

THE RETENTION OF ALKALI BY THE KIDNEY WITH SPECIAL REFERENCE TO ACIDOSIS *

HERMAN M. ADLER, M.D., AND GERALD BLAKE, M.D.

HATHORNE, MASS.

BOSTON

For some time now the conception of an acid intoxication has been familiar to every student and practitioner of medicine. Since the first work of Naunyn on this subject in which many of the pathological phenomena of diabetes were explained by the demonstration of an acid intoxication to which the name "acidosis" was given, a great many facts have been collected and which support in all essentials the original investigations of Naunyn and his pupils. And it has become more and more evident that disturbances, both quantitative and qualitative, in the ability of the body to deal with varying amounts of acid, are not only important but by no means infrequent occurrences. Contrary to the assumption of the early investigators, whose views are to some extent maintained by many at the present time, it may be stated as a demonstrated fact that the reaction of the blood, and probably of the tissues, varies under all conditions during life within such very narrow limits that it may be called constant and neutral. Instead, therefore, of speaking of the "alkalinity" of the blood it will be more accurate to speak of the "neutrality" of the blood. The reasons for this interpretation are of such a nature that we can merely refer to them here, but those interested may find explanation at length in the literature.¹ Since, therefore, the constancy of reaction of the blood seems to be a fundamental condition of life there must necessarily exist some provision by means of which the neutrality may be maintained in spite of the introduction, either pathologically or experimentally, of acid or alkaline substances. Such a mechanism has been demonstrated in recent years by the investigations of Friedenthal, Henderson, and others. Briefly, this consists of a more or less complicated equilibrium between acid substances on one hand, and bases, chiefly bicarbonates and alkaline phosphates, on the other hand. When acid and base are present in suitable proportions the reaction will be neutral no matter what the actual quantities of the various substances may be. From this it will be apparent that it is quite possible to have a variation in titratable acidity or alkalinity without any variation in reaction. This explains the reason for the discrepancy between the results obtained by titrating sam-

* From the Laboratory of the Department of Theory and Practice of Physic, Harvard Medical School.

1. Henderson, L. J.: *Ergebn. d. Physiol.*, 1909, viii, 254-325, Bibliography.

ples of blood or of serum and those obtained by determining the reaction of the blood by means of the concentration cell or by indicators. We assume then that in order to maintain the neutrality of the blood, the organism will meet the introduction of an acid by an increase of base, and that the only important change that we need at present to consider will be a slight increase in concentration. This increase is met by the kidney by an increased excretion. The function of the bases of the blood, therefore, is in the main twofold: in the first place to transport acid, and in the second place to help to maintain the proper concentration. The most important acid which the bases of the blood are called on to transport is carbonic acid. If for any reason more acid is introduced into the circulation than the bases present and in reserve in the tissues are able to neutralize, acid intoxication will result. The stronger, chemically speaking, an acid is, the more readily will it combine with base. Carbonic acid is a weak acid, and will, therefore, be readily replaced by a number of stronger acids which may occur in large quantities under pathologic or experimental conditions. In cases of extreme acidosis in which all available alkali is required to counteract the effect of the pathological increase in acid substances, such as beta-oxybutyric and diacetic acid, the organism is unable to transport a sufficient quantity of carbonic acid from the tissues to the lungs, and a condition will result in the patient which may vary from lethargy to coma and finally end in death. There is one mechanism of which the organism avails itself in extreme cases to combat the effect of an increase of acid; and this mechanism serves at the same time to liberate a certain amount of bases to carry on the carbonic acid transport. In acidosis the organism no longer combines all its ammonia to form urea, but uses the ammonia directly to neutralize the acid substances. The ammonia thus combined is excreted in the urine and the estimation of the amount thus excreted has been the only available means of determining the degree of acid intoxication. While this method has proved of great help, it gives us an index of only one part of the conditions existing within the organism, and leaves us entirely without information in regard to the very important question of the reserve of alkali within the body. While the individual differences in alkali content of the blood and tissues in living beings is at present quite beyond our methods of investigation, it appears that a considerable amount of useful information might be obtained if we could measure, in our acidosis patients, not only the amount of ammonia that is excreted but also the amount of alkali that is retained.

