TABLE II. Summary of Weight, Mortality, Food and Drug Consumption in Dogs Fed Veriloid.

Dog	Wt, kg: Control	6 mo.	12 mo.	At death	Duration drug exposure, days	Mean food intake, g/kg/day	Mean drug intake, μg/kg/day	Remarks
Control	15.2*	17.2*	—	15.8*	(273)	36.3 ± 4.9	Control	Death from acute gastric perforation and hemorrhage
"	10.4*	10.4*	—		(200)	42.8 ± 5.8	"	
"	6.8*	8.7*	9.5*		(378)	40.8 ± 6.2	"	
4a	7.3†	—	—	7.7	21	36.0 ± 7.8	110 ± 23	Delivered pups after 30 days drug exposure
4b	8.3†	—	—	5.3	45	16.1 ± 17.0	59 ± 50	
5	8.6	6.4	8.6	—	350	51.4 ± 26.4	203 ± 68	
6	8.0†	—	—	5.2	138	36.7 ± 6.8	220 ± 53	
7	12.0†	10.9	—	6.0	350	37.6 ± 8.9	195 ± 59	
8	10.9†	6.8	—	6.1	190	33.5 ± 12.3	173 ± 36	
9	7.9	6.4	8.4	—	350	39.9 ± 8.9	223 ± 62	
10	6.8	6.0	8.4	—	350	41.4 ± 10.9	227 ± 57	
11	8.8	7.9	10.9	—	350	40.0 ± 13.2	158 ± 45	
12	11.4	7.8	—	—	172	28.0 ± 12.7	114 ± 39	
13	12.1	7.8	11.6	—	350	33.6 ± 8.6	143 ± 56	
14	12.0	12.3	—	—	172	34.9 ± 6.8	198 ± 57	
Mean	9.8	8.0	9.6	—				
S.D.	2.4	2.2	1.6	—				
Mean†	9.3	—	—	6.1				
S.D.†	2.0	—	—	1.0				

* Not included in mean or S.D.
† Animals which died in course of experiment.

tion of emesis would prevent such occurrence.

Summary. (1) A purified extract of *Veratrum viride*, Veriloid, was fed to growing rats and adult dogs for 12 months. (2) A graded retardation of growth was observed in the rats consuming 3, 5, 8 and 10 mg kg per day of the drug. No such gradation of pathologic change was found. (3) Weight loss and emesis resulted in the dogs. The mean daily intake for this species was limited to 0.19 mg/kg by emesis and failure of animals to eat. (4) No specific organ toxicity was found in either species.

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Effect of ACTH on Decreased Serum Inorganic Phosphorus Induced by Insulin and Glucose. (18628)

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The mechanism of the diabetogenic action of ACTH (adrenocorticotropic hormone) and of 11 oxi-cortico-steroids is little known. Ingle and Thorn(1) have been able to secure evidence against the possibility of a simple increase in neoglucogenesis. Ingle(2), demonstrated the decrease in peripheral utilization of glucose determined by adreno-cortical extracts in the eviscerated rat treated with insulin and his experiments were in harmony with the inverse phenomenon of the facilitation of utilization induced by adrenalectomy in the eviscerated rat as described previously

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by Russell(3). The nature of these changes is not clear at the present time. Conn *et al.* (4) in diabetes produced in man by the administration of ACTH, have afforded proof of the participation of a decrease of SH groups as reflected in a marked drop in blood glutathione levels. At the same time, an increase in uric acid excretion in the urine was noticed. Stetten(5) suggested that the inhibition of hexokinase may be the responsible factor, but this phenomenon takes place in the muscle extracts of diabetic animals and not in the ones from normal animals(6).

