RESPIRATORY STUDIES DURING ANESTHESIA WITH ETHER AND WITH PENTOTHAL SODIUM *

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MUCH attention has been devoted to consideration of the effect of anesthetic agents on respiratory function. Recently this attention has been represented in great part by investigations concerning elimination of carbon dioxide and alterations in acid-base equilibrium (1–8). As a result of these studies important advances have been made in our understanding of these physiologic functions which must accrue to the benefit of our patients to come. However, much work remains to be done. Marked differences of opinion still must be resolved. The resolution of these differences and settlement of controversy can be achieved only after the thoughtful examination of more data than are now available.

PURPOSE

The primary purpose of this report is to contribute in small measure to the information now rapidly accumulating, and on which alone conclusions may some day be drawn. Secondarily, it is our hope that some of the data to be presented may be of value to the reader in clarifying his concept of the physiologic mechanisms considered.

We propose to set forth a summary of observations made on patients undergoing uncomplicated surgical procedures. In all except 1 case these procedures did not involve the thorax and were carried out with the patient in the supine position. These observations include continuous measurement of the expiratory ventilation rate and the depth of anesthesia as indicated by changes in the electro-encephalographic pattern. Coincident with the observations mentioned are intermittent analyses of samples of arterial blood for total carbon dioxide content, total oxygen content and pH. From these data the carbon dioxide tensions of the samples of blood were calculated and are recorded in the tables. Furthermore changes in the fixed acid content of the arterial blood are reflected in calculations of the buffer base. The effect

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of administration of carbon dioxide to the patient on the observations just outlined was then studied.

METHODS

The meaning of an investigation of this kind depends heavily on the accuracy of analytical methods used. For example, determination of carbon dioxide or oxygen content of the blood in the presence of ether vapor is a procedure subject to many errors, the results of which are

TABLE 1

CASE 1: MAN, 43 YEARS OLD, WEIGHING 113 POUNDS AND HAVING 12.4 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Extensive right thoracolumbar sympathectomy.
Anesthesia: Nitrous oxide, oxygen and ether induction. Maintenance with ether and oxygen by machine and for some periods ether and room air (semi-open method).

Time after Start of Study, min.	Arterial blood: Content, vol. per cent O_2	Arterial blood: Content, vol. per cent CO_2	Arterial blood: pH	Arterial blood: pCO_2, mm. Hg	Arterial blood: Buffer, Base, mEq. per liter	EEG Level of Anesthesia	Ventilation Rate, liters per min.	Remarks
3	16.7	55.4	7.49	38.0	50.2			100 per cent O_2 by machine
15	16.0	56.4	7.39	48.0	46.7			Morphine sulfate ¼ grain; pentothal sodium 125 mg. I. V.
15.5	16.0	55.9	7.44	43.5	47.6			
16.0	14.6	52.8	7.45	40.0	45.7			
16.5	16.8	56.0	7.44	44.0	48.5			O_2 continued by machine
17.0	20.0	55.0	7.42	45.0	50.7			
17.5	16.6	53.4	7.41	44.5	46.5			
26.5	21.7	41.9	7.49	29.0	50.0	4		N_2O, O_2 and ether at 18 min.
44	18.8	42.6	7.48	30.0	46.9	3–4		Ether and O_2 by machine
58	19.0	40.0	7.51	27.0	47.1	4		
67	14.4	33.1	7.47	23.5	42.9			Open drop ether, room air
72.5	17.0	30.9	7.47	22.0	42.0			Drop ether and O_2 under mask
96.5	19.4	44.8	7.49	32.5	47.0			
104.5	14.6	44.8	7.47	32.5	47.0			Incision made. Turned on left side
116.5	17.9	41.7	7.50	28.0	44.8			Ether and O_2 by machine .
131.5	17.5	44.3	7.50	30.0	45.6			
143.5	16.2	50.6	7.49	35.5	46.7			Positive pressure, pleura open
161	16.8	45.2	7.50	31.0	45.3			Positive pressure, pleura closed
169	15.7	49.6	7.47	36.0	46.5			Supine; room air
Mean	17.4*	42.4*	7.49*	29.8*	46.0*		11.5†	

* Represents observations after the induction of ether anesthesia eighteen minutes after start of study.
† Observations for 49 minutes only.

reliable only when the analysis has been done by an expert technician well trained in this particular application of the Van Slyke apparatus. So much in the calculated data depends on the estimate of the blood pH, that the method used for this determination should be accurate within narrow limits. The final appraisal of the meaning of the data must be made in the light of a precise estimate of the depth of anesthesia.

Gas Analysis.—The analyses of blood for gas in our study were made on fresh heparinized samples of arterial blood drawn anaerobically and transported to the laboratory in sealed, iced containers. The analytic technic, which was developed in this laboratory, involves the use of a mass spectrometer and will be described elsewhere (5). The accuracy of the method has been demonstrated in calibration studies to be plus or minus 2.5 per cent of the amount of carbon dioxide present. The presence of ether vapor or nitrous oxide has little influence on the result obtained because of the basic nature of mass spectrometric analytic methods. The accuracy of the method of oxygen

TABLE 2

CASE 2: MAN, 67 YEARS OLD, HAVING 11.9 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Choledochoduodenostomy.
Premedication: ⅙ grain of morphine sulfate and 1/150 grain of atropine sulfate.
Anesthesia: Nitrous oxide, oxygen and ether induction. Maintenance with ether and oxygen. 100 per cent nitrous oxide administered between 108 and 114 minutes.

Time of Anesthesia, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
23.5	14.4	49.6	7.39	42	44.2	?	10.0	
37	13.9	50.8	7.36	46	44.0	4	7.0	
42.5	14.4	48.6	7.32	47	43.2	3–4	13.0	CO_2
47.5	15.7	49.3	7.33	47	41.8	?	10.5	
59.5	14.9	44.9	7.40	37	40.8	4	9.5	
76	17.5	49.0	7.35	44.5	43.7	?	10.5	CO_2
81	13.3	48.4	7.35	44.0	39.6	?	9.5	
95	13.8	48.3	7.31	48	39.4	4	6.5	
100.5	15.7	52.2	7.29	54.5	42.0	5	10.0	CO_2
108	13.5	51.0	7.29	53	39.6	4–5	7.5	
114	11.4*	52.9	7.28	57	42.1	5	6.0	N_2O
114.8	9.5*	54.2	7.24	63	41.1	5	6.0	N_2O
120.5	14.7	46.7	7.28	50	40.5	4	8.5	
Mean	14.7*	49.6†	7.32†	48.7†	41.7		8.6‡	

* Periods of induced hypoxia not included in mean.
† Periods of carbon dioxide administration not included.
‡ Observations during entire anesthetic period, except during administration of carbon dioxide and induced hypoxia, included.

analysis employed has been demonstrated to be within plus or minus 5 per cent of the amount present.

pH Determination.—A Cambridge research model pH meter with a glass electrode designed for studies of blood and having a capacity of 0.8 cc. was used. This instrument was standardized before each use on a standard buffer solution having a pH 7.00. The meter can be read with accuracy to 0.01 pH. All determinations were made after the

TABLE 3

CASE 3: MAN, 44 YEARS OLD, WEIGHING 151 POUNDS AND HAVING 13.4 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Premedication: 1½ grains of pentobarbital sodium, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate.

