

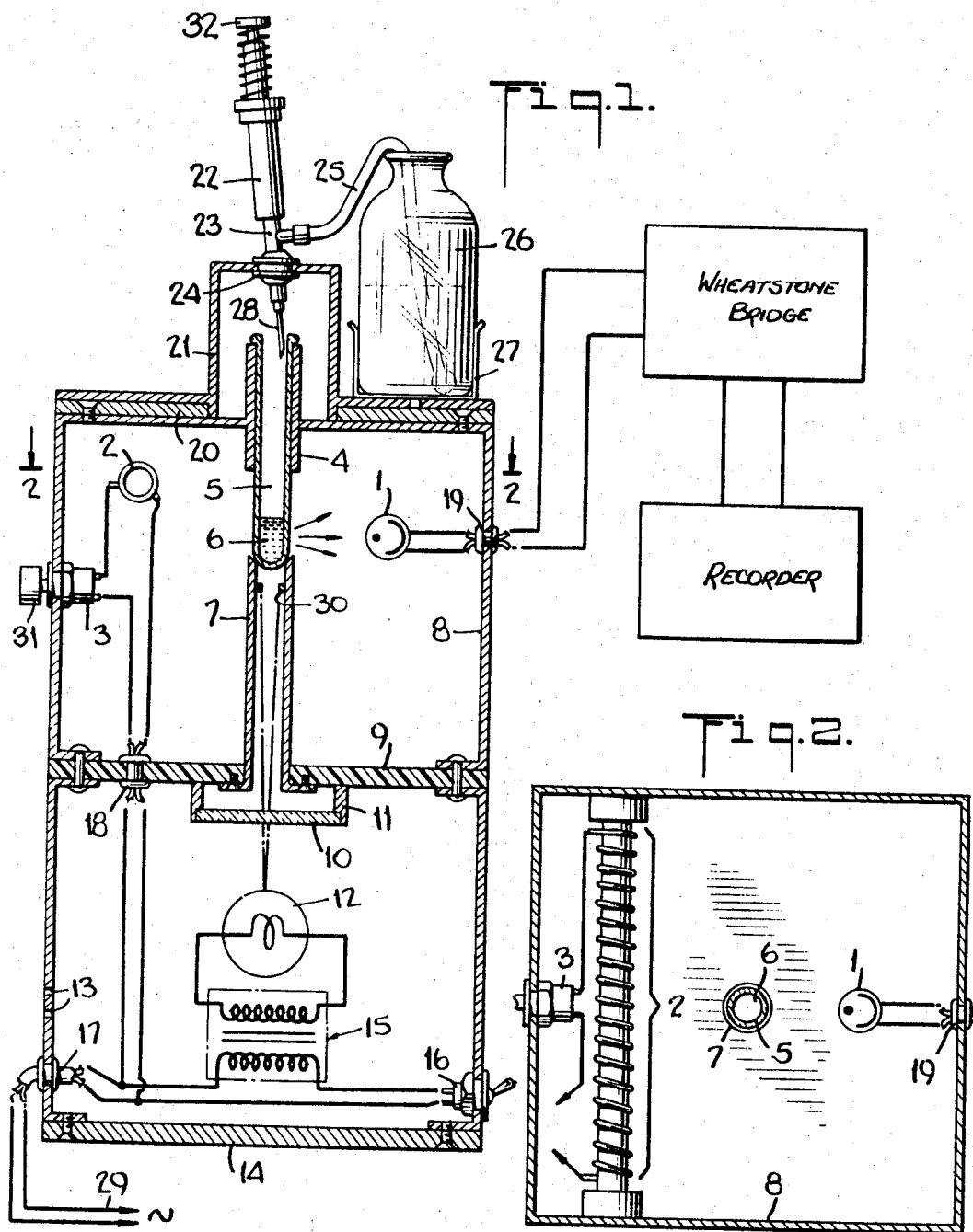
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PROTHROMBIN TIME DETERMINATION

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PROTHROMBIN TIME DETERMINATION

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ABSTRACT OF THE DISCLOSURE

A standard size, disposable test tube containing a blood plasma sample prepared for testing is placed in an enclosed temperature controlled environment. A clotting reagent, contained in a supply bottle, is administered to the test tube containing the sample by means of a self-replenishing-type injector syringe to initiate the clotting reaction, the progress of which is monitored by a photoelectric system which responds to changes in light scattering during coagulation. The photocell output is fed to a resistive bridge circuit, the output of which is sent to a chart recorder which will yield an entire curve of the progress of the coagulation with a sharp endpoint at the instant the clot forms. The prothrombin time is easily read from the curve.

