Glucose Intolerance with Hypokalemia

Failure of Short-term Potassium Depletion in Normal Subjects to Reproduce the Glucose and Insulin Abnormalities of Clinical Hypokalemia

Phillip Gorden, M.D., Bethesda

SUMMARY

The mechanism by which potassium deficiency per se impairs glucose tolerance was studied in seven subjects who were potassium depleted experimentally (mean depletion = 326 mEq.).

In five subjects studied using the oral glucose tolerance test, all showed impairment during the potassium depletion phase compared to the predepletion control period, and four of five subjects showed improvement with potassium repletion. The four subjects with impaired glucose tolerance compared to both control periods showed a delay in the initial phase of total immunoreactive insulin release. None of the five subjects showed a significant variation in the per cent proinsulin-like component from the potassium depletion phase to either control period. Two subjects studied using the intravenous glucose tolerance test showed no impairment of glucose tolerance with potassium depletion, and no evidence of insulin resistance was found following the injection of 0.05 U. per kilogram of insulin. These two subjects did manifest impaired growth hormone responses to the hypoglycemic stimulus, however.

Potassium depletion per se impairs glucose tolerance. The defect is mild; severe glucose intolerance, alterations in total immunoreactive insulin, and plasma insulin components seen in clinical hypokalemic states involve a complex interplay between potassium deficiency and the primary disease state. DIABETES *22*:544-51, July, 1973.

Abnormal glucose tolerance is common in disease states in which hypokalemia is frequently found, including primary aldosteronism,[1] Bartter's syndrome,[2] uremia,[3] cirrhosis,[4,5] congenital alkalosis,[2] ectopic ACTH syndrome,[2] villous adenoma,[6] and following the administration of diuretic drugs.[7,8]

The mechanism of this glucose intolerance is unclear, but at least one important defect appears to be in insulin secretion.[1,2] In addition to alterations in total immunoreactive insulin, we have reported an increased proportion of the biologically less active proinsulin-like component[9,10] in hypokalemic patients.[2]

All previous studies of glucose tolerance and insulin secretion have been carried out in clinical disease or drug-induced states in which potassium deficiency is prominent. In virtually all the diseases, however, abnormal glucose tolerance may be seen regardless of whether hypokalemia is present; the situation is further complicated by the inability to control nutrition and body weight in patients and in experimental animals.

To study the role of potassium per se in the genesis of abnormal glucose tolerance, normal subjects were potassium depleted experimentally to the extent of significant hypokalemia and electrocardiographic changes. In contrast to the hypokalemic patients, these subjects manifested very mild glucose intolerance, small changes in total immunoreactive insulin and essentially no change in the circulating insulin components.

METHODS

Seven young, healthy volunteers were studied as inpatients in an air-conditioned metabolic unit (table 1).

The limit of potassium depletion was that which was found to be safe as determined by previous studies at this institution. Clinical parameters including pulse, blood pressure, cardiac auscultation, electrocardiography, and urinalysis were monitored frequently throughout the study. All subjects remained active and ambulatory.

The typical study protocol is shown in figure 1. A

From the Diabetes Section, Clinical Endocrinology Branch, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, Maryland 20014.

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TABLE 1
Clinical profile of subjects

Subject	Age	Sex	Per cent ideal wt.	#1 GTT HCO_3 mEq./L.	#1 GTT K^+ mEq./L.	#1 GTT Wt. kg.	#2 GTT HCO_3 mEq./L.	#2 GTT K^+ mEq./L.	#2 GTT Wt. kg.	#2 GTT Net K^+ Loss	#3 GTT HCO_3 mEq./L.	#3 GTT K^+ mEq./L.	#3 GTT Wt. kg.
Sch†	20	M	100	29	3.5	64.7	36	2.6	63.4	359	27	3.5	61.9
Bdt†	19	F	100	27	4.3	54.8	31	3.1	51.7	322	26	4.1	51.9
Dus†	23	F	189	26	4.2	103.5	24	2.8	97.2	330	27	4.1	98.6
Syv†	22	F	143	26	4.6	82.5	28	3.3	78.6	313	25	4.2	79.1
Bri†	39	F	180	26	4.2	109.6	31	2.4	107.4	299	22	4.2	103.7
Har*	21	M	97	27	3.5	71.6	30	3.2	70.0	307	30	3.8	68.6
Bog*	21	M	97	28	3.4	76.0	32	3.5	76.6	353	30	4.5	73.8

