my invention may have the following composition in parts by weight:

Example 1

Components of reagent mixture:	Parts by weight
O-tolidine	From 0.5 to 4, preferably 1.
Strontium peroxide	From 5 to 15, preferably 9.
Calcium acetate	From 20 to 60, preferably 60.
Tartaric acid	From 20 to 75, preferably 30.
Corn starch	From 1 to 10, preferably 5.
Sodium bicarbonate	From 0.5 to 1.5, preferably 0.6.

The above components of my preferred reagent mixture are dried, intimately mixed, and placed in an envelope of filter paper which is then sealed around the edges to provide a continuous seal. For a 2" square envelope approximately 2 grams of the reagent mixture has been found satisfactory.

In use, an envelope such as above described, is dropped into a toilet bowl, bed pan or similar receptacle containing water and either feces or urine or both. The envelope is wetted, the tartaric acid (or other dry organic acid) reacts with the sodium bicarbonate (or other gas-supplying salt) and due to the resulting gas formation rises to the surface of the liquid, and if blood is present in either the feces or the urine in even microscopically small amounts of the visible surface of the envelope which is above the surface of the liquid will evidence a definite color change. The intensity of the blue color and the speed of formation is indicative of the quantum of blood present.

The method above described will permit the detection of 1 part of blood in 100,000 of liquid in a toilet bowl, in the presence of urine. In the case of fecal blood, the blood detected is that which is leached out of the feces by the liquid in the toilet bowl. As examples of the sensitivity of the test, it has been found to give a positive test on the feces of a person on a high meat diet or one who has ingested a small quantity of whole blood. It is sufficiently sensitive to check blood in feces resulting from a pathological condition of the alimentary tract, such as a hemorrhage resulting from an intestinal carcinoma or from an ulceration of the stomach mucosa, for example.

While the preferred form of my invention consists of a permeable package or envelope containing encased therein a reagent mixture having the composition set forth in Example 1, the composition of the reagent mixture may be varied. Thus in place of O-tolidine, other reagents may be used such as for example, ortho-toluidine, benzidine, tolidine-o-dihydrochloride, and other well known blood detecting or blood sensitive reagents. For strontium peroxide, barium peroxide, sodium pyrophosphate peroxide, sodium perbor silicate and the like. Other acids such as citric, maleic, succinic and itaconic and the like may be substituted for tartaric acid, provid-

ing that such other acids will liberate acetic acid from the acetate salt present in the mixture. Besides calcium acetate I may use such other acetates as sodium acetate, potassium acetate, lithium acetate and the like. Some examples of fillers other than corn starch which may be used are talc, lactose, flour and similar materials.

The following examples will serve to illustrate other reagent mixtures which I have used successfully in preparing the occult blood detecting device of my invention.

Example 2

Components of reagent mixture:	Parts by weight
O-tolidine	From 0.5–4, preferably 1.
Strontium peroxide	From 5–15, preferably 7.5.
Calcium acetate	From 40–75, preferably 63.
Succinic acid	From 20–75, preferably 39.
Corn starch	From 1–10, preferably 5.
Sodium bicarbonate	From 0.5–1.5, preferably 0.6.

Example 3

Components of reagent mixture:	
O-tolidine	From 1–6, preferably 4.
Sodium perbor silicate	From 8–20, preferably 10.
Calcium acetate	From 20–75, preferably 63.
Succinic acid	From 20–75, preferably 39.
Corn starch	From 1–10, preferably 5.
Sodium carbonate	From 0.5–1.5, preferably 0.6.

Example 4

Components of reagent mixture:	
O-tolidine	From 0.5–4, preferably 1.
Strontium peroxide	From 5–15, preferably 7.5.
Calcium acetate	From 20–75, preferably 63.
Itaconic acid	From 20–75, preferably 39.
Corn starch	From 1–10, preferably 5.
Sodium bicarbonate	From 0.5–1.5, preferably 0.6.

Example 5

Components of reagent mixture:	
Benzidine hydrochloride	From 1–5, preferably 1.
Strontium peroxide	From 5–15, preferably 7.5.
Calcium acetate	From 20–60, preferably 30.
Tartaric acid	From 20–75, preferably 60.
Corn starch	From 1–10, preferably 5.
Sodium bicarbonate	From 0.5–1.5, preferably 0.6.

Example 6

Components of reagent mixture:	
Tolidine-O-dihydrochloride	1.
Strontium peroxide	From 5–15, preferably 7.5.
Calcium acetate	From 20–60, preferably 60.
Tartaric acid	From 20–75, preferably 30.
Corn starch	From 1–10, preferably 5.
Sodium bicarbonate	From 0.5–1.5, preferably 0.6.

