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ACIDOSIS IN ACUTE AND CHRONIC DISEASE *

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The term acidosis as it is used in medicine at the present time does not designate a definite clinical entity, but is applied to a variety of conditions in which, as Sellards¹ expresses it, there is a general impoverishment of the body in bases or substances which readily give rise to bases. This impoverishment in bases may be due to faulty absorption of bases, to an unusual loss of them from the body, or to their neutralization by abnormal amounts of acids. Increase in the amounts of acids in the body may be due to the production of abnormal acids, an overproduction of the usual body acids, or, as Howland and Marriott² have recently suggested, to an accumulation of normal acids due to failure in excretion.

It is difficult, if not impossible, at the present time to estimate what are the normal amounts of bases and acids in the body. Probably considerable variation occurs under different physiologic conditions. Y. Henderson recently emphasized the variations due to changes in elevation above sea level that occur in healthy subjects in some of the tests for so-called acidosis.

The methods used in testing for evidence of so-called acidosis are numerous. They consist in a direct examination of the blood, a study of the urine, a study of the products of respiration, and an estimation of the amount of alkali necessary to render the urine alkaline when administered by mouth or intravenously.

In the direct examination of the blood for evidence of so-called acidosis many studies have been made of the carbon dioxide content of the blood. It has been known for a long time that this acid diminishes in amount in the blood as other acids increase, except when variations in the excitability of the respiratory center occur, as Hasselbalch³ and others have pointed out. A diminution of the carbon dioxide

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1. Sellards: Bull. Johns Hopkins Hosp., 1914, xxv, 101.

2. Howland and Marriott: Bull. Johns Hopkins Hosp., 1916, xxvii, 63.

3. Hasselbalch: Biochem. Ztschr., 1912, xlv, 403.

in the blood, therefore, has been looked on as evidence of acidosis. Pflüger,⁴ Senator,⁵ Geppert,⁶ and Minkowski⁷ were conspicuous among the early workers on the subject of diminished carbon dioxide in the blood in fevers. Their work, which was carried out on animals under different experimental conditions, consisted in direct examination of either the venous or the arterial blood. The lowering of the carbon dioxide content in the blood which they found in fevers was considered to be due to an increase in other acid substances. In 1889 Kraus,⁸ applying this test to man, found that the amount of carbon dioxide in the blood was diminished in fevers. He studied a few cases of typhoid fever, tuberculosis, erysipelas, scarlatina, pneumonia, and acute articular rheumatism. In 1912 Peabody⁹ studied the carbon dioxide content of the blood in pneumonia and found it usually low, occasionally normal, and rarely above normal. In the severer cases and terminal stages of the disease the carbon dioxide was usually low. Van Slyke¹⁰ has recently devised a relatively simple method for estimating the amount of carbon dioxide in the blood. This method should be of great assistance in detecting acidosis.

Studies on the hydrogen ion concentration of the blood for evidence of acidosis have been made by Peabody¹¹ in chronic nephritis and cardiac cases. He found the hydrogen ion concentration of the blood remained quite constant in his cases. Rolly¹² has made an extensive study of the hydrogen and hydroxyl ions in the blood in a variety of diseases and concludes from his observations that the alkalinity of the blood is lowered in diabetes, nephritis, severe anemia, and the gastrointestinal diseases of childhood, while, on the other hand, in diseases of the liver and in exophthalmic goiter the alkalinity of the blood is increased.

In 1888 von Jaksch¹³ reported a diminished alkalinity of the blood in uremia, fever, destructive liver disease, leukemia, chlorosis, primary anemia and carbon monoxide gas poisoning. In 1914 Sellards¹ estimated the titratable alkalinity of the blood in various conditions in which acidosis is present as shown by other tests, and found it diminished. He also found it lowered in certain chronic nephropathies and in some anemias.

