THE EFFECT OF ETHER ANESTHESIA ON THE ALKALI RESERVE *

AN EXPERIMENTAL STUDY

WILLIAM S. CARTER, M.D.

GALVESTON, TEXAS

The alkali reserve can best be determined by measuring the capacity of the blood for combining with carbon dioxid. Many of the observations to determine the influence of anesthesia on the alkali reserve have been made on patients after surgical operations. The alkali reserve may be decreased by the restricted diet or fasting preparatory to surgical operations, and the same condition is usually present in surgical shock, so that ether anesthesia produced experimentally in animals offers the advantage of eliminating these contributing factors.

Caldwell and Cleveland [1] studied the influence of different kinds of anesthesia on the alkali reserve in more than 100 patients, including fifty-five for whom ether anesthesia was used. In those latter cases they found a slight decrease, varying from 4.5 to 7.7 volumes per cent. in the combining capacity for carbon dioxid, but acidosis approaching dangerous proportions was noted only in the case of a diabetic patient who had acidosis before the operation.

Austin and Jonas [2] determined the carbon dioxid combining capacity of blood in sixteen patients after ether anesthesia for various surgical operations. The maximal decrease was 10 volumes per cent. and the lowest amount observed was 47 volumes per cent. The reduction seemed proportionate to the duration of the anesthesia and was maximal at the close of the anesthesia. When a decrease occurred, it apparently persisted with little alteration for about five hours.

Cannon [3] made a number of observations on soldiers who had been wounded in battle and were suffering from varying degrees of shock. In a series of nine cases of moderately severe shock, there was a decrease of approximately 12 volumes per cent. on the average, the maximal reduction being 16 volumes per cent. He found the decrease occurred rapidly when the capacity of the blood for combining with carbon dioxid was low (below 50 volumes per cent.) before the

---

* From the Laboratory of Physiology of the University of Texas.

* Read before the Section on Pathology and Physiology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

1. Surg., Gynec. & Obst. **25**:22, 1917.
2. Am. J. M. Sc. **153**:81, 1917.
3. J. A. M. A. **70**:531 (Feb. 23) 1918.

operation. The maximal decrease following operations when nitrous oxid and oxygen were used for anesthesia was 8 or 9 volumes per cent. Cannon expressed the opinion that the alkali reserve is below normal in shock, and that the reduction is in direct proportion to the degree of shock.

W. H. Morris [4] made a number of observations on patients before and after gynecologic operations. He also made a few experiments on dogs with prolonged ether anesthesia but without any surgical operation which could produce shock. He found that a reduction of the carbon dioxid combining capacity of the blood usually but not invariably occurs and that it does not bear any relation to the duration of the anesthesia. In one case in which the anesthesia only lasted twenty minutes, there was a decrease of 10 volumes per cent.; in another case lasting two hours for a hysterectomy, the decrease was 7.7 volumes per cent. The greatest decrease was 22 volumes per cent., while the least was 0.4 volumes per cent., and in the latter the operation lasted one and a half hours.

Comparing a series of ten patients to whom from 15 to 20 gm. of bicarbonate of sodium had been given intravenously before operation, with the same number who had not received such preliminary treatment, he found the decrease in the carbon dioxid combining capacity of the blood averaged 5.7 volumes per cent. as compared with an average of 9 in those who had not been given sodium bicarbonate.

He etherized two dogs for two hours or more, making carbon dioxid determinations every half hour. He found a reduction of from 10 to 12.5 volumes per cent., that is, from 22 to 24 per cent. of the normal amount. In one dog, the greatest reduction occurred in the third half hour; in the other the most rapid fall took place during the first half hour. Prolonged chloroform anesthesia in one dog caused a reduction of 24 volumes per cent., or 47 per cent. of the normal amount, which was considerably greater than that caused by ether.

Yandell Henderson [5] investigated the subject by experiments on dogs and reached the conclusion that the reduction in the carbon dioxid combining capacity of the blood is due to increased dissociation of the carbon dioxid from the blood, caused by the hyperpnea or increased respiratory activity produced by the irritant ether vapor. He contends that the decrease in the carbon dioxid content and capacity of the blood is due to increased ventilation of the lungs and not to actual reduction in the alkali reserve of the body.