The administration of dextrose in the normal organism is accompanied by a decrease in serum inorganic phosphorus(8,9). This decrease does not occur, and if so, very slightly in the diabetic subject(9,10). The administration of insulin in the normal or pancreatectomized animal is followed by the decrease(7,8,11-13). Most of the experimental work tends to show that the phosphorus leaving the circulatory stream is used for phosphorylization purposes(14,15). Soskin and Levine(16) attributed the decrease in inorganic phosphorus to esterification processes taking place within the blood. Arterio-venous differences in serum inorganic phosphorus are greater after the administration of dextrose in the dog(17). It may be that the decrease in inorganic phosphorus could be used as an approximate index of phosphorylization processes. The treatment with ACTH produces in the dog an inhibition of the mentioned phenomenon after the venous injection of glucose solution(18) that is not parallel with the disturbance of the carbohydrate tolerance; with certain dosages it tends to appear and disappear later than the diabetic type of blood sugar curve(18). It would be interesting to discover if this perturbation of the phosphorus decrease is due to an insulin deficiency or is also a reflection of a peripheral disturbance. The administration of insulin associated with the same amount of glucose used in the mentioned experiments(18) in order to avoid the secondary epinephrine liberation, may give some indications in this regard. The results of such work are here reported.

Methods. Six normal and well nourished dogs were used. They were trained by previous repeated veni-punctures in order to avoid fear and anger reactions. The test performed during the different stages of the experiment consisted of taking a venous blood sample under fasting conditions and giving immediately after an injection by vein of 1 ml per kg of body weight of a 50% glucose solution containing 1 U of insulin zinc crystals per every six ml. Thirty, forty-five and sixty minutes after the injection, venous blood samples were obtained. All the samples were analyzed in duplicate for serum inorganic phosphorus with the procedure of Fiske and Subbarow(19), slightly modified and for blood sugar with the method of Nelson(20). All the absorption readings were done in a Coleman Model 6 Spectrophotometer.

The test was performed in the six dogs and then they received the ACTH. Three dogs were given 20 mg daily in one injection for

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TABLE I. Means and Standard Errors of the Changes of Blood Sugar and Serum Inorganic Phosphorus Taking Place After the Venous Administration of Dextrose (0.5 g/kg body wt), and Insulin (1 U/3 g dextrose) in Dogs Treated with ACTH.

Before ACTH	At end of ACTH	8 days after	28 days after
△ 30′	△ 30′	△ 30′	△ 30′
G. —19 ± 5.1	G. —10 ± 6.8	G. —5† ± 5.6	G. —25 ± 6.8
P. —1.16 ± 0.12	P. —1.10 ± 0.24	P. —0.84* ± 0.09	P. —0.76* ± 0.13
△ 45′	△ 45′	△ 45′	△ 45′
G. —15 ± 3.2	G. —19 ± 6.2	G. 4* ±8.6	G. —12 ± 4.1
P. —1.53 ± 0.17	P. —1.22 ± 0.31	P. —0.71* ± 0.05	P. —0.75* ± 0.17
△ 60′	△ 60′	△ 60′	△ 60′
G. —14 ± 2.9	G. —7† ± 3.08	G. 0.16* ± 5.2	G. — 6* ± 2.9
P. —1.48 ± 0.13	P. —1.04 ± 0.36	P. —0.80* ± 0.07	P. —0.88* ± 0.15

* Statistically significant.
† Moderately significant.
The averages are expressed in terms of differences in mg/100 ml in relation to the initial values.

9 days and the other three were injected twice a day with 20 mg for 5 days (ACTH Armour). The last day of the treatment the test was carried out and then 8 days and 28 days after. All figures were expressed as differences from the fasting value of blood sugar or serum inorganic phosphorus. The statistical significance of the changes found in the different periods in relation with the test done before the treatment with ACTH was studied using the "t" test of Fisher(21).

Results. Initial values for blood sugar did not change significantly and the serum inorganic phosphorus showed a significant drop 8 and 28 days after stopping the treatment (22).

In Table I and Fig. 1 the results are presented.

Discussion. As shown in relation to the effect of the ACTH treatment on the decrease in serum inorganic phosphorus induced by the administration of glucose(18), it was found in the experiments that the injection of insulin plus glucose does not determine a normal decrease. This fact shows that the lack of the usual response of inorganic phosphorus to glucose administration under ACTH treatment does not mean that insulin is not sufficiently produced. The disturbance is probably mainly peripheral. If according to some evidences previously mentioned the inorganic phosphorus disappearing from the serum is used in the phosphorylization processes, the found results may be an indication of the *in vivo* inhibition of such processes determined by stimulation of the adrenal cortex.