Example 7

Components of reagent mixture:	
O-tolidine	From 0.5–4, preferably 1.
Strontium peroxide	From 5–15, preferably 7.5.
Potassium acetate	From 20–75, preferably 60.
Itaconic acid	From 20–75, preferably 30.
Corn starch	From 1–10, preferably 5.
Sodium bicarbonate	From 0.5–1.5, preferably 0.6.

Example 8

Components of reagent mixture:	
Ortho-tolidine	1
Strontium peroxide	9
Tartaric acid	35
Calcium acetate	60
Zonolite (20–80 mesh) (trade name for expanded vermiculite)	7.5

The above materials are intimately mixed and approximately 2 gms. are sealed in a 2" square filter paper envelope.

Example 9

Components of reagent mixture:	
Ortho-tolidine	1
Strontium peroxide	9
Tartaric acid	35
Calcium acetate	60
Styrafoam granules (9 mesh) (a foamed plastic)	2.5

The above materials are intimately mixed and approximately 2 gms. are sealed in a 2" square filter paper envelope.

Example 10

Components of reagent mixture:	
Ortho-tolidine	1
Strontium peroxide	9
Tartaric acid	35
Calcium acetate	60
Calcium hydride, fine granule	2.5

The above materials are intimately mixed and approximately 2 gms. are sealed in a 2" square filter paper envelope. On being wetted, hydrogen is formed, causing the packet to float.

Example 11

Components of reagent mixture:	
Ortho-tolidine	1
Strontium peroxide	9
Tartaric acid	35
Calcium acetate	60

The above materials are intimately mixed and approximately 2 gms. are sealed in a 2" square filter paper envelope. After the envelope has been sealed, ¼" strips of balsa wood are secured to 2 opposite sides covering the seal.

While the preferred technique for imparting "floatability" to the envelope is to incorporate therein an effervescent couple, namely a mixture of a dry acid and a gas-supplying salt, like a bicarbonate and the like, other means useable for imparting floating property to the envelope are the incorporation in or attachment to the envelope of such materials as strips or granules of cork, hollow beads, chips or strips of wood, as balsa wood, granules or strips of foam rubber and so on. Another method is to seal air either into or around the periphery of the envelope or attach other buoyant material to the outside of the envelope. The disadvantage of effecting buoyancy by means other than through the use of an effervescent couple which forms carbon dioxide gas on being wetted as hereinbefore described, is that using such other means the envelope has to be pushed beneath the surface of the liquid to be tested, or dropped with sufficient force to cause a temporary immersion, in order to assure adequate wetting.

The envelope or package, within which the reagent mixture is contained, and which forms an integral part of my composite blood-detecting indicator, may be made of a variety of materials including such sheet materials as paper, closely woven cloth and the like. I have successfully used for this purpose filter paper, which being adsorbent, absorbent and permeable is well suited for my purpose.

While all types of filter paper which have been tried by me have resulted in obtaining positive tests when sufficient blood is present in the medium being tested, not all grades are equally sensitive. I have found that the best papers for this purpose are light weight rapid filter papers which still have sufficient wet strength so that the envelopes formed therefrom do not easily burst when in use. A paper which I have found particularly satisfactory is a paper such as Schleicher and Schuell No. 410, which has a filter speed (Bureau of Standards Methods) of 7–11 seconds, a thickness of 0.006 inch and a basis weight of 18 pounds per 500 sheets each 20" by 20".

The blood detecting indicator of my invention may be made in a variety of ways. For example, two squares of filter paper may be sealed together, with a suitable reagent mixture enclosed therein, by means of a water insoluble cement so as to provide a continuous seal; or the edges of the squares may be coated with a heat sealing material and then crimped together under heat and pressure to bind the edges together. The package may also be formed by applying over the surface of the paper a thin film of heat sealing material so that the paper is still porous, and then heat sealing to provide a continuous sealed edge. The package may likewise be made by applying the heat sealing material in a pattern of diagonal lines before heat sealing, or by applying the heat sealing materials over one-half of the paper, using two such pieces in reverse for the two faces of the package and then heat sealing to provide a continuous unbroken edge.

However the package is made it is important that it be completely sealed around the edge or edges to prevent the contents spilling during the test. It is important also that some part of the unsealed parts of the faces of the package should be porous.

The completed packages should be stored in a closed container such as a bottle or a sealed envelope of moisture vapor proof foil.

While all of the functional aspects of the porous envelope are not entirely understood it appears that besides serving merely as a container for the reagent mixture enclosed therein, the material of which the envelope is made acts as a base, in the form of a capillary network for the diffusion of the surrounding liquid into the packet and for the subsequent formation and absorption of the oxidized reagent onto its exposed surface which floats above the surface level of the liquid.

