

CONCENTRATIONS OF HALOTHANE, ETHER AND CYCLOPROPANE IN INSPIRED ATMOSPHERES DURING CLOSED CIRCUIT ANESTHESIA

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EXCESSIVE depths of anesthesia and delayed recovery may be associated with any method of inhalation anesthesia but would appear particularly noteworthy when potent anesthetic drugs such as halothane (Fluothane), cyclopropane or ether are administered in a closed circuit.

In order to evaluate quantitatively the extent and the time required to produce excessive concentrations in the inspired atmosphere of a closed circuit employing these anesthetics, a clinical study was undertaken. This investigation has included the use of constant inspired tensions of anesthetic gases or vapors as well as the employment of intermittent flow techniques.

METHODS

Subjects in this study were patients ranging in age from 16 to 65 years and who were scheduled to undergo various surgical procedures. These patients ranged in weight from 90 to 230 pounds. The study included values obtained before, during and after the actual surgical procedure.

All patients were premedicated with atropine, 0.4 to 0.6 mg., and either secobarbital, 50 to 100 mg., or meperidine, 50 to 100 mg., given intramuscularly 30 to 60 minutes prior to induction of anesthesia.

Induction of anesthesia in each case was aided by the intravenous administration of 2 per cent thiamylal in doses ranging from 100 to 250 mg.

Continuous electrocardiograms and electroencephalograms were obtained by use of a Grass Polygraph. Blood pressure was obtained by conventional methods.

Presented at the Annual Meeting of the American Society of Anesthesiologists, Inc., New York, New York, October 6, 1960, and accepted for publication February 14, 1961. The authors are in the Department of Anesthesiology, University of Mississippi Medical Center, Jackson, Mississippi.

Gas samples were obtained from the anesthetic machine by insertion of T tubes into the delivery tubing from the machine to the absorber head and into the inspiratory side of the breathing circuit to provide a means for analyzing actual concentrations of gases delivered to the system as well as those which developed in the breathing circuit over a period of time.

Gas samples were obtained at intervals of 1 to 5 minutes during induction and early maintenance. After about 30 minutes, samples were drawn every 10 to 20 minutes until 2 or more gas samples showed similar values. Thereafter, unless the delivered concentration was altered, samples were obtained at intervals of 30 to 60 minutes. Near the end of the procedure after the anesthetic drug had been discontinued, more frequent sampling was carried out to determine the rate of clearance of the drug from the circuit. After an interval of 15 to 20 minutes, the system was flushed with oxygen for 2 or 3 minutes and an additional gas sample was obtained.

Gas analysis was performed by means of gas chromatography employing a Beckman GC-2 gas chromatograph attached to a Minneapolis-Honeywell (Brown) recorder and Brown Integrator. This analytical method provided rapid and accurate determinations of all components in the gas-vapor mixtures from a single sample.¹

In the majority of cases endotracheal intubation was performed to assure a completely gas-tight system. All intubations were facilitated by intravenous injections of from 40 to 60 mg. of succinylcholine. In a few short procedures, a tightly fitting mask was employed.

A flow of 400–500 ml. of oxygen per minute was delivered in each case and manually assisted or controlled respiration was employed routinely in order to assure adequate ventilation at all anesthetic levels.

Closed Circuit Halothane Anesthesia. Following the administration of thiamylal in doses sufficient to produce drowsiness, each patient breathed a mixture containing 50 to 70 per cent nitrous oxide in oxygen for 3 to 5 minutes. During this period the gases were delivered at a total flow rate of 4 to 7 liters/minute. In some cases, 10 per cent cyclopropane was added to this mixture prior to endotracheal intubation. In a few instances halothane in concentrations of 1.0 to 1.8 per cent was added for a period of 2 to 3 minutes in the partial rebreathing system.

The Fluotec Mark II vaporizer was employed in this series. After securing a closed system, the vaporizer control dial was placed initially on the 3 per cent setting at which an oxygen flow of 500 ml./minute through the instrument actually delivered a concentration of 3.8 per cent halothane.

Closed Circuit Cyclopropane Anesthesia. In this group of 20 patients, cyclopropane was administered in either a 50 or 33.3 per cent concentration during induction and early maintenance. After the inspired concentration had stabilized at its maximum level, the delivered concentration was reduced to 33.3 or 25 per cent. This procedure was employed as a means of determining the effects of constant delivered concentrations of high percentages.

