for both urine and feces has been confirmed repeatedly by means of isolation of the crystalline ester and determination of its melting point. This, of course, merely establishes the predominating isomer type in the original mixture.. No discrepancies have been encountered between this and the differential precipitation method as described above.

In order to avoid the necessity of correction for the small residual fluorescence of coproporphyrin I when its initial concentration is less than 20 γ per cent, and for the slight diminution in fluorescence intensity of coproporphyrin III at all concentrations employed (see Fig. 1), a curve has been prepared for various mixtures of the isomers, reference to which permits determination of the percentage of each in a given mixture. These data, together with details of the method as applied to urine and feces and the results obtained in various diseases, will be described in separate communications.

References

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The Use of Ultraviolet Light in Tracing the Course of a Drug Through the Body

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It seems possible, if one takes advantage of the fluorescence of various drugs under ultraviolet light, to trace their course through an animal's body. A timetable of the drug's appearance in the different organs might be set up. The greatest concentration of a drug in, and the disappearance of the drug from, a given organ might be judged by the degree of fluorescence of that organ. This is shown to be true in the case of the quinine derivative, quitenine, which is prepared by oxidizing the vinyl group of quinine to the carboxyl group with a permanganate.

Quitenine was chosen for this purpose because of its intense purple fluorescence and because it can be injected in a fairly sizable dose (2 mM/kg.) without killing the animal. The toadfish (*Opsanus tau*) was used as the experimental animal since considerable knowledge of the action of quitenine on this animal is available (*1*). The drug in doses of 2 mM/kg. as quitenine dihydrochloride was injected subcutaneously into the side of the fish behind the dorsal fin. Sloughs developed at the site of injection in a few days. The fish were killed by a blow on the head and opened just before examination. The source of ultraviolet light was a Hanovia Chemical and Manufacturing Company Inspectolite, which gives a light of about 3,660 A.U.[1] All observations were made in a dark room, with the eyes well dark adapted.

In visible light there is not any significant difference in the appearance of the viscera of the uninjected and injected fish except that there is more variation in the color of the gall bladder in the injected fish. Under ultraviolet light the organs of the uninjected fish show no fluorescence with the following exceptions: the gall bladder shows a faint yellowish fluorescence, and in some cases the full urinary bladder shows a strong white fluorescence.

The injected toadfish were killed at daily intervals, until they showed no more fluorescence than the uninjected fish, and examined under ultraviolet light. For the first six days the markings on the skin are much more noticeable in the injected than in the uninjected fish. The injected animal fluoresces, this being especially noticeable in the eyes. For the first two days after injection the cut edges of the skin and muscles show marked purple fluorescence as does the mixture of blood and body fluid that is in the body cavity. The gut shows a strong purple fluorescence for two days and a weaker one the third day. There is no marked fluorescence at the site of injection until a slough develops. The slough gives a strong purple fluorescence until about the seventh day after injection and then gradually weakens, giving a red fluorescence, probably due to some infection. Organs other than the liver, gall bladder, kidney, ureters, and urinary bladder do not fluoresce with the exception of the ovaries, in which at times the eggs, in injected and uninjected fish, give a brilliant golden fluorescence. This is probably connected with their stage of development and is independent of the drug.

These observations show that when quitenine is injected subcutaneously into the toadfish it is at first widely distributed throughout the body and that a large part of it is rapidly concentrated in the liver. The kidney is a very dense organ, and it would require a high concentration before any fluorescence would show. This is attained by the fourth day, although the excretion had begun on the second day, as is shown by the fact that the craniad end of the ureter shows a purple fluorescence. The drug in the liver begins to disappear on the ninth day, that organ being practically free of the drug by the tenth day. The concentration in the kidney becomes low also on the ninth day, and in at least some fish the detectable concentration in the urine disappears on the tenth

[1] The writer is indebted to Dr. George A. Lavin of the Rockefeller Institute for Medical Research for the use of his ultraviolet lamp and for much needed advice.

day, when the craniad end of the ureter is white and the caudal end shows a purple fluorescence.

It is shown that it is possible to trace the passage of a fluorescent drug through the body with the use of ultraviolet light. If the drug were injected intravenously it would appear and probably disappear from the organs in a much shorter time. Experiments are in progress to trace various fluorescent drugs in mammals after intravenous administration.