4. Pflüger: Arch. f. d. ges. Physiol., 1868, i, 297.

5. Senator: Untersuchungen über fieberhaften Process und seine Behandlung. Berlin, 1873, p. 74.

6. Geppert: Ztschr. f. klin. Med., 1881, ii, 355.

7. Minkowski: Arch. f. exper. path. u. Pharmacol., 1885, xix, 209.

8. Kraus: Ztschr. f. Heilk., 1889, x, 106.

9. Peabody: Jour. Exper. Med., 1912, xvi, 701.

10. Van Slyke: To be published in the Jour. Biol. Chem.

11. Peabody: THE ARCHIVES INT. MED., 1914, xiv, 236.

12. Rolly: München. med. Wchnschr., 1912, lix, 1201.

13. Von Jaksch: Ztschr. f. klin. Med., 1888, xiii, 350.

In 1913 Marriott¹⁴ reported a method for estimating the amount of oxybutyric acid in a small amount of blood collected from a vein, and in 1914¹⁵ showed that although traces of this acid might be present in the blood during health it was increased ten to twenty fold in the acidosis of diabetes. Recently Howland and Marriott¹⁶ have reported that different acid substances, especially the acid phosphates, are increased in amount in the blood of patients with chronic nephritis.

It is to be expected that further studies on human blood will reveal cases in which normal acids are increased in amount in the blood in different diseases, or in which acids are present which are not present under normal conditions.

In considering the methods advocated for detecting the presence of acidosis by examination of the urine no attempt will be made completely to review the subject. Attention will simply be called to certain of the tests which have been used considerably of late by investigators. It must be remembered that just criticism has been raised against most of these urinary tests for acidosis, because they simply show what is excreted, and not what remains in the body. Careful studies have shown that frequently the body is unable to excrete in the urine those substances which have been looked on as indicative of acidosis.

Since Stadelmann¹⁷ discovered oxybutyric acid in the urine of diabetics in 1883, the presence of this substance or diacetic acid or acetone in the urine has been looked on as an indication of acidosis. At one time the amounts of these substances in the urine were used as indications of the degree of acidosis, but it has now been shown definitely that considerable amounts of oxybutyric acid may be present in the blood with only traces of acetone in the urine. On the other hand, there seems to be always some trace of acetone in the urine when there is much oxybutyric acid in the blood. Von Noorden¹⁸ mentions in his book that acetone has been found in scarlatina, measles, typhoid and severe dysentery. Howland and Marriott² consider that it occurs in most of the infectious diseases of childhood, just as fever occurs. In addition to the above, Taylor¹⁹ found acetone in the urine in eclampsia and phosphorus poisoning. It is also well known that acetone bodies occur in the urine in starvation and after anesthesia. Therefore acetone in the urine may be looked on as an indication that abnormal acids

14. Marriott: *Jour. Biol. Chem.*, 1913, xvi, 293.

15. Marriott: *Jour. Biol. Chem.*, 1914, xviii, 507.

16. Howland and Marriott: Reported at meeting of the American Society for the Advancement of Clinical Investigation, 1916.

17. Stadelmann: *Arch. f. exper. Pathol. u. Pharmacol.*, 1883, xvii, 419.

18. Von Noorden: *Metabolism and Practical Medicine*, Chicago Medical Book Co., 1907, ii, 160.

19. Taylor: *Digestion and Metabolism*, Lea & Febiger, Philadelphia, 1912, p. 362.

are present in the blood, but it is no indication of how large a quantity of them are present.

The relation of the amount of ammonia to the total nitrogen in the urine has been studied as an indication of excessive production of acid substances in the body. An increase in the relative amount of ammonia is looked on as an indication of so-called acidosis, although it must be borne in mind that certain diets rich in protein and diseases which cause a large breaking down of protein may show a relative as well as actual increase in ammonia nitrogen in the urine. Boussingault's²⁰ observation in 1850 that the ammonia in diabetic urines was increased was brought to the attention of medical men again in 1880 by Hallervorden.²¹ Since that time many observers have confirmed this fact and used it as a means of determining the degree of acidosis, especially in diabetes. Sellards²² has found the ammonia in the urine increased in Asiatic cholera. Pfaundler²³ reports it increased in diseases of the liver and in gastro-intestinal disorders of children. Palmer and Henderson²⁴ feel that the increase in ammonia in the urine indicates the degree of acidosis only in those cases in which the acidosis is due to the formation of oxybutyric acid. Howland and Marriott²⁵ perhaps sum up the question of the relation between a relative increase in the ammonia in the urine and acidosis by saying that such an increase suggests an acidosis, but needs confirmation by other tests.

In recent years studies have been made on the hydrogen ion concentration of the urine as estimated by Henderson's method. Henderson and Palmer²⁵ found that in certain diseases the average hydrogen ion concentration was lower than in healthy persons, but the individual variations in the different groups make the test unreliable.

