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RESPIRATORY PATTERNS DURING NITROUS OXIDE-OXYGEN-ETHER ANESTHESIA * †

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With the recent revival of interest in respiratory function during general anesthesia, particularly as alterations of this function affect the acid-base status of the subject, it seemed desirable to make a quantitative study of some of the clinically apparent respiratory activities which are influenced by general anesthesia. This paper is a report of such a study. Our investigations were limited to observation of 12 patients undergoing nitrous oxide-oxygen-ether anesthesia for major abdominal operations. In 1 additional case data were obtained during the induction period only. The respiratory parameters considered were ventilation rate, respiratory rate and tidal volume. These were related to simultaneously recorded electro-encephalographic levels of anesthesia based on the classification of Courtin, Bickford and Faulconer (1). Figure 1 shows the seven levels described. The sensitivity of the respiratory center to carbon dioxide stimulation was roughly evaluated by correlation of the observations mentioned with those made after the administration of substantial concentrations of carbon dioxide to the respiratory gas mixture.

Methods

Ventilation Rate.—The volume of the patient's inspirations was measured by passing all of the inspired gas mixture through a volume displacement gas meter. The flow channels in the metering system are schematically represented in figure 2. This system allows only the

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gas respired by the patient to pass through the meter regardless of the flow meter settings on the anesthesia machine. Figure 3 illustrates the arrangement of the gas machine, gas meter and flow channels. This arrangement was later improved by shortening the tubes in parts of the system.

Respiratory Rate.—A signal for recording the respiratory rate was obtained from a strain gauge manometer in the expiratory channel near the face mask. Thus pressure changes in the expiratory channel accompanying each respiratory cycle were signaled on the recording system.

Tidal Volume.—This value was calculated from the record of ventilation rate and respiratory rate.

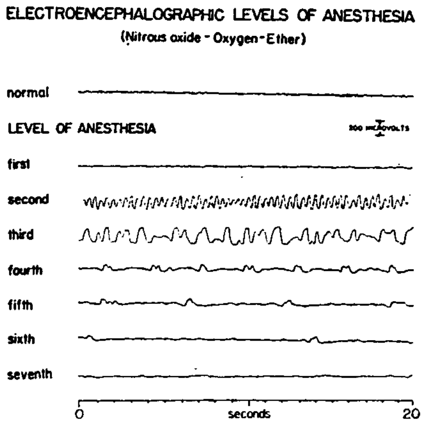

FIG. 1. Classification of electro-encephalographic levels during nitrous oxide-oxygen-ether anesthesia. Levels 3, 4 and 5 occur during safe surgical anesthesia and levels 1 and 2 during induction. Levels 6 and 7 are considered to be unsafe.

Respiratory Gas Analysis.—A small continuous sample of gas was drawn from an end-expiratory sampling device similar to that described by Rahn and Otis (2). A continuous analysis was made, in many subjects, of one or more of the following components of the gas mixtures thus sampled: oxygen, ether, nitrous oxide and nitrogen. This analysis was accomplished with the acoustic gas analyzer and a Beckman oxygen analyzer as described in a previous paper(3).

Recording.—All of the observations mentioned above were recorded optically on 12-inch photosensitive paper, a short sample of which is seen in figure 4. The vertical lines indicate one-minute intervals. The horizontal base line is used as a reference point in making measurements. The next above the base line is a signal line for correlation of the electro-encephalographic record with this one and for the correlation of the record with various clinical notes made during each case study. The next three lines are a record of data from the gas analyzer. The interrupted double lines seen next to the top are a record of ventilation rate, each dash on either one of which represents 500 cc. of inspired gas. The top line is a record of the pressure variation induced in the expiratory tubing by the patient's own respiratory effort. From this the respiratory rate may be counted.