The following investigation was undertaken in order to determine, first, whether any variations occurred in acidosis between the amount of ammonia and the amount of base excreted; second, whether such variations, if they occurred, would give us information in regard to the acid neutralizing power of the organism; third, whether the method employed

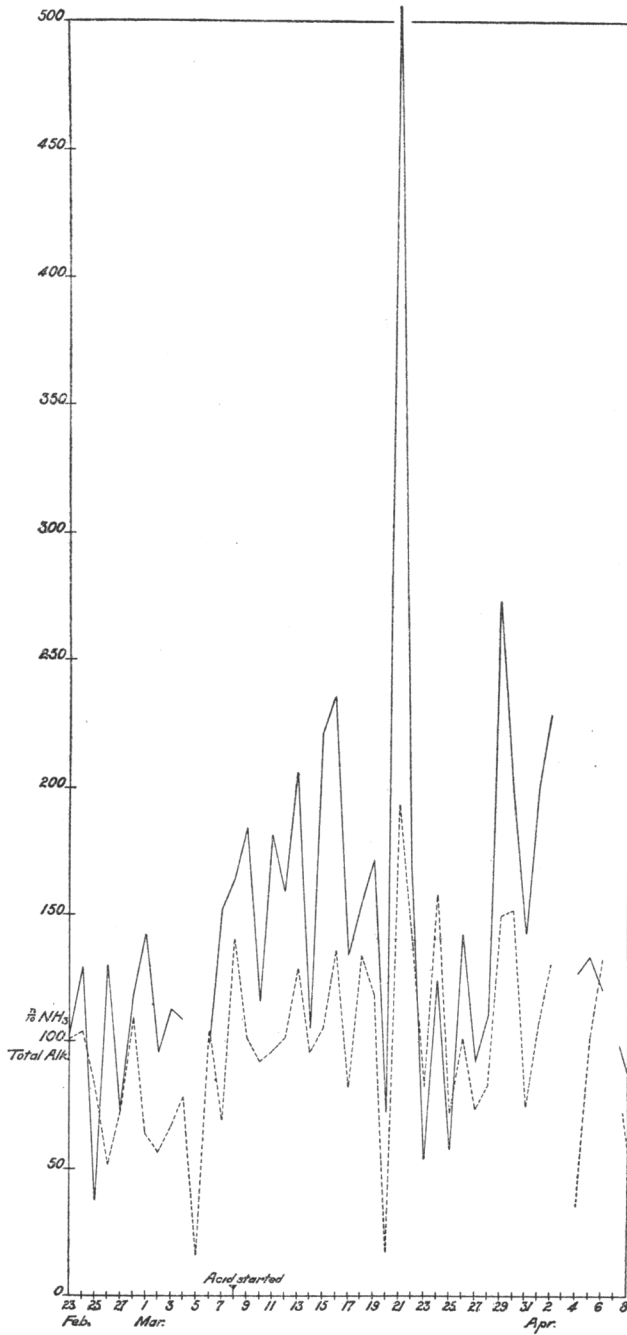


Chart 1.—Diagram of ammonia excretion and alkali retention, Experiment 1, Table 1.

