REFERENCES

[1] Gugliucci, C., O'Sullivan, M., Oppermen, W., et al.: Intensive care of the pregnant diabetic. Am. J. Obstet. Gynecol. *125:* 435, 1976.

[2] Yssing, M.: Long term prognosis of children born to mothers diabetic when pregnant. *In* Diabetes in Early Life, Camerini-Davelos, R., and Cole, H., Eds. New York, Academic Press, 1975.

[3] Victor, A.: Normal blood sugar variation during pregnancy. Acta Obstet. Gynecol. Scand. *53:* 37–40, 1974.

[4] Karlsson, K., and Kjellmer, L.: The outcome of diabetic pregnancy in relation to the mother's blood sugar level. Am. J. Obstet. Gynecol. *112:* 213, 1972.

[5] Cole, H.: Problems in management of infants of diabetic mothers. *In* Diabetes in Early Life, Camerini-Davelos, R., and Cole, H., Eds. New York, Academic Press, 1975.

Mixed Acid-Base Disturbances in Diabetes

Recognition and Terminology

The report of Sanders et al. in this issue of DIABETES CARE illustrates the occurrence of a mixed acid-base disturbance in an elderly female patient with diabetes. The relatively rare occurrence of an alkalemic pH was noted in their case, and the significance of this metabolic abnormality discussed. Reference is made to the prior reports of alkalosis occurring in patients with diabetes[1–4] previously referred to as "diabetic ketoalkalosis." This term is misleading, technically incorrect, and gives reason to review the nature of mixed acid-base disturbances and the role they play in diabetes.

As noted by McCurdy,[5] *alkalosis* is a process that gives rise to an increase in the serum concentration of the base (HCO_3^-), and *acidosis* is a process that provides a loss of HCO_3^- from the body. The state of pure alkalosis, therefore, according to the Henderson-Hasselbach equation, gives rise to *alkalemia* (serum pH greater than 7.45), and, conversely, pure acidosis leads to *acidemia* (serum pH less than 7.35). Utilizing this terminology, unopposed alkalosis and acidosis are metabolic or respiratory processes that ultimately lead to shifts in serum hydrogen ion concentration into the alkalemic or acidemic range. Thus, the simultaneous occurrence of both alkalosis and acidosis can be envisioned, with the resulting pH representing the sum of more than one process. The pH then may be elevated, reduced, or in the normal range.

In the patient with diabetes, the most common acid-base abnormality observed is metabolic acidosis due to increased ketoacid production. This is readily recognized by the usual occurrence of elevated serum and urine concentrations of both glucose and ketone bodies, as well as decrements in serum HCO_3^-, serum pH, and pCO_2. An increase in the absolute difference between the concentration of the serum sodium, on the one hand, and the sum of the serum chloride and bicarbonate, on the other hand, constitutes the "anion gap" and is a cardinal finding in metabolic acidosis. It should not be surprising, however, that in patients with diabetes, other metabolic and/or respiratory abnormalities may also occur. The metabolic alkalosis that is associated with prolonged or severe vomiting or volume contraction is one example. The problem lies not in realizing that mixed acid-base disturbances can exist, but rather in recognizing these mixed disturbances in otherwise unsuspected circumstances, such as in the diabetic patient who presents with glucosuria and ketonuria. In part this problem has been eliminated in recent years with the advent of routine serum pH determinations in cases suspected of having diabetic ketoacidosis. The finding of an alkalemic or normal serum pH in such a patient should suggest the presence of at least one, and possibly two, other primary acid-base disturbances. This should alert the clinician to utilize therapy specifically designed to resolve those processes. In the patient described by Sanders et al. in this issue of DIABETES CARE, and in the previous reports of diabetes with alkalemia, the importance of potassium chloride replacement in the treatment of metabolic alkalosis is demonstrated[6].

Some of the confusion surrounding the occurrence of an alkalemic pH in a patient producing ketones apparently stems from the methods currently used to quantitate serum and urine ketone body concentrations. Both the Ketostix strips and Acetest tablets utilize the nitroprusside reaction to detect both acetone and acetoacetate, the latter with great sensitivity. Positive reactions can be seen with concentrations of acetoacetate less than 1 mM. The nitroprusside reaction does not measure beta-hydroxybutyrate. In the presence of alkalemia, the metabolic equilibrium between beta-hydroxybutyrate and acetoacetate is shifted disproportionately in favor of acetoacetate. Thus, in the absence of enzymatic determinations of ketone bodies, the extent of ketone body production may be overestimated. To fail to recognize the occurrence of a coexistent acid-base abnormality, due to overestimation of the severity of the ketoacidosis, is of obvious significance. As pointed out by Roggin et al.,[2] the proper attention to fluid and electrolyte replacement in their patient was life saving.

In the previous reports describing alkalemia in diabetic patients with ketosis, the unfortunate term "diabetic ketoalkalosis" was used.[3,4] Additionally, the authors suggested that this "entity" was more common than generally recognized.[3] As discussed above, such a designation is misleading and fails to properly identify the problem as a mixed acid-base disturbance.

The occurrence of mixed disturbances in conjunction with diabetic ketoacidosis is probably common. The predominance of a metabolic alkalosis, however, with resulting alkalemia, is not frequently seen, and should be suspected when the appropriate clinical history or laboratory data are obtained.