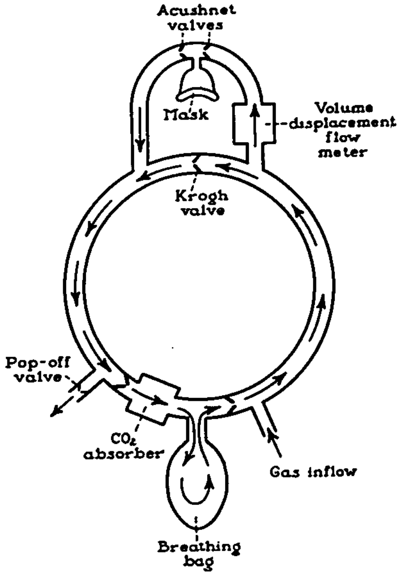

FIG. 2. Diagram of gas flow channels and valves.

Electro-encephalogram.—The electro-encephalographic record was made on a two-channel machine of our own design equipped with Brush pen writers. The technic employed here has been described elsewhere (4). One channel was used to make a continuous electrocardiogram from lead 2. A signal channel recorded signals simultaneously marked on the optical record described above, allowing precise time correlation of the electro-encephalogram with other data.

Blood Gas Analysis.—As a part of another study still in progress, Dr. Robert Patrick analyzed arterial blood samples from several of

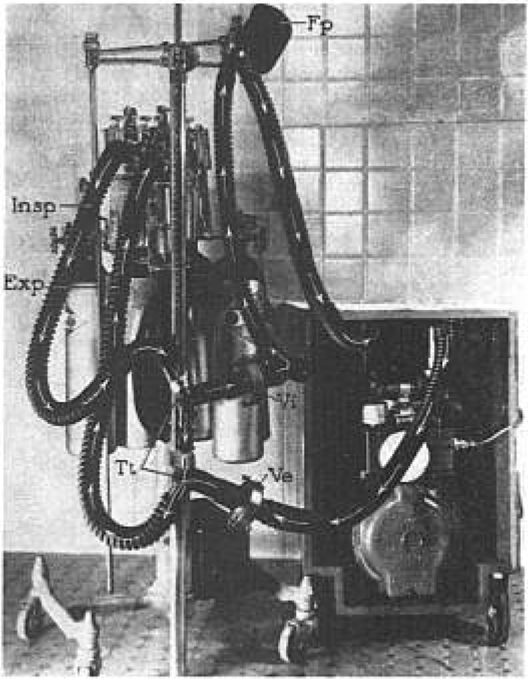

Fig. 3. Gas meter and anesthesia apparatus, showing direction of gas flow. *Fp.*, face piece; *Insp.*, inspiratory gas channel; *Exp.*, expiratory gas channel; *Tt*, T connectors; *Vi*, inspiratory valve; *Ve*, expiratory valve; *G*, gas meter.

the patients considered here, for ether, oxygen, carbon dioxide and pH. These analyses were made with a mass spectrometric method, a description of which is yet to be published. Some of the data thus provided will be presented here with the permission of Dr. Patrick.

Procedure

The premedication used for each of the patients included in this study is shown in table 1. Immediately before induction of anesthesia the electro-encephalograph and the electrocardiograph leads were applied to the patient and short control tracings were taken. The record of respiratory variables and gas analysis commenced with the ap-

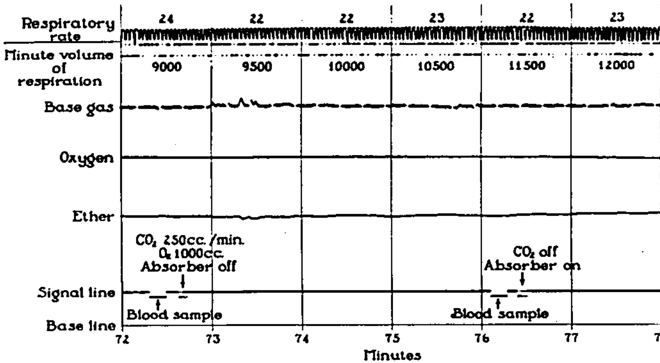

FIG. 4. Sample strip of photographic record showing base line, signal line, ether concentration, base gas, ventilation rate, and respiratory rate.

plication of the anesthesia mask to the patient's face. The induction proceeded with the usual nitrous oxide-oxygen-ether sequence, with complete circle absorption of carbon dioxide from the outset. The carbon dioxide absorber was left in the circuit except during those periods when carbon dioxide was added for the purpose of this study. In a few instances high flows of nitrous oxide were added to the gas mixture at the expense of oxygen to test the effect of anoxia.