Intermittent flows of from 10 to 33 per cent cyclopropane were delivered in 5 patients in order to determine the rapidity of change in inspired concentrations associated with abrupt changes in delivered concentrations.

Closed Circuit Ether Anesthesia. For this portion of the study we were interested in determining the concentrations of ether which might develop during the use of both predictable and unpredictable concentrations delivered into the breathing circuit. Therefore 6 patients in this group were anesthetized by means of a standard Heidbrink wick vaporizer. Either a "copper kettle" or Vernitrol ether vaporizer was used in the remainder of these cases.

Induction of anesthesia in this group of 14 cases was accomplished by the use of nitrous oxide and cyclopropane or nitrous oxide and ether combinations. After endotracheal intubation, a closed circuit system was established

and only an ether-oxygen mixture was administered. An ether concentration of 12 to 16 per cent was delivered for a period of 15 to 30 minutes in the initial period. Following this interval, a maintenance concentration of 10 to 12 per cent was delivered until near the end of the procedure.

In those cases where the ether vaporizer was situated within the breathing circuit, only the actual inspired concentrations of ether could be determined. In each case the vaporizer was located on the expiratory side of the absorber head.

RESULTS

Halothane. At any given halothane concentration delivered from the anesthetic machine into the breathing circuit, an average of 65 minutes was required to develop an inspired concentration amounting to 50 per cent or more of the delivered concentration. The minimum time requirement for any case was 55 minutes and the maximum was 70 minutes. Within 30 minutes from the point at which halothane vaporization was begun, the inspired concentration approached 25 per cent of the delivered concentration.

As a result of the concentrations developed within the breathing circuit during these intervals of time, only one of the 20 patients in this group showed reasonable tolerance to a constant delivered concentration of 3.8 per cent for longer than 30 minutes. For this reason, only this one patient has permitted study of the inspired concentration developing in 60 minutes at this higher concentration delivered from the machine. In this case, a halothane concentration of 1.98 per cent was observed after 65 minutes. At this level, a 42 per cent decrease in blood pressure necessitated the discontinuation of halothane for approximately 40 minutes during which time the inspired concentration gradually decreased to 0.9 per cent. The concentrations obtained throughout this procedure are shown in figure 1.

The remainder of the group (19 patients) required constant delivered concentrations of 1.6 to 2.8 per cent for the first 30 to 45 minutes (Fluotec dial settings of 2.0 and 2.5 per cent respectively) to maintain anesthesia. It was found in each of these cases that inspired concentrations of 0.8 to 1.2 per cent produced

consistently satisfactory levels of anesthesia for most procedures.

In each case when inspired concentrations exceeded 1.2 per cent hypotension became of sufficient significance to warrant a decrease in the concentration delivered from the vaporizer. At inspired concentrations of 0.8 per cent or less, decreases in blood pressure did not exceed 25 mm. of mercury in this series. The record of a representative case from this group is shown in figure 2.

Once equilibration had occurred at any given percentage within the closed circuit, 10 to 15 minutes was required to reduce this concentration significantly by merely discon-

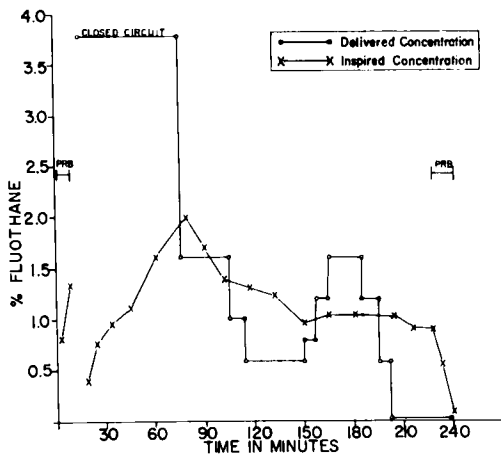


FIG. 1. Inspired concentrations of halothane (Fluothane) developing at an initial delivered concentration of high percentage.

tinuing the vaporization of halothane. By increasing the flow rate of diluting gases or by actual flushing of the system with oxygen, the concentration could be decreased by at least 50 per cent within a minute or two.

Cyclopropane. As shown graphically in figure 3, when constant cyclopropane concentrations were delivered from the anesthetic machine, the inspired concentration approached the delivered concentration rapidly. Within 5 minutes the inspired concentration reached 70 per cent of the delivered concentration. In 10 minutes this value rose to 78 per cent and in 15 minutes reached 86 per cent. Within 30 minutes the inspired concentration of cyclopropane was observed to be 92 per cent of the delivered concentration.