*2500 calorie diet
†1200 calorie diet

diet (see page 546) essentially free of potassium was begun on the first day and continued throughout. Potassium chloride (80 mEq.) was given by mouth from day 1 through day 7; on day 7 a 100 gm. oral glucose tolerance test was performed (#1 GTT). Subjects Har and Bog were studied under an identical protocol except that a 25 gm. intravenous glucose tolerance test was performed at each time interval as indicated above for the oral GTT, followed on the second day by a 0.05 U. per kilogram insulin tolerance test. Following the first glucose tolerance test the potassium chloride supplement was discontinued and 9 α-fluorohydrocorti- (fluoro-F) was given at a dose of 1 mg. per day for five days, followed by chlorothiazide at a dose of 0.5 to 1 gm. per day for three to four days. Following seven days of equilibration to the diet and fourteen days of potassium depletion, a second 100 gm. oral glucose tolerance test was performed (#2 GTT). The 80 mEq. potassium supplement was then resumed for an additional fourteen days and a third glucose tolerance test was performed (#3 GTT).

Serum values for creatinine, sodium, chloride, bicarb-

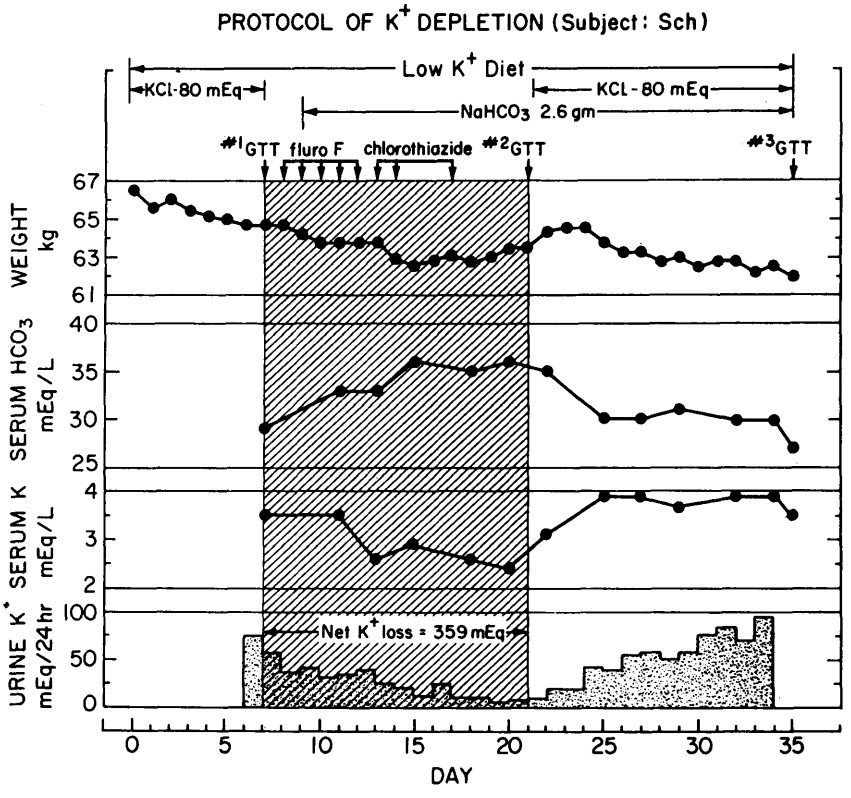

FIGURE 1

Representative example of protocol used for achieving potassium depletion and repletion. For additional details see Methods and table 1.

onate (except where shown, table 1), calcium, phosphate and magnesium were normal at the time of all three glucose tolerance tests and were normal for potassium except for #2 GTT.

The diet was made as palatable as possible and consisted mostly of carbohydrate supplemented by a multivitamin preparation, and additional sodium given as sodium bicarbonate or sodium chloride. The subjects ate all of either a 1200 or 2500 calorie diet daily (table 1). The mineral content of the 2500 calorie diet, analyzed on an aliquot of a homogenate, was as follows: 8 mEq. = potassium, 148 mEq. = sodium, 133 mEq. = chloride, 8 mEq. = calcium, 702 mg. = phosphate, and 5 mEq. = magnesium.

For the purpose of this study the net potassium deficit or net K^+ loss (figure 1 and table 1) is defined as the total amount of potassium excreted in the urine (uncorrected for nitrogen excretion) over the potassium depletion phase of the study, shown by the shaded area in figure 1. No correction is made for the small dietary potassium intake or for the small amount of potassium lost in sweat and feces. (The air-conditioned unit and low-bulk diet make these losses small.) Whole-body potassium was estimated frequently in each subject by measuring 40-K decay in a whole-body counter.[11]

The subjects were weighed daily. Electrolytes were measured in urine every twenty-four hours from the sixth through the thirty-fourth day and in serum every forty-eight hours after the potassium depletion phase was begun. Serum bicarbonate and serum and urine potassium, sodium and chloride were measured in the clinical chemistry laboratory by standard technics.