TABLE 1

INSPIRATORY VENTILATION RATES (MINUTE VOLUME OF RESPIRATION)

Case	Duration of Anesthesia,* minutes	Ventilation Rate, liters per minute			Age, years	Premedication, grains		
		Mean	Low	High		Morphine	Atropine	Nembutal
1	72	6.9	2.0	11.0	21	1/4	1/150	
2	36	9.0	5.5	11.5	55	1/6	1/150	1½
3	74	7.8	5.0	12.5	50	1/4	1/150	1½
4	41	6.7	4.5	11.5	28	1/6	1/150	
5	121	10.9	5.5	14.5	70	1/8	1/150	3
6	59	9.7	5.0	14.5	39	Demerol, 100 mg.	1/150	1½
7	70	9.0	4.0	13.5	36	1/6	1/150	1½
8	83	9.8	7.5	13.0	62	1/6	1/150	
9	49	11.5	7.5	15.0	43		1/150	
10	103	8.6	6.0	11.5	67	1/8	1/150	1½
11	97	9.6	5.5	14.5	68	1/8	1/200	¾
12	133	11.1	7.0	15.5	35	1/4	1/150	1½
13	76	7.1	4.0	12.5	60	1/4	1/150	1½

* Periods of anesthesia during which intervention for investigational purposes occurred (for example, carbon dioxide stimulation) were deleted in compiling these data.

The data obtained were charted for each case as illustrated in figures 5 and 6. Time is reported on the abscissa in minutes starting with the beginning of anesthesia as zero time. The dotted line represents tidal volume which is expressed in cubic centimeters. The solid line indicates the respiratory rate. The next line represents the ventilation rate which is expressed in liters per minute. Next, the electro-encephalographic levels are represented. Trends in the direction of the bottom of the figure indicate increasing depth of anesthesia. Im-

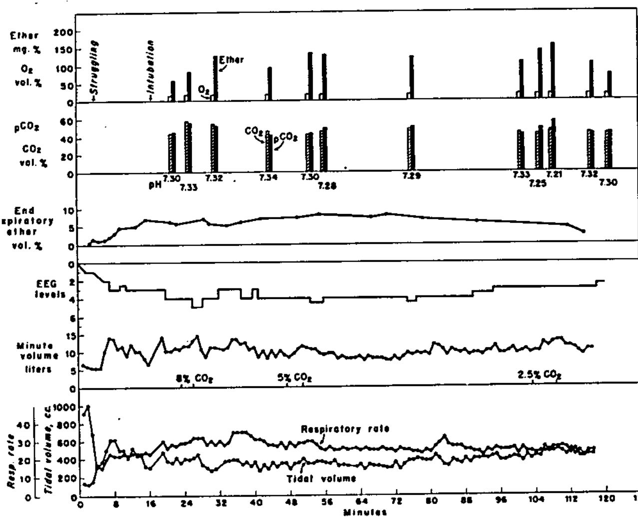

FIG. 5. The top row of bar graphs represents arterial blood levels for oxygen and ether. The second row of bar graphs represents arterial blood levels of carbon dioxide in terms of volumes per cent and carbon dioxide tension. The numerals underneath the lower row of bar graphs represent arterial pH. The next lower variable is the end expiratory ether concentration. Underneath this is indicated the electro-encephalographic level of anesthesia. The lower three lines represent ventilation rate, respiratory rate, and tidal volume respectively.

