

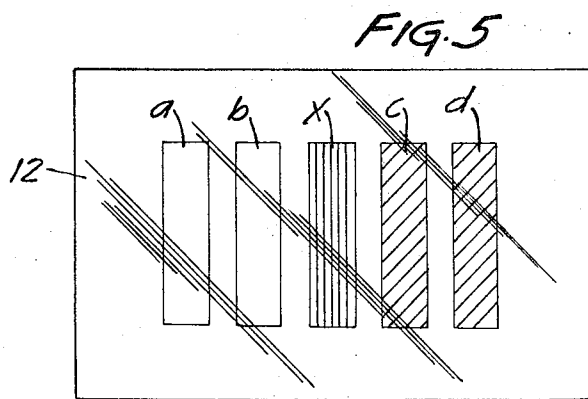
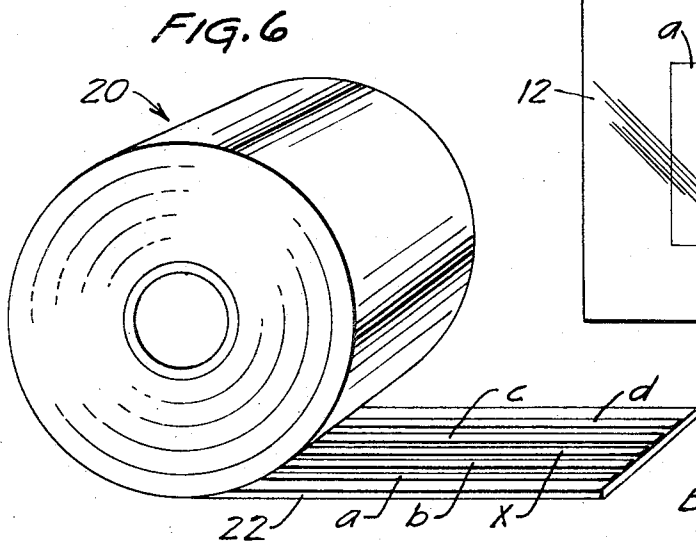
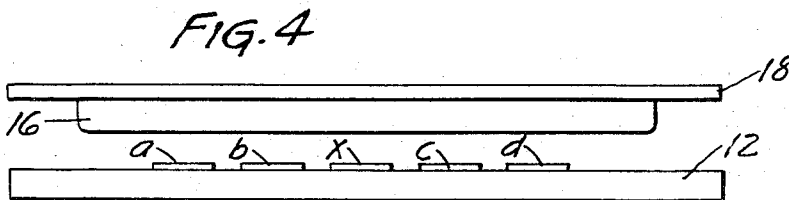
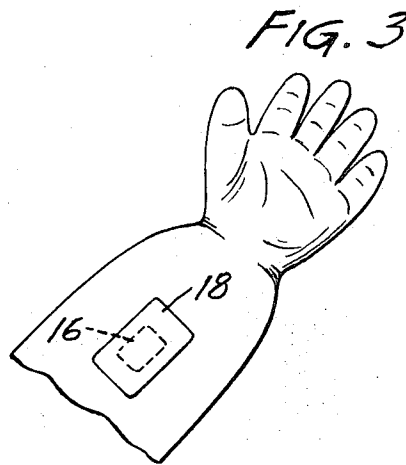
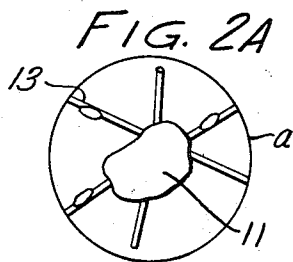
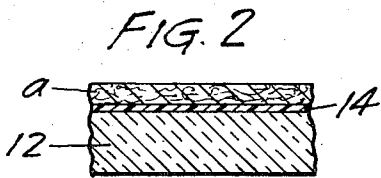
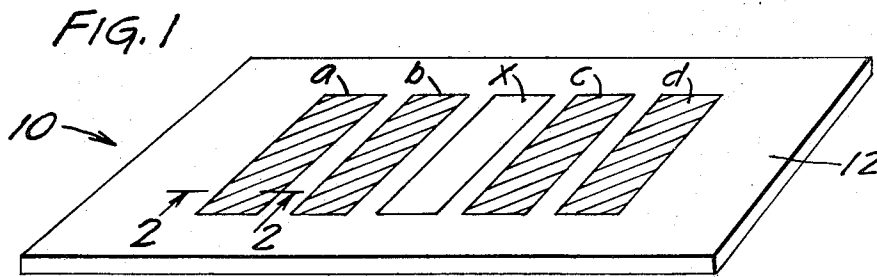
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3,552,929