Previous observations had been made by the Van Slyke apparatus with the plasma alone. Henderson used the whole blood and deter-

4. J. A. M. A. **68**:1391 (May 12) 1917.
5. J. Biol. Chem. **33**:345 (Feb.) 1918.

mined by means of his own apparatus the carbon dioxid content as well as its combining capacity when exposed to an atmosphere containing a uniform amount (5.5 per cent.) of carbon dioxid. He found the maximal decrease in the carbon dioxid content during ether anesthesia was from 14 to 19 volumes per cent., while the greatest decrease in the carbon dioxid combining capacity was from 12 to 15 volumes per cent.

A state of hyperpnea was maintained by artificial respiration in dogs narcotized by chlorbutanol and he states that this produces as great a reduction in the carbon dioxid content and capacity of the blood as that seen in ether anesthesia, although the chlorbutanol alone does not produce that effect. He produced the opposite condition of decreased ventilation of the lungs by morphinizing dogs so as to reduce the respiratory activity, and he found an increase in the carbon dioxid content and capacity of the blood. When he produced light anesthesia with ether, so as to cause an acceleration of the respiration, he found a decrease in the carbon dioxid content and capacity of the blood; when he produced deep ether narcosis with feeble respiratory activity he found that both were increased.

In another series of experiments dogs inhaled ether vapor in an atmosphere containing from 6 to 7 per cent. of carbon dioxid, to which oxygen was added, and Henderson found there was no decrease in the carbon dioxid content or capacity of the blood, although the anesthesia was continued from three to five hours.

This last series of experiments is open to the criticism that the animals were compelled to breathe an artificial atmosphere containing a higher percentage of carbon dioxid than that of the alveolar air. Under such abnormal circumstances it is not surprising that there was an increase in the carbon dioxid of the blood.

EXPERIMENTS

Series 1.—The first series of experiments was made with blood plasma obtained by Van Slyke's method. The jugular vein was exposed after the animal became unconscious at the beginning of ether anesthesia and the first sample of blood was taken as the normal. Other samples were taken after half an hour, one hour, or one and a half hours of anesthesia and the carbon dioxid determinations were made with Van Slyke's apparatus.

Uniform anesthesia was maintained throughout each experiment by causing the animal to breathe ether vapor from a Mason jar of one liter capacity with an adjustable inlet tube and a respiratory valve in the top of the jar (Fig. 1), so that the vapor from the jar entered the cone with each inspiration, while the expired air escaped into the open without entering the jar. The jar was kept in a wooden box, the air of which was warmed by one or two eight-candle power

electric lamps, so that the air containing ether vapor was warmed before it entered the lungs.

The results are shown in Table 1. Only one out of twelve dogs did not show any decrease in the carbon dioxid combining capacity of the blood. Eleven showed a decrease varying from 5.6 to 23.3 volumes per cent., or from 15 to 46 per cent. of the normal. The average decrease at the end of the anesthesia was 10.8 volumes per

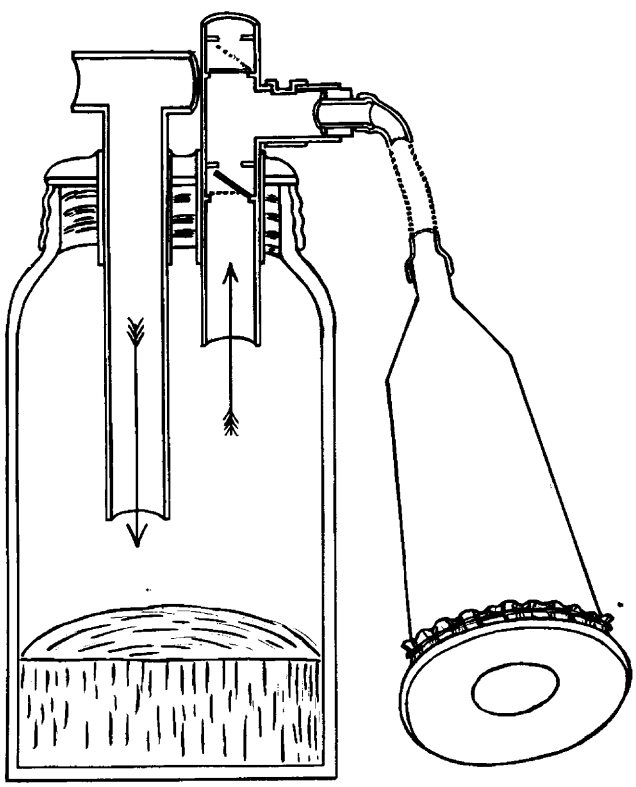

Fig. 1.—Sectional view of ether jar with respiratory valve on top. The continuous lines show the position of the light aluminum disks of the respiratory valve during inspiration, while the broken lines show the position of these disks during the phase of expiration.

