Letters to the Editor

Hyperkalemia in Diabetic Ketoacidosis

J. Malone and S. Brodsky reported on the value of ECG monitoring in diabetic ketoacidosis (Diabetes Care 3: 543–47, 1980). We want to stress the importance of this procedure by the following case report.

A 37-yr-old man with type I diabetes mellitus of 16-yr duration, and with diabetic neuropathy and retinopathy, was admitted to the hospital in diabetic ketoacidotic coma. Apart from his insulin, he was not known to take drugs influencing electrolyte behavior. Immediately after admission to the emergency ward, he developed an almost fatal heart arrest due to cardiac arrythmia (Figure 1). After successful resuscitation, a complete electrocardiogram was obtained in the intensive care unit, revealing a tracing with large T waves, taller than its accompanying QRS complex, consistent with severe hyperkalemia (Figure 2). Between chemical determinations (Table 1), the initial serum potassium value of 7.8 meq/L confirmed the previous ECG findings. After correction requiring high quantities of potassium-free fluids, appropriately accompanied by insulin and bicarbonate, the metabolic balance and the cardiac rhythm normalized in 24 h. The patient was able to be discharged 10 days later.

As in the Malone and Brodsky report, initial serum electrolyte values were not available at the moment of admission. However, knowledge of the serum potassium level during diabetic ketoacidosis is of paramount importance, as the delay in obtaining accurate serum potassium results before instituting appropriate therapy can lead to severe life-threatening cardiac arrhythmias and heart arrest. This report

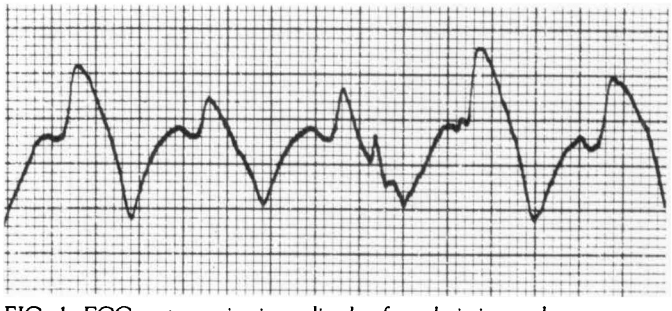

FIG. 1. ECG scope tracing immediately after admission to the emergency room: arrythmia with large tall T waves.

clearly demonstrates that not only potassium depletion is important in diabetic ketoacidosis; hyperkalemia, although rare, also has to be considered as an important element.

In his study on the value of ECG monitoring as a guide to potassium replacement, Soler et al. (Diabetes 23: 610–15, 1974) only reported 3/23 patients with initial ECG signs of hyperkalemia (>6.5 meq/L). We are convinced that severe electrolyte disturbances such as hyperkalemia and hypocalcemia have to be listed as major causes of death in diabetic ketoacidosis.

In conclusion, we want to confirm the Malone and Brodsky paper on the importance of immediate ECG monitoring as a necessary parameter in the approach of diabetic ketoacidosis.

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TABLE 1
Laboratory values on admission and after treatment

	Glycemia (mg/dl)	pH	Na^+ (meq/L)	K^+ (meq/L)	Cl^- (meq/L)	HCO_3^- (meq/L)	Lactate (mg/dl)
Admission	1750	6.77	111	7.8	63	4.5	43.6
After 12 h	525	7.30	125	3.8	82	23	33.0
After 24 h	360	7.41	141	4.0	98	30	15.0