Anesthesia: Nitrous oxide, oxygen and ether induction. Maintenance with ether and oxygen. 100 per cent nitrous oxide administered between 143 and 150 minutes.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
22	20.0	40.9	7.42	33	44.5	4	15.0	
26.5	19.1	45.2	7.36	42	43.9	4	15.0	CO_2
38.5	19.8	42.1	7.38	37.5	43.8	3–4	16.5	
43.5	20.1	37.2	7.37	33	42.0	3	16.5	
47.5	19.5	42.2	7.31	43	41.6	3	17.0	CO_2
58	20.4	44.0	7.34	42	43.9	3	14.5	
80.5	20.1	46.4	7.27	52	42.7	3	16.0	
99	20.0	48.6	7.25	56	42.9	3	13.0	
106	19.9	47.1	7.20	61	40.7	3	14.0	CO_2 absorber off
119	20.2	51.0	7.20	66	41.4	3–4	11.0	
142.5	20.0	46.6	7.25	54	42.0	3–4	15.5	
150	16.3*	53.0	7.10	87	39.1	5	3.5	100 per cent N_2O (143–150 min.)
157	20.6	57.6	7.03	106	38.9	4–5	3.0	
161	18.3	53.9	7.05	98	38.2	2–3	4.0	
Mean	19.8*	47.4†	7.24†	60.4†	41.8		14.2‡	

* Period of induced hypoxia not included in mean.

† Does not include periods of administration of carbon dioxide.

‡ Observations during entire period of anesthesia, except during administration of carbon dioxide and induced hypoxia, included.

blood came to room temperature, and corrections were made for the temperature. The determinations were made within a period of time demonstrated by calibration studies to have produced no significant change in the pH of the blood as freshly drawn.

Ventilation Rate.—This was measured by directing the patient's expired air through a dry flow gas meter equipped to record continuously by signal marker every 500 cc. of gas moved.

Depth of Anesthesia.—A single-channel recording electro-encephalograph with bipolar fronto-occipital needle electrodes attached to the patient's scalp provided a continuous record of electro-encephalographic patterns in each case. From these patterns an estimate of the depth of anesthesia was made and related to other observations. The classification used for the etherized patients was that of Courtin, Bickford and Faulconer (10). For patients undergoing pentothal sodium anesthesia the classification of Kiersey, Bickford and Faulconer (11) was used.

TABLE 4

CASE 4: MAN, 68 YEARS OLD, WEIGHING 146 POUNDS AND HAVING 12.2 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Anterior sigmoid resection.
Premedication: ¾ grain of pentobarbital sodium, ⅙ grain of morphine sulfate and 1/150 grain of atropine sulfate.
Anesthesia: Nitrous oxide, oxygen and ether induction. Maintenance with ether and oxygen.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
22	15.1	43.5	7.30	45	40.3	3	11.0	
25.5	16.0	57.6	7.33	55	47.0	3–4	12.0	CO_2
31.5	16.8	52.6	7.32	51	44.8	5	10.5	
44	17.0	44.2	7.34	41	41.9	3–4	10.0	
49.5	16.9	41.1	7.31	41	39.8	4	10.0	CO_2
51.0	18.0	42.1	7.30	43	39.8	4	11.5	CO_2
56.5	17.0	45.4	7.28	48.5	40.7	4	9.5	
73.5	17.4	47.6	7.29	50	41.8	4	8.0	
101	18.0	43.4	7.33	41.5	41.2	4	10.0	
106.5	17.8	42.5	7.25	48	38.4	4	12.0	CO_2
108.5	19.2	45.3	7.21	55	38.6	4	12.5	CO_2
117	17.7	42.9	7.32	42	40.8	3	10.5	
121	16.0	41.9	7.30	43	39.7	3	—	Room air
Mean	17.2*	45.2†	7.31†	45.3†	41.1		9.6‡	

* Does not include observation during breathing of room air.
† Does not include periods of administration of carbon dioxide.
‡ Observations during entire anesthetic period, except during administration of carbon dioxide, included.

Carbon Dioxide Tension.—The carbon dioxide tension (pCO_2) was calculated from the carbon dioxide content of whole blood, and the pH and oxygen content of the blood sample by the method of Sendroy and Van Slyke (12) and the application of the Henderson-Hasselbalch equation.

Buffer Base.—An effective means of determining the direction and manner of change of the acid-base equilibrium is offered by calculating the value for buffer base in whole blood (13). Buffer base is repre-

sented by the sum of the cations bound by the protein and bicarbonate anions (fig. 1). Although the proportion of these may vary as the pH of the blood changes, this sum will remain the same in the absence of any gain or loss of acid or base in the blood. Thus, any variation in blood pH in the presence of a constant value for buffer base represents respiratory acidosis or alkalosis as the case may be. This value

TABLE 5

CASE 5: MAN, 35 YEARS OLD, WEIGHING 116 POUNDS AND HAVING 14.3 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Cholecystectomy, subtotal pancreatectomy and splenectomy.
Premedication: 1½ grains of pentobarbital sodium by mouth, ½ grain of morphine sulfate and 1/150 grain of atropine sulfate.
Anesthesia: Nitrous oxide, oxygen and ether induction. Maintenance with ether and oxygen.

Time, min.	Arterial Blood				EEG Level	Ventilation Rate, liters per min.	Remarks
	CO_2 Content, vol. per 100 cc.	pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
21	42.1	7.41	35.5	46.0	4	14.5	CO_2
24	45.1	7.37	42	46.0	4	11.0	CO_2
39	39.9	7.39	34.5	44.6	4	8.5	
44.5	41.6	7.27	47	42.7	5	12.5	CO_2
52.5	43.3	7.29	47	42.9	5	13.0	
62.0	36.8	7.36	33.5	42.3	4–5	14.0	Assisted respiration 8 min.
71	34.1	7.41	28	42.6	?	11.5	
94.5	44.3	7.32	44.5	44.2	?	7.5	
131	33.5	7.43	27	43.0	2	9.0	
135.5	36.0	7.37	32.5	42.2	4	12.0	100 per cent N_2O
136.5	37.6	7.37	34	42.9	4	12.0	
147	36.7	7.42	30	44.0	3	9.5	
Mean	38.2*	7.38*	34.7*	43.6		11.1†	

* Does not include periods of administration of carbon dioxide and assisted respiration.
† Observations during entire anesthetic period, except during administration of carbon dioxide, assisted respiration and induced hypoxia, included.

may be determined from a knowledge of the concentration of reduced hemoglobin, oxyhemoglobin and bicarbonate in whole blood when the pH is known. Since plasma protein plays such a small role as a buffer mechanism, it was assumed to be constant in this series.

