EDITORIAL

SYRUPY BLOOD

From time to time reports are published of patients with blood sugar levels reaching 1,000 mg. per 100 ml. or higher. Such concentrations occur in the course of severe diabetic acidosis and have been known to exceed even 2,000 mg. per 100 ml. Some years ago Lawrence observed an adult patient with fatal ketoacidosis in whom the concentration prior to therapy was 2,060 mg. per 100 ml.[1] More recently, Myer and Salt reported an eight-year-old boy who survived in whom a pretreatment blood sugar level of 1,076 mg. per 100 ml. rose after sixteen hours of therapy to 2,100 mg. per 100 ml.[2] During the period of treatment 320 gm. of glucose had been given intravenously. Certainly in diabetic acidosis a blood sugar concentration in excess of 1,000 mg. per 100 ml. prior to therapy indicates a grave prognosis, for the degree of insulin insufficiency must be marked indeed to produce both ketosis and such hyperglycemia.

In recent years attention has been directed toward extreme hyperglycemia in states other than ketoacidosis. One type of current interest is that associated with coma and other central nervous system symptoms in diabetic individuals in whom there are no apparent accompanying disorders or events to which to relate the hyperglycemia. In this group even higher blood sugar concentrations have been reported. There have been several instances of levels in the 2,000 range, and Jackson from Cape Town describes a patient with the astonishing concentration of 3,120 mg. per 100 ml.[3] The world's record appears to be held in France, however, where a level of 4,800 mg. per 100 ml. is reported.[4] Many cases of this type of hyperglycemia have now been reported, and reviews of the clinical aspects have appeared in this Journal[5] and elsewhere.[6] Dehydration may be severe, and laboratory tests have revealed serum osmolality above 400 mOsm/L., hypernatremia and azotemia. The mortality has been high, but in some cases treatment was successful with moderate insulin dosage and fluid therapy aimed at correction of dehydration, both extra- and intracellular.

The pathogenesis of this type of hyperglycemia and related findings is not understood. All patients were known or proved to be diabetic and, in some, excessive carbohydrate intake in combination with insulin insufficiency may have led in part to the blood sugar elevation. The failure of ketosis to develop implies some degree of carbohydrate utilization caused perhaps by the high concentration of substrate. The reasons for the neurologic symptomatology are unknown, though it has been suggested that intracellular water loss brought about by the high osmotic presence of the extracellular fluid or toxic effects of the glucose itself may be responsible.[7] The development of hypernatremia is also poorly understood. Possibly massive glucose diuresis may be partly at fault, for hypernatremia can appear in the course of acute and chronic solute loading with diuresis. It is interesting that hypokalemia noted in other conditions of hypernatremia was seen in the present cases as well.

A second example of marked elevation of the blood sugar concentration without ketosis is that reported in the course of severe burns. Concentrations have ranged up to 1,660 mg. per 100 ml.[8] Moreover, hypernatremia has been present also to add to the already elevated tonicity. Nor is the pathogenesis of this type of hyperglycemia understood. In several cases the elevated blood sugar followed intakes of over 400 gm. of carbohydrate daily, amounts which have been shown experimentally to produce little hyperglycemia in the normal person not under stress.[9] Accordingly, it has been suggested for these cases as well that beta cell insufficiency was present due to subclinical diabetes or overt islet cell damage.[8,10] In either event, the administration of large amounts of carbohydrate could lead to hyperglycemia. That early diabetes might be the cause is suggested by glucose tolerance tests a year later in three patients which yielded diabetic curves in one and normal tolerance in the other two.[7] On the other hand, some support for the concept of pancreatic damage is available from the observations of Sevitt[11] who described islet cell damage in burned patients. It will be necessary to determine the prevalence of this type of hyperglycemia and establish its role in the mortality of burned patients.