Since Haldane and Priestley²⁶ in 1905 devised a relatively simple method for determining the amount of carbon dioxide in the alveolar air, this test has been much used for studies on acidosis. It is well known that the alveolar carbon dioxide corresponds closely to that in the arterial blood, and that as other acids increase this acid diminishes in amount in the blood. Thus a reduction of the tension of the carbon dioxide in the alveoli is looked on as an indication of acidosis, unless changes in the irritability of the respiratory center are present.

Von Rubow²⁷ and Beddard and Pembrey²⁸ in 1908 found a lowered

20. Boussingault: *Jour. f. prakt. Chem.*, 1850, li, 281.

21. Hallervorden: *Arch. f. exper. Path. u. Pharmacol.*, 1879-1880, xii, 237.

22. Sellards and Shaklee: *Philippine Jour. Sc.*, 1911, vi, 53.

23. Pfaundler: *Jahrb. f. Kinderh.*, 1904, lx, 719; *ibid.*, 1901, liv, 247.

24. Palmer and Henderson: *THE ARCHIVES INT. MED.*, 1913, xii, 153.

25. Henderson and Palmer: *Jour. Biol. Chem.*, 1913, xii, 393.

26. Haldane and Priestley: *Jour. Physiol.*, 1905, xxxii, 225.

27. Von Rubow: *Festschr. b. d. Einweihung der Finzeninst Klinik für innere Krankh.*, 1908, p. 26.

28. Beddard and Pembrey: *Brit. Med. Jour.*, 1908, ii, 580.

carbon dioxid tension in the alveolar air in cardiac cases which showed cyanosis. Fitzgerald²⁹ also found the carbon dioxid tension in the alveolar air below normal in cases of congenital heart disease. Beddard and Pembrey²⁸ found evidence of acidosis by this test in diabetes. Porges, Leimdörfer and Markovici³⁰ confirmed this finding and found also that the carbon dioxid tension was lowered in cardiac dyspnea. Friderica and Olsen³¹ report evidence of acidosis as shown by this test in some cases of erysipelas, mumps and angina, but not uniformly. Straub and Schlayer³² in 1912 found the carbon dioxid tension diminished in the alveolar air in cases of chronic nephritis. Evidence of acidosis in certain cases of chronic nephritis as shown by this test has also been found by Peabody,³³ Porges and Leimdörfer³⁴ and others. Roth³⁵ reports evidence of diminished carbon dioxid tension in the alveolar air in cases of obesity and in certain surgical cases.

The estimation of the degree of acidosis by determining the amount of sodium bicarbonate taken by mouth or intravenously which is necessary to render the urine alkaline has been used extensively by Sellards. He³⁶ found increased tolerance to sodium bicarbonate in some of the nephropathies, Asiatic cholera, some anemias, rheumatic fever and diabetes. Palmer and Henderson²⁴ in 1913 applied the principle of this test in a somewhat different form and found evidence of acidosis in nephritis. Peabody³⁷ has also found evidence of acidosis by the so-called soda tolerance test of Sellards in nephritis.

It is evident from this short review that signs of so-called acidosis, as detected by various tests, may exist in numerous diseases. In each disease, however, all the tests may not be positive, as for example acetone may be found in diabetes and in diseases in children, while in chronic nephritis it is not present; yet all of these conditions may show the alveolar carbon dioxid lowered or the sodium bicarbonate tolerance increased. It would seem, therefore, that so-called acidosis is not due in each case to the same abnormal factors.

It has been the object of this work to study on the same case at the same time several of these tests for so-called acidosis with a view of finding out how the cases in which an acidosis is supposed to exist react to the different tests. Also, it was thought that evidence of

29. Fitzgerald: *Jour. Path. and Bact.*, 1909-1910, xiv, 328.

30. Porges, Leimdörfer and Markovici: *Ztschr. f. klin. Med.*, 1911, lxxiii, 389.

31. Friderica and Olsen: *Deutsch. Arch. f. klin. Med.*, 1912, cvii, 236.

32. Straub and Schlayer: *München. med. Wchnschr.*, 1912, lix, 569.

33. Peabody: *THE ARCHIVES INT. MED.*, 1914, xiv, 236.

34. Porges and Leimdörfer: *Ztschr. f. klin. Med.*, 1913, lxxvii, 464.

35. Roth: *Jour. Am. Med. Assn.*, 1915, lxxv, 413.

36. Sellards: *Bull. Johns Hopkins Hosp.*, 1914, xxv, 141.

37. Peabody: *THE ARCHIVES INT. MED.*, 1915, xvi, 955.

acidosis might appear in certain diseases in which its presence has not as yet been expected.