mediately above the graph of electro-encephalographic levels will be seen the end expiratory concentration of ether expressed in volumes per cent. The bar graphs appearing at the top of the figure represent the arterial blood gas analysis on samples drawn at the times indicated. The lower row of bars represents the carbon dioxide content of the arterial blood in volumes per cent (the shaded bar). The cross-hatched bar associated with each of these determinations represents the carbon dioxide tension in millimeters of mercury determined by calculation from the carbon dioxide content and the pH of the same sample (Henderson-Hasselbalch equation). The pH for each of the samples is indicated numerically beneath each of the pair of bars. The top row of bars represents a determination of the ether content and oxygen content of each of the arterial samples. The unshaded one indicates oxygen in volumes per cent. The black bar represents the arterial content of ether in milligrams per 100 cc. Certain clinical notes deemed to be of significance in this study are placed in the proper time relation-

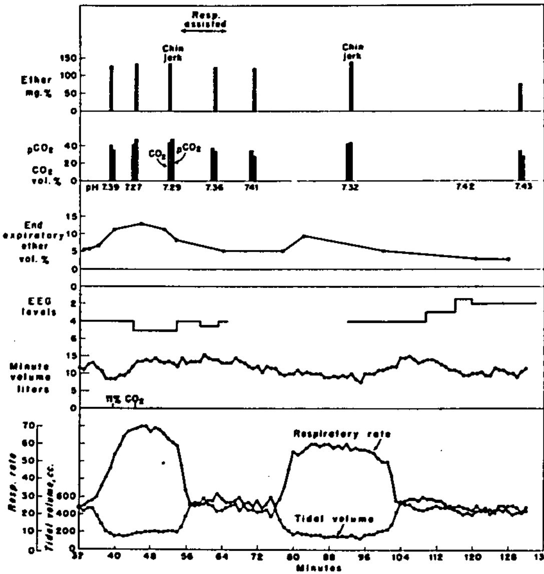

FIG. 6. The top row of bar graphs represents arterial blood level for ether. The second row of bar graphs represents arterial blood levels of carbon dioxide in terms of volumes per cent and carbon dioxide tension. Underneath the lower row of bar graphs the arterial pH is indicated. The next lower variable is the end expiratory ether concentration. Underneath this is given the electro-encephalographic level of anesthesia. The lower three lines represent ventilation rate, respiratory rate, and tidal volume, respectively.

ship along the top of the figure. This presentation of the data for each of the cases studied greatly facilitated analysis.

RESPIRATORY PATTERNS DURING ANESTHESIA ALONE

Ventilation Rate (Minute Volume of Respiration).—The mean ventilation rates and the ranges, the ages of the subjects and the premedication are presented in table 1. The mean of the means for the

13 cases was 9.1 liters. The range of the means was 6.7 to 11.5 liters. The values for all observations of the minute volumes ranged from 2 liters to 15.5 liters. The ventilation rates were consistently higher than those usually accepted for the normal resting state (5 to 7 liters). In some instances these elevated ventilation rates existed in the presence of a pH higher than 7.40 and carbon dioxide tensions below 30 mm. of mercury (fig. 6). This strongly suggests that ether acts as a primary respiratory stimulant. The average minute volume as illustrated in figure 5 was 9.6 liters. The marked variation in the first minutes of anesthesia from a low value of 5.5 to a high of 14 liters per minute is to be noted. These variations are characteristic of the induction period and depend upon many factors not subjected to analysis in this paper.

Partial obstruction of the airway accounts for certain episodes of diminished ventilation rate during the crucial induction period. When the partial obstruction is relieved the ventilation rate then rises to a level much higher than the normal. In 1 of the cases in this series in which no endotracheal tube was used an insidious type of partial obstruction developed several times during the course of anesthesia. When this obstruction was relieved the patient had a marked compensatory increase in the ventilation rate.