DIAGNOSIS MEANS

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DIAGNOSIS MEANS

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9 Claims

ABSTRACT OF THE DISCLOSURE

A device for detecting halide ion concentration in fluids. The device comprises a transparent backing material and a substrate adhered thereto. The substrate is divided into a plurality of distinct regions which contain different, predetermined amounts of halide-sensitive reagent.

This invention relates to a means and method for the rapid and approximate determination of the concentration of chemical constituents of human body fluids, such as perspiration, urine, blood or mucous, and a device therefore. More particularly the invention is concerned with determining chloride ion concentration in human perspiration as a method of diagnosing the disease, cystic fibrosis.

The relatively recent development (1962) of a successful treatment for cystic fibrosis has much increased the importance of its accurate detection. If the disease is not recognized or its symptoms are misdiagnosed—as pneumonia, for example, which is often the case because of the similarity of its effect on the lungs—it is very often fatal, particularly in infants. It has been noted that a great number of infants admitted to pneumonia wards very often exhibit, and subsequently die from, the lung lesions normally present in cystic fibrosis.

It has been known since 1953 that patients afflicted with cystic fibrosis have a high chloride ion concentration in their perspiration (Darling, et al., *Pediatrics*, 12:549, 1953) and this fact has since been recognized as being more diagnostic of the disease than any other factor. This observation has been corroborated many times over by other researchers.

In the past the determination of chloride concentration in human perspiration has not been as rapid as is desirable for frequent routine tests such as might be carried out in screening large numbers of patients for the presence of cystic fibrosis. The present standard chemical analysis of chloride levels in human perspiration employed in diagnosing cystic fibrosis comprises inducing sweating in the patient, collecting a perspiration sample by saturation of a piece of preweighed, dry filter paper, reweighing to determine sample weight, leaching the paper with a known volume of distilled water, and running any one of several standard chloride analyses on the solution. The total procedure requires approximately two hours per patient and is susceptible to error in the two weighing steps and in the manipulation of the wet paper. It is apparent that an analysis as described above requires reliable laboratory personnel and methods.

Several attempts have been made to introduce more rapid screening tests for determining chloride ion levels in various test solutions, including body fluids, see, e.g., Gluck, *Pediatrics*, 23: 731-737 (1959); Knights, *J. Am. Med. Assoc.* 169, 12:1279 (1959); Hoffman et al., *New York J. Med.*, 64, 15:1988 (1964). Essentially these tests all employ variations of the titration of chloride ion with silver nitrate and potassium chromate reagents to form silver chromate which acts as an indicator. While these tests all provide a visible color change on a substrate in the presence of chlorides, a true quantitative indication

of chloride ion concentration is not presented. Often an estimation of the chloride level is made only on the basis of visual examination of the degree of color presented by the indicator or by comparison to known standards. Furthermore, the substrate materials employed in prior art devices, e.g., filter or blotting paper, are often susceptible to uneven wetting by the sample to be tested such that reaction between the reagent impregnated in the substrate and the test solution may occur before the substrate is uniformly wetted over its whole area. The result is a mottling or blotching of the substrate which may cause inaccurate test results. Qualitative recognition of "high" or "normal" chloride levels based on human observation of the intensity of a color change produced on a patch of filter paper is not diagnostically acceptable without accurate quantification by scientific methods.