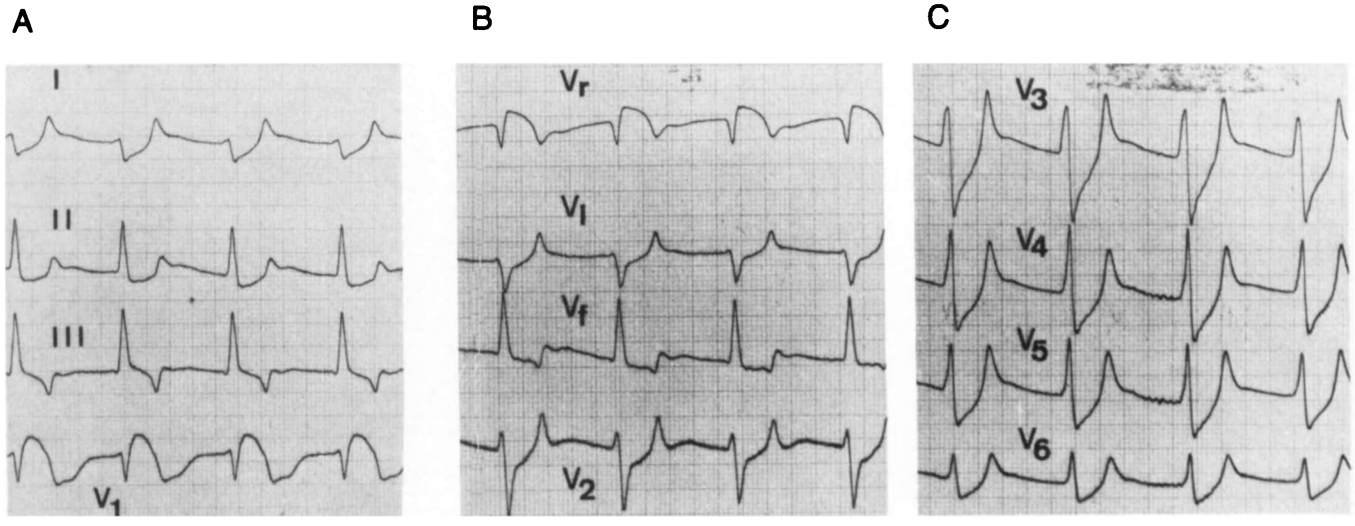

FIG. 2A–C. ECG tracing revealing large T waves, in V_2–V_3 taller than its accompanying QRS complex, consistent with hyperkalemia.

Is NIDDM Just a Receptor Disease?

Recent advances in our knowledge of the nature and function of hormone receptors has greatly expanded our conception of endocrine physiology. The density and properties of receptors within the plasma membrane, cytoplasm, or nucleus may share equal billing with hormone concentrations in the regulation of cell metabolism. However, the new emphasis on receptors should not distort our perspective with regard to the importance of the hormones, which must still amplify the signals transmitted by their receptors for a specific intracellular pathway to be activated or deactivated.

In a stimulating review of the role of receptors in human disease,[1] Roth classifies non-insulin-dependent diabetes mellitus (NIDDM), whether in obese or normal-weight subjects, as a disorder in which the target cell is the primary site of abnormality; he considers the availability of hormone (i.e., the plasma insulin concentration) to be discordant with the clinical state of hyperglycemia. According to this view, it is insulin resistance due to a decrease in the number of insulin receptors rather than a deficiency of insulin that causes hyperglycemia. This construct ignores a number of studies[2–7] to the contrary. These clearly demonstrate that in obese diabetic patients, plasma insulin responses are low in relation to body weight and that hyperglycemia is inversely related to insulin levels. Even in diabetic patients with insulin responses in the "normal range," there is reason to believe that the beta-cells are not secreting promptly as much insulin as they contain, thus permitting hyperglycemia to develop.[8] Furthermore, though caloric restriction and weight reduction reduce insulin resistance as the number of insulin receptors increases, in some patients, plasma insulin responses also increase simultaneously with abatement of hyperglycemia.[9–12] Taken together, these observations support the view that a decrease in receptor number ± an intracellular impediment to insulin action may produce insulin resistance as the initiating event, but clinically significant diabetes develops when insulin availability becomes compromised for that individual or, in Roth's words, "when plasma hormone concentration becomes concordant with the clinical state."

The apparently divergent views of NIDDM, as a receptor versus a hormone deficiency problem, could be reconciled if the receptor abnormality were broadened to include the beta-cell. If there is, in fact, a glucose receptor,[13,14] a failure to respond to normal levels of glycemia would lead to at least relative insulin deficiency. This liability in hormone secretion would render the patient unable to rise completely to the challenge of insulin resistance and hyperglycemia would progress as the beta-cell receptor abnormality worsened. NIDDM would then be viewed as a generalized disorder in glucose uptake, involving receptors in peripheral cells (liver, muscle, and adipose tissue), beta-cells, and even alpha-cells of the islets.[15] To pursue this speculative hypothesis further, one might ask why both an insulin receptor and a glucose receptor should be affected by a single disorder. An even more speculative answer might be that the abnormal receptor is one and the same molecule in different states of conformation (Figure 1). A single receptor molecule might interact with insulin in its target cell membranes to activate a glucose carrier and with glucose in the beta-cell membrane to activate an insulin carrier (or the mechanism of insulin release). A reduced number of these receptor molecules, e.g., as a result of caloric excess in the case of obesity, would then simultaneously create insulin resistance and relative insulin deficiency. The prevailing degree of hyperglycemia would reflect the balance between the two. Such a hypothesis might even explain the dual sites of action of sulfonylureas in NIDDM. While these drugs appear to increase receptor number[16] and lower insulin resistance,[17,18] they also reset the beta-cell to secrete the same amount of insulin with a lesser glucose stimulus.[19]

This hypothesis, if true, would demand answers to numerous questions. Would the putative receptor facilitate rapid insulin release by interacting with free insulin molecules in