cent. The anesthesia lasted one hour in three experiments and one and a half hours in nine experiments. Very little decrease occurred during the first half hour; the greatest decrease occurred during the second half hour, with a further fall during the third half hour period.

The same dog was used in Experiments 4, 5 and 6 on three consecutive days. There was no fall on the third day although there was a decrease on each of the first two days.

The same dog was used in Experiments 7, 8 and 9. The fall was no greater in Experiment 9, although a condition of shock was produced during the last two periods of that experiment by exposing and handling the abdominal viscera, so that the mean blood pressure was reduced from 140 mm. to less than 100 mm., and kept at that level.

One dog was also used for Experiments 11 and 12. This animal showed the greatest reduction in the alkali reserve on the first day, but less on the second day.

TABLE 1.—SUMMARY OF THE FIRST SERIES OF EXPERIMENTS. ORDINARY ETHER ANESTHESIA. UNIFORM ETHER VAPOR INSPIRED FROM ETHER JAR. EXPIRED AIR ESCAPED INTO THE OPEN WITHOUT ENTERING THE JAR. CARBON DIOXID DETERMINED BY VAN SLYKE'S METHOD

Experiment	Dog's Weight and Date of Experiment	Normal Carbon Dioxid Capacity of Blood	After ½ Hour of Anesthesia	After 1 Hour of Anesthesia	After 1½ Hours of Anesthesia	Decrease in Volume per Cent. (1-1½ Hrs.)	Decrease in Percentage of Normal
1	10.5 kg.	54.3	....	36.0	....	18.3	33.7
2	13 kg.	51.9	....	....	39.9	12.0	23.1
3	9.5 kg. Aug. 20.	59.7	50.4	46.7	....	13.0	21.8
4	Same dog Aug. 22.	44.0	....	37.4	37.4	6.6	15.0
5	Same dog Aug. 23.	41.2	....	33.8	33.8	7.4	17.9
6	Same dog Aug. 24.	39.3	....	39.3	....	0.0	0.0
7	13 kg. Aug. 27, 10 a.m.	35.7	....	33.9	30.1	5.6	15.7
8	Same dog Aug. 27, 3 p.m.	33.9	....	26.4	24.6	9.3	27.4
9	Same dog Aug. 28.	42.1	43.0	41.2	34.7	7.4	17.5
10	7.7 kg.	52.05	42.2	37.5	39.3	12.7	24.4
11	5.0 kg. Sept. 5.	49.7	43.2	31.05	26.4	23.3	46.8
12	Same dog Sept. 7.	59.9	54.3	54.3	46.1	13.8	23.0
	Average.	46.98	46.6	37.95	34.7	10.8	22.1

Series 2.—In the second series of experiments, the normal blood was obtained before the anesthetic was started, by injecting procain and exposing the jugular vein without causing pain or struggling by the animal. Duplicate determinations were made from the normal blood to avoid error and these are given as the first and second normals.

In this series, and in all subsequent experiments throughout this investigation, the whole blood was used for determining the carbon dioxid content and the carbon dioxid combining capacity of the blood by Yandell Henderson's method and his apparatus was used in all experiments after the first series. The results by this method are more uniform and there is less danger of error than there is by Van Slyke's method.

The ether vapor was inhaled from a Mason jar of 1 liter capacity with the respiration valve in the top as in the first series. Anesthesia was maintained for two hours. Determinations of the carbon dioxid content and carbon dioxid combining capacity of the blood were made at the end of one and two hours of anesthesia, respectively, and also half an hour and one hour after the end of the anesthesia, to determine the after-effect.

The details of these experiments are not given for each separate experiment but they may be summarized by giving the averages of the different periods in the five experiments of this series (Table 2).

All of the experiments of this series showed a decrease, varying from 4.0 to 8.6 volumes per cent. in the carbon dioxid combining capacity of the blood. The results were quite uniform and did not show as much variation as in the first series.