This invention relates to improvement in the method of and apparatus for performing blood plasma prothrombin time determinations. A general object of this invention is the substantial improvement in accuracy and reproducibility of such determinations utilizing a novel system of photoelectric detection in a temperature-controlled environment, enclosed so that the sample is isolated from dust, debris, chemical fumes and other outside factors that are responsible for inaccurate determinations. This method eliminates end point determination by human eyesight and avoids agitation of the mixture during the clotting process, thus preventing side factors due to mixing by hand or even by mechanical means from affecting the rate of the reaction, yet it provides for homogeneity of reactants by means of a rapid initial blending before the reaction is under way.

A further object is the provision for obtaining an electronic read-out in graphical form of the progress of the coagulation reaction which will yield an entire curve of such progress as well as a sharp, significant endpoint at the instant the clot forms.

Another object is the provision of an apparatus called a "Prothrombinometer," wherein the entire prothrombin time determination is performed, from the mixing of the reagent with plasma to the detection of the blood coagulation endpoint or clot.

Advantages include ease of operation and rapidity with which the tests can be made, close conformation with clinical procedure—such as in the use of standard size disposable test tubes, and the simplicity of operation, requiring a minimum of technical skill.

The accompanying drawing illustrates the device used in practicing the aforementioned method.

FIGURE 1, is a cross-sectional view of the device;

FIGURE 2, is a transverse-sectional view taken on the line 2—2 of FIGURE 1.

In FIGURE 1, the numeral 1 indicates a resistive photocell (photoconductive cell) selected from available models; numeral 2 is a heating contrivance consisting of a resistive heating-element wire wound around a blackened porcelain or ceramic rod which is affixed to opposing walls of the upper compartment and supplies heat therein at a controlled 37° C. temperature; a total resistance of 1000 ohms serves nicely; numeral 3 is an on-off bimetallic strip type thermostat switch, selected from commercial models

which controls the temperature and is connected in series with heating-element No. 2. It is affixed to the wall of the device as shown in FIGURES 1 and 2, with the control knob No. 31 on the outside to set the thermostat-switch No. 3 for desired temperature; numeral 4 is an aluminum tube painted or anodized black on both surfaces and edges, and is force-fitted or aluminum soldered through a central hole in the top of the upper compartment so as to extend about one inch above and one-half inch below said top; numeral 5 is a disposable standard three inch test tube (.4 inch diameter); numeral 6 is the plasma sample to be tested; numeral 7 is a metal tube, painted black on the outside surface, that is force-fitted through a hole in the compartment divider No. 9 with its flanged base securely screwed to the underside of the aforesaid divider, and with a beveled edge at the top for the base of test tube No. 5 to rest upon; numeral 8 indicates the aluminum walls of the box-like device, of which there are four, painted or anodized black on their inner faced surfaces; numeral 9 indicates the divider of the upper and lower compartments of the device and consists of a slab of masonite or stiff thermal insulating material, painted black on its upper surface; numeral 10 is a heat absorbing glass of approximately one and one-half inches diameter, set in a mounting No. 11, which is attached to the underside of the divider No. 9; numeral 12 is a low voltage light bulb (automobile tail-lights or exciter lamp type) positioned approximately in the center of the lower compartment directly beneath No. 10; numeral 13 indicates a louvre of air vent; numeral 14 is the square base of the device consisting of Masonite or similar material; numeral 15 is a step down transformer to operate lamp No. 12; numeral 16 is an S.P.S.T. switch to turn off lamp No. 12; numeral 17 is a plastic or rubber grommet in hole of the wall of lower compartment which permits lead-in from 115 v. A.C. line to pass through wall No. 8; numeral 18 is another grommet in hole of divider No. 9 to allow leads from 115 v. A.C. line to pass through into the upper compartment, and is sealed with black cement to make the connection light-tight and air-tight; numeral 19 is another grommet to allow leads from photocell No. 1 to pass through wall of device, and is sealed in the same fashion as No. 18; numeral 20 indicates the upper plate consisting of a square slab of Masonite or similar material with a circular hole in its center to permit snug fitting of top-piece No. 21, and is fastened to the aluminum top of the device; numeral 21 is a removable top-piece of cylindrical shape with a flange extending over the entire surface of the top of the device and made to fit snugly thereto, so as to make a light-tight shield over test-tube No. 5; numeral 22 designates a syringe with spring-return on plunger No. 32 set to deliver a specified quantity of the reagent; numeral 23 is a self replenishing valve arrangement on syringe No. 22; numeral 24 indicates a tightly locked ball-joint, set into the top of No. 21, holding the syringe at a set inclination from the vertical; numeral 25 is a flexible tube leading syringe No. 22 to the reagent bottle No. 26; numeral 27 indicates clips attached to the flange of the top-piece No. 21 to hold the reagent bottle No. 26; numeral 28 is the needle of syringe No. 22; numeral 29 indicates the 115 v. A.C. line leading to an electric outlet; numeral 30 is a metal cuff or ring force-fitted into the upper part of metal tube No. 7 at a set distance from the top thereof.