CASES STUDIED

Ether.—Six adult patients (cases 1 to 6) were studied. All 6 were in good general physical condition and were undergoing anesthesia with ether and oxygen. The anesthesia in 5 cases was for abdominal procedures; in the other case (case 1) extrapleural thoracolumbar sympathectomy was performed. The pleura was inadvertently opened near the termination of the procedure. Premedication was used in the

TABLE 6

CASE 6: MAN, 61 YEARS OLD, WEIGHING 106 POUNDS AND HAVING 15.9 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Cholecystectomy.

Premedication: 1½ grains of pentobarbital sodium by mouth, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate.

Anesthesia: Nitrous oxide, oxygen and ether induction. Maintenance with ether and oxygen.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
36	22.7	47.6	7.34	47.3	48.8	4	7.0	
48.5	22.2	43.9	7.35	42	45.9	4	7.0	
60.0	22.2	46.3	7.34	45	46.6	4	5.5	
63	22.3	47.1	7.29	51	45.2	4	9.5	CO_2
67.5	22.6	48.5	7.21	63	43.3	4	13.0	CO_2
72.8	23.2	49.4	7.26	58	46.1	4	6.5	
79	22.6	41.6	7.29	46	43.3	4	7.5	
89.5	23.8	43.7	7.34	43	46.9	1–2	7.5	
Mean	22.7	45.4*	7.32*	46.9*	45.8		7.1†	

* Periods of administration of carbon dioxide not included.

† Observations during entire anesthetic period, except during administration of carbon dioxide, included.

TABLE 7

CASE 7: WOMAN, 47 YEARS OLD, WEIGHING 175 POUNDS AND HAVING 11.2 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Stripping great saphenous veins, bilateral.

Premedication: 1½ grains of pentobarbital sodium by mouth, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate intravenously 5 minutes before induction.

Anesthesia: Pentothal sodium by intermittent intravenous injection and 100 per cent oxygen. Total pentothal given: 2,375 mg.

Time, min.	Content in Arterial Blood, vol. per 100 cc.		EEG Level	Ventilation Rate, liters per min.	Remarks
	O_2	CO_2			
29.5	14.7	47.9	2	5.5	
37	15.5	47.4	2	6.0	
45	15.6	48.4	2–3	5.0	
49.5	15.3	47.3	2	5.5	
54	15.5	51.5*	2–3	12.0	5 per cent CO_2
55.5	15.5	51.8*	2	12.0	
60.5	15.3	47.2	2	7.5	
75	16.5	48.5	2	7.0	
94	15.5	45.1	2	6.5	
97.5	15.5	52.5*	2	11.5	5 per cent CO_2
101.5	15.9	49.2*	2	14.5	CO_2 absorber off
108	16.9	47.1	2	8.5	
113.5	16.3	47.5	2	7.0	
Mean	15.7	47.4*		6.2†	

* Periods of administration or accumulation of carbon dioxide not included.

† Observations during entire anesthetic period, except during administration or accumulation of carbon dioxide, included.

usual manner consisting of small doses of barbiturate, morphine and atropine. These patients were permitted to inhale substantial concentrations of carbon dioxide intermittently and for short intervals on eleven occasions.

Pentothal Sodium.—Seven adult patients (cases 7 to 13) were studied. All were in good general physical condition and were anesthetized with pentothal sodium and oxygen for surgical stripping of varicose veins in the lower extremities. Premedication consisted of

TABLE 8

CASE 8: WOMAN, 59 YEARS OLD, WEIGHING 168 POUNDS AND HAVING 12.4 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Stripping of great saphenous veins on both sides.

Premedication: 1½ grains of pentobarbital sodium by mouth, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate intravenously 5 minutes before induction.

Anesthesia: 2½ per cent solution of pentothal sodium by intermittent intravenous injection and 100 per cent oxygen. Total pentothal given: 2,850 mg.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
20	17.9	50.5	7.43	39	46.8	2–3	7.0	
36	17.8	50.4	7.38	43.5	45.4	2–3	5.5	
39	16.4	50.1	7.34	46.5	43.2	2–3	5.5	
40.5	16.1	50.4	7.35	46	43.0	2–3	7.0	
42	17.6	49.5	7.38	44	45.0	2–3	10.0	5 per cent CO_2
44	17.4	51.4	7.33	49	44.2	2–3	11.0	
46.5	18.6	53.4	7.35	48.5	46.6	2–3	11.0	
48	18.0	49.7	7.37	43.5	45.5	2–3	10.5	
52	17.9	50.6	7.41	41.5	46.6	2–3	6.5	
68.5	17.6	53.6	7.35	48.5	45.9	5	4.5	
73	17.7	56.4	7.31	56	46.3	4–5	4.0	
75.5	16.7	56.2	7.31	56	45.3	5	5.5	5 per cent CO_2
77	18.5	54.7	7.36	49.5	47.5	5	6.0	
89	17.9	54.0	7.40	44.5	47.7	4	5.5	
Mean	17.6	52.1*	7.38*	45.2*	45.6		4.9†	

* Periods of administration of carbon dioxide not included.

† Observations during entire anesthetic period, except during administration of carbon dioxide, included.

1½ grains (0.1 Gm.) of pentobarbital sodium, ⅙ grain (0.01 Gm.) of morphine and 1/150 grain (0.00043 Gm.) of atropine. A mixture of 5 per cent carbon dioxide in oxygen was administered sixteen times to the 7 patients for brief intervals.

RESULTS DURING ANESTHESIA WITH ETHER

The complete results during anesthesia with ether and with pentothal sodium as obtained by observation and calculation appear in

tables 1 through 14 and are illustrated graphically in part by figures 1 through 9.

Electro-encephalographic Levels.—The levels of anesthesia, as estimated by the electro-encephalograph ranged from 1 through 5. Levels 3, 4 and 5 represent light, moderate and deep surgical levels of ether anesthesia, respectively (10).

Ventilation Rate.—The average of the mean ventilation rates of patients in this series was 9.6 liters per minute with a range of 7.1 to

TABLE 9

CASE 9: WOMAN, 67 YEARS OLD, WEIGHING 154 POUNDS AND HAVING 12.8 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Stripping of great saphenous veins on both sides.

Premedication: 1½ grains of pentobarbital sodium by mouth, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate intravenously 5 minutes before induction.

