THE ANALYSIS OF SMALL CONCENTRATIONS OF TRICHLOROETHYLENE VAPOR BY INTERFEROMETRY * †

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Since its recommendation for clinical anesthesia in 1942 (1) trichloroethylene has received increasing attention as a drug which possesses considerable analgesic potency. Its ability to relieve pain when self-administered by the patient has been stressed particularly. Its usefulness as an analgesic adjunct to such drugs as nitrous oxide and pentothal sodium in general anesthesia has been thought also to be important. However, this is a potent drug which is capable of producing undesirable side effects on the respiratory and cardiovascular systems when sufficiently high concentrations are employed. There has been a lack of objectivity in determining what ranges of use may be considered safe in the average patient. This has arisen because adequate methods of ascertaining vapor concentrations of trichloroethylene have not been available. Technics have been described, but they entail sufficient time and effort to be impractical for repeated assays (2). To fill this need a method has been devised in which the Zeiss interferometer (3) and the purified medical preparation, "trilene®," ‡ have been used. It has been possible to determine rapidly concentrations delivered under various circumstances, and thus to calibrate the several inhalers and vaporizers used clinically.

In this communication the method employed will be described and the vapor concentrations which may be obtained with different instruments will be enumerated.

Trichloroethylene is a colorless liquid at room temperature, with a molecular weight of 131.5, chemical formula C_2HCl_3 and a boiling point of 87.15 C. at a pressure of 760 mm. of mercury. Because of its low vapor pressure, only small concentrations exist in the gaseous state under standard conditions. For example, the vapor pressure at 25 C. is 73 mm. of mercury or about one-tenth atmosphere: that is, a

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‡ Supplies of "trilene" were obtained from Ayerst, McKenna, Harrison, Ltd., New York, New York.

saturated solution at 25 C. and 760 mm. of mercury would contain only about 10 per cent trichloroethylene (fig. 1). Fortunately, trichloroethylene is a very potent drug and can produce analgesia in concentrations as low as 0.5 per cent. This by most methods is a difficult quantity to measure accurately. With the Zeiss interferometer, however, concentrations of this order can be determined with considerable sensitivity and accuracy.

Since the elaboration of the technic of interferometry is beyond the scope of the present discussion, suffice it to say that each gas has a different refractive index, be it ever so slight. Given, therefore, two gas mixtures identical except for one component, the unknown quantity

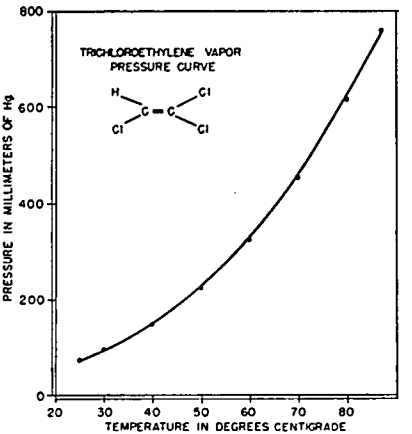

FIG. 1.

of this component can be accurately determined by comparing the refractive indexes of the two mixtures (4).

As the refractive index of trichloroethylene is not well known, and as there are many variables such as temperature, pressure and the presence of small quantities of other gases, an empirical calibration was found to be more practical for the present study than the more indirect methods described.

A weighed amount of trichloroethylene was placed in a flask and pure oxygen passed over it until total vaporization had occurred. Both gases were carried into a water-sealed spirometer, and then this was filled with an excess of pure oxygen until it contained 100 liters of gas kept constantly mixed with a fan. A sample of this gas was pulled through one chamber of the interferometer. For control, a sample of pure oxygen in another water-sealed spirometer was drawn through

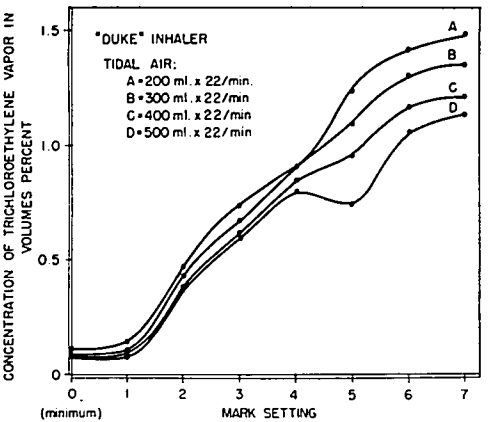

FIG. 2.