Glucose was given either as a 100 gm. oral load or a 25 gm. intravenous bolus; samples were collected as previously described.[12] Blood glucose was measured by an AutoAnalyzer technic,[12] and total plasma insulin was measured by radioimmunoassay.[9,12] The proinsulin-like and insulin components were separated by gel filtration and measured in an insulin radioimmunoassay.[12,13] Plasma growth hormone was measured by radioimmunoassay.[14]

RESULTS

Clinical and laboratory evidence of potassium deficiency occurred in all seven subjects. In the initial control period serum potassium ranged from 3.4 to 4.6 mEq. per liter, during potassium depletion from 2.4 to 3.5 mEq. per liter, and in the subsequent control period from 3.5 to 4.5 mEq. per liter. The net total body potassium deficit ranged from 299 to 359 mEq. Frequent measurements of total body potassium (40-K decay in whole-body counter[11]) reflected the qualitative trend in potassium depletion and repletion (table 2). While the qualitative trend in 40-K decay agrees generally with the balance data, it is clear that the total body potassium measurements in these studies are not precise and cannot be considered quantitative. In six of the seven subjects serum bicarbonate was higher during the potassium depletion period (table 1 and figure 1). All seven subjects manifested the typical electrocardiographic changes of hypokalemia,[15] including bradycardia, prolongation of Q-T interval, ST-T segment depression, flattening of T waves and the appearance of U waves. These electrocardiographic changes were completely corrected by potassium repletion. One subject (Syv) had a transient bigeminal rhythm rapidly corrected by a small oral dose of potassium chloride. All subjects noted a mild sense of lassitude and weakness during the hypokalemic phase.

In spite of the complete consumption of the diet at both the 1200 and 2500 calorie level, all subjects had some degree of weight loss which was always greatest in the potassium repletion control period (table 1).

Five subjects were studied using 100 gm. oral glucose tolerance tests. The initial predepletion test (#1 GTT) was normal[12,16] except in subject Bri who had a borderline elevation of the glucose value at two hours after oral glucose (figure 2). Following potassium depletion (#2 GTT) there was no change in the fasting glucose value or in the initial response to oral glucose; ninety minutes after the glucose load there was some degree of impairment in all five subjects in glucose tolerance with respect to the predepletion control period. In four of the five subjects the impairment in glucose tolerance was corrected in the potassium repletion control period (#3 GTT). (Subject Bdt

TABLE 2

Total body potassium* (mEq.)

	Sch	Bdt	Dus	Syv	Har	Bog
#1 GTT	3,960	2,450	3,075	2,920	4,360	4,470
	4,050	2,090	2,630	2,755	3,700	4,020
	3,960	1,925	3,560	2,580	3,500	3,810
				2,490	3,430	4,090
#2 GTT	3,865	1,945	2,815	2,090	3,010	3,140
	3,490	2,300	4,380		3,635	3,360
	4,525	1,975	2,760		3,690	4,020
		2,065	2,705	2,645	3,910	4,120
#3 GTT	3,465	1,990	2,990	3,021	3,890	4,000