For this purpose cases were selected from the wards of the Peter Bent Brigham Hospital for study. So far as possible cases were chosen which presented an uncomplicated picture of a single disease. In each case the carbon dioxid tension in the alveolar air was determined, the soda tolerance test was carried out, and the twenty-four-hour specimen of urine was examined for the presence of acetone, for its hydrogen ion concentration, for the total nitrogen and for the ammonia nitrogen.

The Plesch³⁸ method as modified by Higgins³⁹ was used for collecting the alveolar air, which was then examined by the method devised by Haldane⁴⁰ for gas analysis. That this method is satisfactory even in cases in which the patient is breathing rapidly or is unable to cooperate with the investigator has been shown by Walker and Frothingham.⁴¹ We (Walker and Frothingham) compared the results obtained by this method with the results obtained by examination of the venous blood direct, as recommended by Van Slyke, and found that they agreed very well in most cases. With this method under these conditions it seems fair to call the carbon dioxid tension normal when it falls between 39 and 45 mm. The alveolar air in each case was collected for examination at some time during the twenty-four hours in which the urine was collected or just after the twenty-four hours were up on the following morning before the soda tolerance test was started. Most of the samples of alveolar air were collected about two or three hours after a meal.

In studying the amount of sodium bicarbonate necessary to make the urine alkaline to litmus, 5 gm. at a time were given by mouth. At the end of two hours the patient voided the urine and if it was still acid the dose was repeated. If the patient was unable to void the next dose was put off until after the next urination. If the test was carried on through the night the patients were not aroused, so the intervals became longer. It usually takes from 5 to 15 gm. of sodium bicarbonate to change the reaction of a healthy person's urine from acid to alkaline. In a few cases the urine became amphoteric, in which cases the test was continued until it became definitely alkaline to litmus. This test was performed on the morning after the twenty-four-hour urine had been collected.

In the twenty-four-hour urines a small amount of toluol was used

38. Plesch: *Ztschr. f. exper. Path. u. Therap.*, 1909, iii, 380.

39. Higgins: Publication No. 203, Carnegie Inst. of Washington, 1915, p. 168.

40. Haldane: *Methods of Air Analysis*, London, Charles Griffin & Co., Ltd., 1912.

41. Walker and Frothingham: *Tr. Am. Soc. for the Advancement of Clinical Investigation*, 1916. Now published in *THE ARCHIVES INT. MED.*, September, 1916.

as a preservative. In some cases, due to contamination with feces or to errors on the part of those collecting the urines, the full twenty-four-hour amount was not obtained, but it was felt that probably these losses made little difference in the relation of ammonia to the total nitrogen.

The ammonia is recorded as ammonia nitrogen. This and the total nitrogen of the urine were estimated by Folin's⁴² method. The ammonia nitrogen is usually estimated under normal conditions at from 2 to 7 per cent. of the total nitrogen.

The hydrogen ion concentration of the urine was determined by Henderson's method and recorded as the logarithm with the minus sign omitted. Henderson and Palmer²³ found the average of 100 healthy cases to be P_H^+ 6.3. The presence of acetone was looked for by shaking the urine with glacial acetic acid and sodium nitroprussid and then adding ammonia. No attempt was made to determine quantitatively this substance.

The results of these studies are presented in the form of tables. Cases of the same disease are grouped together in one table and a few words of explanation are added to emphasize the interesting points. The actual date of the observation and the medical number of the patient are recorded so that by reference to the hospital records the exact condition of the patient at the time of the tests may be ascertained.

TABLE 1.—SYPHILIS

Date	Med. No.	Alveolar Air CO ₂ Tension, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P_H^+	Acetone	
11/ 5/15	3540	42	2.9	7.3	0	5
1/ 6/16	3857	44.2	2.8	5.9	0	10
2/17/16	4143	43.2	5.5	5.8	0	5

In Table 1 are grouped three cases of syphilis which showed evidence of a generalized infection with the spirochetes. It will be readily seen that in each case all the tests fall within normal limits and therefore no suggestion of acidosis is present.