It is obvious that misdiagnosis of such a highly fatal disease is intolerable. If the disease is not recognized, the patient may die; by the same token, if by reliance on an inaccurate chloride ion reading, cystic fibrosis is suspected, the patient is often subjected to unnecessary emotional as well as financial strain in having to undergo further diagnostic testing. Medical practitioners at cystic fibrosis clinics have indicated many patients referred to them have been improperly diagnosed as having the disease simply because the chloride value relied on by the referring physical was incorrect.

It is therefore an object of the present invention to provide a new and improved means for rapidly and accurately determining the concentration of halide ion in fluids.

It is a further object of this invention to provide a new and improved means for diagnosing cystic fibrosis by measuring the chloride ion concentration of human sweat which means provides an accurate diagnosis, which means may be employed rapidly by persons without specialized chemical or biochemical training, for example, by the nursing staff of a hospital, and which allows the total chloride determination to be carried out in the immediate vicinity of the patient without the use of laboratory equipment.

A further object of the invention is to provide a chloride ion detection means which is self contained and inexpensive and which can rapidly accomplish the equivalent of an analytical titration for chloride ion such that large scale screening operations involving large numbers of patients can be carried out rapidly by unskilled personnel who need only apply the sample to be tested to the detection means.

Other objects and advantages inherent in the invention will become apparent from the following detailed but nonlimiting description.

In accomplishing the noted objects, the detection means of the present invention provides a general means of incremental analysis wherein chloride sensitive reagents in a plurality of correlated and different predetermined concentrations are imbedded in an absorptive substrate of convenient dimensions. The absorptive substrate must be capable of successively absorbing equal volumes of a reagent-containing liquid and a test liquid. The absorptive substrate may be divided into a plurality of distinct regions or may be in the form of individual strips, with each of said regions or strips containing chloride-sensitive chemical reagents in a predetermined amount relative to the volume of test liquid absorbed by said region or strip when saturated therewith. The concentration of the reagents impregnated into each region or strip differs from the concentration in each of the other regions or strips such that a visible color change is effected in a particular region or strip when a predetermined amount

3

of halide ion is encountered therein when saturated with a liquid to be tested. The substrate regions or strips are adhered to a transparent backing such that the reagents imbedded therein are arranged in some order of increasing concentrations. Analytical titration of chloride ion in the test liquid takes place within the substrate when the impregnated regions or strips are wetted by the test liquid. Observation of the result is through the transparent backing so that the color change at the interface of backing and strip or region is observed rather than that which may occur at the exposed surface of the strip or region through which the test liquid is wicked.

While in testing for cystic fibrosis the invention ordinarily includes four strips containing chloride-sensitive reagents, it will be understood that the number of strips may be varied to include any number of separate strips suitable or convenient for a given application. It will also be understood that the spacial arrangement and shape of the strips can be varied to suit aesthetic requirements or to prevent confusion by the user.

The invention can be better understood with reference to the accompanying drawings wherein:

FIG. 1 is a perspective view of a means in accordance with the invention for determining chloride ion concentration in human perspiration;

FIG. 2 is an enlarged cross-sectional view of the means of FIG. 1 taken substantially along the plane of section line 2—2;

FIG. 2A is a micrographic representation of a portion of the means of FIG. 1;

FIG. 3 is a diagrammatic view illustrating a method of collecting a sample of perspiration to be analyzed;

FIG. 4 is an elevational view of the invention illustrating the transfer of perspiration sample from a saturated collection patch to the reagent-impregnated strips of the chloride ion concentration determining means;

FIG. 5 is a perspective view of the invention illustrating the color change after the reagent-containing strips have been saturated with perspiration; and

FIG. 6 is a perspective view of a modified detection means in roll form.

