Effect of Acetazoleamide (Diamox) on Glucose Tolerance. (21146)

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Acetazoleamide (Diamox),* a carbonic anhydrase inhibitor, is now often employed for the diuretic effect on the kidney which results through enzymatic blocking produced by this compound(1). The widespread participation of carbonic anhydrase in the enzymatic functions of tissue other than the kidney, namely, erythrocytes(2-4), stomach(5-7), pancreas (8), and brain(9), has centered considerable attention upon these organs in the clinical uses of acetazoleamide.

This investigation was undertaken following the observation of insulin shock in a patient with diabetic nephropathy, who had been given acetazoleamide as a diuretic. Previously she had been easily and well controlled with 25 units of NPH (Lilly) insulin. She was eating an adequate daily diet consisting of 1800 calories composed of 180 g of carbohydrate, 90 g of protein, and 80 g of fat. It was noted on 3 separate occasions that insulin shock occurred approximately 3 to 5 hours following the administration of 0.5 g of acetazoleamide. The reaction was promptly corrected by intravenous infusion of 50 cc of 25% glucose solution. To determine the cause for this reaction this preliminary study was undertaken in an effort to evaluate the effects, if any, of acetazoleamide on glucose tolerance of normal subjects.

Method. The first subjects studied were 6 normal, healthy medical students on whom 2 oral glucose tolerance tests were performed by the method to be described later. The first test was used as a control; 0.5 g of acetazoleamide was administered orally 30 minutes before the second test. There was no apparent difference in the results of these 2 tests except an indication that acetazoleamide might cause a lowering of blood sugar levels after 2 to 3 hours; therefore, in later tests acetazoleamide was administered 2 to 3 hours before glucose was administered. These 6 subjects are not included in any of the figures and tables.

For this study 2 glucose tolerance tests were performed on 14 non-diabetic medical and psychiatric patients, the first test being used as a control and the second followed 2½ to 3½ hours after one oral dose of acetazoleamide. Nine patients received the standard oral glucose tolerance test using 100 g of glucose after a minimum fasting period of 12 hours. Blood samples were collected at fasting, 30-, 60-, 120-, and 180-minute intervals (Fig. 1). Five patients received the intravenous glucose tolerance test after a minimum fasting period of 12 hours. Glucose, 0.5 g per kg of body weight, was administered as a 20% solution, and blood samples were collected at fasting, 30-, 60-, 90-, and 120-minute intervals (Fig. 2), following the intravenous infusion of the glucose solution. In 3 to 5 days the same procedure was repeated on all patients with one oral dose of acetazoleamide 2½ to 3½ hours before administration of glucose. Acetazoleamide was administered in doses of 0.5 and 1.0 g with no difference in the glucose tolerance curve.

All of these patients had been maintained on a regular hospital diet, containing a minimum daily average of 300 g of carbohydrate, for 3 to 5 days prior to performing the first test.

The concentration of blood glucose was determined by a modified Folin-Wu method using the spectrophotometer(10). Urinary sodium and potassium excretions were determined on 5 subjects during both the control test and following the acetazoleamide administration. Quantitative urinary sugar determinations after acetazoleamide administration failed to reveal an increase in glucose excretion over the control glucose tolerance test in any of the groups.

Discussion. In this investigation it was shown in 5 subjects that urinary potassium

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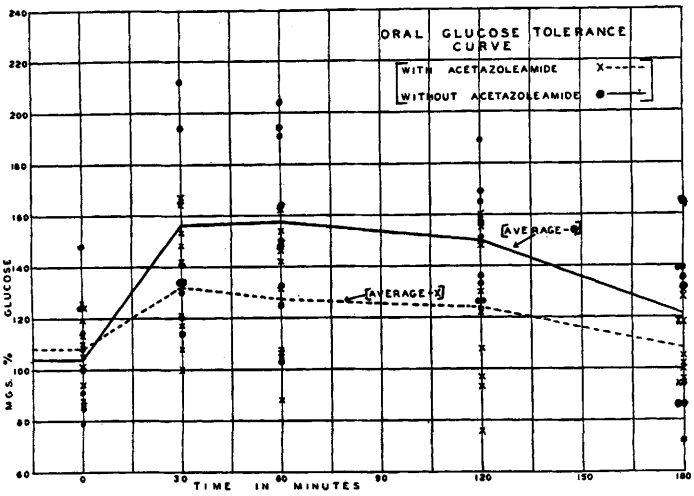

FIG. 1.

excretion was decreased after administration of acetazoleamide during glucose tolerance test (Table I); however, it has been reported that in normal subjects acetazoleamide increased urinary potassium excretion(11). Friedberg *et al.*(12) have clearly shown that in patients with congestive heart failure and receiving acetazoleamide, urinary potassium was increased by approximately 50%. An explanation for the diminished potassium in our investigation may be due to increased glycogenesis. The effect of insulin and glucose on urinary potassium is well known, however, the exact mechanism is poorly understood. It is thought that the migration of potassium ions from the intracellular spaces into the cells is related to glycogenesis. Therefore, a glycogenic effect initiated by acetazoleamide may be suggested by the decreased urinary potassium excretion.