Anesthesia: 1 per cent solution of pentothal sodium by continuous drip intravenously and 100 per cent oxygen. Total pentothal given: 1,660 mg.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
41	19.8	71	7.36	66.5	55.5	2	3.5	
53	19.5	71.9	7.28	79	53.1	4	0.5	
60	18.9	73.5	7.25	85.5	52.3	5	0.5	
63	18.6	66*	7.31	68	50.7	5	3.5	Assisted respiration (60 to 63 minutes)
69	20.2	74.5	7.20	97	52.0	5	0.5	
81.5	19.8	77.3	7.14	112	50.8	4-5	1.0	
86	20.3	76.8*	7.19	101	52.7	3	2.5	5 per cent CO_2
87.5	19.5	74.6	7.20	96	51.7	3	2.5	
92.5	17.4	75.5	7.18	106	49.6	3-4	2.0	
111	18.7	70.0	7.12	111	46.4	4-5	3.0	
120	19.0	74.6	7.11	114	48.1	4	3.5	
123	19.0	74.7*	7.16	98	50.2	4	4.5	5 per cent CO_2
126	19.2	71.2	7.23	86	50.7	4	4.0	
129.5	19.4	68.1	7.24	81	50.1	4	4.5	
Mean	19.2	72.9*	7.21*	94.0*	51.0		2.1†	

* Periods of administration of carbon dioxide or assisted respiration not included.

† Observations during entire anesthetic period, except during administration of carbon dioxide, included.

11.5 liters per minute. The mean ventilation rate in case 3 (table 3) was 14.2 liters per minute; this was omitted from the calculated mean of all patients because of excessive rebreathing on the part of this patient due to faulty equipment. Individual observations during periods in which respiration was influenced by the administration of carbon dioxide or by purposely induced hypoxia were omitted. No correlation could be made between the mean ventilation rate or minute volume and the level of anesthesia observed.

Concentration of Hemoglobin and Oxygen.—Oxygen content as tabulated represents that physically dissolved in blood in addition to that in combination with hemoglobin. The mean oxygen content of the blood of each of 5 patients was as follows: 17.4, 14.7, 19.8, 17.2 and 22.7 volumes per cent. The preoperative concentrations of hemoglobin of the same patients were, respectively: 12.4, 11.9, 13.4, 12.2 and 15.9 Gm. per 100 cc. This indicates that the oxygen saturation of the hemoglobin was nearly complete in all instances. High concentrations of oxygen were used at all times except when indicated in the tables. Therefore,

TABLE 10

CASE 10: WOMAN, 50 YEARS OLD, WEIGHING 153 POUNDS AND HAVING 11.9 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Stripping of right great saphenous vein.

Premedication: 1½ grains of pentobarbital sodium by mouth, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate intravenously 5 minutes before induction.

Anesthesia: 1 per cent solution of pentothal sodium by continuous intravenous drip and 100 per cent oxygen. Total pentothal given: 2.3 Gm.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
30	17.9	60.7	7.32	60	48.2	5	2	
36.5	17.9	59.8	7.31	61	47.6	4	4	
40.5	18.4	58.8	7.32	58	48.1	4	2.5	
43	18.4	62.7	7.27	70	48.2	4	1.5	5 per cent CO_2
45	18.2	62.8	7.27	70	48.1	5	3.5	
50	17.8	62.6	7.25	73	47.0	4	3.5	
53	18.1	60.7	7.22	74	45.6	4	3	5 per cent CO_2
54.5	18.7	62.6	7.23	75	47.0	4	3.5	
56.5	18.6	60.5	7.23	72.5	46.0	4	3	
59	17.8	59.3	7.29	63	46.8	4	3.5	
Mean	18.2	60.3*	7.29*	64.6*	47.3		3.2†	

* Periods of administration of carbon dioxide not included.

† Observations during entire anesthetic period, except during administration of carbon dioxide, included.

fluctuations in oxygen content are believed to represent variations in hemoconcentration.

Carbon Dioxide Content.—The average of the mean carbon dioxide contents of all cases was 44.7 volumes per cent with a range of 38.2 to 49.6 volumes per cent.

pH.—The average of the mean pH's in all cases except case 3 was 7.36 with a range of 7.31 to 7.49. The mean pH in case 3 was 7.24.

Carbon Dioxide Tension.—The average of the mean carbon dioxide tensions of all cases except case 3 was 41.1 mm. of mercury. The range of those included was 29.8 to 48.7 mm. of mercury. The mean tension in case 3 was 60.4 mm. of mercury.

Buffer Base.—The mean value for buffer base in each instance was 46.0, 41.7, 41.8, 41.1, 43.6 and 45.8 mEq. per liter. The values early in the period of anesthesia and at its termination were 46.5 and 46.5, 44.2 and 40.5, 44.5 and 38.2, 40.3 and 39.7, 46.0 and 44.0, and 48.8 and 46.9 mEq. per liter, respectively. The average decrease in buffer base was 2.4 mEq. per liter.

Administration of Carbon Dioxide and Anoxic Anoxia.—The administration of increased concentrations of carbon dioxide in the

TABLE 11

CASE 11: WOMAN, 46 YEARS OLD, WEIGHING 185 POUNDS AND HAVING 12.8 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Stripping of both great saphenous veins.

Premedication: 1½ grains of pentobarbital sodium by mouth, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate intravenously 5 minutes before induction.

Anesthesia: 1 per cent solution of pentothal sodium by continuous intravenous drip and 100 per cent oxygen. Total pentothal given: 3,830 mg.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
35.5	18.7	52.6	7.31	55.0	45.7	2-3	5.0	
50.5	20.4	53.6	7.35	50.5	48.4	2-3	7.5	
54	18.6	53.8	7.35	50.5	46.8	2-3	8.5	5 per cent CO_2
57	18.3	52.3	7.29	56.5	44.3	3	10.0	
64.5	17.9	51.8	7.33	51	44.7	4	7.0	
74.5	18.5	47.6	7.43	38	46.1	2-3	8.5	
78.5	18.9	52.1	7.35	48	46.2	2-3	8.5	5 per cent CO_2
81.5	19.6	51.0	7.28	56	44.4	2-3	12.0	
85.5	18.6	50.1	7.34	48	45.1	2-3	9.0	
100	19.5	48.4	7.38	43	46.2	2	7.5	
119	20.4	48.6	7.38	43	47.3	2	8.0	
123.5	19.8	50.0	7.30	52.5	44.6	2	10.0	5 per cent CO_2
126	19.5	50.8	7.32	51	45.4	2	11.5	
134.5	19.9	49.3	7.36	46	46.4	2	6.5	
Mean	19.2	50.2*	7.36*	46.8*	45.8		7.4†	

* Periods of administration of carbon dioxide not included.

† Observations during entire anesthetic period, except during administration of carbon dioxide, included.

inspired gas mixture resulted in a mean increase in the ventilation rate of 44.9 per cent with a range of 21 to 83 per cent. The per cent of increase was calculated from the amount by which the highest minute volume attained exceeded the minute volume immediately before the period of administration.