In figure 5 there is indicated a period of forty minutes of uncomplicated anesthesia from the sixtieth to the hundredth minute. The ventilation rate varies from 7.5 to 12 liters per minute. As one ascends from electro-encephalographic level 4 to level 3 there is a small but definite increase in the ventilation rate. The elevation at the eighty-first minute is unexplained and may represent a reflex response to surgical manipulation.

Respiratory Rate.—There is considerable variation in the respiratory rate from patient to patient under ether anesthesia. In the patients studied there was a consistent rise in rate through the induction period. With the onset of surgical anesthesia the rate rose to 30 or more per minute although it often did not remain this high throughout anesthesia. In the deeper levels of anesthesia the rate was commonly seen to be very high. Figure 6 illustrates this point. The first elevation in rate occurs in levels 4 and 5 and the second elevation occurs in level 4. In both of these periods of rapid respiration the arterial ether concentrations were at a higher level than seen at other times during the procedure.

Tidal Volume.—This was calculated from the simultaneous observations of ventilation rate and respiratory rate. The ventilation rate in cubic centimeters per minute divided by the respiratory rate equals the tidal volume. At the beginning of induction, tidal volume is consistently high ranging around 500 cc. In the first few minutes of induction it falls to about half the value observed in the beginning of induction. From this point throughout the remainder of the anesthesia the tidal volume consistently bears a reciprocal relationship to the respiratory rate. This observation is well illustrated in figure 6. Thus, when the respiratory rate rises to values in excess of 50 per minute, the tidal volume often approaches that of the assumed anatomic dead space. It might be thought, on a basis of this fact, that the actual alveolar ventilation becomes nil. This does not appear to be the case when one considers the observations made of the carbon dioxide tension in the arterial blood during these periods. In figure 6, during the interval from the eightieth to the ninety-fifth minute the tidal volume does not exceed 200 cc. which is the approximate anatomic dead space plus the dead space of the apparatus used. Yet an arterial sample drawn at the end of the fifteen-minute period revealed a carbon dioxide tension of only 44 mm. of mercury and a pH of 7.32. It must be concluded from these observations that the actual alveolar ventilation is considerably in excess of that calculated on the basis of the assumed anatomic space. Similar observations were made repeatedly throughout this series of studies.

RESPIRATORY PATTERNS IN RESPONSE TO CARBON DIOXIDE STIMULATION DURING ANESTHESIA

During this study 13 patients were given carbon dioxide-enriched inspiratory gas mixtures a total of 36 times for periods varying from two to five minutes. During these intervals the carbon dioxide absorber was removed from the circuit. These observations were made in various electro-encephalographic levels of anesthesia.

Ventilation Rate.—The response of ventilation rate to this stimulation is reported in terms of per cent change. The percentage is calculated as the difference in observed ventilation rate between that recorded immediately prior to carbon dioxide administration and the highest ventilation rate occurring during or immediately following the administration of carbon dioxide. In the 36 observations made in this manner the mean per cent increase in ventilation rate was 45 with a range from 4 to 86. These observations were made on occasions when the patients were in electro-encephalographic levels of anesthesia 3, 4, 5 and 6. No correlation could be made between the extent of increase of ventilation rate and the electro-encephalographic level of anesthesia except that in the only 2 observations made in level 6 an initial decrease in ventilation rate with the addition of carbon dioxide to the inspiratory gas mixture was observed. In each of these 2 instances the ventilation rate subsequently increased coincidentally with a change in electro-encephalographic levels of anesthesia from 6 to 5. In all instances in which arterial gas analyses were made during electro-encephalographic levels of anesthesia down to and including level 5 the observed increase in minute-volume respiration appeared to be effective in coping with the temporary increase in carbon dioxide tension and decrease in pH resulting therefrom. Thus, it may be seen in figure 5 that after administration of carbon dioxide from the twenty-third to the twentysixth minute the arterial carbon dioxide tension changed from 45 to 55 mm. of mercury while the ventilation rate was increasing 38 per cent. The arterial gas analysis revealed a slow return from the peak carbon dioxide tension reported to 41 mm. of mercury at the forty-fourth minute.