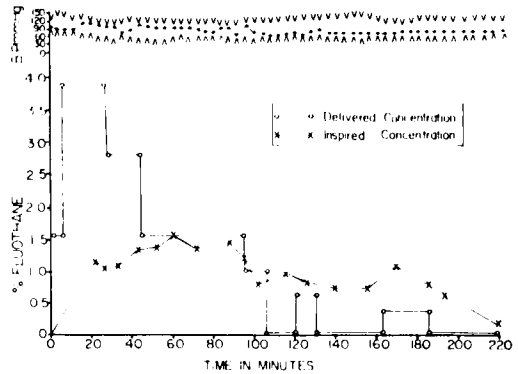


FIG. 2. Representative data obtained from patient during closed circuit halothane (Fluothane) anesthesia. Upper portion of photograph shows blood pressure and pulse. Remainder of photograph shows delayed changes in actual inspired concentrations of halothane following changes in delivered concentrations.

The clearance rate of cyclopropane from the system also was observed to be rapid. A decrease of 50 per cent in the inspired concentration of cyclopropane was observed within 10 minutes when the circuit remained closed and no cyclopropane was added. A flushing period of 1 to 2 minutes produced a 90 per cent decrease in the inspired concentration. Samples taken from the system 5 minutes after this period of flushing, however, showed concentrations of cyclopropane of up to 5 per cent in the inspired atmosphere.

The rapidity of changes in the inspired atmosphere associated with intermittent changes

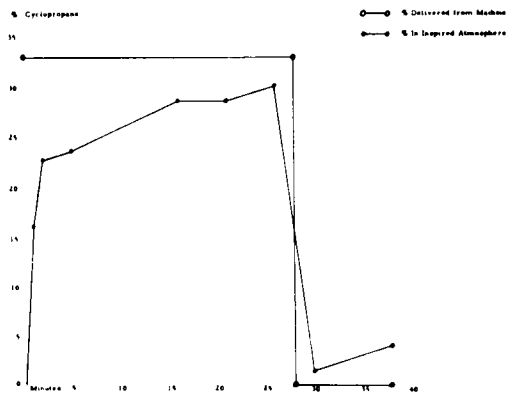


FIG. 3. Development of actual inspired concentrations when delivered concentration of cyclopropane remains constant. Note rapid rate of clearance from the circuit when cyclopropane is discontinued.

in the delivered concentration is shown well in figure 4.

It was found that inspired concentrations of cyclopropane ranging from 12 to 14 per cent were satisfactory for most procedures in this series and produced an anesthetic plane 2 of Stage III (EEG level 3 to 4). At inspired concentrations of 20 per cent cyclopropane only slight increases in depth were detectable.

When inspired concentrations greater than 25 per cent occurred during maintenance of anesthesia, pupillary dilatation became evident, muscle relaxation was extreme and the electroencephalogram showed periods of burst suppression exceeding 10 seconds (level 6) in most patients.

Ether. Because of temperature and vapor pressure variations which occur during the vaporization of ether, this portion of the study has presented considerable difficulty in ascertaining average percentage values. Even with the use of "copper kettle" or Vernitrol vaporizers, we have observed variations of from 1 to 2 per cent ether vapor in inspired atmospheres occurring during induction and early maintenance of anesthesia as a result of fluctuations in delivered concentrations.

The data shown in figure 5 are those obtained from one such case and illustrate the variations which occurred during induction and early maintenance. In this instance a

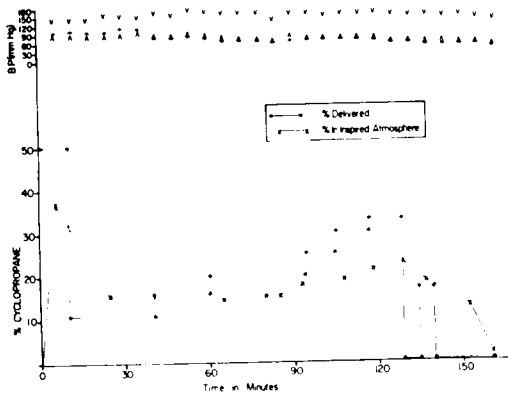


FIG. 4. Representative data obtained from patient during closed circuit cyclopropane anesthesia. Upper portion of photograph shows blood pressure and pulse. Remainder of photograph shows delayed changes in actual inspired concentrations of cyclopropane following changes in delivered concentrations.