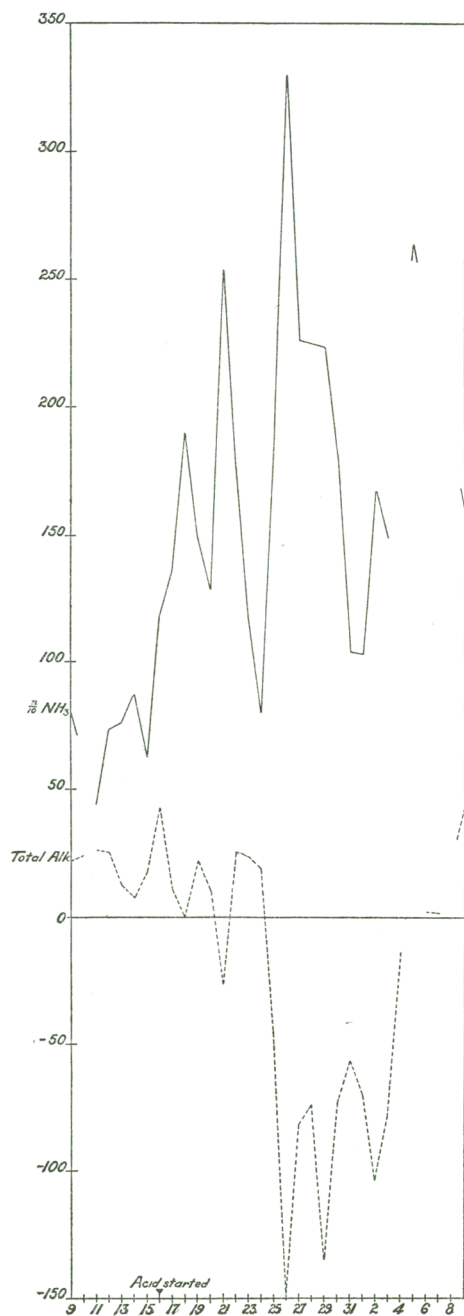


Chart 2.—Diagram of ammonia excretion and alkali retention, Experiment 2, Table 2.

was of sufficient accuracy and simplicity to make it of use in the clinical laboratory.

I. METHOD

The method employed in this investigation is the one reported by Henderson and Adler.² It consists in comparing the properly prepared urine with a standard solution so made up as to correspond in concentration and reaction to blood. The method depends on the facts that neutral red changes color at the exact point of reaction of the blood;³ and furthermore, that this change, while a fairly rapid one, shows intermediate shades of color between the full red of acid and the lemon-yellow of alkali. At the reaction of the blood the neutral red in solution is a reddish yellow; at the ordinary reaction of urine it approaches a light burgundy. If then a solution corresponding to blood in reaction be used as the standard, with neutral red as an indicator, a second specimen of urine made up under similar conditions as regards dilution and the quantity of neutral red used, may be titrated with a one-tenth normal sodium hydrate until the color of the urine specimen corresponds exactly to that of the standard solution. Obviously in titrating back to the reaction of the blood it is necessary to add to the acids of the urine precisely the amount of alkali which, formerly combined with them in the blood, has been retained by the kidney in the preparation of the urine. In addition to this retention of alkali another portion of base has been saved to the body by the substitution of ammonia for fixed alkali. Clearly, these two quantities are additive. Together they measure the effective work of the kidney in saving basic substances for the further neutralization of acid and transport of carbonic acid.

The solutions required are as follows:

1. A stock solution containing 36.2 gm. anhydrous di-sodium phosphate and 5.4 gm. anhydrous mono-sodium phosphate per liter. This solution when diluted in the ratio 1 to 80 gives the reaction of normal blood and is used for comparison of colors with the indicator.
2. A 25 per cent. aqueous solution of neutral red.
3. A solution of potassium oxalate approximately normal.

The procedure is as follows:

Three c.c. of the phosphate solution are placed in a 300 c.c. flask.

One c.c. of the neutral red solution is added and water to 240 c.c. This is the standard.

Ten c.c. of urine are treated with 1 c.c. of the oxalate solution and allowed to stand ten minutes. The urine is then filtered into a 300 c.c. flask, the precipitate washed, 1 c.c. neutral red solution added and the whole made up to about 240 c.c. One-tenth normal hydrate sodium solution is then run into the urine from a burette until the color matches that of the standard. The number of cubic centimeters of alkali thus used are calculated to the total volume of urine and the figure thus obtained represents the alkali retention.⁴

2. Henderson, L. J., and Adler, H. M.: *Jour. Biol. Chem.*, 1909, vi, p. xxii.

3. Salm, E.: *Ztschr. f. physik. Chem.*, 1906, lvii, 471.

4. Folin, O.: *Am. Jour. Physiol.*, 1903, ix, 265.

EXPERIMENTS

Three sets of experiments were performed. In the first the animals were kept on a constant diet of dog biscuit and water and were given varying quantities of a 0.8 per cent. hydrogen chlorid solution by the

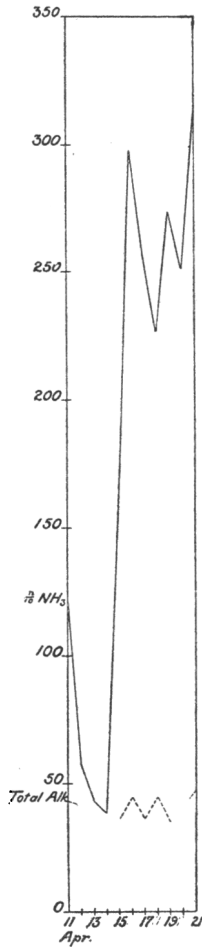


Chart 3.