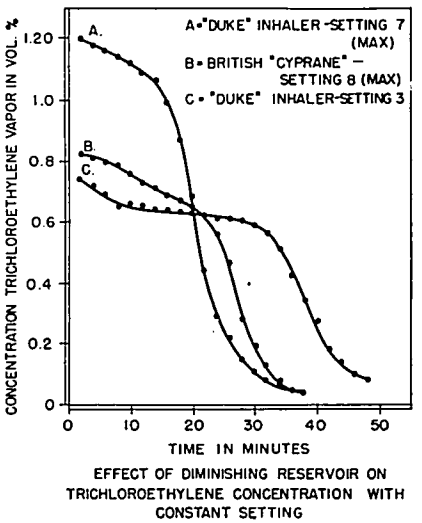

FIG. 3.

the other chamber. Each chamber is 100 cm. long and 1.0 cm. in diameter. Since the temperature was kept constant for the entire system, the effect of saturating the gas mixtures with water vapor in both spirometers was canceled. The gases were pulled through each interferometer chamber by a vacuum pump at a measured rate of 1 liter per minute with a pressure drop of less than 3 mm. of mercury in the entire system and with no appreciable pressure differences between the two chambers. This process was repeated for concentrations of trichloroethylene of approximately 0.5, 1.0 and 1.5 per cent and the calibrating factor of 681 interferometer scale units obtained. The micrometer scale on the interferometer reads directly and easily to the nearest unit. Trichloroethylene may be diluted with gases other

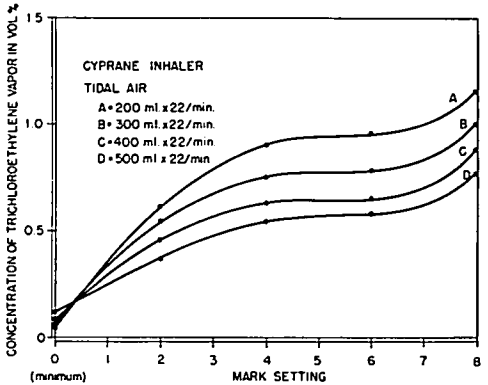

FIG. 4.

than oxygen and water with no appreciable difference in the calibration factor. One disadvantage of this dynamic system is the large volume of gas required for equilibrium, but it should be realized that the absolute quantity of trichloroethylene involved is quite small. For example, 2 liters of a 1.7 per cent mixture, which contains about 200 mg. of trichloroethylene, brings the reading to within 0.1 per cent, and another 200 mg. to within 0.01 per cent, of the correct value.

In an attempt to reproduce clinical methods of use, human volunteers acted as subjects for the initial calibrations, but they became confused and anesthetized before equilibrium was established in the interferometer. A pulmotor, therefore, was employed to give an intermittent flow of ambient air through the inhalers and vaporizers at a desired rate. Both tidal air and breathing rate could be varied

to stimulate different human respiratory conditions, but a fixed breathing rate of 22 breaths per minute and tidal airs of 200, 300, 400 and 500 milliliters were selected for these studies. A continuous flow of gas was pulled off to the interferometer through a side tube attached just distal to the vaporizer. Beyond the side tube was an exhaust tube, approximately 2.5 cm. in diameter and 1 meter in length, which served to prevent back diffusion of gases.

CALIBRATION OF INHALERS AND VAPORIZERS

1. The "Duke University" inhaler (Ayerst, McKenna & Harrison, Ltd.) was designed at Duke University School of Medicine (5) and has eight settings, arbitrarily designated as: Minimum, Mark 1, and so on, through Mark 7 (Maximum). It may be observed (fig. 2):

a. The maximal concentration produced is 1.48 per cent.
b. There is an almost linear increase of concentration with corresponding increase in setting, excluding extreme settings.
c. The concentration decreases with time as the reservoir of trichloroethylene diminishes. This was further investigated and it was observed (fig. 3) that it takes thirty-eight minutes to exhaust 10 ml. of trichloroethylene to within 0.04 per cent.
d. The concentration decreases with increasing tidal air. This might have clinical value, acting like a safety valve, since a patient who is hyperventilating would receive relatively less trichloroethylene, thereby reducing the danger of the drug reaching toxic concentrations in the blood stream.

2. The "Cyprane" inhaler (Ohio Chemical Co.). This has nine settings arbitrarily designated as: Minimum, Mark 1, and so on, through Mark 8 (Maximum). It may be observed (fig. 4):

a. The maximal concentration produced is 1.16 per cent.
b. There is an almost linear increase of concentration with corresponding increase in setting, excluding extreme settings.
c. The concentration decreases with time as the reservoir of trichloroethylene diminishes. This was further investigated and it was observed (fig. 3) that it takes thirty-eight minutes to exhaust 10 ml. of trichloroethylene to within 0.04 per cent.
d. The concentration decreases with increasing tidal air.