Referring now to the accompanying drawings in detail FIGS. 1 and 2 illustrate a chloride ion concentration detection means 10 to be employed in diagnosing cystic fibrosis. A backing 12 is provided in the form of a glass slide 12, e.g., a standard 3" x 1" size may be used. Adhered to the backing 12 by an adhesive 14 (FIG. 2) are four filter paper strips, *a*, *b*, *c* and *d* in a linear arrangement and impregnated with chloride-sensitive reagents in incrementally varying concentrations. As illustrated these are normally of a brown color. A fifth filter paper strip X, impregnated with a water-sensitive indicator (e.g., nonvolatile base and phenol phthalein dissolved in acetone) which exhibits a color change in the strip X when all of the strips become fully saturated with test solution is optionally, but desirably, provided. As illustrated this strip is normally white.

Reagent-containing indicator strips *a*, *b*, *c* and *d* are prepared by saturating sheets or ribbons of porous substrate material, e.g., fine textured filter paper, with solutions containing the desired reagents in known but differing concentration (e.g., when analyzing for chloride ion concentration, the preferred reagents are Ag_2CrO_4 and AgNO_3). Each sheet or ribbon thus is made to contain a known but different amount of reagent materials from its companion sheets or ribbons. After saturation and drying, separate strips of desired dimensions are cut from each of the impregnated and dried sheets or ribbons and adhered to the transparent, liquid-impermeable backing in any desired order or spacial arrangement as strips *a*, *b*, *c* and *d*. An arrangement in order of increasing incremental concentrations is preferred in order to minimize confusion of results. Each strip is then assigned a value corresponding to the concentration of silver ion

4

(in meq./liter) of the reagent solutions with which each is saturated. Thus a strip saturated with a solution containing 50 meq./liter of silver ion is assigned a value of 50 meq./liter.

The adhesive 14 (FIG. 2) used to attach the substrate strips to the backing should be transparent and preferably colorless; it must be substantially non-migratory such that it will not penetrate the strips too deeply so as to coat the reagents contained therein and thereby impede the reaction. The adhesive must, however, be sufficiently tacky to maintain the strips securely in position on the backing upon wetting. Generally, acceptable adhesives are those with sufficiently high molecular weight to impart the nonmigratory characteristic when applied to the substrate, such as acrylates, vinyl ethers, polyolefins, polyisobutylenes and rubber resin-terpene adhesives without tackifiers. Rubbery viscoelastic polymers disclosed in U.S. Pat. No. 3,121,021 in the form of thin cohesive, pressure-sensitive adhesive strips have been found to provide a particularly satisfactory adhesive when the reagent strips consist of fine textured filter paper.

The backing 12 employed is limited only in that it must be liquid impermeable and sufficiently transparent to permit visual observation through the underside of the backing. In place of the glass slide, any one of several polymeric materials such as cellophane, vinyl polymers, polyethylene terephthalate or other polyester, or the like, in film form could be used as the backing. However, a rigid backing such as that provided by the glass slide is generally preferred. The adhesive 14 serves both to maintain the strips in position on the backing 12 and to prevent the indicator strips from becoming wetted through the surface adjacent to the backing, which reverse wetting can obscure the accuracy of the results. Color changes are to be read through the backing on the strip surface at the interface of the strip surface with the adhesive bonding it to the backing. Since the test solution saturates from the exposed surface of the strip, there will usually be some change in color at that surface due to the concentration of chloride ion there.

The materials used in the formation of the indicator strips must be liquid-absorptive and porous and must be capable of absorbing equal volumes of reagent-containing solutions and test solution. Materials such as filter paper, cloth, microporous polymers, and random web materials have been found to be adequate. Preferred materials are those having minimum variations in porosity, thickness and other properties which affect the absorption characteristics of the material. Acceptable indicator strip material is a conventional filter paper having a thickness of at least .003" to .004". Fine textured filter paper such as that commonly used in vacuum filtration, having a thickness of approximately .006" is preferred as it provides little resistance to saturation while remaining dimensionally stable when saturated.