IRWIN KLEIN
MIAMI, FLORIDA

REFERENCES

[1] Bleicher, S.: Ketosis not always acidosis: 'Heartburn' can be relevant. Diabetes Outlook *2*: 3–4, 1967.

[2] Roggin, G., et al.: Ketosis and metabolic alkalosis in a patient with diabetes. J.A.M.A. *211*: 296–98, 1970.

[3] Walsh, C., and Lim, K.: Diabetic ketoalkalosis: a readily misdiagnosed entity. Br. Med. J. *2*: 19, 1976.

[4] Melrose, E., et al.: Diabetic ketoalkalosis. Br. Med. J. *2*: 237, 1976.

[5] McCurdy, D. K.: Mixed metabolic and respiratory acid-base disturbances; diagnosis and treatment. Chest *62* (Suppl.): 35–44, 1972.

[6] Kassirer, J. P., Berkman, P. M., Lawrenz, D. R., and Schwartz, W. B.: The critical role of chloride in the correction of hypokalemic alkalosis in man. Am. J. Med. *38*: 172–81, 1965.

The Editors are pleased to report that DIABETES CARE has been selected for inclusion in the National Library of Medicine's MEDLARS data base and, accordingly, will be indexed in *Index Medicus*.

The opinions expressed in editorials represent those of the authors and do not reflect official policy of the American Diabetes Association or of the institution with which the author is affiliated.

STATEMENT OF OWNERSHIP, MANAGEMENT AND CIRCULATION

(Act of August 12, 1970: Section 3685. Title 39. United States Code)

1. TITLE OF PUBLICATION: Diabetes Care

2. DATE OF FILING: September 30, 1978.

3. FREQUENCY OF ISSUE: Bi-monthly

4. LOCATION OF KNOWN OFFICE OF PUBLICATION: 600 Fifth Avenue, New York, NY 10020

5. LOCATION OF THE HEADQUARTERS OF GENERAL BUSINESS OFFICES OF THE PUBLISHERS: 600 Fifth Avenue, New York, NY 10020.

6. NAMES AND ADDRESSES OF PUBLISHER, EDITOR AND MANAGING EDITOR: Publisher, American Diabetes Association, Inc., 600 Fifth Avenue, New York, NY 10020. Editor, Jay S. Skyler, M.D. 600 Fifth Avenue, New York, NY 10020. Managing Editor, Susan Lovell, 600 Fifth Avenue, New York, NY 10020.

7. OWNER: (If owned by a corporation, its name and address must be stated and also immediately thereunder the names and addresses of stockholders owning or holding 1 per cent or more of total amount of stock. If not owned by a corporation, the names and addresses of the individual owners must be given. If owned by a partnership or other unincorporated firm, its name and address, as well as that of each individual must be given.) Name, American Diabetes Association, Inc. (A nonprofit voluntary health agency—no stockholders), Address, 600 Fifth Avenue, New York, NY 10020.

8. KNOWN BONDHOLDERS, MORTGAGES, AND OTHER SECURITY HOLDERS owning or holding 1 per cent or more of total amount of bonds, mortgages, or other securities: NONE.

9. *For completion by non-profit organizations authorized to mail at special rates (Section 132.122, Postal Manual)*: The purpose, function, and nonprofit status of this organization and the exempt status for Federal income tax purposes have not changed during the preceding 12 months.

10. Extent and nature of circulation: (A) Total No. copies printed (Net Press Run): Average No. copies each issue preceding 12 months: 22,452. Actual number of copies of single issue published nearest to filing date: 20,132. (B) Paid circulation: (1) Sales through dealers and carriers, street vendors and counter sales: Average No. copies each issue during preceding 12 months: 0. Actual number of copies of single issue published nearest to filing date: 0. (2) Mail subscriptions: Average No. copies each issue during preceding 12 months: 3,761. Actual number of copies of single issue published nearest to filing date: 3,761. (C) Total Paid Circulation: Average No. copies each issue during preceding 12 months: 3,761. Actual number of copies of single issue published nearest to filing date: 3,761. (D) Free distribution by mail carrier or other means samples, complimentary, and other free copies: Average No. copies each issue during preceding 12 months: 15,725 (including 3,307 of nondeductible Association member subscriptions). Actual number of copies of single issue published nearest to filing date: 13,419 (including 3,285 of nondeductible Association member subscriptions). (E) TOTAL DISTRIBUTION (sum of C and D): Average No. copies each issue during preceding 12 months: 19,486. Actual number of copies of single issue published nearest to filing date: 17,180. (F) Copies not distributed: (1) Office use, left over, unaccounted, spoiled after printing: Average No. copies each issue during preceding 12 months: 2,966. Actual number of copies of single issue published nearest to filing date: 2,952. (2) Returns from news agents: Average No. copies each issue during preceding 12 months: 0. Actual number of copies of single issue published nearest to filing date: 0. (G) Total (Sum of E and F—should equal net press run shown in A): Average No. copies each issue during preceding 12 months: 22,452. Actual number of copies of single issue published nearest to filing date: 20,132.

11. I certify that the statements made by me above are correct and complete. WILLIAM A. ASPINWALL, Director of Finance.