CVIII. A METHOD FOR DETERMINING THE ACCURACY OF ANALYSES OF ETHYL IODIDE VAPOUR FOR MEASUREMENTS OF THE CIRCULATION OF THE BLOOD IN MAN.

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(Received July 17th, 1926.)

THE use of ethyl iodide, inhaled as a very dilute vapour in air, for measuring the circulation of the blood in man seems now to be assured of extensive adoption [see Mobitz, 1926]. For this measurement samples of inspired, expired, and alveolar air of about 250 cc. each, containing from 0.2 to 0.5 mg. of ethyl iodide, are analysed by passing them through a U-tube of iodine pentoxide heated to about 170°. The iodine thus liberated is collected by passing the effluent air through 10 cc. of 5 % potassium iodide solution. It is then measured by titrating the solution with sodium thiosulphate with starch as the indicator in the usual manner.

This method of analysis is well known for determining carbon monoxide, and has a wide applicability to volatile organic substances. It is essential, however, to determine the reliability of the particular preparation of iodine pentoxide employed, and also to determine the speed, or volume per minute, at which air containing the vapour can be passed without allowing any appreciable amount to escape oxidation. It has been found that the rate of flow (about a litre a minute) advised in the paper of Henderson and Haggard [1925] describing the ethyl iodide method is initially much too rapid for complete oxidation. This does not invalidate the circulation rates determined by analyses so conducted, for the reason that it is the relative, not the absolute, amounts of iodine and ethyl iodide found in the three airs from which the circulation of the blood is calculated. If all three analyses are too low by x % the circulation is as correctly estimated as if the analyses were precise.

In the desire for a more nearly absolute precision, however, the following method of checking the accuracy of analysis has been worked out. It may be mentioned here incidentally that when the glass wool, in which the iodine pentoxide is held, turns brown the colour is probably due to iron, not iodine, and does not affect the analyses.

Make a micropipette as follows: warm a thermometer which has a narrow capillary and reads up to 250° or 300° until the greater part of the capillary is full of mercury. Break off the bulb and the top of the thermometer. Note

the number of degrees of the graduation through which the column of mercury extends. Blow the mercury out into a tared watch-glass and weigh. From this weight, the specific gravity of mercury and the number of degrees (noted above), calculate the volume in per cent. of a cubic millimetre represented by one degree on the thermometer. Multiply by 1.944 (the specific gravity of ethyl iodide), and thus obtain the weight of ethyl iodide corresponding to one degree on the thermometer. If the capillary is as small as it should be, the volumes used are from 25° to 50° , which give 0.5 to 1.0 mm.³, and weights of 1 to 2 mg. of ethyl iodide.

Fit a two-holed rubber stopper into the neck of a 200 cc. bottle. The micropipette is inserted up to its middle, or a little more, through one hole. A glass tube passes through the other hole and down to the bottom of the bottle. (See Fig. 1.)

Fig. 1.

The stopper is taken out and held so that the micropipette is horizontal. A drop of ethyl iodide is touched to the end of the capillary and a column 60° or 70° in length is allowed to run along the capillary. The excess is then wiped off the end, and the length of the column is reduced by touching the end of the capillary with a finger. Then the pipette is tilted until the column runs a few millimetres away from the end. Any of the ethyl iodide on the surface of the pipette is evaporated off by fanning.

The bottle is slipped on over the pipette and glass tube and the stopper is pressed in. Then the bottle is stood upright. The glass tube through the stopper is connected by a rubber tube to the U-tube of iodine pentoxide which is to

be tested. From the other side of this U-tube a glass tube passes down through a two-holed rubber stopper into a large, thick-walled, test-tube containing 10 cc. of 5 % potassium iodide solution. A second glass tube through the other hole in this stopper enables this test-tube to be connected to a second U-tube of iodine pentoxide which in turn leads to a second test-tube containing potassium iodide solution. The two U-tubes stand side by side in an air-bath heated electrically to 170°. From the second test-tube a rubber tube leads to a bottle containing 4 or 5 litres of water. The water in this bottle is drained off through a vertical tube, and a current of air is thus drawn through the whole train.

After air has thus been drawn through the micropipette for 10 or 15 seconds, thus sweeping the ethyl iodide into the bottle, the stopper in the 200 cc. bottle is loosened enough to allow air to pass in around the stopper.

The flow of air through the train is measured by means of a graduated cylinder into which the large bottle of water is drained. The flow should be set at 300 cc. a minute for 2 minutes, then at about a litre per minute for 4 or 5 minutes. The first period draws the ethyl iodide into the U-tube, the second, at the more rapid rate, washes the iodine liberated into the potassium iodide solution. No iodine escapes at even the most rapid flow in the second period. But it is possible that when the flow in the first period is too rapid some ethyl iodide may escape oxidation in the first U-tube, and in part also even in the second. If this occurs, the experiment should be repeated with an air flow of 200 cc. or 100 or even 50 cc. per minute until 500 or 600 cc. have been drawn through the train. Then a rapid flow should be maintained for 4 or 5 minutes to wash out the iodine. That iodine, once liberated, is not lost by a rapid flow is easily demonstrated by putting a second test-tube containing a little starch paste into the train just after the first test-tube. That ethyl iodide may escape complete oxidation in the first U-tube is shown by the appearance of iodine in the test-tube placed after the second U-tube.

That the rate of flow is correct, and that the U-tube of iodine pentoxide is working properly, is demonstrated by finding that the fluid in the first test-tube requires on titration an amount of thiosulphate corresponding to the amount of ethyl iodide put into the micropipette.

For the standardisation of the titration weigh out exactly 50 mg. of iodine and dissolve in 100 cc. of 5 % solution of potassium iodide. Weigh out approximately 1.1 g. of sodium thiosulphate and dissolve in 1000 cc. of distilled water. Using starch paste as the indicator titrate 5 cc. of the iodine solution and calculate the amount of iodine in mg. decolorised by 1 cc. of thiosulphate. This amount multiplied by 0.341 gives the amount of ethyl iodide which on oxidation with iodine pentoxide should liberate enough iodine to require 1 cc. of thiosulphate. The factor 0.341 is derived from the figure 0.81, which is the weight of iodine in 1.0 of ethyl iodide, and from the equation of oxidation

In recent tests of U-tubes of iodine pentoxide by this procedure, I have

obtained results balancing to a difference of less than 1 %. A balance to within 5 % is, however, usually sufficient owing to the fact that the calculation of the volume of the circulation of the blood through the lungs depends, not upon the absolute, but upon the relative amounts of ethyl iodide found in the inspired, expired and alveolar airs.

In conclusion I wish to express my thanks to Mr Francis H. Carr of the British Drug Houses for very practical assistance in developing satisfactory U-tubes of iodine pentoxide without which the general introduction of the method in England would be greatly impeded. Especially am I indebted to Prof. Joseph Barcroft for the hospitality of his laboratory, and to Mr Henry Barcroft for collaboration.

REFERENCES.

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