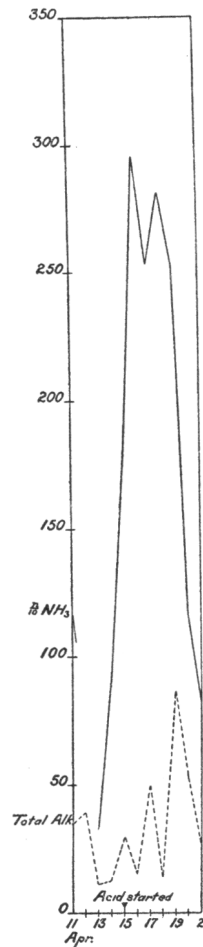


Chart 4.

Chart 3.—Diagram of ammonia excretion and alkali retention, Experiment 3, Table 3.

Chart 4.—Diagram of ammonia excretion and alkali retention, Experiment 4, Table 4.

stomach-tube. In the second series a constant diet of flour was substituted for the dog biscuit in order to reduce the amount of nitrogen and salts and thus the available alkali. In the third series the animals were given no food or acid and only a measured amount of water. In all

the experiments the urine was examined daily and the total quantity, the ammonia content, and the titratable bases were determined. The urine was furthermore examined for albumin or sugar, acetone and blood. At no time did we find either albumin or sugar, and, as was to have been expected in dogs, at no time did acetone appear in the urine even in the severest, fatal, case. The ammonia determinations were made according to the method of Folin.⁵

EXPERIMENT 1 (Table 1).—Feb. 23, 1909. Large male mongrel dog. Constant diet of 250 gm. dog biscuit and 600 c.c. of water mixed together and made into thick paste. In addition the dog received water of which he took varying amounts as indicated in the table. The acid feeding was begun March 8 and continued until the 23d. From March 18 he was given two feedings of acid a day. On March 19 diarrhea set in and persisted until the end of the experiment.

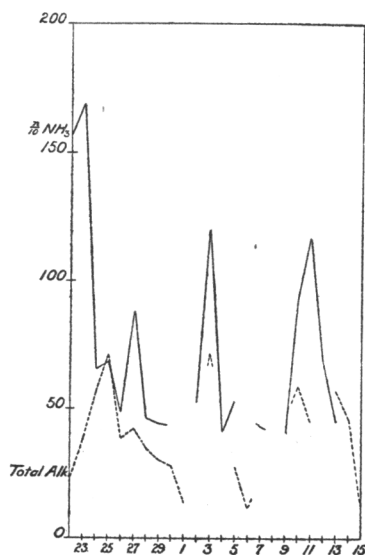


Chart 5.—Diagram of ammonia excretion and alkali retention, Experiment 5, Table 5.

On March 26 the dog vomited shortly after the acid feeding and continued this until the end of the experiment. Vomitus consisted at first from 10 to 20 c.c. of mucus mixed with the acid solution. Later small amounts of food appeared in the vomitus.

EXPERIMENT 2 (Table 2).—March 8, 1909. Small fox terrier bitch. Same amount of food given and under the same conditions as in Experiment 1. The acid feeding was begun on March 15 and continued daily until April 9. The animal appeared well and was very lively during the entire experiment. On March 21 diarrhea set in and continued until the end of experiment, but this did not seem to interfere with the general health. About March 20 it was noted that she was in heat and the table and the curve show that the amount of alkali excreted rose to enormous proportions. Although this entirely vitiated the

5. Folin, Otto: *Ztschr. f. physiol. Chem.*, 1902, xxxvii, 161.

experiment the results seem to us of sufficient interest to warrant continuing the experiment and to record the results. The dog showed a gain of one-quarter of a pound during the experiment.

EXPERIMENT 3 (Table 3).—April 9, 1909. Same dog as in Experiment 1. Dog was kept on a constant diet of 250 gm. of wheat flour, which was made up into a dough with water and without other additions baked into a dry biscuit. This was fed to the dog daily, together with 600 c.c. of water, of which the dog took varying amounts as shown in the table. A double feeding of 0.8 per cent. hydrogen chlorid was given daily throughout the experiment. The dog had soft movements from the beginning and vomited about 10 to 20 c.c. of mucus once or twice a day, usually shortly after the acid feeding. Practically no acid, however, was lost in this way. The dog kept constant weight throughout the experiment.