*Whole body counter[11]
Subject Bri not studied

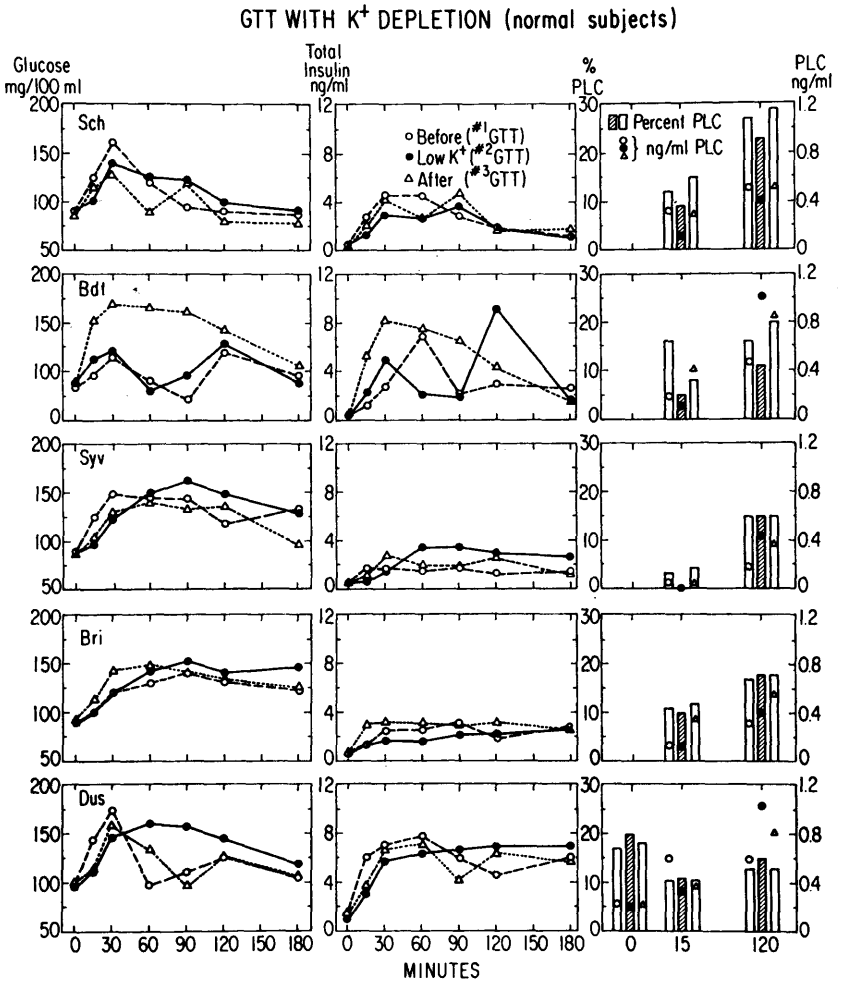

FIGURE 2

Oral glucose tolerance test (100 gm.). Left panel = glucose responses, center panel = total insulin responses and right panel = concentration of proinsulin-like component shown by symbols and the percentage proinsulin-like component shown by the bars. For details on each subject see tables 1 and 2.

showed further impairment for unexplained reasons; see figure 2.)

In the four subjects who manifested impairment of #2 GTT with respect to #1 and #3 GTT, there was a delay in the initial phase of total insulin secretion, i.e. #2 GTT showed a lower total insulin concentration at fifteen minutes after the glucose load than in #1 and #3 GTT (figure 2). There were no other significant alterations in total immunoreactive insulin.

The pattern of response of the proinsulin-like component was highly consistent in a given subject over several different measurements and indistinguishable from patterns previously reported for normokalemic subjects.[12,13] The proinsulin-like and insulin components were measured at fifteen minutes and 120 minutes following the glucose load in all five subjects and in one subject in the basal state. In all three phases of the study, regardless of the potassium status, the concentration and per cent proinsulin-like component were low at fifteen minutes after the glucose load and both the concentration and per cent proinsulin-like component increased 120 minutes after the glucose load. In the subject studied in the basal state, the basal percentage proinsulin-like component was highest, decreasing at fifteen minutes after the glucose load and returning toward the basal state at 120 minutes following glucose (figure 2). There was no consistent difference in the per cent proinsulin-like component in either of the three glucose tolerance tests.

Two subjects (Bog and Har) were studied using a 25 gm. intravenous glucose tolerance test. There was no significant impairment of either glucose tolerance or total insulin secretion from the hypokalemic period to either normokalemic control period (figure 3).

To determine whether potassium depletion produced a clinical state of insulin resistance, two subjects (Bog and Har) were given 0.05 U. of porcine insulin per kilogram body weight, and the glucose responses were