In Table 2 are included two patients with epilepsy on whom the tests were taken between attacks, which came in only infrequent intervals. In these cases there is no evidence of acidosis in any of the tests used.

42. Folin and McCallum: Jour. Biol. Chem., 1912, xi, 523. Folin and Farmer: Ibid., 493.

Six cases of diabetes are presented in Table 3. In five of these cases it will be seen that there is evidence of acidosis and, furthermore, that each of these five cases shows variations from the normal in all of the tests used except in the hydrogen ion concentration of the urine. As will be observed in the other groups, this test shows such marked variation in the individual cases that it does not seem to be reliable as

TABLE 2.—EPILEPSY

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H +	Acetone	
11/ 3/15	3517	42.7	5.0	5.6	0	10
11/ 3/15	3514	39.1	6.3	5.8	0	10

a guide to acidosis. The remaining case was a mild case and showed no evidence of acidosis by any of the tests. If we assume that the acidosis of diabetes is due entirely to the presence of increased amounts of oxybutyric acid, we may expect that acidosis due to this cause in other diseases will give positive results with all these tests except the hydrogen ion concentration of the urine. Of course other factors than oxybutyric acid may take part in the acidosis of diabetes.

TABLE 3.—DIABETES

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H +	Acetone	
12/14/15	3738	34.7	18.2	6.2	+	35
12/15/15	3746	36.6	11.2	5.1	+	45
12/15/15	3757	34.6	18.9	below 4.7	+	65
1/ 4/16	3880	32.3	20.4	5.9	+	{ 60 amphoteric 90 total 10
1/24/16	4008	40.8	4.6	5	0	
1/25/16	3988	35.5	10.3	5.5	+	

Quite a different condition from the acidosis in diabetes is seen in the nine cases of exophthalmic goiter in Table 4. These cases represent various degrees of activity of the disease. In some of these cases the carbon dioxide tension in the alveolar air was quite high. Acetone was never present and the urine became alkaline on small amounts of sodium bicarbonate in four of the cases. The percentage of ammonia nitrogen to total nitrogen varied considerably, but in no case did it

reach 10 per cent. The hydrogen ion concentration shows variations from one end of the scale used to the other.

Eight cases of primary anemia with quite marked blood changes are shown in Table 5. Evidence of acidosis is suggested in the alveolar air and soda tolerance tests in two cases, but both of these

TABLE 4.—EXOPHTHALMIC GOITER

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H +	Acetone	
11/ 4/15	3434	54.4	2.8	7.3	0	15
11/16/15	3591	47.2	2.8	6.3	0	{ 10 amphoteric 15 total
12/16/15	3792	43.5	6.9	6.4	0	
12/16/15	3748	45.4	7.0	5.8	0	10
1/13/16	3896	47.7	2.1	4.7	0	5
1/21/16	3989	41.2	7.6	5.9	0	0
1/27/16	4040	40.9	4	7	0	5
2/ 1/16	4075	40.6	6.4	6.2	0	{ 5 10 amphoteric 15 total
3/17/16	4311	43.9	7.3	below 4.7	0	

TABLE 5.—PRIMARY ANEMIA

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H +	Acetone	
10/23/15	3139	40.2	6.9	5.3	0	20
10/26/15	3435	41.2	4	6.6	0	10
11/ 9/15	3538	39.7	5.8	5.2	0	10
11/29/15	3690	39.3	5.5	5.6	0	{ 15 amphoteric 20 total
1/12/16	3863	36.7	7.5	5.6	0	
2/ 4/16	4063	42.5	6.9	6.3	0	15
2/29/16	4064	38.6	4	5.2	0	20 taking 1 c.c. di- lute HCl t.i.d.
2/29/16	4223	46.2	5.3	5.4	0	10

patients were receiving 1 c.c. of dilute hydrochloric acid three times a day. In other cases the amount of sodium bicarbonate necessary to render the urine alkaline was slightly elevated. The study of the ammonia-nitrogen ratio and the hydrogen ion concentration showed nothing remarkable. Certainly no appreciable degree of acidosis exists in this condition which is detectable by these tests.