Where fibrous materials are to be employed as the strip-forming material, e.g., filter paper or cloth, it has been surprisingly observed that the accuracy and reliability of the invention is greatly improved when the impregnated strip-forming material has been treated with a protective polymeric material which is either not wetted by water or only very slowly wetted by water. Electron micrographs of reagent-impregnated filter paper indicator strips of FIG. 1 of this invention treated with such a protective polymer (not readily illustratable in the drawings, but generally depicted in FIG. 2A) indicate that a discontinuous polymeric coating forms about the surface of the fibers of the paper. It appears that microscopic globules 11 of polymer accumulated at points where fibers 13 cross and contact one another. The result is a retardation of the wetting rate of the filter paper which slows the penetration of the test solution (sweat or aqueous chloride solution) into the paper fibers and thereby allows the strip to wet evenly and uniformly over its whole area before much reaction occurs between the sample chloride and

the reagents imbedded within the paper. Theoretically it appears that the surface tension of the aqueous sample liquid and the protective properties of the polymeric coating effectively retard the rate of entry of the sample liquid into the paper fibers. It has been observed that without the polymeric coating, the paper is wetted in an uneven manner with respect to the chloride ion in the test solution. Although the entire strip may be wetted with water, the distribution of chloride ion throughout the body of the strip is not uniform. The reason for this phenomenon appears to be the fact that the test solution, when introduced at any site on an untreated fibrous substrate, wicks its way laterally by capillary action into the body of the substrate, reacting with imbedded reagents as they are encountered, thereby depleting the chloride ion contained in the test solution. Thus while it appears that a given substrate may be uniformly wetted with water, the reagents in the substrate may not be uniformly reacted with chloride ion. The result is that a strip may exhibit a color change at the site where test solution is introduced while adjacent areas retain their original color since they may be wetted by test solution already depleted of chloride ion. A blotched indicator strip is not quantitatively representative of the chloride ion concentration present in the test solution.

The polymeric coating provided by the present invention apparently functions to retard the rate at which the lateral wicking movement of test solution occurs. The surface tension of the test solution is believed to substantially slow its movement past the microscopic polymer globules into and through the substrate. This effect of retarding the wetting rate of the test solution allows the test solution sufficient time to cover the surface of a substrate strip uniformly before lateral wicking can occur. Thus solution containing chloride ion accurately representative of that actually contained in the bulk of the test solution is distributed throughout the strip before a color change occurs. The result is a color change visible over the entire area of the strip and blotching is eliminated.

The polymeric coating is applied by immersing the reagent-containing strip-forming material in solvent containing the selected polymer for a few seconds, removing the material and allowing the solvent to evaporate. It will be understood that the solvent should be chemically inert with respect to the reagents, the strip forming material, and the backing, and it should not degrade the adhesive during the relatively short period it is in contact therewith.

While it is to be understood that a large variety of protective polymers such as cellulose acetate, polystyrene and silicones will function in the desired manner, the preferred polymer is polymethylmethacrylate. An optimum coating on the strip is obtained by immersing the impregnated strip-forming material in a chloroform solution containing 0.05% ($\pm 0.02\%$) by weight polymethylmethacrylate for a few seconds and then drying at moderate heat (60°C.) to remove the solvent. The polymer itself, like the solvent in which it is dissolved must be chemically inert with respect to the reagents, the fibrous strip, the adhesive and the backing.

The preferred reagents with which the strips *a*, *b*, *c* and *d* are impregnated when testing for chloride (or halide) concentration are silver chromate and silver nitrate. The substrate strips contain equivalent amounts of silver chromate and incrementally varying excess amounts of silver nitrate, the silver chromate imparting the same brown color to each of the strips. When the strips become saturated with a solution believed to contain chloride ion, e.g., perspiration, the chloride ion reacts first with silver ion supplied by the silver nitrate and then with silver ion supplied by the silver chromate which is less soluble than the silver nitrate. Each strip retains its brown color until the chloride ion available from the test solution exceeds the total silver ion available from the reagents imbedded in a particular strip. After the silver ion avail-

able from the silver nitrate is precipitated as silver chloride, the remaining chloride ion attacks the silver chromate causing it to lose its brown color leaving a white or very pale yellow. The reaction is nearly stoichiometric in that test solutions having chloride ion concentrations differing by only ± 3.0 meq./liter from the silver ion concentration of the solution originally impregnating a particular substrate strip can be detected. It is important that each strip absorb equal volumes of reagent and test solutions and practically all of the strip should be of a common substrate material. The chloride concentration of the test solution is determined by observing a colorless strip adjacent to a strip which retains its brown color. The chloride ion concentration can then be determined as being greater than the value ascribed to the last strip to lose its color and less than the value ascribed to the strip adjacent to it which retains its brown color. Since the quantitative accuracy of any given strip is approximately ± 3.0 meq./liter, the incremental values differentiating successive strips from one another may be as little as 6.0 meq./liter.