One important fact brought out by this series is that there was practically no decrease in the alkali reserve at the end of one hour of etherization, but the entire reduction occurred during the second hour. This has a practical bearing as it shows that the danger of decrease in the alkali reserve is greater from prolonged anesthesia than it is when this is not continued for more than an hour.

TABLE 2.—SUMMARY OF FIVE EXPERIMENTS. ORDINARY ETHER ANESTHESIA. CARBON DETERMINATIONS BY HENDERSON'S METHOD

Periods for Which Averages Are Given in Last Two Columns	Average Carbon Dioxid Content of Blood	Average Carbon Dioxid Combining Capacity of Blood
First normal (blood obtained by procain)	48.27	48.77
Second normal (blood obtained by procain)	48.04	49.02
After 1 hour of ordinary ether anesthesia	48.45	48.28
After 2 hours of ordinary ether anesthesia	42.86	42.71
One-half hour after end of anesthesia	42.70	43.28
One hour after end of anesthesia	47.09	46.79
Average decrease in volume per cent.	5.38	6.09
Average decrease in percentage of normal	.....	12.5

The reduction in the carbon dioxid content and combining capacity of the blood continued for half an hour after the end of anesthesia in each experiment but both had practically returned to the normal at the end of one hour.

Series 3.—A third series of experiments was made to determine whether there is an actual reduction in the alkali reserve from ether anesthesia, or if this is an apparent condition caused by the hyperpnea or increased respiratory activity as a result of the irritant effects of ether vapor, as claimed by Henderson. The normal blood was obtained from the vein after it had been exposed by the use of procain. The animal was first etherized in the ordinary way until tracheotomy could be performed and etherization was then continued by connecting the tracheal tube to a metal tube in the top of a 2-quart Mason jar containing ether. A large rubber tube from the Hans Meyer artificial respiration apparatus was connected to another tube in the top of the ether jar. This apparatus can be adjusted to force through the ether jar and into the lungs the same amount of air that is breathed in natural respiration by animals of different size. The tidal air had been determined by means of a spirometer for each animal before

the experiment started, and the artificial respiration apparatus was adjusted to furnish the same amount. It also aspirates from the jar and lungs in expiration the same volume of air that is forced in under positive pressure during inspiration. Of course the air in the jar, 2 liters, was added to the dead air space of the upper respiratory passages and analysis of this air in each experiment showed that it contained on the average from 2.6 to 3.0 per cent. of carbon dioxid. The animals used in the third series were, therefore, furnished with ether in a uniform vapor density, in an atmosphere containing approximately 3 per cent. of carbon dioxid. This accounts for the increase in the carbon dioxid content and combining capacity of the blood which occurred after one hour of anesthesia maintained in this way. The increased carbon dioxid of the air would tend to keep up the carbon dioxid of the blood, even if there were a condition of hyperpnea. Hyperpnea was prevented in this series by the artificial respiration which maintained a uniform respiratory rate and volume throughout the entire experiment.

TABLE 3.—SUMMARY OF THREE EXPERIMENTS OF SERIES III. EFFECT OF ETHER ANESTHESIA BY ARTIFICIAL RESPIRATION TO MAINTAIN A UNIFORM RESPIRATORY RATE AND VOLUME, THUS ELIMINATING HYPERPNEA

Periods for Which Averages Are Given	Carbon Dioxid Content of Blood	Carbon Dioxid Combining Capacity of Blood
First normal (blood obtained by use of procain).....	51.82	54.18
Second normal (blood obtained by use of procain).....	51.95	53.02
After one hour of anesthesia by artificial respiration through a two liter jar containing 2.6-3.0 per cent. carbon dioxid..	53.62	56.15
After two hours of anesthesia.....	46.06	50.06
After three hours of anesthesia.....	42.12	44.75
Average decrease in volume per cent. after two hours etherization	5.82	3.54
Average decrease in volume per cent. after three hours etherization	9.76	8 85
Maximal decrease in percentage of the normal amount.....	18%	16.5%

The elimination of hyperpnea in the experiments of the third series shows that this condition is not responsible for the reduction in the alkali reserve in the experiments of the first and second series where ordinary ether anesthesia was used. In spite of the increased percentage of carbon dioxid in the tidal and stationary or alveolar air, which in itself caused an increase in the carbon dioxid content and combining capacity of the blood during the first hour of anesthesia, there was a decided fall during the second hour and a further fall during the third hour. The fall during the second hour was less than that in the second series, but when the increase during the first hour is taken into consideration, the results are practically the same in both series. The reduction for three hours of anesthesia by artificial respiration is greater than that in the second series and almost as great as the average of the experiments in the first series.