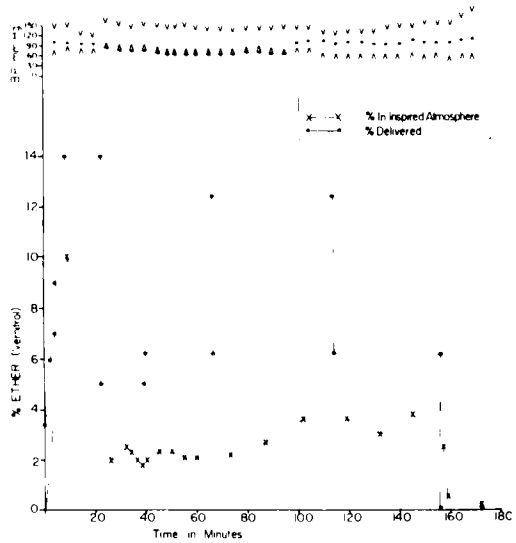


FIG. 5. Representative data obtained from patient during closed circuit ether anesthesia. Upper portion of photograph shows blood pressure and pulse. Remainder of photograph shows delayed changes in actual inspired concentrations of ether following changes in delivered concentrations.

partial rebreathing system was employed for administering nitrous oxide and ether prior to tracheal intubation.

The results obtained in cases where the vaporizer was situated within the expiratory side of the breathing circuit showed even greater variations in the vapor concentrations in inspired atmospheres. This variability precludes the presentation of reasonable averages but a representative case is illustrated in figure 6.

DISCUSSION

In this study we have attempted to analyze the concentrations of anesthetics most commonly used in the closed circuit method of inhalation anesthesia under actual clinical circumstances and including all variables with which the anesthetist must be concerned in daily practice. For this reason we purposely planned a relatively uncontrolled study on unselected patients.

Robson and others² in an investigation of closed circuit halothane anesthesia found that the concentration of halothane within the circuit usually did not exceed 50 per cent of the concentration delivered from the vaporizer in

a series of 25 cases. Our results tend to corroborate the findings of those workers in the 20 cases included in our series.

The over-all results obtained in this study may be summarized graphically as in figure 7. A number of interesting features present themselves in this illustration and correlate well with the clinical responses of patients which we have observed in the various series.

Of particular interest is the rate of clearance associated with each anesthetic compound from the breathing circuit when a closed system is maintained after the discontinuation of the anesthetic.

Cyclopropane is seen to build up rapidly in the system when a given concentration is delivered constantly into the breathing circuit. It is evident also that concentrations of this drug may be decreased rapidly in the inspired atmosphere by merely discontinuing the flow. It will be noted, however, that even after 30 minutes, approximately 10 per cent of the concentration previously delivered still recirculates in the circuit. Following the prolonged delivery of concentrations in excess of 25 per cent, the eventual equilibration of this recirculating cyclopropane with that being released from tissues may well predispose to prolonged recovery. This has been observed frequently in this group of patients.

Both halothane and ether concentrations were observed to develop rather slowly in the closed circuit and elimination of these vapors

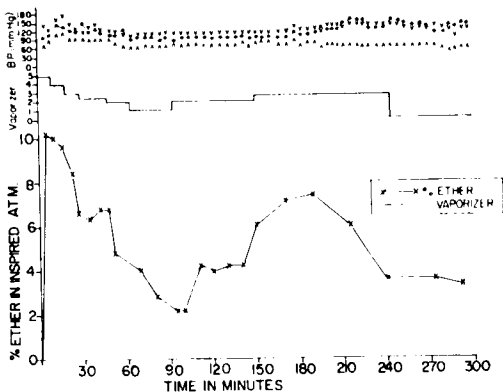


FIG. 6. Data obtained from case in which Heidbrink 'wick' vaporizer was employed within the breathing circuit. Note marked variations in concentration as setting of arbitrary numbers on vaporizer dial are changed.

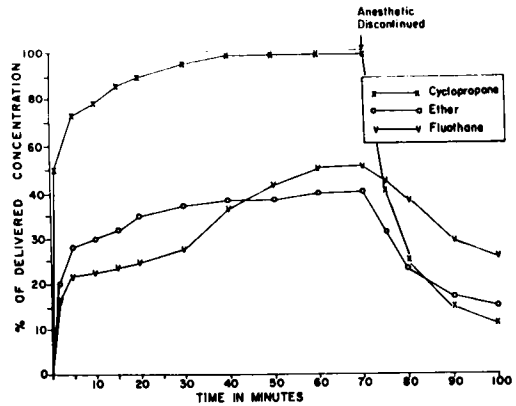


FIG. 7. Graphic summary of changes in inspired atmospheres which occurred when constant delivered concentrations were employed. (Values are expressed in terms of percentages of a constant delivered concentration). Circuit remaining closed after anesthetic discontinued.

was quite delayed, as might be anticipated, unless high flow rates of diluting gases were employed at the end of the procedure.