In case 3 the ventilation rate was increased during the greater part of the period of anesthesia (fig. 3). Analysis of the arterial blood revealed progressively increasing carbon dioxide tension, and analysis

of samples of inspired gas revealed concentrations of carbon dioxide of 2.4 and 1.2 per cent in the ninety-sixth minute and the 139th minute respectively. Administration of high concentrations of nitrous oxide in the inspired mixture from the 143rd to the 150th minute resulted in decreased arterial oxygen content and a precipitous decrease in ventilation rate. Carbon dioxide tension at this time increased to a level of 106 mm. of mercury.

TABLE 12

CASE 12: WOMAN, 57 YEARS OLD, WEIGHING 153 POUNDS AND HAVING 11.9 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Stripping of both great saphenous veins.

Premedication: 1½ grains of pentobarbital sodium by mouth, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate intravenously 5 minutes before induction.

Anesthesia: 2½ per cent solution of pentothal sodium by intermittent intravenous injection and 100 per cent oxygen. Total pentothal given: 1,950 mg.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
20	15.8	50.9	7.40	41.5	44.5	2		Room air
38.5	17.6	51.7	7.33	49.0	44.8	2-3	4.0	
41.5	19.5	54.9	7.28	61.0	46.0	2-3	7.0	5 per cent CO_2
44.0	19.1	59.1	7.27	66.5	47.2	2-3	7.5	
50.0	17.6	51.6	7.33	49	44.6	2	4.5	
61.0	17.3	50.6	7.32	49	43.7	2	5.5	
78.5	17.8	53.0	7.32	51.5	45.0	2-3	5.5	
82.5	18.3	52.6	7.31	52.5	45.1	2-3	8.0	5 per cent CO_2
85.0	17.7	51.7	7.29	54.5	43.6	2-3	8.0	
93.0	17.6	49.9	7.32	48	43.7	2-3	5.0	
Mean	18.1*	51.3†	7.34†	48.0†	44.8		4.6‡	

* Oxygen content during breathing of room air not included.

† Periods of administration of carbon dioxide not included.

‡ Observations during entire anesthetic period, except during administration of carbon dioxide, included.

RESULTS DURING ANESTHESIA WITH PENTOTHAL SODIUM

Electro-encephalographic Levels.—Patterns of electro-encephalographic tracings representing levels 1 through 5 were observed during pentothal sodium anesthesia. Level 2 has been established by Kiersey (11) as providing sufficient anesthesia for a surgical procedure involving the stripping of varicose veins.

Ventilation Rate.—The average of the mean ventilation rates for all patients was 5.4 liters per minute (table 14) with a range of 2.1 to 9.1 liters per minute. The mean ventilation rate during level 2 anesthesia was 7.1, during level 3, 6.1, during level 4, 3.6, and during level 5, 2.2 liters per minute (fig. 8). In cases 9 and 10 levels of anesthesia were deeper than was actually required for the surgical procedure. If ob-

servations in these cases are not included in the calculation of the average of the mean ventilation rates, its value would be 6.4 liters per minute.

Concentration of Hemoglobin and Oxygen.—The concentrations of hemoglobin in each instance before anesthesia were 11.2, 12.4, 12.8, 11.9, 12.8, 11.9 and 13.9 Gm. per 100 cc. Corresponding mean oxygen contents were 15.7, 17.6, 19.2, 18.2, 19.2, 18.1 and 22.3 volumes per cent, respectively. High tensions of oxygen were available in the inspired gas mixture at all times, and the variations observed in the blood of each patient from time to time are assumed to be due to fluctuations in concentration of hemoglobin.

TABLE 13

CASE 13: MAN, 32 YEARS OLD, WEIGHING 196 POUNDS AND HAVING 13.9 GM. OF HEMOGLOBIN PER 100 CC. OF BLOOD

Operation: Stripping of both great saphenous veins.

Premedication: 1½ grains of pentobarbital sodium by mouth, ¼ grain of morphine sulfate and 1/150 grain of atropine sulfate intravenously 5 minutes before induction.

Anesthesia: 2½ per cent solution of pentothal sodium by intermittent intravenous injection and 100 per cent oxygen. Total pentothal given: 3,125 mg.

Time, min.	Arterial Blood					EEG Level	Ventilation Rate, liters per min.	Remarks
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter			
	O_2	CO_2						
15	21.0	44.9	7.37	41	44.1	2	8.0	
22	21.6	48.7	7.34	47	47.1	2	8.0	
26.5	21.6	49.3	7.34	47.5	47.3	2	9.5	5 per cent CO_2
30.5	22.8	48.6	7.33	48	47.5	2	9.5	
48	22.4	46.6	7.37	43	47.9	1–2	12.5	
52	22.8	46.4	7.37	43	48.0	1–2	15.5	} 5 per cent CO_2
54	21.9	46.8	7.36	44	47.0	1–2	17.0	
60.5	22.2	46.4	7.39	41	48.3	1–2	9.0	
74	23.0	48.1	7.33	47.5	48.6	2–3	9.5	
77.5	23.5	51.4	7.30	56	48.3	2–3	10.0	} 5 per cent CO_2
80.5	21.4	50.0	7.30	54	46.4	2–3–4	15.0	
87.5		49.4	7.34	48	47.8	3	8.5	
101	18.9*	55.1	7.25	65	47.2	2	5.5	N_2O 75 per cent O_2 25 per cent
121.5	22.3	49.3	7.27	56.6	45.4	2	10.0	
132.5	22.4	48.1	7.32	49	46.9	2	9.0	
Mean	22.3*	48.5†	7.33†	48.6†	47.2		9.1‡	

* Observation during administration of nitrous oxide not included.

† Periods of administration of carbon dioxide not included.

‡ Observations during entire anesthetic period, except during administration of carbon dioxide, included.

Carbon Dioxide Content.—The average of the mean carbon dioxide contents of the arterial blood of all patients was 54.7 volumes per cent with a range of 47.4 to 72.9.

pH.—The average of the mean pH's was 7.32 with a range of 7.21 to 7.38.

Carbon Dioxide Tension.—The average of the mean carbon dioxide tensions as calculated was 57.9 mm. of mercury with a range of 45.2 to 94.0.