The apparent difference between the oral and intravenous glucose curves (Fig. 1 and 2) following acetazoleamide administration suggests that gastrointestinal absorption of glucose may also be influenced by acetazoleamide. By what mechanism it would be operative is not known, unless some derangement in the rate of phosphorylation is produced.

It has also been demonstrated that sulfonamides, by competing with the thyroid for iodine, prevents the formation of diiodotyrosine, and consequently thyroxine(13). Whether this inhibition by acetazoleamide, (theoretically 50 to 400 times as potent a carbonic anhydrase inhibitor as sulfonamide) is of significant degree to influence carbohydrate metabolism is purely speculative.

Summary. Two glucose tolerance tests were performed on each of 14 subjects (9 oral glucose tolerance tests, 5 intravenous glucose

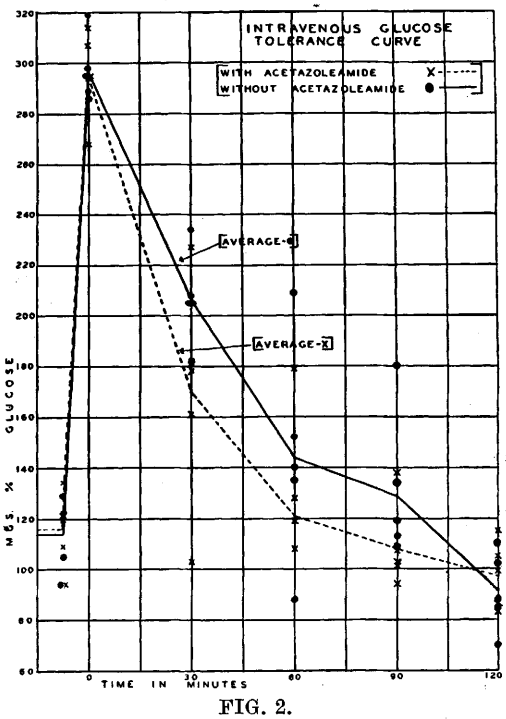

FIG. 2.

TABLE I. Urinary Sodium and Potassium Excretions. 5 subjects in each series.

Normal	Total urinary Na excretion Acetazoleamide	% increase
4.4 MEQ	58.4 MEQ	1225
10.5	76.2	635
49.0	82.3	68
15.5	40.2	58
54.6	121.7	123
	Avg % increase	440
Normal	Total urinary K excretion Acetazoleamide	% decrease
12.3 MEQ	4.9 MEQ	60
7.1	3.8	47
7.2	2.4	67
8.4	1.6	81
11.0	5.8	47
	Avg % decrease	60

tolerance tests). The first glucose tolerance test was used as a control. A second test was performed 2½ to 3½ hours after the administration of acetazoleamide. These tests showed a tendency for the acetazoleamide to increase the oral glucose tolerance. The administration of acetazoleamide 2½ to 3½ hours prior to the intravenous administration of glucose did not result in as marked a degree of change in the glucose tolerance curve. After administration of acetazoleamide to patients receiving oral glucose tolerance tests a diminution of the urinary potassium excretion was observed.

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Possible Occurrence of Multiple Antigens in Type 2 Poliomyelitis and GDVII Mouse Encephalomyelitis Viruses.* (21147)

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(Introduced by S. A. Koser.)

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The occurrence of at least two distinct antigens has been established for a number of mammalian viruses(1) and for *B. coli* T2 bacteriophage(2) by complement fixation and precipitin tests. The viruses for which such antigens have been separated and characterized are of relatively large size ranging from about 100 mμ to 450 mμ. However, very little information is available concerning the presence of multiple antigens in viruses considerably smaller in size. The foot and mouth disease virus, one of the smallest known viruses, has been found to have 2 complement fixing components(3,4); one associated with virus particles (infectivity) which measures about 20 mμ in diameter on the basis of sedimentation studies, and the other a smaller component of 6.5 mμ(4).

This report concerns the possible presence of 2 complement fixing antigens in GDVII mouse encephalomyelitis virus, estimated to be

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