

Effect of Carbutamide on Serum Inorganic Phosphate. (23109)

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Study of the group of hypoglycemia-producing benzene sulfonamide compounds began with the work of Janbon *et al.*(1), and Loubatieres(2). Most investigations were carried out with p-amino-benzene-sulfonamide-isopropyl-thiodiazole (P.A.S.I.T., RP 2254). Interest in the field was enhanced after studies of German workers on N₁-sulfanyllil-N₂-n-butylcarbamide (BZ-55, carbutamide)(3,4,5), etc. and the introduction of 1-butyl-3-p-tolyl-sulfonylurea (D-860, tolbutamide)(6,7,8).

Insulin produces a decrease in serum inorganic phosphate in normal and diabetic subjects(9,10,11). In this note, the action of carbutamide on this blood constituent in normal dogs is reported. While this paper was being prepared for publication, contradictory reports appeared. Renold *et al.*(12), mentioned that there is no change in serum inorganic phosphate or urinary phosphate excretion in human subjects after administration of carbutamide or tolbutamide, and Goetz *et al.*(13) reported that tolbutamide produces a decrease in serum inorganic phosphate.

Methods. Six apparently normal dogs weighing between 13.5 and 17.5 kilos were used for the carbutamide experiments. They were fed *ad libitum* on Purina Chow and twice weekly with meat; all foods were withdrawn 14 to 16 hours before experiments were performed. The animals were previously trained with repeated venipunctures to avoid fear and anger reactions. A blood sample was taken

and an injection by vein of the sodium salt of carbutamide (20% solution) using 0.25 g/kg body weight was given within one minute. Venous blood samples were then withdrawn at 15', 30', 45', 60' and 120'. Blood samples were used for duplicate determinations of blood sugar(14) and serum inorganic phosphate(15). In different dogs, 6 experiments with glucose (0.5 g/kg) in 50% solution by vein, and 6 experiments with glucagon free insulin (0.1 U/kg by vein) were carried out for comparative purposes. Blood samples were taken up to 60'. All results are expressed in terms of differences from initial values, in mg/100 ml (Deltas).

Results. The results are shown in Table I and Fig. 1.

Discussion. In our experiments on normal dogs, carbutamide (sodium salt) injected by vein induces a decrease in blood sugar. This change in blood sugar is not accompanied by a significant decrease in serum inorganic phosphate. Insulin produces a marked lowering of serum phosphate, and glucose will also lower this blood constituent. The effect of glucose does not take place in the pancreatectomized animal(16), and seems to be due to an insulin discharge(17) determined by pancreatic stimulation. Since carbutamide shows a very definite hypoglycemic action without exerting any effect on serum inorganic phosphate, this suggests that its action is not mediated through extra insulin secretion. However, since the decrease in blood

TABLE I. Averages and Standard Errors of Initial Values and Deltas of Blood Sugar and Serum Inorganic Phosphate after Administration of Carbutamide, Insulin or Glucose. 6 animals/series.

	0'	15'	30'	45'	60'	120'
Blood sugar, mg/100 ml						
Carbutamide	72 ± 2	- 9 ± 2	- 19 ± 2	-25 ± 1	-29 ± 2	-31 ± 3
Insulin	74 ± 3	- 31 ± 3	- 35 ± 4	-32 ± 6	-20 ± 4	
Glucose	78 ± 3	+63 ± 14	+17 ± 9	- 3 ± 4	- 9 ± 2	
Serum inorganic phosphate, mg/100 ml						
Carbutamide	3.80 ± .15	-.07 ± .03	-.08 ± .02	-.07 ± .01	-.08 ± .02	-.10 ± .02
Insulin	3.93 ± .23	-.40 ± .07	-.76 ± .16	-.86 ± .15	-.66 ± .25	
Glucose	4.86 ± .45	-.17 ± .10	-.49 ± .11	-.41 ± .11	-.14 ± .15	

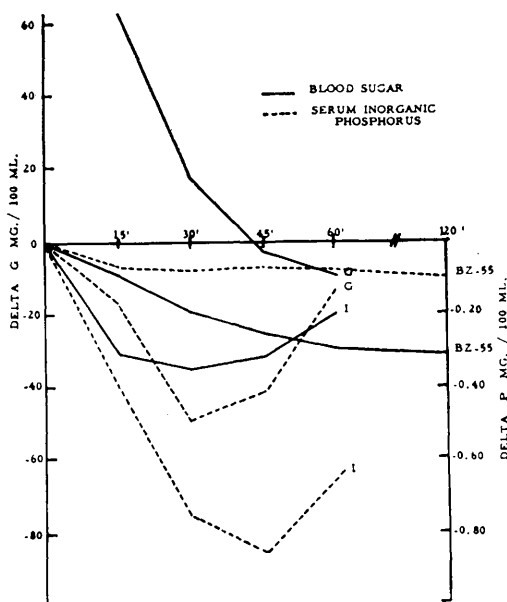


FIG. 1.

sugar induced by carbutamide is gradual, it may be that this time will allow for correction by homeostatic mechanisms, of decrease of serum phosphate, which will thus become masked. Another alternative is that the drug may simultaneously affect the phosphorylation processes.

Summary. The normal trained dog, in fasting conditions, injected by vein with the sodium salt of carbutamide shows a definite decrease of blood sugar, but not significant changes in serum inorganic phosphate. Insulin and glucose produce a definite lowering of serum inorganic phosphate. It seems then, that carbutamide may not lead to a discharge of insulin by the pancreas. However, since the effect of carbutamide on blood

sugar is gradual, it may be that its possible action on serum phosphate is masked by other mechanisms.

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