The details of each experiment are not given on account of limited space. The results were quite uniform in the three experiments and these are summarized in Table 3 by giving the averages for the different periods.

Series 4.—This series of experiments was made to determine whether the ventilation of the lungs is increased in proportion to the acceleration of the respiratory rate during ordinary anesthesia; also to devise a method of overcoming the reduction in the carbon dioxid content and capacity of the blood that might be produced by a simple hyperpnea, or increased in the volume of air moved in and out of the lungs, occurring with natural respiration.

The experiments were divided into four periods of half an hour each. The respiratory volume, as measured by a spirometer, and the rate were taken for two or three minutes and averaged for one minute periods. At least six observations were made in each period at intervals of from three to five minutes and the average was taken for the entire period of half an hour.

During the first period the animal breathed through the cone and Mason jar with the respiration valve in the top, but without ether in the jar. The expired air escaping from the top of the respiration valve was collected and measured in a spirometer. This period was taken as the normal for comparison with the other periods.

During the second period the dog breathed through a jar with a respiration valve on the far side from the animal (Fig. 2). In this way the inspired and expired air passed through the jar, the contents of which became part of the dead air space of the cone and upper respiratory passages. Analysis of the air of the jar showed that it contained from 16 to 17 per cent. of oxygen and from 2.5 to 3.0 per cent. of carbon dioxid. Jars of different size (1, 2 and 3 liters) were used, but the composition of the air did not vary much. When such jars are used for vaporizing ether the large size (3 liters) is desirable as the vapor density of the ether does not then exceed the amount desirable for anesthesia.

The third period was like the first, except that ether was placed in the jar for ordinary ether anesthesia.

The fourth period was like the second, except that ether, in sufficient amount to keep the bottom covered, was placed in the jar through which the inspired and expired air passed, so that the animal inhaled ether vapor in an atmosphere containing from 16 to 17 per cent. of oxygen and from 2.5 to 3 per cent. of carbon dioxid.

Six experiments were made in this series and the averages for the different periods are given in Table 4, together with the percentage for each period over the normal. It will be seen that an atmosphere containing from 2.5 to 3 per cent. of carbon dioxid (Period B)

increased the respiratory volume 74 per cent., but only increased the rate 7 per cent. The greater depth of the respirations is caused by the chemical stimulation of the respiratory center produced by the increased tension of carbon dioxid in the blood.

Ether vapor alone in the ordinary atmosphere (Period C) increased the respiratory rate 107 per cent., but only increased the respiratory volume 33 per cent. This indicates that the acceleration of the respiratory rate in ordinary ether anesthesia is three times greater than the increase in the ventilation of the lungs, and that the hyperpnea is not so great as it appears to be when the number of shallow respirations alone are considered.

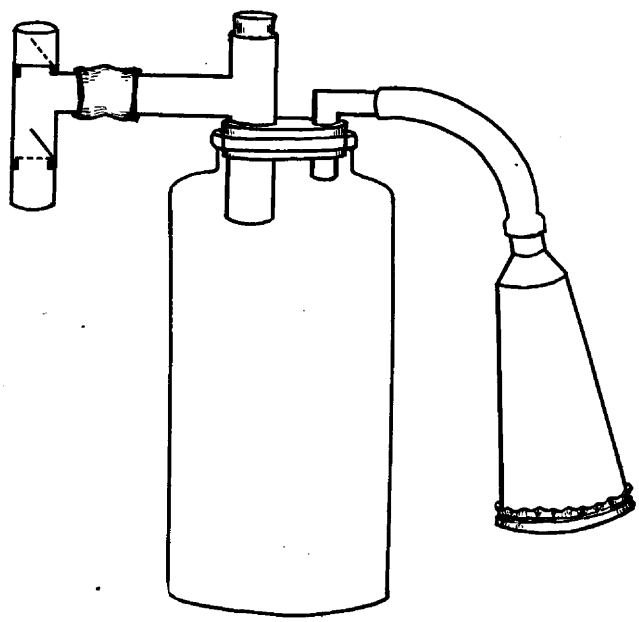

Fig. 2.—Ether jar with respiratory valve on the far side from the cone. The continuous lines show the position of the disks of the valve during inspiration, while the broken lines show the position during expiration.