Reference

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Modification of Metabolism Apparatus[1]

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Basal metabolism in man is commonly calculated on the basis of oxygen consumption. Clinical types of testing apparatus are designed for determining either (1) the amount of oxygen consumed during a definite period of time or (2) the time required for the consumption of a definite quantity of oxygen. The principal advantages in using a clinical type of apparatus are in their simplicity of operation and in computation of results. This type of apparatus is, however, not well adapted for metabolism studies that involve other than resting or basal conditions. The purpose of this report is to describe a modification of a standard type apparatus to broaden its usefulness in studies of oxygen consumption under various conditions of activity.

The essential feature of the present modification is the inclusion of a regulator valve and rate-meter tube (Rotameter),[2] which is inserted in the oxygen intake line of a standard closed-circuit apparatus of the Benedict-Roth type. The setup is shown in Fig. 1. With these additions, oxygen can be delivered at constant and measured rates simultaneously with the consumption. By adjusting the flow from a predicted demand (from standard tables) to the actual requirements a direct reading of the consumption can be made. In this case the oxygen-consumption line becomes parallel to a horizontal base line (Fig. 2, line A).

A brief discussion of the data shown in Fig. 2 will illustrate a method of using the apparatus and suggest further applications.

[1] I am especially indebted to Mr. George K. Porter, of Hatboro, Pennsylvania, technical authority on Rotameters; to Mr. Harold A. Hopkins, Philadelphia service representative for Benedict Roth apparatus; and to Mr. Warren E. Collins of Boston, who supplied some of the materials with which a bellows type apparatus (mentioned in text) was constructed.

[2] The "Rotameter" is a flow-rate meter of the "variable area" type. The metering element is a rotating free float operating in a precision, taper-bore tube, which is calibrated to give a direct reading of the rate of flow.

The initial oxygen-consumption line (A) was obtained on a subject by adjusting the flow to 260 cc. O_2 per minute, at which point the delivery and consumption balanced. This amount was delivered at 30 lbs. pressure throughout the test period, and represents the oxygen requirement under resting conditions (after one hour reclining). At (B) the subject was

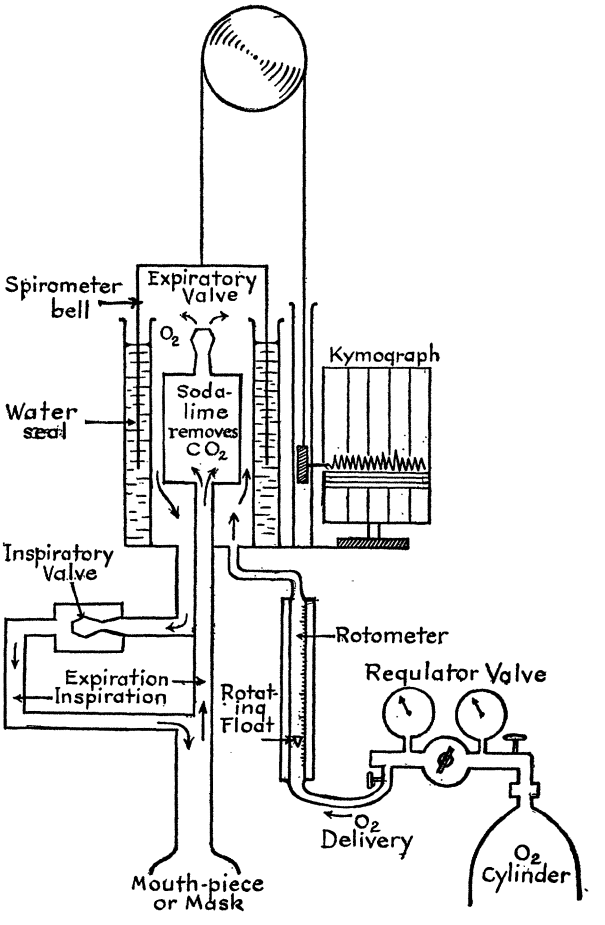

FIG. 1. A diagram of metabolism apparatus of the Benedict-Roth type showing the assembly of the regulator valve and Rotameter.

detached from the circuit, and while prevented from respiratory exchange with outside air, he ran down and up a flight of stairs and then was reconnected into the circuit. The duration and character of the recovery period (payment of oxygen debt) is shown by the curve (C), and the amount of oxygen required for performing the work is represented by the vertical distance between the level of the initial resting line (A′) and the secondary oxygen consumption line (D). The line (D), in leveling off, shows that full recovery has been effected.

Calibrations of the particular Rotameter which we have been using give accurate deliveries within a range