When testing human perspiration for chloride ion concentration with the present invention, sweating may be initially induced in the patient by known procedures (see, e.g., Gibson, et al., *Pediatrics* 23:545 (1959)). A sample of perspiration to be analyzed may be collected as illustrated in FIG. 3 by touching the area of skin where sweating has been induced with an absorptive sweat collecting patch **16** under a polyethylene pad or the like **18** until the patch is saturated with sweat. The overlying pad **18** is simply to prevent evaporation and to facilitate handling of the saturated patch **16** without contamination. When the collection patch **16** becomes saturated with sweat, it is pressed against each of the reagent-impregnated substrate strips as illustrated in FIG. 4 simultaneously whereby test solution is transferred to and saturates said strip. The chloride level is then read by visually observing which of the strips change color as illustrated in FIG. 5. As noted hereinbefore, an additional strip X containing an indicator which exhibits a visual color change when saturated can be added to the detection means **10** as a precaution to assure that all the strips are thoroughly saturated with perspiration.

Assuming a value of 10 for strip *a*, 30 for strip *b*, 50 for strip *c* and 70 for strip *d*, has been assigned, these values corresponding to the concentration of silver ion (in meq./liter) of the reagent solutions with which each strip is initially saturated in FIG. 5, it is observed that strips *c* and *d* have exhibited no color change and strips *a* and *b* have become colorless indicating the chloride ion concentration in the test sample to be between 30 and 50 meq./liter.

In the modification illustrated in FIG. 6, the detection means is in the form of a roll of tape **20** having a transparent backing, e.g., cellophane, to which strips *a*, *b*, *c*, *d*, and, optionally X, are adhered by means of an adhesive **14** (see FIG. 2) as previously described. In use, the tape can be mounted on a dispenser and pieces of the desired length for use as a detection means cut therefrom.

In order to further illustrate the novel improvements of the invention and preferred embodiments thereof, the following examples are provided:

Example I.—Analysis of chloride (bromide or iodide)

Four large pieces of Whatmann Filter Paper No. 50 were saturated with an aqueous solution containing 10 meq./liter of potassium chromate by complete immersion of the paper in the solution and then allowed to dry. Each piece was then saturated in the same manner with aqueous solutions containing 15, 30, 60 and 100 meq./liter of silver nitrate, respectively. The result was the precipitation of approximately 10 meq./liter of silver chromate within each piece of paper, imparting an equal brown color to each piece and leaving an excess of silver nitrate in each piece, the amount of excess increasing

from piece to piece in accordance with the silver nitrate concentration in each piece. The pieces were again allowed to dry. The impregnated pieces were then cut into strips 1/4" x 1/16" and adhered to one side of a 3" x 1" glass slide in order of increasing silver concentration using a co-

then removed from the polyethylene backing and rapidly analyzed for chloride content. One paper was pressed to the incremental titrating device and the second was analyzed using the referee method. Results are given below:

TABLE II

	Referee Cl- strip	15 meq./l. strip	30 meq./l. strip	60 meq./l. strip	100 meq./l. strip
Patient:					
1	15	White	Brown	Brown	Brown
2	18	Light brown	do	do	Do.
3	28	White	Light brown	do	Do.
4	20	(Sweat volume too low to fill strips)			
5	11	Brown	Brown	Brown	Brown
6	14	do	do	do	Do.
7	35 (±3)	White	Light brown	do	Do.
8	18	Brown	Brown	do	Do.
9	20	White	do	do	Do.
10	43	do	White	do	Do.
11	35	(Sweat volume too low to fill strips)			
12	(Not analyzed, sweat volume too low to fill strips)				
13	32	White	Light brown	Brown	Brown
14	28	do	Brown	do	Do.
15	28	do	do	do	Do.
16	34	do	White	do	Do.
17	27	do	Brown	do	Do.
18	15	Light brown	do	do	Do.
19	20	White	do	do	Do.
20	25	do	do	do	Do.
21	27	do	do	do	Do.
22	13	Brown	do	do	Do.
23	39	White	White	do	Do.