Buffer Base.—The mean value for buffer base as calculated for 5 patients was 45.6, 51.0, 47.3, 45.8, 44.8 and 47.2 mEq. per liter. Values early in the period of anesthesia and at its termination were 46.8 and

TABLE 14

MEAN OF THE DETERMINATION FOR ALL PATIENTS AND THE AVERAGE VALUES OF THE MEANS

Case	Arterial Blood					Ventilation Rate, liters per min.
	Content, vol. per 100 cc.		pH	pCO_2, mm. Hg	Buffer Base, mEq. per liter	
	O_2	CO_2				
			Ether			
1	17.4	42.4	7.49	29.8	46.0	11.5
2	14.7	49.6	7.32	48.7	41.7	8.6
3	19.8	47.4	7.24*	60.4*	41.8	14.2*
4	17.2	45.2	7.31	45.3	41.1	9.6
5		38.2	7.38	34.7	43.6	11.1
6	22.7	45.4	7.32	46.9	45.8	7.1
Average		44.7	7.36	41.1		9.6
			Pentothal sodium			
7	15.7	47.4				6.2
8	17.6	52.1	7.38	45.2	45.6	4.9
9	19.2	72.9	7.21	94.0	51.0	2.1
10	18.2	60.3	7.29	64.6	47.3	3.2
11	19.2	50.2	7.36	46.8	45.8	7.4
12	18.1	51.3	7.34	48.0	44.8	4.6
13	22.3	48.5	7.33	48.6	47.2	9.1
Average		54.7	7.32	57.9		5.4

* Not included in the average of the means because of excessive rebreathing on the part this patient due to faulty equipment.

47.7, 55.5 and 50.1, 48.2 and 46.8, 45.7 and 46.4, 44.5 and 43.7, and 44.1 and 46.9 mEq. per liter, respectively. The mean decrease in buffer base was 0.5 mEq. per liter which probably has little significance in view of the random increases and decreases.

Administration of Carbon Dioxide.—The administration of 5 per cent carbon dioxide in oxygen to the patients induced a mean increase in ventilation rate of 64.1 per cent. The range was 14.3 to 138 per cent. The mean increase during levels of anesthesia 2 and 3 was 71.8 per cent and during levels 4 and 5 was 40.6 per cent.

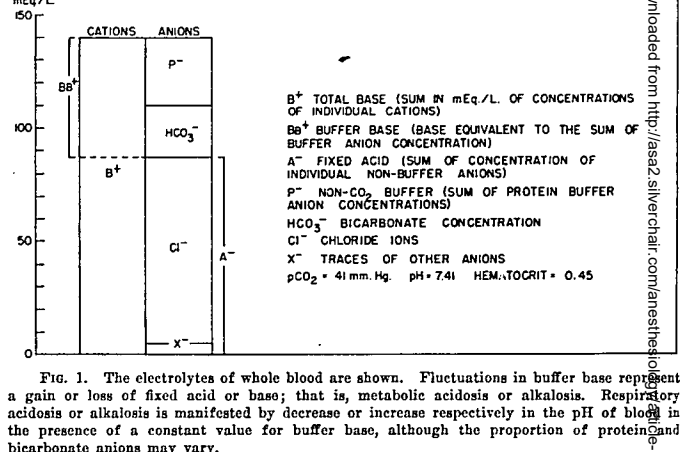

FIG. 1. The electrolytes of whole blood are shown. Fluctuations in buffer base represent a gain or loss of fixed acid or base; that is, metabolic acidosis or alkalosis. Respiratory acidosis or alkalosis is manifested by decrease or increase respectively in the pH of blood in the presence of a constant value for buffer base, although the proportion of protein and bicarbonate anions may vary.

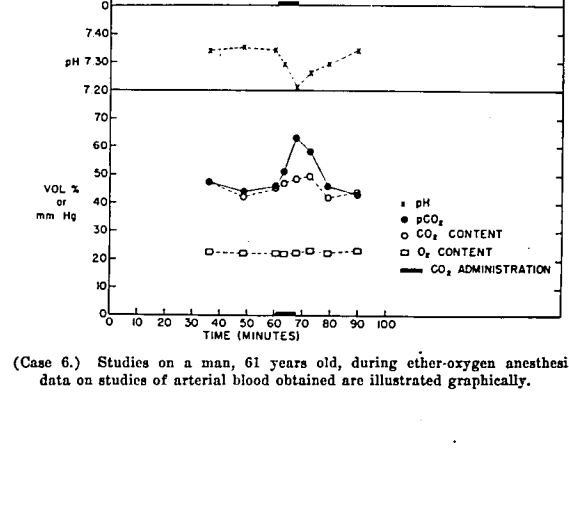

FIG. 2. (Case 6.) Studies on a man, 61 years old, during ether-oxygen anesthesia. The data on studies of arterial blood obtained are illustrated graphically.

COMMENT

Ventilation Rate.—The normal ventilation rate or minute volume of a conscious resting individual is near 8 liters per minute (14, 15). Observations on these patients indicate that ether has little or no depressant effect on minute volume of respiration. On the contrary, in certain instances, it apparently has a stimulating effect as evidenced

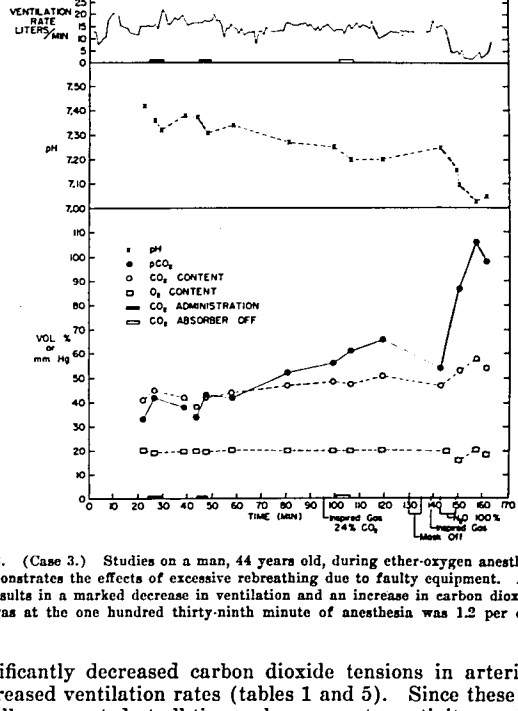

FIG. 3. (Case 3.) Studies on a man, 44 years old, during ether-oxygen anesthesia. This graph demonstrates the effects of excessive rebreathing due to faulty equipment. A period of hypoxia results in a marked decrease in ventilation and an increase in carbon dioxide tension. Inspired gas at the one hundred thirty-ninth minute of anesthesia was 1.2 per cent carbon dioxide.

by significantly decreased carbon dioxide tensions in arterial blood and increased ventilation rates (tables 1 and 5). Since these patients were well oxygenated at all times, chemoreceptor activity can be eliminated as a factor tending to increase respiratory activity. Several possibilities remain: ether may stimulate respiration by an irritant action on the mucous membranes of the respiratory tract; it may increase the sensitivity of various peripheral respiratory reflexes, or it

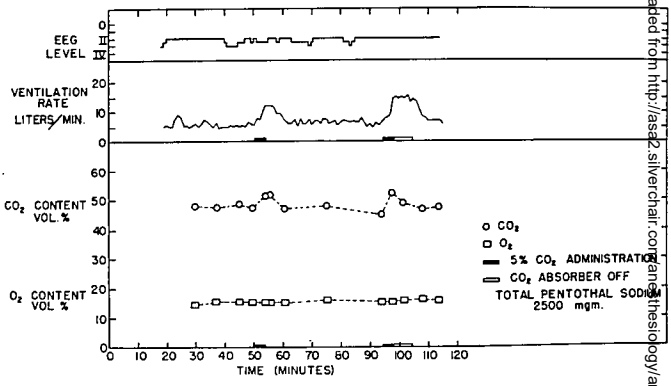

FIG. 4. (Case 7.) Studies on a woman, 47 years old, during pentothal sodium-oxygen anesthesia. The data obtained in this case illustrate the conspicuous increase in ventilation induced by the administration of 5 per cent carbon dioxide.