Again as shown in figure 5, carbon dioxide was added to the inspiratory gas mixture from the hundred and fourth to the hundred and ninth minute. During this period of stimulation the carbon dioxide tension rose from 42 to 55 mm. of mercury while the ventilation rate increased 37 per cent. During this period the electro-encephalographic tracing remained in level 3. By the end of the hundred and seventeenth minute the carbon dioxide tension had returned to 42 mm. of mercury in the arterial blood. It may be of interest to note that the pH of the arterial blood immediately prior to the stimulation was 7.33. At the height of stimulation (seven minutes later) it was 7.21 and by the end of the hundred and seventeenth minute it was 7.32. On a basis of all of these observations it appears that the respiratory center is active and sensitive to carbon dioxide stimulation to the extent that there is effective respiratory compensation to changes in the patient's acid-base status induced by the added carbon dioxide. It does appear, however, that there is a significant reduction in the sensitivity of the center to carbon dioxide stimulation in the sixth electro-encephalographic level of anesthesia.

Respiratory Rate and Tidal Volume.—The increase in the ventilation rate reported above was the result of an increase in both tidal volume and respiratory rate in 23 of the 36 observations. In regard to the tidal volume, there was an increase 33 times, decrease 1 time and no change 2 times. The rate showed an increase 26 times, a decrease 6 times and no change 4 times. These observations indicate that both tidal volume and respiratory rate play an important role in the increase of the ventilation rate that occurs with carbon dioxide stimulation.

It may be of interest to note that the clinical phenomenon designated as "chin jerk" was observed 3 times when simultaneous arterial blood gas analyses were done. Two of these occasions are seen in figure 6. In both instances illustrated here the carbon dioxide tension was near the highest point reached during the anesthesia but not at a level to be considered excessive. The arterial blood pH on 1 occasion was 7.29 and on the other 7.32. It may also be of interest to note that both of these occasions were marked by arterial ether concentrations which were the highest observed during this anesthesia. The other observation of chin jerk was made at a carbon dioxide tension of 36 and a pH of 7.04.

SUMMARY

1. A method has been described for correlating the following variables during surgical anesthesia: ventilation rate, respiratory rate,

tidal volume, respiratory gas analysis, electro-encephalographic level of anesthesia, and blood gas determinations including oxygen, ether, carbon dioxide content, carbon dioxide tension and pH.

2. Changes in the ventilation rate, the respiratory rate and tidal volume in 13 patients undergoing nitrous oxide-oxygen-ether anesthesia for major surgical procedures are considered. It was observed that (a) the mean ventilation rate was 9.1 liters per minute with a range of the means from 6.7 to 11.5 liters per minute; (b) the respiratory rate consistently increased during the induction of anesthesia and frequently remained above 30 during maintenance. Rates above 50 were commonly seen in electro-encephalographic levels 4, 5 and 6; and (c) the tidal volume decreased during induction, and during maintenance bore a reciprocal relation to the respiratory rate. Values for the tidal volume during deep anesthesia may be less than the anatomic dead space. This may occur in the absence of an excess carbon dioxide tension in the arterial blood indicating that alveolar ventilation still takes place despite the low tidal volume.

Carbon dioxide stimulation was performed a total of 36 times. It was observed that (a) the mean increase in ventilation rate was 45 per cent; (b) this increase in ventilation rate was dependent upon an increase in both tidal volume and respiratory rate in 23 of the 36 observations; and (c) in electro-encephalographic levels of anesthesia 3, 4 and 5, the increase in carbon dioxide tension and decrease in pH of the arterial blood were partially compensated for by increase in the ventilation rate thus indicating that the respiratory center was still sensitive to carbon dioxide in these levels of anesthesia.

Chin jerk was observed 3 times in this study. Twice it was accompanied by an elevated arterial carbon dioxide tension and once it was not.

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