¹ Meq./liter.

monomer of isoctyl acrylate-acrylic acid in the form of a thin strip of pressure-sensitive adhesive. The assembled strips were then saturated by immersion in a solution of 0.05% by weight of polymethylmethacrylate in chloroform as a solvent. The assembly was then allowed to dry at 60° C.

Devices thus assembled were then tested by contacting with filter papers wetted with solutions containing known amounts of either chloride, bromide or iodide ions. Halide concentration was determined by observing a colorless strip adjacent to one which remained brown and noting the silver ion concentration of the last strip to turn colorless. The experimental results obtained are described in the following table:

TABLE I

Halide conc., meq./liter	15 meq./liter strip	30 meq./liter strip	60 meq./liter strip	100 meq./liter strip
105 Cl-	White	White	White	White
98 Cl-	do	do	do	Brown
63 Cl-	do	do	do	Do.
60 Cl-	do	do	Light brown	Do.
57 Cl-	do	do	Brown	Do.
33 Cl-	do	do	do	Do.
27 Cl-	do	Light brown	do	Do.
18 Cl-	do	Brown	do	Do.
12 Cl-	Light brown	do	do	Do.
60 Br-	White	White	Light brown	Do.
30 Br-	do	Light brown	Brown	Do.
15 Br-	Light brown	Brown	do	Do.
60 I-	White	White	Light brown	Do.
30 I-	do	do	Brown	Do.
15 I-	Light brown	Brown	do	Do.

Table I indicates halide concentration increments of 3 milliequivalents per liter from the values selected for the device strips can be detected.

Example II.—Analysis for chloride ion in human perspiration

The chloride concentration of human perspiration was analyzed using the above described invention while simultaneously checking the results against referee analytical methods (Bergmann et al., Anal. Chem. 29:241 (1957)). Sweating was induced in 23 adult human males using pilocarpine nitrate admitted to the body by iontophoresis (as described by Gibson et al. in Pediatrics 23:545 (1959)). Sweat from the pilocarpine-treated area of the forearm was collected on a pair of patches (such as 16 of FIG. 5) under a polyethylene overlayer (to prevent evaporation), each patch comprising a 1/2" x 1" piece of filter paper. The collection patches were applied to the forearm for approximately 20 to 30 minutes and

In addition to the above experiments, further testing was carried out using substantially similar referee methods in which of the 50 patients screened, 17 were suffering from cystic fibrosis. The results based on sweat chloride concentration values obtained utilizing the present invention provided accurate diagnoses of all (17 of 17) the positive cases as having cystic fibrosis.

Example III.—Analysis of chloride ion in aqueous solutions using silver nitrate and fluorescein as reagents

The analysis of chloride ion in aqueous solution was accomplished using this invention but employing silver nitrate and fluorescein in the paper matrix rather than silver nitrate-silver chromate as described in Example I. The papers were prepared by saturating each piece of Whatmann Filter Paper No. 50 with one of the solutions containing 15, 30 or 60 milliequivalents per liter silver nitrate plus 200 milligrams per liter fluorescein in 30/70 water-ethyl alcohol solvent. The papers were dried, cut into strips, assembled and treated with polymethylmethacrylate as described in Example I.

The assembled incremental devices were tested by touching to filter papers wetted with standard chloride solutions. They were yellow when prepared and became red when wetted with a chloride solution containing a lower chloride concentration than was contained in a substrate strip. When the strips were exposed to a chloride solution containing a higher chloride concentration than was contained in a strip, the strip was yellow. Thus, the said incremental device is observed as having a red strip adjacent to a yellow strip and the chloride concentration of the solution being tested is thus known to be between the limits defined by said strips. Table III summarizes the experimental results obtained in a series of tests done as described above.