EXPERIMENT 4 (Table 4).—April 9, 1909. Male bull terrier pup, about four months old. The condition of the experiment was as in Experiment 3. The acid feeding began on April 14 and continued once a day until the 20th. The dog was lively throughout the experiment and did not vomit. He had soft move-

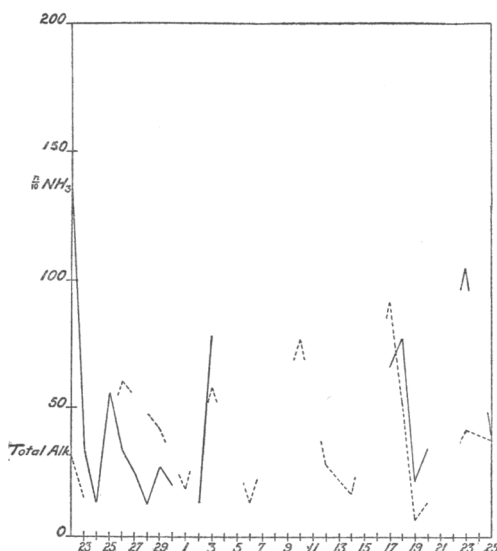


Chart 6.—Diagram of ammonia excretion and alkali retention, Experiment 6, Table 6.

ments during the period of acid feeding. The weight throughout the experiment remained the same.

EXPERIMENT 5 (Table 5).—April 22, 1909. The same dog as used in Experiments 1 and 3. Neither food nor acid was used during this experiment, but the starvation depended on to aggravate the acidosis induced by immediately preceding acid feeding. The stools throughout the experiment were normal. There was no vomiting. There was a rapid loss of weight throughout the experiment from 19½ pounds at the beginning to 12 pounds at the end. On May 13 the animal appeared languid and indifferent. On the 15th he died in coma. The urine early became scanty in amount in spite of the fairly large quantities of water that the dog consumed. This necessitated the omission of either the ammonia or the alkali determinations on certain days.

EXPERIMENT 6 (Table 6).—April 22, 1909. The same dog as in Experiment 4. Same conditions as in Experiment 5. Dog weighed at the beginning of the experiment 13¼ pounds and weighed 8¼ at the end of the experiment on May

25. The movements were normal throughout the experiment. The same difficulty as in Experiment 5 was met in obtaining an adequate quantity of urine. The animal was weak and torpid at the end of the experiment, but rapidly recovered on being fed.

DISCUSSION

From the comparison of the curves, omitting the second, it is apparent that the results of this method of determining the alkali retention not only vary with the conditions in the organism as indicated in the ammonia output, but are sufficiently regular and sufficiently large to be of value by themselves in estimating the capacity of the organism for withstanding acid. When the results obtained thus are added to the ammonia determinations we get a very much more accurate idea, not only of how much acid the organism has to combat, but also how far the alkali reserve has been involved in the struggle. The clinical material that we have been