It is seen that a fundamental and unique aspect of the present invention lies in the concept of encasing the reagent mixture in a porous envelope or package, preferably of paper such as filter paper, but suitably of any similar water permeable sheet material. It is this enclosing of the reagent mixture in an envelope or package of the character above described which characterizes the most important feature of my invention, and which in fact, makes the test work. In this connection it is desired to point out that when an occult blood detecting composition, either such as herein described or any other occult blood detecting reagent or composition is dropped, either in powder or tablet form into a fluid containing feces, blood and urine, there is no color reaction with any but gross hemorrhage from the bowel. Such a test is therefore not practicable as a diagnostic procedure.

It is only when the reagent composition is enclosed in an envelope such as I have described that the characteristic blue color developes in the presence of small but pathologic traces of blood. This color appears only upon the surface of the paper (envelope) and not in the fluid into which the packet is placed.

The advantages of the present invention are numerous and important, particularly in connection with the diagnosis of such diseases as cancer of the digestive organs and peritoneum which accounts for a substantial proportion of all cancer deaths. Cancer of the intestinal tract usually is "silent" until its later, secondary manifestations such as anemia appear. While microscopic oozing hemorrhage is known to appear early in most cases of cancer of the bowel, the prompt detection of such hemorrhage by means of occult blood determinations on the feces has not been as extensive as would be desirable due to the impracticabilities of the presently available procedures for testing for occult blood, as hereinbefore described.

My invention, by providing a simple test for the detection of occult blood which can be carried out by the patient himself—who may be any unskilled person—quickly, conveniently and accurately, is thus of tremendous assistance in the early diagnosis of those diseases where the detection of occult blood plays such an important part.

This application is a continuation of my co-pending application Serial No. 148,745, filed March 9, 1950, now abandoned. It is to be understood that the description and examples contained herein are for purposes of illustration only, and it is not intended that the present invention be limited in scope except as required by the appended claims.

I claim:

1. A device for testing for blood in fluids, said device comprising in combination, a closed envelope formed of a sheet material which is permeable to electrolytes but impermeable to solid materials and an occult blood detecting composition enclosed therein, said device being adapted to be wetted by and to float to the surface of said fluid to provide a surface of said sheet material above the surface of the said fluid and to develop color on the above surface visible portion of said sheet material when occult blood is present in the fluid.

2. A method for testing for blood in an aqueous fluid which comprises dropping a closed envelope containing a blood detecting composition into a quantity of said fluid, said envelope being formed of a sheet material which is readily permeable to electrolytes but impermeable to solid materials and adapted to float to the surface of said fluid to provide a surface of said sheet material above the surface of the said fluid, whereby in the presence of occult blood a color formation results on the above-surface visible portion of said sheet material.

3. A device for detecting the presence of occult blood, comprising a substantially dry mixture containing an effervescent couple, a small amount of a compound selected from the group consisting of o-tolidine, benzidine, o-toluidine, and the salts thereof, said mixture being enclosed within permeable sheet material, and means integral with the device for causing it to float in an aqueous liquid and provide a surface of the sheet material above the surface of the liquid for color development when occult blood is present in said aqueous liquid.

4. A device for detecting the presence of occult blood in an aqueous fluid containing urine, said device being adapted to be wetted by and to float on said fluid and provide a surface of a porous permeable membrane above the surface of said fluid, and to acquire color on the above-surface visible portion of said membrane when occult blood is present in said fluid, said device comprising a closed package formed of a porous permeable membrane containing an acetate, an oxidizing agent, a compound selected from the group consisting of o-tolidine, o-toluidine, benzidine and salts thereof, and a material capable of reacting with the said acid to produce a gas for lifting the device to the surface of the fluid.

5. A composite indicator for detecting occult blood in a fluid medium comprising a closed package formed of a porous permeable membrane and containing a compound selected from the group consisting of alkali acetates and alkaline earth acetates, an organic acid in dry form and stronger than acetic acid, an oxidizing agent of the peroxide type, a salt capable of reacting with said organic acid to produce a gas, and a compound selected from the group consisting of o-tolidine, o-toluidine, benzidine, and salts thereof, said device being adapted to float on and be wetted by said fluid medium and, thus, provide a surface of the membrane above the surface of the fluid for color development when occult blood is present.

6. An article for detecting occult blood in a fluid medium comprising a porous envelope having sealed therein a mixture of ingredients having the following composition:

	Parts
Ortho-toluidine	1
Strontium peroxide	9
Calcium acetate	60
Tartaric acid	30
Corn starch	5
Sodium bicarbonate	0.6

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UNITED STATES PATENT OFFICE

CERTIFICATE OF CORRECTION

Patent No. 2,838,377 June 10, 1958

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It is hereby certified that error appears in the printed specification of the above numbered patent requiring correction and that the said Letters Patent should read as corrected below.

Column 6, line 54, for "Ortho-toluidine" read -- Ortho-tolidine --.

Signed and sealed this 5th day of August 1958.

(SEAL)

Attest:

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