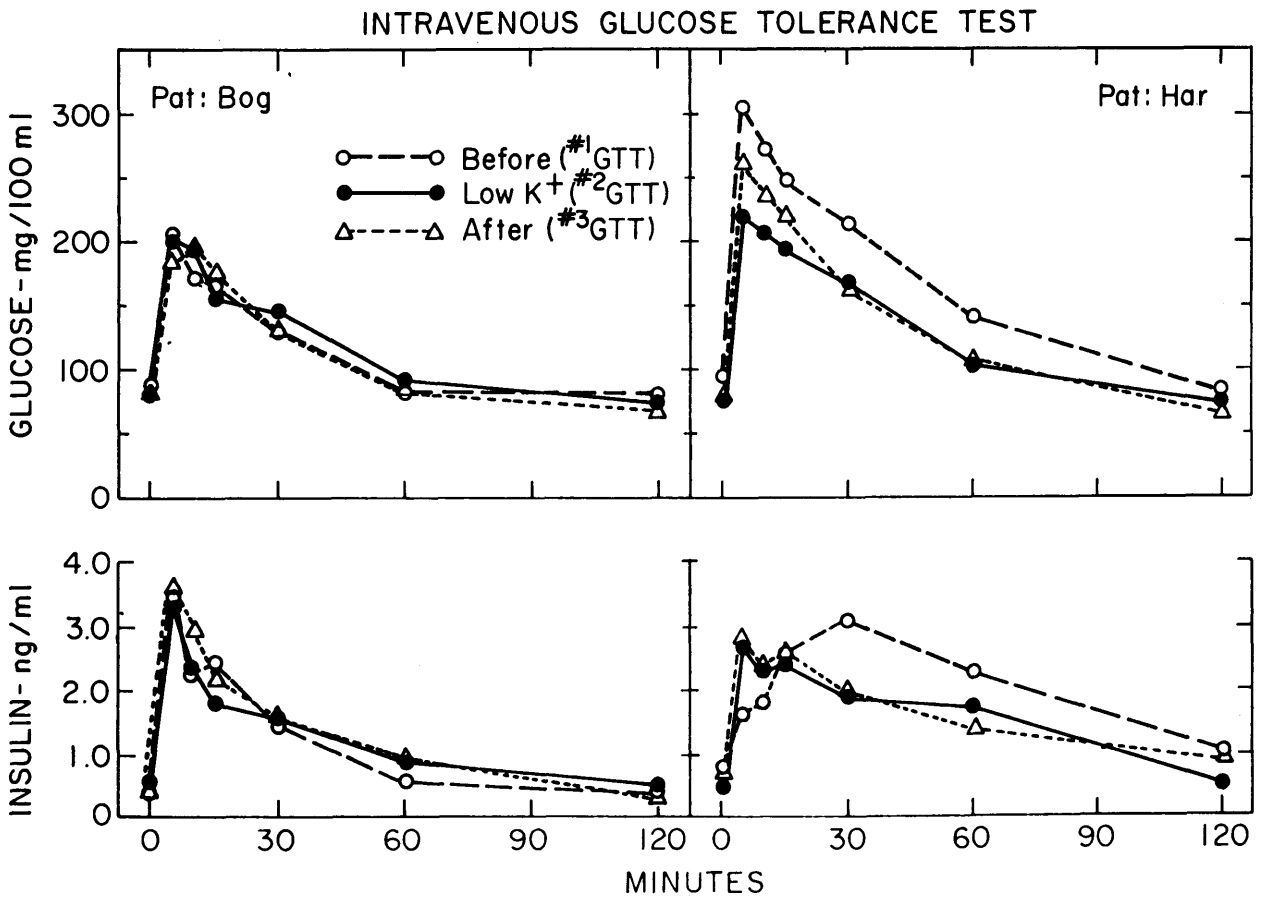

FIG. 3. Intravenous glucose tolerance test (25 gm.). For details on each subject see tables 1 and 2.

measured. There was no consistent difference in the decrement in blood glucose from the hypokalemic period to the normokalemic control periods (figure 4).

In order to see whether other polypeptide hormones show a secretory impairment similar to plasma insulin, plasma growth hormone concentration was measured during the insulin tolerance test. Compared to the initial normokalemic control period, growth hormone secretion was blunted in both subjects, and in subject Bog growth hormone secretion was diminished in the hypokalemic period with respect to both normokalemic control periods. In subject Har the decrement in blood glucose was less in the third period (normokalemic) for unexplained reasons and the rise in growth hormone concentrations was less (figure 4).

DISCUSSION

These studies indicate that impairment of glucose tolerance can be produced by potassium depletion per se and that the defect can be corrected by potassium repletion. However, the impairment is mild with up to 10 per cent total body potassium depletion and in the presence of significant hypokalemia. There is a delay in the initial phase of insulin release but no other significant alterations in total insulin secretion. Since the change in total insulin secretion was small, there was no significant alteration in the individual proinsulin-like or insulin components.

We have previously reported that in patients with chronic hypokalemia from various causes there is an increased percentage of the proinsulin-like component.[2] These changes, however, are seen only in patients with significant insulinopenia. Data reported in preliminary form suggest that cirrhotic patients with low total body potassium and hypoinsulinemia have a higher percentage proinsulin-like component than cirrhotic patients with normal total body potassium and more normal plasma insulin values.[17] We have emphasized the difficulty in ascribing all the changes in insulin secretion to the deficiency in the potassium ion in patients with