The average for the fourth period (Period D) showed that the ether vapor in an atmosphere containing 3 per cent. of carbon dioxid caused an increase of 80 per cent. in the rate but the volume is increased less than 5 per cent. The latter varies with the depth of anesthesia, but the increase in the volume is never as great as with ether alone, or an atmosphere of 3 per cent. of carbon dioxid alone. Apparently the depression of the respiratory center by the ether lessens its irritability to chemical stimulation by an increased tension of carbon dioxid

in the blood. The method used in this last period makes it possible to study the effect of etherization on the alkali reserve with natural respiration when there is comparatively little increase in the ventilation of the lungs. Any increase in the volume of air is fully offset by the increased percentage of carbon dioxid in the alveolar air. This was shown by the increased amount of carbon dioxid in the blood which was found in numerous experiments.

TABLE 4.—SUMMARY OF SIX EXPERIMENTS TO DETERMINE THE EFFECT OF (1) ORDINARY ETHER ANESTHESIA ON RESPIRATORY RATE AND VOLUME; (2) BREATHING THROUGH A JAR CONTAINING 16-17% OXYGEN AND 2.5-3% CARBON DIOXID; (3) ETHER VAPOR IN A JAR CONTAINING 2.5-3% CARBON DIOXID. SIX OBSERVATIONS MADE FOR EACH PERIOD AT INTERVALS OF THREE TO FIVE MINUTES

Half-hour Periods for Which Averages Were Made	Average Respiratory Rate per Minute	Percentage Increase Over Normal	Average Respiratory Volume (Cubic Inches per Minute)	Percentage Increase Over Normal
A. Normal respiration through Mason jar with respiration valve in top, i. e., breathing ordinary atmosphere.....	26	...	109	
B. Breathing through jar with respiration valve on far side. "Dead air space" in jar contained 16-17% oxygen and 2.5-3.0% carbon dioxid.....	28	7	190	74
C. Ether anesthesia. Uniform ether vapor from jar with valve in top, i. e., expired air escaped without entering jar	54	107	145	33
D. Ether anesthesia through jar with valve on far side, i. e., ether vapor in air containing 16-17% oxygen and 2.5-3.0% carbon dioxid	47	80.7	113	3.7

It was not practicable to make simultaneous observations of the respiratory rate and volume and of the carbon dioxid of the blood in many experiments, but the following experiment shows no decrease in the carbon dioxid combining capacity of the blood during one and one half hours of ordinary ether anesthesia, although there was considerable hyperpnea. During the second period of one and one-half hours in the same animal, when the animal inhaled ether vapor in air containing from 3 to 3.5 per cent. of carbon dioxid, there was a decided decrease in the alkali reserve of the blood, although the respiratory volume was practically the same as it had been during the first period.

Series 5.—The experiments of this series were made to determine the effect on the carbon dioxid content and combining capacity of the blood produced (1) by natural respiration through a 3 liter jar containing approximately 3 per cent. of carbon dioxid, and (2) by inhaling ether vapor from such a jar for two or three hours. Observations were also made one and one-half hours after the end of the anesthesia

when it was found that the alkali reserve of the blood had practically returned to normal.

Six experiments were made in this series which are summarized in Table 6 by giving the averages for each period. The dogs breathed through a 3 liter bottle with the respiratory valve on the distal side from the animal and described in discussing results in Period D of Series 4. The air of the bottle was vitiated by respiration so that it contained from 16 to 17 per cent. of oxygen and 3 per cent. of carbon dioxid. The bottom of the bottle was kept covered with ether.