TABLE III

Chloride conc., meq./liter:	15 meq./liter strip	30 meq./liter strip	60 meq./liter strip
63	Yellow	Yellow	Yellow.
57	do	do	Red.
33	do	do	Red.
27	do	Red	Red.
18	do	Red	Red.
12	do	Red	Red.

What is claimed is:

1. A device for facilitating the rapid and approximate determination of halide ion in fluids which comprises a transparent, liquid-impermeable backing, a liquid-absorptive, porous substrate capable of successively absorb-

ing equal volumes of a reagent-containing liquid and a test liquid, a substantially colorless non-migratory adhesive adhering said substrate to the backing, said substrate being divided into a plurality of distinct regions, each of said regions containing halide-sensitive chemical reagent in predetermined amount relative to the volume of test liquid absorbed by said region when saturated therewith, the amount of reagent in each region differing from the amount in each of the other regions, whereby a visible color change is effected in a particular region when a predetermined amount of halide ion is encountered therein when saturated with a liquid to be tested.

2. A means for facilitating the rapid and approximate determination of chloride ion concentration in body fluids which comprises a transparent, liquid-impermeable backing, a plurality of liquid-absorptive porous strips capable of successively absorbing equal volumes of a reagent-containing liquid and a body fluid, the strips being adhered to the backing, each of said strips containing chloride-sensitive chemical reagents in predetermined amounts relative to the volume of a liquid absorbed by said strip when saturated therewith, the amounts of the reagents in each strip differing incrementally from the amounts in an adjacent strip, said strips being treated with a discontinuous polymer coating compatible with the strips and the reagents contained therein to reduce the possibility of blotching or mottling of the strips when saturated with body fluid, whereby a uniformly visible color change is effected in a particular strip when a predetermined amount of chloride ion is encountered therein upon being saturated with body fluid to be tested.

3. The device of claim 2 wherein said strips contain equal amounts of silver chromate or fluorescein and differing amounts of silver nitrate such that each strip exhibits a visible color change when exposed to an amount of chloride ion at least equivalent to the amount of silver ion available from the reagents in each strip.

4. Means for rapidly detecting the presence of undue concentrations of chloride ion in aqueous fluids at the fluid collection site comprising a transparent backing having a plurality of parallel strips of a common porous fibrous substrate material adhered thereto by means of a transparent adhesive, each strip being saturated with a chloride ion detecting reagent which changes color when the chloride ion present in a saturating aqueous liquid exceeds a predetermined amount, each of said strips changing color at a different chloride ion concentration

level than any of the other strips, said strips having a discontinuous polymeric coating in the fibers thereof facilitating more uniform wetting of said strips.

5. The means of claim 4 wherein all of said strips contain equal amounts of a first chloride ion reactive agent and each strip contains a second chloride ion reactive agent more soluble in aqueous chloride ion containing liquids than said first agent, the amount of said second agent in each strip being greater than the amount of said first agent in said strips, the amount of said second agent in each strip being different from the amount of said second agent in every other strip.

6. The means of claim 5 wherein said first agent is silver chromate or fluorescein and said second agent is silver nitrate.

7. The means of claim 4 wherein said means is in the form of a continuous tape wound in roll form.

8. The means of claim 4 wherein said backing is a rigid element.

9. A device for the rapid and approximate determination of chloride ion in fluid which comprises a transparent, liquid-impermeable backing; a liquid-absorptive, fibrous substrate adhered to said backing, the fibers of said substrate bearing a discontinuous polymethylmethacrylate coating, said substrate being divided into a plurality of distinct regions which contain a predetermined amount of chloride-sensitive chemical reagent, the amount of said reagent in each region differing from the amount in each of the other regions, whereby a visible color change is effected in a particular region when a predetermined amount of halide ion is encountered therein.

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