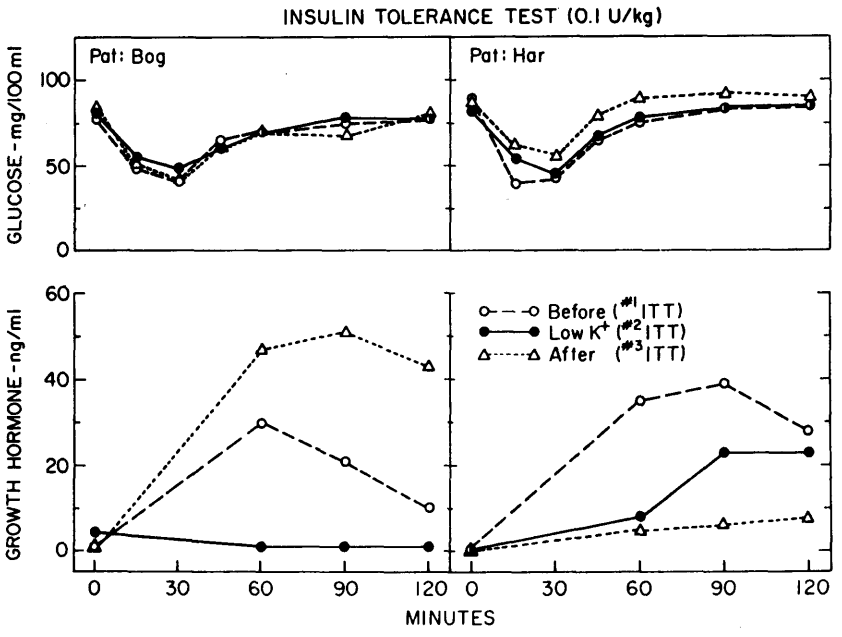

FIGURE 4

Insulin tolerance test. Porcine insulin (0.05 U. per kilogram) was given to each subject by rapid intravenous injection. Upper panel = glucose response and lower panel = growth hormone response. For details on each subject see tables 1 and 2.

complicated underlying diseases.[2] As previously mentioned, most disease states characterized by abnormal glucose tolerance and hypokalemia may manifest the glucose tolerance abnormality after the potassium deficit has been repaired. In primary aldosteronism, abnormal glucose tolerance is seen in approximately 50 per cent of patients, and a delay in the early phase of insulin release has been demonstrated.[1] Potassium administration will restore insulin secretion to a more normal state in these patients and improve glucose tolerance. However, correction of the hypokalemia by removal of the adrenal adenoma does not result in a normal glucose tolerance in a significant number of patients.[18]

In the present study no underlying disease is present and other modulating influences such as diet and weight have been reasonably well controlled. However, clinical potassium deficiency was not completely simulated in these studies, as the potassium depletion was of short duration and the degree of depletion was quantitatively limited. Patients may be potassium deficient for a longer period of time and the degree of potassium deficiency may be much greater.

The initial effect of potassium deficiency appears to be impairment of the early phase of insulin release. A similar defect is seen in diabetic patients with mild to moderate glucose intolerance.[19,20] These patients have normal or even increased total insulin secretion and the percentage of their circulating proinsulin-like component is usually not greater than 20 to 30 per cent of the total immunoreactive insulin.[12,13,21] By contrast, with more severe glucose intolerance, there is usually insulinopenia. This is true in both hypokalemic patients[2] and in normokalemic patients, i.e. juvenile-type diabetes mellitus[22] and pheochromocytoma;[23] in both situations there is an increased proportion of the biologically less active proinsulin-like component.[24] Thus the changes in total insulin secretion appear to determine the proportions of the individual plasma insulin components regardless of the mechanism by which the abnormality in glucose tolerance is produced. While it is reasonable to suggest that the impaired glucose tolerance is related to a defect in insulin secretion, the defect in insulin secretion is not specific and shows a similar pattern to other abnormalities that affect islet cell function.

In the only other study of experimental potassium deficiency, Sagild et al. found impairment of intravenous glucose tolerance.[25] Sagild's studies suggest that the impaired glucose tolerance does not result from an abnormal gastrointestinal factor. However, we have been unable to confirm Sagild's studies in our subjects who had approximately the same levels of serum potassium and the same degree of potassium depletion. The reasons for these differences are not completely evident but most likely result from the methods used to achieve the potassium depletion. In the present study the diet was kept constant throughout all phases to exclude effects of dietary manipulations. Dietary influences are a problem in studying not only hypokalemic patients and nor-

mal subjects but also experimental animals.[26-29] Neither Sagild's studies nor ours show any evidence of clinical insulin resistance in the potassium-depleted subjects, and no evidence of insulin resistance was seen in rats made potassium deficient.[28]