TABLE 5.—EXPERIMENT 12. SHOWING SIMULTANEOUS OBSERVATIONS ON RESPIRATORY RATE AND VOLUME AND CARBON DIOXID CONTENT AND CAPACITY OF THE BLOOD (A) DURING ORDINARY ETHER ANESTHESIA AND (B) DURING ETHER ANESTHESIA WHILE BREATHING 3.5% CARBON DIOXID

	Respiratory Volume (Cubic Inches per Minute)	Respiratory Rate per Minute	Carbon Dioxid Content of Blood	Combining Capacity of Blood
9:30 a. m. First normal (blood taken by procain)	...	...	55.72	57.30
Second normal	...	...	53.80	58.70
Average	...	...	54.76	58.00
9:40–9:50 Average of 4 observations	90	31		
10.00 Started ether anesthesia				
10:00–10:25 Average of 8 observations	186	41		
10:30	...	...	50.90	60.70
10:55–11:25 Average of 7 observations	212	54		
11:30 After 1½ hours of ordinary ether anesthesia	...	...	59.20	63.00
11:32 Began inhalation of ether vapor with 3.5% carbon dioxid by breathing through a 3 liter jar				
11:40–11:55 Average of 4 observations	242	83		
12:00 m.	...	...	46.70	49.94
12:45–12:55 Average of 3 observations	210	86		
1:00 p. m. After 3 hours of anesthesia, i. e., 1½ hours with ordinary air and 1½ hours of ether vapor with 3–3.5 carbon dioxid	...	...	45.92	47.94
Decrease	...	...	8.84	10.06

In the experiments of Series 3, artificial respiration was used through a 2 liter ether jar; in those of Series 5, natural respiration was used through a 3 liter ether jar. In both series the jar contained approximately 3 per cent. of carbon dioxid. Hyperpnea was completely eliminated in Series 3, but not in Series 5. Even if there were any hyperpnea in Series 5, it did not cause any increased dissociation of carbon dioxid from the blood on account of the increased percentage of carbon dioxid in the tidal and in the alveolar air. This is clearly shown by the increase in the carbon dioxid content and combining capacity of the blood when the animal breathed through the jar for half an hour before the anesthetic was started. The animals breathed

quietly during this time and did not struggle. Under such conditions any decrease in the carbon dioxid combining capacity of the blood that occurred in the six experiments of Series 5 could not have been due to hyperpnea.

The reduction was practically the same as that in Series 2, in which the animals inhaled ether vapor in the ordinary atmosphere, and it was three-fourths as great (6.4 volumes per cent.) as that in Series 3 (8.85 volumes per cent.).

TABLE 6.—SERIES 5. SUMMARY OF SIX EXPERIMENTS WITH NATURAL RESPIRATION. ETHER VAPORIZED IN A THREE-LITER JAR CONTAINING 3 PER CENT CARBON DIOXID

Periods for Which Averages Are Given in Last Two Columns	Average Carbon Dioxid Content of Blood	Average Carbon Dioxid Combining Capacity of the Blood
First normal (vein exposed by procain)	52.1	52.3
Second normal	53.2	54.1
After breathing through 3 liter bottle containing 3% carbon dioxid (without ether) for one-half hour	56.3*	57.6
After one hour of etherization (ether vaporized in jar containing 3% carbon dioxid through which the animal breathed)	54.6	54.6
After two hours of anesthesia (6 experiments)	48.5	49.4
After three hours of anesthesia (3 experiments)	46.1	45.4
Average decrease in volumes per cent.	6.16	6.4
Average decrease in percentage of the normal amount	11.1%	11.6%
One and one-half hours after end of anesthesia (4 exper.)	52.7	52.1

As an atmosphere containing 3 per cent. of carbon dioxid causes a distinct increase of 3 or 4 volumes per cent. in the carbon dioxid content and combining capacity of the blood, this method seems much better than the one used by Henderson, in which the animals breathed an atmosphere containing 6 or 7 per cent. of carbon dioxid with the addition of oxygen.

That hyperpnea is not a factor in the decrease in the alkali reserve produced by ether anesthesia is also evident from the fact that the decrease does not occur during the first hour of anesthesia, when the greatest acceleration of the respiratory rate occurs, but during the second or third hour when the respirations are uniform in rate. It is also evident from the six experiments of Series 4 that the increase in respiratory volume is only about one-third as great as the increase in rate in the hyperpnea which occurs early in ether anesthesia.

THE EFFECT OF DECREASED OXYGEN

It is a well known fact that a decreased supply of oxygen to the tissues may produce a decrease in the alkali reserve. In order to determine whether the decrease in the oxygen in the 3 liter jar, through which the animal breathed in order to increase the carbon

dioxid of the tidal and alveolar air, was responsible for the decrease in the carbon dioxid combining capacity of the blood during ether anesthesia by this method, three control experiments were made.