TABLE 1.—EXPERIMENT 1, ACIDOSIS IN DOG WITH DIET OF DOG BISCUIT, WATER AND 0.8 PER CENT HYDROGEN CHLORID

Date	Water c.c.	Acid c.c.	Urine c.c.	Total NH ₃ c.c.	n/10NH ₃ c.c.	Total Alk. c.c.	n/10NH ₃ + Total Alk. c.c.
2/23	565	0	140	.1827	103.1	100.8	203.9
2/24	565	0	160	.2197	129.2	104.0	233.2
2/25	625	0	80	.0636	38.0	83.2	121.2
2/26	605	0	70	.221	130.0	51.6	181.6
2/27	555	0	120	.123	72.3	72.8	145.1
2/28	550	0	140	.199	117.5	109.2	226.7
3/1	750	0	100	.243	142.9	64.0	206.9
3/2	545	0	130	.167	95.2	56.5	151.7
3/3	500	0	95	.193	112.9	66.5	179.4
3/4	615	0	105	.184	108.2	78.7	186.95
3/5	610	0	15	15.7	short day
3/6	525	0	120	.1688	99.2	104.4	203.6
3/7	0	0	125	.259	152.3	69.7	222.05
3/8	100	72	180	.279	164.1	140.4	304.5
3/9	750	72	130	.313	184.1	101.4	285.5
3/10	575	70	105	.196	115.2	92.4	207.6
3/11	500	70	115	.309	181.7	96.6	278.3
3/12	580	72	90	.271	159.4	101.7	261.1
3/13	475	70	140	.351	206.4	129.0	335.4
3/14	550	70	85	.179	105.2	96.0	201.2
3/15	995	72	110	.377	221.7	105.6	327.3
3/16	645	74	160	.401	235.8	136.0	371.8
3/17	705	72	65	.228	134.1	82.2	216.35
3/18	800	153	140	.263	154.1	134.4	288.5
3/19	630	153	110	.291	171.7	118.8	290.5
3/20	505	147	50	.123	72.3	17.5	89.8
3/21	175	153	215	.860	505.8	193.5	699.3
3/22	945	155	115	.277	162.9	138.0	439.9
3/23	665	156	70	.092	54.1	83.3	137.4
3/24	575	100	140	.211	124.8	158.2	283.0
3/25	525	149	75	.0994	58.5	72.7	131.2
3/26	720	152	85	.251	142.8	102.0	244.8
3/27	225	78	70	.157	92.9	74.2	167.1
3/28	445	161	100	.188	111.2	84.0	195.2
3/29	585	156	200	.464	273.6	150.0	423.6
3/30	595	160	160	.336	198.4	152.0	350.4
3/31	480	160	60	.241	142.6	75.0	217.6
4/1	600	160	80	.338	199.6	107.2	306.8
4/2	490	78	105	.389	229.3	131.2	360.5
4/3	595	82	16
4/4	360	164	240	.214*	126.7	36.0*	162.7
4/5	235	160	110	.226*	133.7	102.3*	236.0
4/6	450	160	120	.204*	120.9	133.2*	254.1
4/7	490	170	16
4/8	420	161	40	.150	88.8	60.0	148.8

*Part lost.

TABLE 2.—EXPERIMENT 2, ACIDOSIS IN DOG UNDER SAME CONDITIONS AS EXPERIMENT 1

Date	Water c.c.	Acid c.c.	Urine c.c.	Total NH ₃ c.c.	n/10NH ₃ c.c.	Total Alk. c.c.	n/10NH ₃ + Total Alk. c.c.
3/ 8- 9	545	40	0	.136	80.0	22.0	102.0
3/ 9-10	350	...	0
3/10-11	350	90	0	.074	44.2	26.1	70.3
3/11-12	405	80	0	.124	73.6	25.6	99.2
3/12-13	430	50	0	.129	76.0	12.5	88.5
3/13-14	445	75	0	.147	87.7	7.5	95.2
3/14-15	460	65	0	.106	62.8	17.5	80.3
3/15-16	450	110	72	.200	118.	42.9	160.9
3/16-17	420	80	75	.221	136.	10.4	146.4
3/17-18	460	150	76	.323	190.	0	190.0
3/18-19	385	110	75	.253	149.	22.	171.0
3/19-20	420	100	75	.219	129.	10.	139.0
3/20-21	200	110	78	.425	254.	— 26.4	227.6
3/21-22	575	90	75	.300	177.	25.2	202.2
3/22-23	320	65	77	.188	117.	24.0	141.0
3/23-24	305	65	77	.134	79.4	18.8	98.2
3/24-25	330	60	78	.306	182.4	— 45.0	137.4
3/25-26	290	120	77	.561	330.	—148.	182.0
3/26-27	220	75	74	.384	226.	— 81.7	144.3
3/27-28	260	85	75	.382	225.	— 73.9	151.1
3/28-29	290	75	69	.379	223.	—135.	88.0
3/29-30	200	55	74	.307	181.	— 72.6	108.4
3/30-31	200	45	76	.176	104.	— 56.2	47.8
3/31- 1	200	35	76	.186	103.	— 70.0	33.0
4/ 1- 2	200	55	75	.285	168.	—103.4	64.6
4/ 2- 3	200	50	77	.253	149.	— 78.5	70.5
4/ 3- 4	200	40	77	— 13.6
4/ 4- 5	200	110	76	.448	264.
4/ 5- 6	200	20	77	2.0
4/ 6- 7	200	10	80	1.7
4/ 7- 8	200	65	57
4/ 8- 9	600	60	62	.272	160.	43.2	203.2