It is interesting to point out the lack of parallelism between the changes in blood sugar and serum inorganic phosphorus after the injection of insulin and dextrose induced by the ACTH treatment, because it gives an indication about their relative independence.

A latent period is required after the beginning of the ACTH administration in order to produce the defect of the fall in serum inorganic phosphorus. The inhibition was greater 8 days after the end of the treatment and still noticeable 28 days after when the blood sugar values were already practically normal.

Summary. The effect of ACTH on the decrease of serum inorganic phosphorus induced by the administration of glucose and insulin in the normal dog has been studied. Three dogs were given 20 mg of ACTH daily in one injection for 9 days and the other 3 were injected twice a day with 20 mg for 5 days. A significant reduction of the decrease of serum inorganic phosphorus produced by the insulin and dextrose administration was registered 8 days after the end of the treatment and persisted, but not as marked, 28 days after. The defect in the hypoglycemic action of insulin was noticed at the end of the treatment, was more marked 8 days after and almost disappeared 28 days later. The results show that the inhibition of the decrease in serum inorganic phosphorus after the administra-

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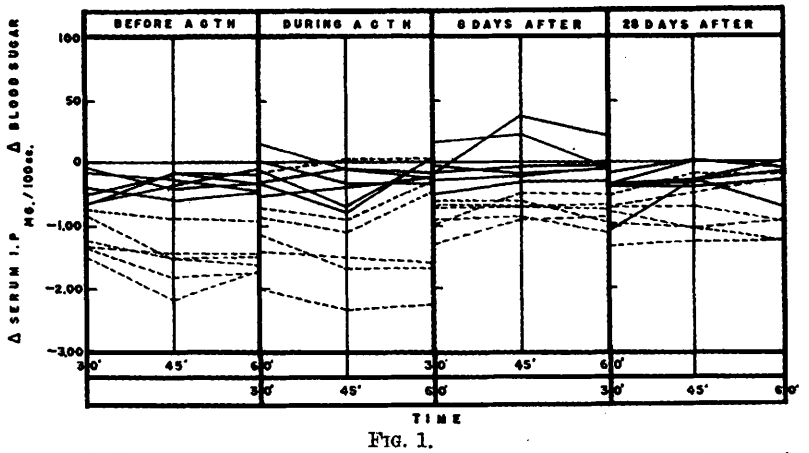

FIG. 1.

The individual variations of blood sugar (solid lines) and serum inorganic phosphorus (dotted lines) from the initial values during the different periods of the experiment.

tion of glucose alone(18) that occurs under the influence of ACTH is not due to a deficiency in insulin production. It was possible to observe that the changes of blood sugar tended to appear and disappear sooner than the modifications in inorganic phosphorus which suggest that they are independent in its mechanism although closely related phenomena. It may be that these experiments could be interpreted as an *in vivo* reduction of the rate of phosphorylization induced by adreno-cortical stimulation.

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Effect of Renal Venous Occlusion on Intrarenal Pressure.* (18629)

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When the veins leaving a tissue are occluded, the hydrostatic pressure from the heart is in part transmitted into the tissue. Burch and Sodeman(1) and Wells, *et al.*(2) found an increase in subcutaneous tissue pressure of 1-3 cm H_2O during prolonged venous congestion. In muscles the same occurs: Wells, *et al.*(2) report that in venous congestion, the intramuscular pressure of the gastrocnemius rises 20 cm H_2O and that of the soleus rises 50 cm H_2O. In the case of the kidney, we have reported that renal venous occlusion causes a pronounced rise in the pressure within the kidney parenchyma(3,4). Gottschalk(5) has also studied the same phenomenon, reporting that the intrarenal pressure does not rise with partial renal venous occlusion until the renal venous pressure exceeds the preexisting interstitial pressure. The present study will describe further experiments in which the effect of both partial and total renal venous occlusion on intrarenal

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