To operate the "Prothrombinometer," the thermostat knob No. 31 is adjusted to the desired temperature (37° C.). The electrical input lead No. 29 is plugged in and the system is allowed several minutes to come to the designated temperature, then the lamp switch No. 16 is turned on. The top-piece No. 21 is removed manually, exposing the tubular opening No. 4 leading into the upper

compartment. A three inch disposable test tube No. 5 containing the blood plasma prepared for testing in a manner well known to practitioners of the art, is placed into the tube opening No. 4 with its base resting on top of the metal tube opening of No. 7. The top-piece No. 21 is replaced and secured. The needle plunger No. 32, set to deliver a specified quantity of the clotting reagent from bottle No. 26 (reagent may be kept at desired temperature by an immersion heater kept in bottle No. 26), is depressed, and a jet stream of reagent is sent down the wall of the test tube No. 5 causing instant mixing with the blood plasma therein, no further agitation being necessary. At this point, clotting begins at No. 6.

The electric lamp No. 12 provides a light beam which passes through the heat absorbing glass No. 10 and through the hollow tube No. 7 where it narrows at No. 30. It then passes through the blood plasma mixture No. 6. As the clotting proceeds, the light rays become scattered at the base of test tube No. 5 at right angles to the direction of the light beam and strike photocell No. 1. These scattered light rays intensify as the end point is approached causing a response in the photocell which is fed into a bridge circuit as shown in FIGURE 1 of the drawing (one arm of the bridge being the photocell) and then to a chart recorder for a graphical interpretation of the progress of the coagulation reaction from which the "prothrombin time" is easily and accurately read. (If an electric timer is used instead of a chart recorder, it should be driven by an electronic amplifier or Wheatstone bridge and relay system, the parameters of which are set to stop the timer the instant the clot forms as indicated by photocell response. The timer may be started by a switch activated by depressing the syringe plunger or by the initial response of the photocell to the discharge of the clotting reagent).

It should be noted that the amount of clotting reagent required varies with the type of reagent used. Hence the syringe should be adjusted to deliver the proper amount. The apparatus described herein was designed to best accommodate a combined clotting mixture of prepared plasma sample and clotting reagent in the neighborhood of $\frac{1}{4}$ to $\frac{1}{2}$ milliliter. This condition is satisfied if, for example the prothrombin time determination is performed in accordance with the procedures described in Part II of Laboratory Techniques in the Control of Anticoagulant Therapy—U.S. Department of Health, Education and Welfare (No. 1017) February 1963—using .2 ml. of clotting reagent and .1 ml. of plasma sample. This by no means limits the use of the novel method herein described, however; for, modifications in the apparatus such as to allow accommodation of a different size test tube give rise to adaptation to larger or smaller amounts of reagent and plasma—as preferred by practitioners of the art.

It is also understood that variations in materials of construction and suggested methods of fabrication of the apparatus may be used so long as there is no departure from the underlying principles of the invention.

Having described the invention, that which is claimed

as new and desired to be secured by Letters Patent is:

1. An apparatus for prothrombin time determination, comprising an enclosed chamber, a heating source for maintaining the proper temperature within said chamber, a removable top-piece for inserting the test tube containing the plasma sample to be tested, a self-replenishing-type injector syringe for administering the clotting reagent mounted on said top-piece with a flexible tube leading to the reagent supply, a light source located outside the heat controlled enclosed chamber, the light rays from the light source being beamed through the base of the test tube and plasma, and a photocell mounted inside the aforesaid chamber and positioned at a fixed distance from the test tube with the light detecting side facing at right angles to the direction of light transmission, whereby changes in light scattering may be detected as the clotting reaction proceeds; with the electric leads passing outside the chamber to a recording device for the signal from the photocell, with a switch provided for the light source, and a control knob for regulating means to control the above said heating source.

2. An apparatus for prothrombin time determination, comprising an enclosed chamber, a heating source for maintaining the proper temperature within said chamber, a removable top-piece for inserting the test tube containing the plasma sample to be tested, a self-replenishing-type injector syringe for administering the clotting reagent mounted on said top-piece with a flexible tube leading to the reagent supply, a light source located outside the heat controlled enclosed chamber, the light rays from which are beamed through the base of the test tube and plasma, and a photocell mounted inside the aforesaid chamber and positioned at a fixed distance from the test tube with the light detecting side facing at right angles to the direction of light transmission, whereby changes in light scattering may be detected as the clotting reaction proceeds; with the electrical leads passing outside the chamber to the recording device, with a switch provided for the light source, and a control knob for regulating means to control the above said heating source, with the light source located in a chamber below the heat controlled chamber, the light projected upward through a heat absorbing glass and on through a hollow tube extending into the heat controlled chamber, and with the test tube containing the sample resting on top of said hollow tube.

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