TABLE 3.—ACIDOSIS IN DOG WITH DIET OF DRY BISCUIT, WATER, AND 0.8 PER CENT. HYDROGEN CHLORID

Date	Water c.c.	Acid c.c.	Urine c.c.	Total NH ₃ c.c.	n/10NH ₃ c.c.	Total Alk. c.c.	n/10NH ₃ + Total Alk. c.c.
4/ 9-10	120	161	lost
4/10-11	140	163	90	.205	120.5	43.2	163.7
4/11-12	365	0	30	.098	57.6
4/12-13	340	155	25	.074	43.5
4/13-14	290	163	30	.065	38.2
4/14-15	380	158	110	.265	155.8	36.3	192.1
4/15-16	210	156	155	.506	297.6	44.9	342.5
4/16-17	260	164	130	.435	255.8	36.4	292.2
4/17-18	300	151	180	.384	225.8	45.0	270.8
4/18-19	450	0	160	.465	273.5	35.2	308.7
4/19-20	0	163	135	.426	250.5
4/20-21	580	76	190	.535	314.7	47.5	362.2

TABLE 4.—EXPERIMENT 4, ACIDOSIS IN DOG UNDER SAME CONDITIONS AS EXPERIMENT 3

Date	Water c.c.	Acid c.c.	Urine c.c.	Total NH ₃ c.c.	n/10NH ₃ c.c.	Total Alk. c.c.	n/10NH ₃ + Total Alk. c.c.
4/ 9-10	100	...	10
4/10-11	150	...	100	.199	117.0	35.0	152.0
4/11-12	320	...	110	39.6
4/12-13	220	...	40	.054	31.7	11.2	42.9
4/13-14	300	...	80	.159	93.5	12.8	106.3
4/14-15	295	80	200	.306	180.0	30.0	210.0
4/15-16	205	77	195	.503	295.8	15.6	311.4
4/16-17	140	72	125	.430	252.9	50.0	302.9
4/17-18	300	80	210	.479	281.7	14.0	295.7
4/18-19	590	0	310	.428	251.7	86.8	338.5
4/19-20	600	75	230	.198	116.4	52.9	169.3
4/20-21	195	...	135	.142	83.5	27.0	110.5

TABLE 5.—ACIDOSIS IN DOG UNDER STARVATION REGIME

Date	Weight c.c.	Water c.c.	Urine c.c.	Total NH ₃ c.c.	n/10NH ₃ c.c.	Total Alk. c.c.	n/10NH ₃ + Total Alk. c.c.
4/21-22	19½	460	125	.266	157.	23.7	180.7
4/22-23	365	160	.287	169.	38.4	207.4
4/23-24	350	85	.111	65.6	56.2	121.8
4/24-25	300	75	.116	68.6	71.2	139.8
4/25-26	450	51	.083	49.0	39.0	88.0
4/26-27	320	65	.151	89.0	42.2	131.2
4/27-28	16 5/16	220	50	.078	46.8	35.0	81.8
4/28-29	335	40	.074	44.8	30.8	75.6
4/29-30	225	40	.073	43.8	28.4	72.2
4/30- 1	200	20	14.4
5/ 1- 2	300	40	.088	52.4
5/ 2- 3	600	55	.204	120.3	71.5	191.8
5/ 3- 4	225	35	.069	41.1
5/ 4- 5	15	180	40	.090	53.7	28.0	81.7
5/ 5- 6	245	20	11.8
5/ 6- 7	135	30	.074	43.9
5/ 7- 8	80
5/ 8- 9	150	30	.066	39.2
5/ 9-10	90	75	.158	93.2	59.2	152.4
5/10-11	220	65	.198	117.0	45.5	162.5
5/11-12	12¾	240	80	.115	68.8
5/12-13	90	60	.076	45.6	57.0	102.6
5/13-14	100	80	46.4
5/14-15	60	15	12.9