Four of the six cases of advanced chronic nephritis in Table 6

show evidence of acidosis by the alveolar air test and the soda tolerance test. The percentage of ammonia is low in most of the cases, which agrees with observations of other workers. Whether this is due to faulty elimination or to the fact that ammonia is not used by the body to make up the deficiency in base met with in chronic nephritis is not clear. As there is no acetone in the urine it is evident that this acidosis is due to some other factor than that which is present in diabetes. The hydrogen ion concentration is fairly constant in these cases and somewhat lowered. Several other cases, not included in the table because all five of the tests could not be completed, showed a very marked reduction in the alveolar air carbon dioxide tension. In one case it was as low as 19 mm.

TABLE 6.—CHRONIC NEPHRITIS

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ - N ₂ per Cent.	P _H ⁺	Acetone	
11/ 5/15	3507	44	6.5	6.2	0	10
11/ 8/15	3520	38.7	1	4.8	0	25+
11/ 8/15	3369	40.1	2.2	5.1	0	50
11/22/15	3597	37.3	4.3	5.1	0	10
1/21/16	3990	39.5	4.2	5.8	0	25
3/ 4/16	4253	29.9	2.8	5.5	0	40+

Twenty-one observations on fifteen cases of pneumonia are recorded in Table 7. In those cases in which two observations were made the second one was after the crisis. Several of these pneumonias terminated fatally. Although the respirations in many of these cases were elevated the results of the carbon dioxide tension determinations in the alveolar air checked up well with the estimation of carbon dioxide in the venous blood. Some of these cases during the course of the disease showed evidence of acidosis by this alveolar air test, while others showed just the reverse. This fits in with Peabody's observation on the blood in pneumonia. He found the carbon dioxide low in some, normal in some and elevated in a few. In a few of the cases the ammonia fraction of the total nitrogen in the urine was elevated appreciably above normal. The hydrogen ion concentration of the urine was quite variable, but on the whole tended to be toward the acid end of the scale. In one case acetone was present. In most of the cases during the height of the fever the amount of sodium bicarbonate necessary to render the urine alkaline was considerably increased. In the cases in which a plus sign is put after the number of grams it signifies that the sodium bicarbonate was discontinued for some

reason before the urine became alkaline. This test certainly suggests that an acidosis is present during the course of the fever in some of these cases. An interesting feature in this group is the fact that the different tests for acidosis show more variable results than in other diseases with acidosis. It suggests, therefore, that if an acidosis is present in pneumonia, it may be due to some other factors besides those that produce the acidosis in diabetes or chronic nephritis.

TABLE 7.—PNEUMONIA

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Blearb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H +	Acetone	
11/13/15	3608	37.9	26.5	5.5	+	10
11/23/15	3608	39.7	8.3	6.2	0	5 convalescent
11/18/15	3630	40.3	5.8	5.4	0	55
11/23/15	3630	33.8	2.5	6.4	0	10 crisis passed, beginning em- pyema
11/19/15	3642	34.5	12.3	5.7	0	35+ discontinued
11/26/15	3677	44.2	7.6	5.1	0	40
11/29/15	3699	45.9	9.8	5.3	0	15
12/ 7/15	3699	47.6	7.7	6.1	0	15 convalescent
12/ 8/15	3744	40.6	8.1	5.2	0	35+ discontinued
12/31/15	3883	34.2	7.1	...	0	110
1/10/16	3883	44.7	3.3	5.6	0	15 convalescent
12/31/15	3882	34.7	5	...	0	30
1/10/16	3882	41.9	2.9	6	0	5 convalescent
1/ 4/16	3885	42	5.6	5.4	0	25
1/14/16	3944	38.1	10.7	6.2	0	{ 20 amphoteric 35 total
1/19/16	3965	41.6	5.6	5.2	0	20 brochopneu- monia?
1/27/16	4046	45.1	7.5	5.1	0	25
2/ 5/16	4046	45.1	6	5.4	0	15 convalescent (Crisis on day
3/17/16	4263	36.3	11.8	5.2	0	5 before toler- ance test was done
3/ 7/16	4280	43.1	3.3	4.9	0	15
3/17/16	4237	38.8	9.7	4.7	0	20

In Table 8 are ten observations made on eight cases of acute articular rheumatism. These patients were taking sodium salicylate at the time of the observations. In several of the cases evidence of acidosis was shown by the alveolar air studies, but not in all of them. In one case acetone was present and in another the ammonia was elevated to nearly 10 per cent., but in the other cases these tests showed no evidence of acidosis. Four of the cases showed an increase in the soda

tolerance test. The hydrogen ion concentration of the urine showed too marked variation to be of value in forming an opinion in this disease. It seems fair to say that some form of acidosis occurs in certain of these cases of acute rheumatism, which shows up in one or the other of these tests, but not consistently in any one.