The potassium ion may influence multiple cellular processes related to carbohydrate metabolism including the transfer of high energy phosphates[30] and formation of liver glycogen.[31] In potassium-deficient animals the major sites of depletion are serum and muscle.[26-29] The predominant effect on glucose tolerance appears to be mediated through alterations in insulin, however. In vitro studies of the effect of potassium on proinsulin biosynthesis and conversion to insulin are inconclusive.[32] It is difficult to compare in vitro studies of insulin secretion: In rabbit pancreatic slices, insulin secretion is diminished by a potassium-deficient media;[33] in pieces of rabbit pancreas, insulin secretion is enhanced by a potassium-free media.[34]

Supra-physiologic concentrations of potassium cause insulin secretion in the isolated perfused rat pancreas[35] and in vivo in the dog.[36] These studies, as well as the studies in man, raise questions of nonspecific cation effects on hormone secretion. The general dampening effect of potassium deficiency on insulin secretion appears well documented. The preliminary observations of this study as well as those of Podolsky[37] suggest a similar effect on growth hormone secretion. Furthermore, it is well known that potassium deficiency inhibits aldosterone secretion.[38]

It seems reasonable to conclude from these studies that potassium deficiency affects glucose tolerance, predominantly by way of insulin secretion. However, in the clinical setting the net effect on glucose tolerance results from a complex interplay of the primary disease state and potassium deficiency.

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REFERENCES

[1] Conn, J. W.: Hypertension, the potassium ion and impaired carbohydrate tolerance. N. Engl. J. Med. *273*:1135-43, 1965.

[2] Gordon, P., Sherman, B. M., and Simopoulos, A. P.: Glucose intolerance with hypokalemia: An increased proportion of circulating proinsulin-like component. J. Clin. Endocrinol. Metab. *34*:235-40, 1972.

[3] Spergel, G., Bleicher, S. J., Goldberg, M., Adesman, J., and Goldner, M. G.: The effect of potassium on the impaired glucose tolerance in chronic uremia. Metabolism *16*:581-85, 1967.

[4] Conn, H. O.: Cirrhosis and diabetes IV. Effect of potassium chloride administration on glucose and insulin metabolism. Amer. J. Med. Sci. *259*:394-404, 1970.

[5] Podolsky, S., Zimmerman, H. J., Burrows, B. A.: Relation between total body potassium and growth hormone and insulin response in cirrhosis. J. Clin. Invest. *49*:75a, 1970 (abstract).

[6] Rabinowitz, P., Farber, M., and Friedman, I. S.: A depletion syndrome in villous adenoma of the rectum. Arch. Int. Med. *109*:265-69, 1962.

[7] Rapoport, M. I., and Hurd, H. F.: Thiazide-induced glucose intolerance treated with potassium. Arch. Int. Med. *113*: 405-08, 1964.

[8] Chowdhury, F. R., and Bleicher, S. J.: Chlorthalidone-induced hypokalemia and abnormal carbohydrate metabolism. Hormone Metab. Res. *2*:13-16, 1970.

[9] Roth, J., Gorden P., and Pastan I. "Big Insulin": A new component of plasma insulin detected by immunoassay. Proc. Natl. Acad. Sci. USA *61*:138-145, 1968.

[10] Sherman, B. M., Gorden, P., Roth, J., and Freychet, P.: Circulating insulin: The proinsulin-like properties of "big" insulin in patients without islet cell tumors. J. Clin. Invest. *50*: 849-58, 1971.

[11] Andrews, H. L., Peterson, D. C., Murphy, R. E. and Myers, E. J.: An organic plastic, localizing whole-body counter. J. Nucl. Med. *6*:667-78, 1965.

[12] Gorden, P., and Roth, J.: Plasma insulin: Fluctuations in the "big" insulin component in man after glucose and other stimuli. J. Clin. Invest. *48*:2225-34, 1969.

[13] Gorden, P., Sherman, B. M., and Roth, J.: Proinsulin-like component of circulating insulin in the basal state and in patients and hamsters with islet cell tumors. J. Clin. Invest. *50*:2113-22, 1971.

[14] Roth, J., Gorden, P., and Brace, K.: Efficacy of conventional pituitary irradiation in acromegaly. N. Engl. J. Med. *282*:1385-91, 1970.

[15] Clinical Scalar Electrocardiography. Lipman, B. S., and Massie, E., Eds. Year Book Publishers, 1959, p. 180.

[16] Gorden, P., Griggs, R. C., Nissley, S. P., Roth, J., and Engel, W. K.: Studies of plasma insulin in myotonic dystrophy. J. Clin. Endocrinol. Metab. *29*:684-90, 1969.