TABLE 6.—ACIDOSIS IN DOG UNDER SAME CONDITIONS AS EXPERIMENT 5

Date	Weight c.c.	Water c.c.	Urine c.c.	Total NH ₃ c.c.	n/10NH ₃ c.c.	Total Alk. c.c.	n/10NH ₃ + Total Alk. c.c.
4/21-22	13 5/16	130	125	.229	135.5	31.2	166.8
4/22-23	135	115	.0578	34.0	14.9	48.9
4/23-24	120	30+	.0219+	12.9+
4/24-25	290	85	.093	55.7
4/25-26	50	55	.056	33.8	60.4	94.2
4/26-27	80	30	.048	24.7
4/27-28	40	30	.020	12.3
4/28-29	11 5/16	100	40	.045	27.3	42.0	69.3
4/29-30	135	35	.032	19.8
4/30- 1	80	20	18.6
5/ 1- 2	290	25	.0204	12.3
5/ 2- 3	410	40	.132	78.8	58.0	136.8
5/ 3- 4	140
5/ 4- 5	40
5/ 5- 6	10 5/16	100	15	13.5
5/ 6- 7	65
5/ 7- 8	65
5/ 8- 9	205
5/ 9-10	60	50	77.0
5/10-11	115	5
5/11-12	100	25	28.
5/12-13	9 1/16	120
5/13-14	150	15	16.2
5/14-15	100
5/15-16	175
5/16-17	300	70	.112	65.8	91.7	157.5
5/17-18	275	100	.132	78.0	52.	130.0
5/18-19	9.0	375	50	.0374	22.0	7.0	29.0
5/19-20	300	125	.057	34.6	13.7	48.3
5/20-21	300	25
5/21-22	225	120
5/22-23	440	230	.170	104.8	41.4	146.2
5/23-24	440	125
5/24-25	440	90	.066	39.6	37.8	77.4

TABLE 7.—ACIDOSIS IN HUMAN SUBJECTS

Subject	Date	Urine cc.	Acetone	Total NH ₃	n/10NH ₃	Total Alk.	n/10NH ₃ + Total Alk.
C	Apr. 1-2	1301	+	1.18	697.3	78.0	775.3
..	May 4-5	1520	+	1.30	826.0	15.2	841.2
..	May 4-5	1552	+	1.26	744.0	77.6	821.6
..	May 16-17	1171	+	.906	533.0	156.3	689.3
B	May 10-11	243	..	.297	174.9	102.0	276.9
..	May 10-11	870	..	.887	522.0	252.0	774.0
R	May 12-13	1555	..	.792	466.0	279.0	745.0
..	May 12-13	874	..	.666	392.0	183.5	575.5

C. Severe case. Diacetic acid constantly present with a minus carbohydrate balance of about 30 during most of the time. Given 30 gm. soda bicarbonate daily.

B. Moderately severe case. No diacetic acid for nine months. Never given soda bicarbonate. Has a plus carbohydrate balance of about 30-50.

R. Moderately severe case with diacetic acid present occasionally. Given 20 gm. soda bicarbonate up to May 3, none after May 3. Diet contains about 16 gm. carbohydrate; about 9 gm. nitrogen.

able to observe has necessarily been scanty, but as can be seen in the specimens presented in Table 7, the same general observations that were made experimentally hold here as well. In the curves it will be observed that the higher the ammonia curve reaches above the base line the higher ordinarily the alkali retention line runs. In these cases, as a rule, while the acidosis is severe, the organism is in no immediate danger of coma. The starvation experiment, which ended fatally, is not absolutely corroborative of this, because the animal died undoubtedly from exhaustion due to the previous acid intoxication. Even here, however, it will be observed that toward the end this alkali retention curve falls considerably below the ammonia curve. It is interesting to note that in Experiment 2 the alkali retention is decreased instead of increased almost proportionately, as the ammonia is increased. Whether this be due to alkaline secretion from the vagina entirely or in part also to the added condition of acidosis, it is clear that we are dealing here with an unfermented urine which is more alkaline than the blood, a condition which, except in those cases in which large amounts of alkali have been fed, has been considered by many an impossibility.

CONCLUSIONS

1. The amount of base excreted in the urine in acidosis, while following in general the variations in the amount of ammonia, may show differences which are of importance in estimating the power of the organism to resist intoxication.

2. Whether the amount of base excreted varies with the amount of ammonia or not, it is important to determine both quantities as they represent two distinct mechanisms of defense.

3. The method employed in this investigation is of such simplicity and accuracy as to recommend itself as a valuable aid to the clinician.

We wish to thank Dr. Francis A. Benedict of the Carnegie Institution Nutrition Laboratory, and Dr. Elliot P. Joslin for the clinical material used; Dr. L. V. Henderson for his kind interest, and Mr. R. S. Titus for assistance in the preliminary work.

Danvers State Hospital, Hathorne—212 Beacon Street, Boston.