3. The "McGill" vaporizer (6). With an initial load of 50 ml. of trichloroethylene, a tidal air of 500 ml., and a breathing rate of 22 per minute (giving an intermittent flow of 11 liters per minute) a curve was obtained for concentrations for the various arbitrary machine settings (fig. 5). This calibration was carried out with the side orifice open—as it is used commonly. The curve has a dip at Mark 6 which could be explained by the decreasing efficiency of the Bernouille effect be-

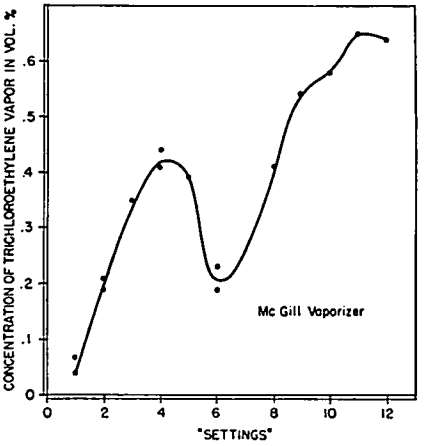

FIG. 5.

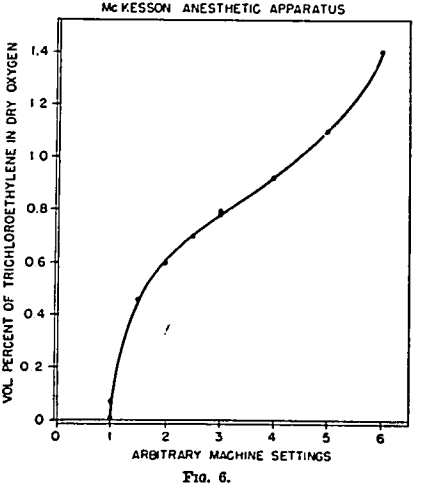

FIG. 6.

cause of a wider orifice at this point. However, further investigation would be necessary to confirm this.

4. The McKesson anesthetic apparatus (Toledo, Ohio). A standard "McKesson" machine with a Nargraf head was employed using oxygen, under pressure of 5 mm. of mercury, which was passed over trichloroethylene placed in the ether bottle. The gas sampling was drawn off continuously through a small side tube and analyzed for trichloroethylene content at various arbitrary machine settings. In the

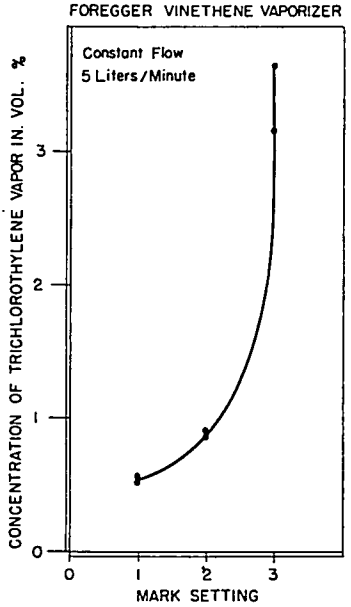

FIG. 7.

range of operational use it was noted that the machine performed essentially linearly (fig. 6).

5. The "Foregger Vinethene®" vaporizer (Foregger Co., New York). A Foregger machine was tested using the small amber "vinethene" bottle attached directly to the gas outlet of the machine. The settings on this attachment consist of lines which were designated as Mark 1, Mark 2, Mark 3. With a flow of 5 liters per minute of pure oxygen from the gas machine, the maximal concentration obtained was

3.68 per cent (fig. 7). The arbitrary settings on the machine represent a nonlinear increase in trichloroethylene vapor concentration.

SUMMARY

A procedure for measuring the concentration of trichloroethylene vapor in gas mixtures has been described. The Zeiss interferometer is used, which offers a rapid, easy, stable and accurate method for calibration of the various apparatus. Because of the relatively great difference in the refractive indexes of oxygen or nitrogen as contrasted with trichloroethylene vapor, the high precision accuracy of 0.01 per cent could be obtained. Several vaporizers and inhalers have been calibrated by this method, including the "Cyprane," "Foregger," "McGill," "McKesson" and "Duke."

ACKNOWLEDGMENT

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