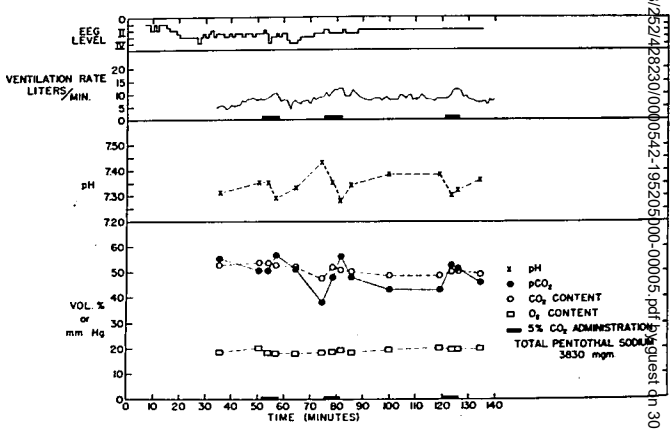

FIG. 5. (Case 11.) Studies on a woman, 46 years old, during pentothal sodium-oxygen anesthesia. Moderate increases in ventilation rate occurred with the administration of 5 per cent carbon dioxide. There was no progressive increase in carbon dioxide tension although the values are for the most part somewhat above the normal threshold of the respiratory center.

may lower the threshold of response of the respiratory center itself in some manner. However, an increase in effective ventilation was not observed in every case, and no conclusive statement to the effect that ether is a respiratory stimulant can be made from these studies.

Since the concentration of carbon dioxide administered to these patients was variable, it may be stated only that the respiratory center was capable of responding to the administration of substantial concentrations of carbon dioxide as evidenced by an increased ventilation rate in all levels of anesthesia observed.

The studies on patients undergoing anesthesia with pentothal sodium indicate strongly that this agent is a respiratory depressant,

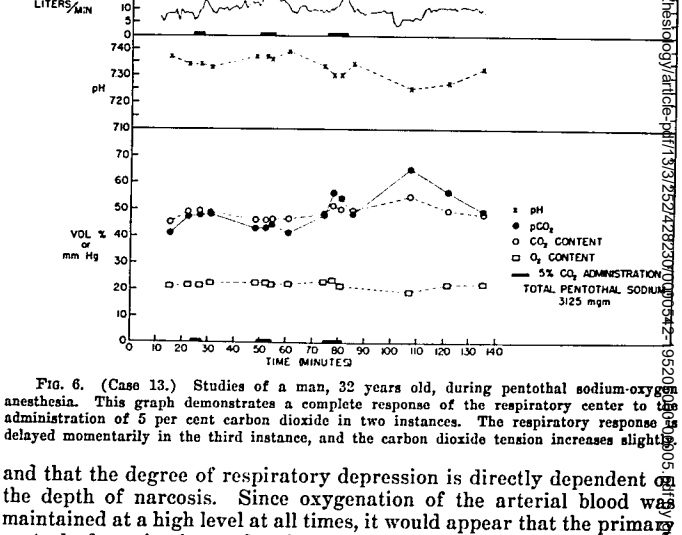

FIG. 6. (Case 13.) Studies of a man, 32 years old, during pentothal sodium-oxygen anesthesia. This graph demonstrates a complete response of the respiratory center to the administration of 5 per cent carbon dioxide in two instances. The respiratory response is delayed momentarily in the third instance, and the carbon dioxide tension increases slightly.

and that the degree of respiratory depression is directly dependent on the depth of narcosis. Since oxygenation of the arterial blood was maintained at a high level at all times, it would appear that the primary control of respiration under these circumstances is maintained by the respiratory center rather than by the chemoreceptors. Moreover, the respiratory center retained the ability to increase the ventilation rate in response to an increase in carbon dioxide tension, although this response was significantly greater in light levels than in deep levels. Figure 6 illustrates a complete response of the respiratory center to the administration of carbon dioxide. During the first two periods of administration of carbon dioxide, the carbon dioxide tension increased only slightly or not at all, indicating that ventilation had increased

sufficiently to maintain the tension at a constant level. The third administration of carbon dioxide to this patient, however, resulted in an increased tension. The respiratory response in this instance was delayed momentarily. This is due apparently to a decreased sensitivity of the center at a slightly deeper level of anesthesia, or possibly because of a cumulative depressant effect of pentothal sodium.

The ventilation rate, although markedly diminished in several instances, appeared to have little or no effect on the oxygen content of

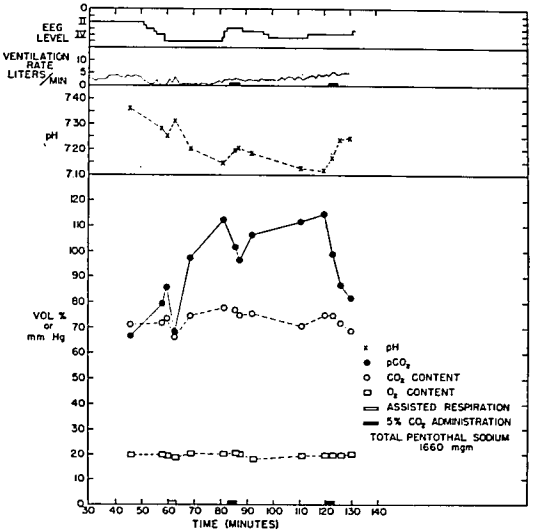

FIG. 7. (Case 9.) Studies on a woman, 67 years old, during pentothal sodium-oxygen anesthesia. A striking respiratory depression occurred. The effect of assisted respiration on carbon dioxide tension can be seen. High oxygen contents are evident in spite of greatly diminished ventilation rates in several instances.

arterial blood. This is especially evident in case 9 (table 9, fig. 7). These findings are in accord with the investigations of Draper and Whitehead (16), who were able to maintain high oxygen saturation of the hemoglobin of dogs in the absence of any respiratory activity. Three requirements must be satisfied to insure adequate oxygenation under these conditions. These requirements include an adequate airway, effective denitrogenation and a high concentration of oxygen in the mask.