TABLE 8.—ACUTE ARTICULAR RHEUMATISM

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H ⁺	Acetone	
12/ 2/15	3715	33.2	5.1	5.7	0	10
12/ 7/15	3715	41	2.6	4.9	0	10 convalescent
12/ 2/15	3712	37.1	6.5	5.4	+	15
12/ 3/15	3662	35	5.1	7.1	0	20
12/ 8/15	3662	31.2	4.2	5.1	0	10
2/ 3/16	4088	33.2	6.4	5.3	0	20
3/23/16	4371	38.2	7.6	Below 4.7	0	40
3/27/16	4396	33.1	5.8	7.2	0	10
3/29/16	4417	44.5	6.4	5.6	0	20
4/21/16	4534	43.3	9.8	4.9	0	15

TABLE 9.—SUBACUTE NEPHRITIS

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H ⁺	Acetone	
3/ 2/16	4160	39.5	7.1	6	0	10
3/22/16	4245	46.2	3.6	4.9	0	15
3/22/16	4314	48.5	2.9	5.2	0	10

TABLE 10.—LUNG ABSCESS

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H ⁺	Acetone	
1/12/16	3884	40.4	3.2	5.6	0	15
3/ 7/16	4226	41.2	8.2	5.2	0	10

Three cases of subacute nephritis of a mild grade are presented in Table 9 and show no evidence of acidosis by any of the tests. In two the carbon dioxide tension in the alveolar air was rather high.

Two cases of lung abscess shown in Table 10 also give no evidence of acidosis.

In two cases of gastric cancer (Table 11) the amount of sodium bicarbonate necessary to render the urine alkaline was increased above normal in both. This may possibly have been due to some disturbance in absorption rather than an acidosis. Of the other tests the alveolar air suggested acidosis in one case. The ammonia was high in this case also. The hydrogen ion concentration in the urine represented the two extremes of the scale.

TABLE 11.—GASTRIC CANCER

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H ⁺	Acetone	
3/20/16	4836	39.2	7.2	Below 4.7	0	{ 80 amphoteric 45 total
3/23/16	3799	37.4	12.8	7.1	0	{ 5 amphoteric 35 total

TABLE 12.—ADDISON'S DISEASE

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H ⁺	Acetone	
10/29/15	3521	28.8	8.3	Below 4.7	0	35
3/11/16	4299	38.7	2.4	Below 4.7	0	15

TABLE 13.—CIRRHOSIS OF THE LIVER

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H ⁺	Acetone	
2/ 2/16	4007	43.7	11.5	5.8	0	10
2/18/16	4170	38.2	6	5.1	0	25 (ascites)

In two cases of Addison's disease (Table 12) the carbon dioxide tension was just below the lower limit of normal. In one case the soda tolerance test showed an increase. It is interesting to note that in both the cases the hydrogen ion concentration was more acid than a P_H⁺ of 4.7, but conclusions from these two cases are hardly justifiable.

In one of the cases of cirrhosis of the liver (Table 13) the ammonia was elevated, as has been noted in diseases of the liver. In the

patient who had ascites the soda tolerance test was increased. This has been the finding in other of our cases of ascites from portal obstruction and probably has some relation to the portal obstruction rather than to an acidosis.

In Table 14 are grouped six cases of chronic cardiac disease. In these cases compensation was fairly well established as long as the patients were quiet in bed. Most of them preferred to have the head somewhat elevated. Except for a diminished carbon dioxid tension in one case and a slightly increased percentage of ammonia in another, there is no evidence of acidosis. In both these cases the other signs of an acidosis were absent. The hydrogen ion concentration of the urine showed such marked variation that no conclusions could be drawn from it.

