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Lessened Insulin Hypophosphatemia Following N-Sulfanilyl-N′-Butylurea (BZ-55 or Carbutamid).* (22934)

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N-sulfanilyl-N′-butylurea (BZ-55 or Carbutamid) was administered to juvenile diabetics prior to insulin tolerance tests in an attempt to determine whether the amelioration of clinical diabetes reported, at a conference, with this compound can be attributed to potentiation or prolongation of insulin action.

Materials and methods. Twenty-seven juvenile diabetics, previously maintained for 3 to 5 days on short-acting insulin received *per os* 100 mg of BZ-55/kg body weight 45 minutes before start of intravenous insulin tolerance test, 0.1 u of crystalline insulin/kg given at zero time. Samples of venous blood obtained without stasis at –45, –20, 0, 30, 60, 90, 120 minutes, and in some patients at 3 and 4 hours, were analyzed for concentrations of sugar by Hagedorn-Jensen procedure. Levels of inorganic phosphorus, potassium, total carbon dioxide, chloride, and sodium in sera of venous bloods drawn between zero and 2 hour points were measured by standard procedures(1). The patients were fasted and at bed rest. Control insulin tolerance tests were made in 14 juvenile diabetics under the same circumstances save that BZ-55 was not given and blood sampling at –45 and –20 minutes was omitted.

Results. From Fig. 1 it is evident that BZ-55 neither potentiates nor prolongs the hypoglycemic action of exogenous insulin. The mean decrements in blood sugar concentrations at 30 minutes (–52 and –36 mg % without and with BZ-55) and at 60 minutes (–77 and –69 mg % without or with BZ-55, respectively) are of the same order of magnitude in the 2 groups with p values of 0.11 and 0.56. On the other hand the decrease in serum inorganic phosphorus which accompanies the hypoglycemia is distinctly less in patients receiving BZ-55, p value of 0.02 (Fig. 1), with mean values of –0.53 and –0.80 mg % at 30 minutes. Changes in serum carbon dioxide content, potassium, chloride and sodium were not influenced by BZ-55.

Discussion. A number of possible explanations have been advanced for amelioration of diabetes mellitus in certain patients by N-sulfanilyl-N′-butylurea, including suppression of pancreatic alpha cell activity(2), decreased absorption from the gastro-intestinal tract (3), decreased gluconeogenesis, increased hepatic glycogenation(4), diminished glucose-6-phosphatase activity(5), inhibition of cytochrome oxidase(6), increased production of insulin(7), and inhibition of insulin destruction(8,9). Insofar as the last of these is concerned there is no evidence in our studies that BZ-55 intensifies or prolongs hypoglycemia which follows administration of insulin in these dosages to juvenile diabetics. As a matter of fact the lesser degree of hypophosphatemia is in keeping with a diminution of

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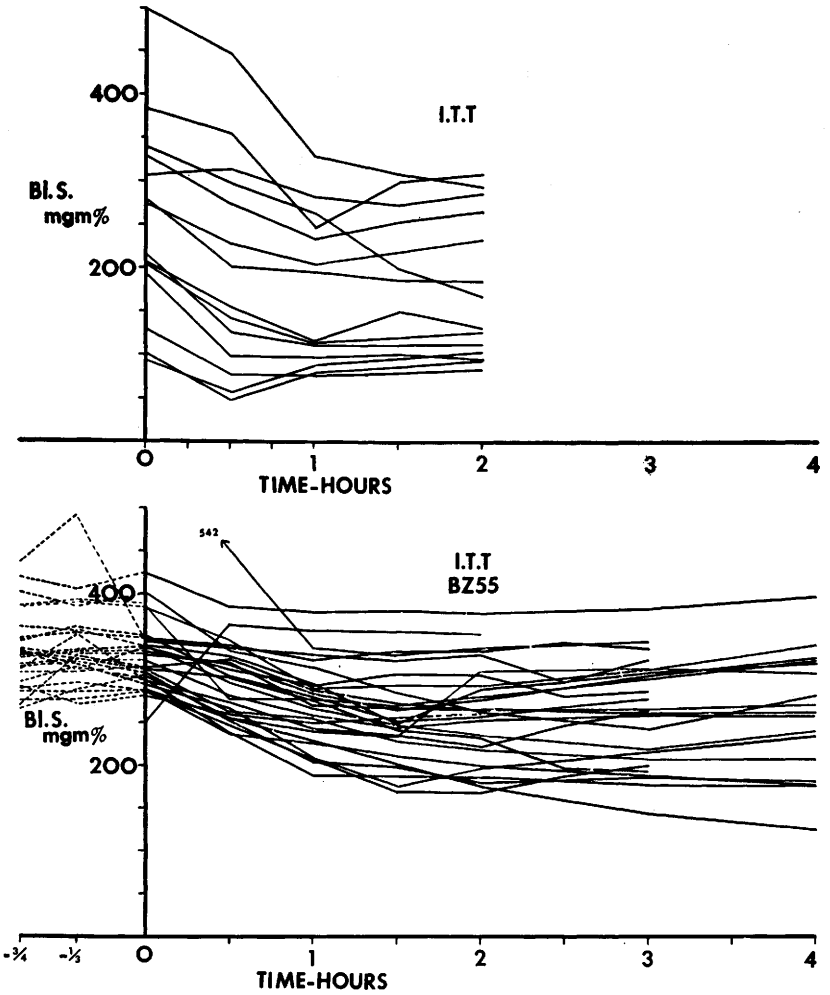