Carbon Dioxide Tension.—The average of the mean carbon dioxide tensions of the patients undergoing ether anesthesia was well within

the normal range in the neighborhood of 40 mm. That of the patients undergoing pentothal sodium anesthesia was greater than normal. Two of these patients were narcotized to deeper levels than the surgical procedure actually required (tables 9 and 10, fig. 7). Examination of the data obtained from the other patients reveals that the carbon dioxide tension does not progressively increase with the maintenance of anesthesia, although a comparatively constant level is usually evident somewhat above the normal threshold of the respiratory center. This fact lends more evidence to the assumption that during lighter levels of anesthesia the center retains the ability to control respiration in response to its normal stimulus, although its threshold may be somewhat elevated. If all or nearly all sensitivity of the respiratory center were lost, one would expect the carbon dioxide tension to increase pro-

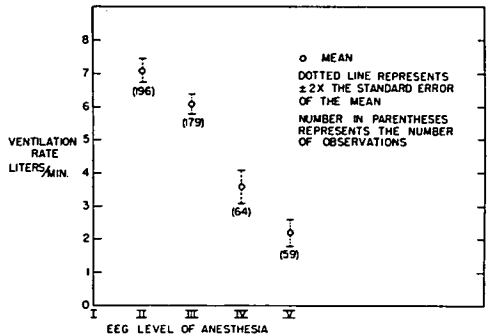

FIG. 8. The statistically significant effect of the intensity of narcosis as measured by the electro-encephalograph on ventilation rate during anesthesia with pentothal sodium. The mean ventilation rates during lighter levels of anesthesia (levels 2 and 3) were more than 6 liters per minute.

gressively with the duration of the anesthesia. In only 1 case (case 9) did the respiratory center appear to lose its sensitivity to a major degree as evidenced by increasing carbon dioxide tension (table 9, fig. 7). However, near the termination of the procedure, a level of anesthesia was attained which enabled the respiratory center rapidly to decrease the carbon dioxide tension.

Buffer Base.—As has been stated previously, the value for buffer base gives a true index of change in acid-base balance. A decrease in buffer base indicates a real decrease of fixed base or an increase of fixed acid (fig. 1). Unfortunately, the conditions under which this study was made did not permit withdrawal of arterial blood samples before induction of anesthesia. A comparison of values early in the period of ether anesthesia and at its termination reveals a consistent decrease in buffer base in all cases but one. However, this decrease is

not significantly different statistically from the apparently more random increases and decreases observed in patients undergoing pentothal sodium anesthesia. Moreover, it must be assumed that factors other than the administration of an anesthetic agent may produce alterations in acid-base equilibrium under the conditions of these observations. In addition normal, conscious individuals may show moderate variations over short periods of time (17).

Examination of individual determinations of buffer base discloses that the values remain relatively constant in spite of rather marked variations in the pH of the blood during pentothal sodium or ether anesthesia. This seems to indicate that alterations in acid-base

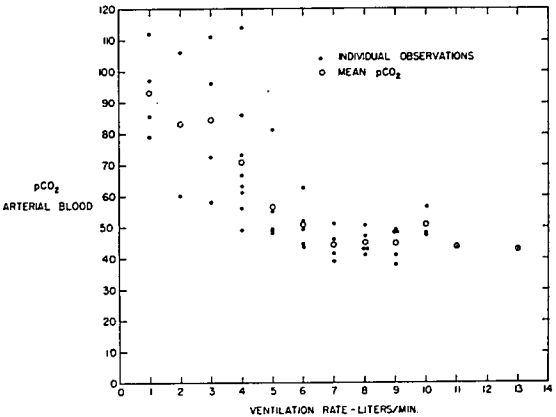

FIG. 9. Mean carbon dioxide tensions when the ventilation rate was 6 liters per minute or more, were only slightly greater than the normal tension during pentothal sodium anesthesia.

equilibrium are primarily due to alterations in ventilation, and it can safely be assumed that neither ether nor pentothal sodium induces any marked degree of metabolic acidosis under these conditions.

Pentothal Sodium Anesthesia and Respiratory Acidosis.—The effect of the degree of narcosis on the ventilation rate or minute volume during pentothal sodium anesthesia is illustrated in figure 8. At lighter levels of anesthesia or electro-encephalographic patterns 2 and 3, the mean ventilation rate is more than 6 liters per minute. Examination of figure 9 reveals that at a ventilation rate of 6 liters or more per minute, the mean carbon dioxide tension is only slightly greater than normal.

Kiersey (11), in a study of 50 patients undergoing pentothal sodium

anesthesia under these same conditions demonstrated that in most cases, level 2 anesthesia provided sufficient anesthesia for the surgical procedure performed. The patients exhibited no signs indicating intolerance to placing of skin clips, incision and retraction of the wound edges, stripping of the varicosities, or closure of the incision. Therefore, it would appear that, under these conditions, pentothal sodium anesthesia when skillfully managed, will not induce an accumulation of carbon dioxide in amounts sufficient to be detrimental to the welfare of the patient, and yet will produce a degree of narcosis sufficient for a surgical procedure capable of initiating many painful stimuli.

SUMMARY AND CONCLUSIONS

Six patients undergoing ether anesthesia and 7 undergoing anesthesia with pentothal sodium were studied. Measurements included the estimation of level of anesthesia by the electro-encephalograph and determination of the expiratory ventilation rate. Intermittently collected samples of arterial blood were analyzed for oxygen content, carbon dioxide content and pH. Carbon dioxide tension and buffer base of whole blood were calculated. The following observations were made:

1. The ventilation rate during ether anesthesia remained within the normal range during all levels of anesthesia observed (electro-encephalographic levels 1 through 5). The ventilation rate increased in every instance in response to an increased concentration of carbon dioxide in the inspired gas mixture.

2. The mean ventilation rate during pentothal sodium anesthesia decreased progressively as the degree of narcosis increased. The respiratory center, under these conditions, was capable of increasing the ventilation rate in response to the administration of 5 per cent carbon dioxide in oxygen. The response was greater in light levels of anesthesia than in deep levels.

3. The oxygen content of arterial blood remained at high levels during both ether and pentothal sodium anesthesia in this series.

4. The carbon dioxide tension of arterial blood during ether anesthesia in most instances remained within normal limits.

5. The arterial blood carbon dioxide tension in patients undergoing pentothal sodium and oxygen anesthesia was not unduly elevated except for periods during which respiration was markedly depressed by deep narcosis.

6. Variations in the acid-base equilibrium in all patients in both ether and pentothal sodium series were primarily due to alterations in ventilation, and no highly significant degree of metabolic acidosis was evident.

7. Pentothal sodium has proved under these conditions to be an anesthetic agent adequate for the performance of a surgical procedure

capable of provoking many painful stimuli; yet no undue depression of respiration occurred, except when purposely induced, as evidenced by relatively normal carbon dioxide tension and normal oxygen content of the arterial blood.

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