The dogs were kept quiet by giving chlorbutanol to produce narcosis after the normal sample of blood had been taken by exposing the vein with the use of procain. They were then made to breathe through the jar of 3 liters capacity for three hours and the carbon dioxid content and capacity of the blood were determined as before. Analysis of the air in the jar showed an average of 16.3 per cent. oxygen and 3.9 per cent. carbon dioxid. The averages of the three experiments are shown in Table 7.

TABLE 7.—EFFECT OF DECREASED OXYGEN

	Carbon Dioxid Content	Carbon Dioxid Combining Capacity
Normal blood	58.5	62.6
After one-half hour of chlorbutanol narcosis	48.7	55.7
After breathing through 3 liter jar for 1 hour	59.2	60.0
After breathing through 3 liter jar for 2 hours	57.0	58.4
After breathing through 3 liter jar for 3 hours	60.1	58.6

These experiments show conclusively that the decrease in the oxygen in the air breathed from the jar was not responsible for the decrease in the alkali reserve of the blood. The chlorbutanol narcosis seemed to cause a distinct decrease until the respiratory center was stimulated by the increased tension of carbon dioxid in the blood which resulted from a higher percentage of carbon dioxid in the alveolar air. Henderson states that chlorbutanol does not influence the carbon dioxid combining capacity of the blood. However, it lessens the respiratory activity decidedly.

AFTER-EFFECT OF ETHER ANESTHESIA

All five of the experiments of the second series showed that the reduction in the alkali reserve at the end of etherization for two hours continued for half an hour after the anesthesia ended, but the carbon dioxid content and capacity returned almost to the normal at the end of one hour after the anesthesia.

Four of the experiments in Series 5 showed that the carbon dioxid content and capacity of the blood had returned to the normal one and a half hours after the termination of the anesthesia, which lasted for two hours in two experiments, and for three hours in two experiments.

Two other experiments were made to determine if there is a secondary fall. There was an average reduction of 8.5 volumes per cent. in the carbon dioxid combining capacity at the end of two hours

of ordinary anesthesia and this continued for one hour. At the end of two and one half hours the alkali reserve had returned to normal and remained so at the end of four and five hours, respectively, after the anesthesia.

CONCLUSIONS

1. Ordinary ether anesthesia, without any of the contributing conditions that attend surgical operations, causes a distinct decrease in the alkali reserve. The decrease in carbon dioxid combining capacity of the blood of dogs is usually from 6 to 10 volumes per cent.

2. There is comparatively little diminution during the first hour but it occurs almost entirely after that time and is in direct proportion to the duration of the anesthetic.

3. There is an actual decrease in the alkali reserve and not an apparent condition due to hyperpnea. The latter is most marked early in the anesthesia but there is little or no dealkalization during the first hour. The usual decrease occurs when anesthesia is maintained by artificial respiration which provides a uniform respiratory volume; also when an animal breathes an atmosphere containing 3 per cent. of carbon dioxid in which ether has been vaporized.

4. Breathing an atmosphere containing 16 per cent. of oxygen and 3.5 per cent. of carbon dioxid for three hours does not diminish the alkali reserve.

5. The greatest decrease in the alkali reserve produced by ether anesthesia occurs at the end of the anesthesia and remains at that level for from one-half to one hour after the anesthesia, at a time when there is decreased respiratory activity. Following this brief after-effect, there is a rapid increase in the alkali reserve and it returns to the normal in from one to two hours after the anesthesia.

All of the experiments presented in this paper were performed on normal dogs. The decrease in the alkali reserve never reached a dangerous level and it only continued for a short time after the anesthesia. It is impossible to conclude from them what might occur if there is a reduction from altered metabolism before a surgical operation, or when a patient is in a condition of surgical shock which is attended by a reduction in the carbon dioxid combining capacity of the blood. Such conditions, added to that produced by ether, may be more serious. It should also be remembered that it is extremely difficult to produce in dogs the condition known as acidosis, even by injecting large amounts of a mineral acid into the circulation, as they are able to protect themselves against acids by the alkali reserve of the body and by the ability to form ammonia salts from protein metabolism.