TABLE 14.—CHRONIC CARDIAC

Date	Med. No.	Alveolar Air CO ₂ Ten- sion, Mm.	24-Hour Urine			Sodium Bicarb., Gm.
			NH ₃ /N ₂ -N ₂ per Cent.	P _H +	Acetone	
11/ 9/15	3523	34.8	3.7	6.4	0	5
11/10/15	3539	46.4	3.8	5.4	0	10
11/17/15	3632	39.1	4.8	7.4	0	5
12/28/15	3730	43.2	6.4	4.7	0	10
12/30/15	3460	40.2	11.7	4.7	0	10
1/31/16	4036	46.3	4.7	5.8	0	5

In Table 10 are grouped seventeen cases representing as many different conditions. In several of them interesting responses to the different tests are seen. In some of them quite marked evidence of acidosis occurs. Acetone was not found in any of these cases, so the type of acidosis was probably different from that found in diabetes. In the cases with an acute infection involving the kidney, in the case of probable miliary tuberculosis and in the case of typhoid fever evidence of acidosis was shown by the alveolar air study and the soda tolerance test. In two of these cases the hydrogen ion concentration of the urine showed it to be strongly acid. One case of gout was interesting, in that it showed no evidence of acidosis. The case of portal thrombosis was of interest in that it showed a high percentage of ammonia nitrogen in the urine, as is reported in liver disorders and a high sodium bicarbonate tolerance, which is probably due to the portal obstruction rather than to an acidosis. The cases of lymphatic leukemia, portal thrombosis and myxedema show a very slight reduction in the carbon dioxid tension of the alveolar air, but too slight to make one feel that any appreciable acidosis exists. The case which

suggested typhus was interesting in that the sodium bicarbonate tolerance was increased, suggesting an acidosis, while the carbon dioxide tension in the alveolar air was high, suggesting just the reverse.

From these studies it seems fair to conclude that the study of the hydrogen ion concentration in the urine is not reliable as an index of acidosis, and therefore it will not be considered further in this summary. It is also clear from this study that evidence of acidosis appears at times in certain diseases, while in other diseases no evidence of it is found. Those diseases which showed an acidosis at times by some

TABLE 15.—MISCELLANEOUS CASES

Date	Med. No.	Alveolar Air CO ₂ Tension, Mm.	24-Hour Urine			Sodium Blearb., Gm.	Diagnosis
			NH ₃ /N ₂ -N ₂ per Cent.	P _H +	Acetone		
12/21/15	3780	27.4	7.6	Below 4.7	0	80+	Acute infection involving kidney
10/29/15	3423	41.6	3.1	5.6	0	15	Chronic arthritis
10/27/15	3522	36.4	7.9	6.1	0	20	Typhoid fever
10/29/15	3457	28.7	2.6	Below 4.7	0	30	Probably military tuberculosis
11/ 3/15	3559	42.2	4.6	5.6	0	20	Tumor in right kidney region
11/10/15	3480	42.5	9.8	5.8	0	15	Fever, mild, unknown cause
11/12/15	3566	41.7	7.8	7.3	0	10	Acute endocarditis
12/14/15	3787	41.9	5.2	5.0	0	10	Acute bronchitis
3/24/16	4359	46.7	6.4	6.4	0	10	Polycythemia
1/ 6/16	3905	39.9	7.1	5.3	0	15	Gonorrheal arthritis
1/12/16	3955	41.9	6.1	5.6	0	15	Perirenal abscess
1/24/16	4025	45.9	7.5	5.4	0	30	Typhus (?)
1/25/16	4035	43.5	3.4	6.6	0	10	Erythema nodosum
2/16/16	4166	45.9	5.4	5.2	0	15	Gout and alcohol
2/21/16	4180	38.3	5.6	4.7	0	10	Lymphatic leukemia
2/ 1/16	3281	38.5	27.8	5.8	0	65	Portal thrombosis
2/28/16	4197	38.3	5.6	6.0	0	15 amphoteric 20 total	Myxedema

of these tests are diabetes, chronic nephritis, pneumonia, acute articular rheumatism and several acute febrile conditions in the miscellaneous group. Cases of exophthalmic goiter, epilepsy, syphilis, chronic cardiac disease, subacute nephritis, lung abscess, and many in the miscellaneous group distinctly did not show any evidence of acidosis by these tests. The results in the cases of primary anemia, gastric cancer, Addison's disease, and cirrhosis of the liver were not so clearly defined and in some of the tests suggested a slight acidosis.

It is evident from these tests that the acidosis found in diabetes

is due to different causes, in part at least, from those that produce it in other conditions. It also seems likely that the acidosis met with in different diseases is due to various causes, since the response to these tests varies somewhat in the different conditions.

Of these tests, either the estimation of the carbon dioxid tension in the alveolar air or the so-called soda tolerance test showed variation from the normal in all the cases of acidosis. They also seem to be of value in detecting the degree of acidosis.

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