It is emphasized also that the inspired concentrations represented in the graph do not reflect totally the proportional concentrations which may occur in blood. Actually the alveolar and blood concentrations of cyclopropane should exceed the delivered concentrations as a result of oxygen consumption.

In the cases of halothane and ether, the concentrations in blood would probably be quite dissimilar for the two drugs due to the greater solubility of halothane in blood. For this reason, one would expect relative blood concentrations of halothane to develop at a considerably faster rate than those of ether.

SUMMARY

A study has been made of the concentrations of halothane, cyclopropane, and ether which may develop in a closed anesthesia circuit over a given period of time and of the rate with which these drugs are eliminated from inspired atmospheres.

At constant delivered concentrations, it was found that cyclopropane was by far the most rapid in attaining high concentrations in the breathing circuit and in rate of clearance from the system.

The slow rate of development and clearance

of ether and halothane concentrations in this system have been notable.

Correlations of these data with the clinical responses of anesthetized patients are made and emphasis is placed on the desirability of utilizing high flow rates of gases for induction and for several minutes at the end of the procedure in order to speed both induction and recovery time when the closed circuit method is to be employed for anesthetic maintenance.

Supported in part by a grant from Ayerst Laboratories, New York, New York.

REFERENCES

1. Fabian, L. W., and Carnes, M. A.: Gas chromatography as analytical tool in anesthesiology, *ANESTHESIOLOGY* 21: 98, 1960.
2. Robson, J. G., Gillies, D. M., Cullen, W. G., and Griffith, H. R.: Fluothane (halothane) in closed circuit anesthesia, *ANESTHESIOLOGY* 20: 251, 1959.

HYPOTHERMIA AND DIGITALIS At temperatures between 21 and 32 C. one third of the average lethal dose of tincture of digitalis, calculated from data obtained in cats at normal body temperature, was injected intravenously at five-minute intervals until death of the animal occurred. The lethal dose of digitalis was larger in the hypothermic animals. A correlation appeared to exist between the degree of hypothermia and the lethal dose. The lower the temperature the greater the lethal dose. (*Szekely, P., and Wynne, N. A.: Effects of Digitalis on Hypothermic Heart, Brit. Heart J. 22: 647 (Nov.) 1960.*)

NERVE BLOCK Sodium-free solutions cause complete block of conduction in all myelinated and nonmyelinated fibers of the cat spinal roots. This blocking occurs at different rates, a large proportion of the alpha and beta fibers still conducting when the gamma, delta, and nonmyelinated fibers are completely blocked. Recovery of fibers of all sizes occurs within seconds of applying the normal solution and is complete within one minute. Solutions containing between 10 and 25 per cent of the normal amount of sodium block the fiber groups differentially. A solution containing 15 per cent of the normal amount of sodium blocks the gamma, delta, and nonmyelinated fibers without blocking a

significant proportion of the alpha and beta fibers. Solutions containing 20 per cent of the normal amount of sodium block delta and nonmyelinated fibers, but a proportion of the gamma fibers continue to conduct at diminished velocity. Slowing of conduction velocity is conspicuous with concentrations of sodium near to the threshold for blocking, especially with nonmyelinated nerve fibers. The nonmyelinated fibers continue to conduct at diminished velocity in a solution which blocks the very smallest myelinated fibers. (*Nathan, P. W., and Sears, T. A.: Differential Nerve Block by Sodium-Deficient Solutions, J. Physiol. 154: 41P (Nov.) 1960.*)

PROLONGED LOCAL ANESTHESIA The duration of local anesthesia provided by a mixture of lidocaine and Dextran has been investigated. The subcutaneous injection of a solution containing 1 per cent lidocaine and 10 per cent Dextran with 1/250,000 epinephrine produced analgesia for 10 hours. When injected about operative wounds to block sensory nerves, it considerably reduced the need for other analgesics in patients who had undergone thoracic or upper abdominal operations. (*Loder, R. E.: Local-Anaesthetic Solution with Longer Action, Lancet 2: 346 (Aug. 13) 1960.*)