FIG. 1. Blood sugar levels in insulin tolerance tests in juvenile diabetics: effects of BZ-55. There is no evidence that BZ-55 increases hypoglycemia following intravenous administration of crystalline insulin 0.1 u/kilo of body weight at zero time (p values of 0.11 and 0.56 for the 30 and 60 minute points, respectively, in the 2 groups).

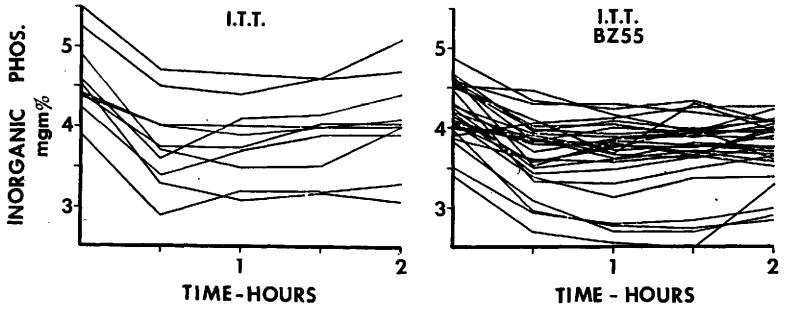

FIG. 2. Insulin tolerance tests in juvenile diabetics: serum inorganic phosphorus concentrations with and without BZ-55. Prior administration of BZ-55 decreases hypophosphatemia present at 30 minutes following intravenous insulin from –0.80 mg % in control group to –0.53 in BZ-55 group (p value of 0.02).

anaerobic glycolysis and could represent either a blockade or other loss of insulin action or result from a decrease in the glucose load. Either or both of these alternatives is compatible with decreased gluconeogenesis, enhanced glycogenation or decreased glycogenolysis as mechanisms whereby BZ-55 may lessen the insulin requirement in some diabetics.

Summary. Insulin tolerance tests in juvenile diabetics following administration of N-sulfanilyl-N′-butylurea (BZ-55 or Carbutamid) failed to show potentiation or prolongation of the usual insulin hypoglycemia and hypophosphatemia. Actually, the decrease in serum inorganic phosphorus which followed administration of insulin to juvenile diabetics was less pronounced, suggesting a diminution in anaerobic glycolysis, either as a result of interference with the usual action of insulin or as a consequence of a decreased glucose load. Both of these possibilities are compatible with decreased gluconeogenesis, increased glycogenation, or diminished glycogenolysis as factors in the decreased insulin requirement which follows administration of this agent to certain patients with diabetes mellitus.

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Abnormal Serum Protein and Bone Destruction in Transmissible Mouse Plasma Cell Neoplasm (Multiple Myeloma). (22935)

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Plasma cell neoplasms of the C3H/HE strain mouse are rare and most often originate in an ulcerated lesion in the ileocecum. Neoplasms of this type have previously been described pathologically and one has been transplanted in this laboratory successfully through 50 transfer generations(1,2,3,4). Plasma cell neoplasms of other mouse strains have been described(5,6,7). The resemblance of these neoplasms to multiple myeloma of man has been made on the basis of microscopic pathology only. The subject of this report is another successfully transplanted C3H strain plasma cell neoplasm of ileocecal origin (X5563), which resembles multiple myeloma of man, not only microscopically, but also by producing an abnormal serum electrophoretic pattern and multiple osteolytic lesions.

Materials and methods. 1. *Origin of tumor, serum sources and methods of transplantation.* The plasma cell neoplasm X5563 originated in a 22½-month-old female of C3H/HE/CRGL strain which had been gonadectomized at the age of 2 months. This animal developed an abdominal mass, and at autopsy there was found a large neoplasm in the wall of the ileocecum, and an enlarged

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