A third category of unusual hyperglycemia without ketosis has been observed in induced hypothermia. In three cases reported, the sugar levels were not as high as those described above, being 680, 940 and 1,040 mg. per 100 ml.[12,13] The rise in blood sugar occurred rapidly and followed the administration of only small amounts of glucose. In one of Wright and Gann's[12] pa-

tients the concentration was in excess of 900 mg. per 100 ml. when 75 gm. of glucose had been given intravenously, and in Wynn's[13] patient, 1,040 mg. per 100 ml. was found after administration of only 65 gm. of glucose. Also, hypo- rather than hypernatremia occurred, an event probably related to the short duration of the hyperglycemia. As a result, the serum osmolarity was unchanged in Wright and Gann's experience, the effect of hyponatremia offsetting that of hyperglycemia. Coma or other neurologic symptoms which might be attributed to the effect of hypertonicity on the central nervous system were not observed. Here again the pathogenesis of the hyperglycemia is unclear, though Wynn in his investigations of glucose metabolism in hypothermic dogs arrived at the opinion that lowering of body temperature markedly decreased glucose utilization.[13]

Finally, extreme hyperglycemia without ketosis may complicate hemodialysis when high glucose concentrations in the dialyzing bath are used to reduce edema. In this situation the deleterious effects are clearly described in a case study by Potter[14] wherein with 5 per cent bath glucose concentration there was marked central nervous symptomatology and with 7 per cent concentration death ensued. The blood sugar level in the latter situation was 3,400 mg. per 100 ml.

The total prevalence of extreme hyperglycemia is unknown. Indeed, high concentrations may occur more commonly than suspected, not only in the conditions listed above but in others as well. Busy hospital laboratories do not always have time to dilute blood specimens to determine the true concentrations. Hypertonicity can be lethal in itself, and it certainly is not favorable for a situation already grave for other reasons. It behooves clinicians to be more aware of this abnormal state, because proper treatment administered early may save lives.

REFERENCES

[1] Lawrence, R. D.: Extreme hyperglycemia in diabetic coma. Brit. Med. J. *1*:377, 1934.

[2] Meyer, P. C., and Salt, H. B.: Unusually high blood sugar in a boy. Brit. Med. J. *1*:171, 1951.

[3] Jackson, W. P. U., and Forman, R.: Hyperosmolar nonketotic diabetic coma. Diabetes *15*:714-19, Oct. 1966.

[4] Larcan, A., Huriet, C., Vert, P., and Thibaut, G.: Comas-metaboliques non acidocetosiques chez des diabetiques. Diabete *11*:99, 1963.

[5] Danowski, T. S., and Nabarro, J. D. N.: Hyperosmolar and other types of nonketoacidotic coma in diabetes. Diabetes *14*:162, 1965.

[6] Di Benedetto, R. J., Crocco, J. A., and Soscia, J. L.: Hyperglycemic nonketotic coma. Arch. Int. Med. *116*:74, 1965.

[7] Maccario, Micheline, Messis, C. P., and Vastola, E. F.: Focal seizures as a manifestation of hyperglycemia without ketoacidosis. Neurology *15*:195, 1965.

[8] Rosenberg, S. A., Brief, D. K., Kinney, J. M., Herrera, M. G., Wilson, R. E., and Moore, F. D.: The syndrome of dehydration, coma and severe hyperglycemia without ketosis in patients convalescing from burns. New Eng. J. Med. *272*:931, 1965.

[9] Seltzer, Holbrooke S., and Harris, Virginia L.: Exhaustion of insulogenic reserve in maturity-onset diabetic patients during prolonged and continuous hyperglycemic stress. Diabetes *13*:6, 1964.

[10] Hyperglycemia and Diabetes after Burns. Leading Article. Lancet *2*:225, 1965.

[11] Sevitt, S.: Hyperglycemia after burning. Lancet *1*:566, 1955.

[12] Wright, H. K., and Gann, D. S.: Hyperglycemic hyponatremia in nondiabetic patients. Arch. Int. Med. *112*:344, 1963.

[13] Wynn, Victor: Electrolyte disturbances associated with failure to metabolise glucose during hypothermia. Lancet *2*:575, 1954.

[14] Potter, Daniel J.: Death as a result of hyperglycemia without ketosis—a complication of hemodialysis. Ann. Int. Med. *64/2*:399, 1966.

HARVEY C. KNOWLES, JR., M.D.
Cincinnati