[17] Podolsky, S., Gutman, R. A., Zimmerman, H. J., and Burrows, B. A.: Effects of potassium on insulin, proinsulin and growth hormone release in cirrhotics with abnormal carbohydrate tolerance. Diabetes *20* (Suppl. 1):372-73, 1971. Abstract.

[18] Conn, J. W.: Personal communication.

[19] Yalow, R. S., and Berson, S. A.: Immunoassay of endogenous plasma insulin in man. J. Clin. Invest. *39*:1157-75, 1960.

[20] Seltzer, H. S., Allen, E. W., Herron, A. L., Jr., and Brennan, M. T.: Insulin secretion in response to glycemic stimulus: Relation of delayed initial release to carbohydrate intolerance

in mild diabetes mellitus. J. Clin. Invest. *46*:323-35, 1967.

[21] Goldsmith, S. J., Yalow, R. S., and Berson, S. A.: Significance of human plasma insulin Sephadex fractions. Diabetes *18*:834-39, 1969.

[22] Parker, M. L., Pildes, R. S., Chao, K. L., Cornblath, M., and Kipnis, D. M.: Juvenile diabetes mellitus; a deficiency in insulin. Diabetes *17*:27-32, 1968.

[23] Vance, J. E., Buchanan, K. D., O'Hara, D., Williams, R. H., and Porte, D., Jr.: Insulin and glucagon responses in subjects with pheochromocytoma: Effect of alpha adrenergic blockade. J. Clin. Endocrinol. Metab. *29*:911-16, 1969.

[24] Gorden, P., and Roth, J.: Circulating proinsulin-like component: An increased proportion in severe hypoinsulinemic states in man. Clin. Res. *20*:623, 1972 (abstract).

[25] Sagild, U., Andersen, V., and Andreasen, P. B.: Glucose tolerance and insulin responsiveness in experimental potassium depletion. Acta Med. Scand. *169*:243-51, 1961.

[26] Gardner, L. I., Talbot, N. B., Cook, C. D., Berman, H., and Uribe, R. C.: The effect of potassium deficiency on carbohydrate metabolism. J. Lab. Clin. Med. *35*:592-602, 1950.

[27] Fuhrman, F. A.: Glycogen, glucose tolerance and tissue metabolism in potassium-deficient rats. Am. J. Physiol. *167*: 314-20, 1951.

[28] Mondon, C. E., Burton, S. D., Grodsky, G. M., and Ishida, T.: Glucose tolerance and insulin response of potassium-deficient rat and isolated liver. Am. J. Physiol. *215*:779-87, 1968.

[29] Spergel, G., Schmidt, P., Stern, A., and Bleicher, S. J.: Effects of hypokalemia on carbohydrate and lipid metabolism in the rat. Diabetes *16*:312-18, 1967.

[30] Boyer, P. D., Lardy, H. A., and Phillips, P. H.: Further studies on the role of potassium and other ions in the phosphorylation of the adenylic system. J. Biol. Chem. *149*:529-41, 1943.

[31] Hastings, A. B., and Buchanan, J. M.: The role of intracellular cations on liver glycogen formation in vitro. Proc. Natl. Acad. Sci. USA *28*:478-82, 1942.

[32] Sherman, B. M., and Gorden, P.: Unpublished observations.

[33] Howell, S. L., and Taylor, K. W.: Potassium ions and the secretion of insulin by islets of Langerhans incubated in vitro. Biochem. J. *108*:17-24, 1968.

[34] Hales, C. N., and Milner, R. D. G.: The role of sodium and potassium in insulin secretion from rabbit pancreas. J. Physiol. *194*:725-43, 1968.

[35] Grodsky, G. M., and Bennett, L. L.: Cation requirements for insulin secretion in the isolated perfused pancreas. Diabetes *15*:910-13, 1966.

[36] Hiatt, N., and Davidson, M. B.: Effect of potassium chloride (KCl) infusions on insulin secretion in vitro. Program of the 53rd Meeting of The Endocrine Society. San Francisco, June 1971, p. 56. Abstract.

[37] Podolsky, S., Burrows, B. A., and Pattavina, C.: Effect of chronic potassium depletion on growth hormone release in man. Second International Symposium on Growth Hormone. Excerpta Medica #236. Milan, May 1971, p. 50.

[38] Gann, D. S., Delea, C. S., Gill, J. R., Jr., Thomas, J. P., and Bartter, F. C.: Control of aldosterone secretion by change of body potassium in normal man. Am. J. Physiol. *207*:104-08, 1964.