been carried out to determine the effect of LSD and bufotenine on climbing time of trained rats. 2. Both drugs produced similar effects in these animals. However, LSD was effective at smaller doses but had a shorter duration of action than bufotenine. 3. Tolerance to repeated LSD injections was found and a similar tolerance to bufotenine was demonstrated. 4. Prolongation of climbing produced by submaximal doses of both LSD and bufotenine was potentiated when brain serotonin levels were altered by pretreatment of animals with reserpine, 5-HTP or iproniazid. Highly effective doses of LSD and bufotenine were inhibited by 5-HTP pretreatment. 5. Based on evaluation of climbing time delay produced in trained rats the psychogenic activity of LSD and bufotenine appears to depend on a similar mechanism of action.

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Received September 14, 1959. P.S.E.B.M., 1959, v102.

Effect of Glucagon on Renal Functions in the Dog.* (25368)

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Glucagon, in addition to effects on carbohydrate metabolism(1) has been reported to increase urinary excretion of electrolytes in dog (2) and in man(3,4). These authors agree that the electrolyte effects of glucagon are independent of its hyperglycemic action. They also feel that the effects of glucagon on electrolyte excretion probably result from a direct action on the renal tubule since they observed only occasional or slight increases of equivocal significance in glomerular filtration rate (GFR) and renal plasma flow (RPF). Glucagon does not alter peripheral blood flow as measured by finger plethysmography(5), but does produce a marked increase in hepatic blood flow(6). In view of the equivocal data available regarding glomerular filtration rate and renal plasma flow after glucagon administration, and since small changes in glomerular filtration rate could produce large changes in electrolyte excretion, this problem has been further investigated in the dog. In addition, the effect of glucagon on maximum rate at which the renal tubules can reabsorb glucose (Tm glucose) was investigated. In a recent study(7), glucagon was found to have no effect on Tm_G in 2 volunteer subjects.

Materials and methods. Seven healthy trained unanesthetized female mongrel dogs between 45 and 55 lb in weight were used in this study. Exogenous creatinine clearance (GFR), p-amino hippurate (PAH) clearance (RPF) and Tmglucose (Tm_G) were measured by standard technics(8,9). Briefly, creatinine and PAH or creatinine and glucose were administered at a constant rate by means of an infusion pump. After a suitable period allowed for equilibrium, urine was collected by catheter. Each collection period was terminated by a bladder rinse with distilled water. Urine collection periods were accurately timed. Blood was obtained at mid-

* Aided by grants from U. S. Public Health Service and Otho S. A. Sprague.

TABLE I. Effect of Glucagon (HGF) on Glomerular Filtration Rate (GFR), Renal Plasma Flow (RPF) and Filtration Fraction (FF) in Dog.

Function	Procedure	No. dogs	No. exp.	Renal function — Basal	Exp.	Δ	P (paired comparison of basal *vs* exp. groups)
GFR (ml/min.)	Control infusions	5	9	66.2	69.3	+ 3.1	>.1
	Glucagon	7	26	59.9	75.2	+15.3	<.001
RPF "	Control infusions	3	4	230	282	+52	
	Glucagon	3	14	190	256	+66	<.001
FF (%)	Control infusions	3	4	32.5	29.6	− 2.9	
	Glucagon	3	14	28.7	28.9	+ .2	>.5

point of each collection period. Arterial plasma glucose was measured when Tm_G was to be calculated. After appropriate dilutions plasma and urine were analyzed for PAH(9), creatinine(10) and glucose(11). The plasma filtrates were treated with Folin decalso and Lloyd reagent to remove creatinine prior to the glucose analysis. Glucose in the concentration range achieved in our experiments did not alter creatinine values.

Following 3 control periods, crystalline insulin-free glucagon† (HGF) was administered by single injection intravenously or intraperitoneally, or by continuous intravenous infusion at a measured constant rate by means of an infusion pump. Vehicles for HGF included 0.85% saline, glycine-NaOH buffer (pH 8.5) and dog plasma. Renal functions were measured for 3 or more 10 to 20 minute periods during the continuous infusion of HGF at 6 to 45 μ per minute, or for 15 to 30 minute periods after the single intraperitoneal or intravenous injection of 0.2 to 0.5 mg HGF. Frequent measurements of rectal temperature and mean arterial blood pressure were made during 5 experiments. No significant changes were observed. As controls, similar measurements of renal functions were made before and during continuous intravenous administration of glycine-buffer, saline or glucose in amounts used for the Tm_G measurements. As a further control, renal functions were similarly measured when HGF which had been heated to 100°C for 1 or 12 hours in buffered solution at pH = 7.04 was administered by continuous intravenous infusion in 3 experiments.

In long term studies, HGF in saline was given intraperitoneally, 0.5 mg once daily for 145 days in Dog 1, and 0.5 mg twice daily for 140 days in Dog 2. Renal functions were measured at intervals throughout the experimental periods. Urine was tested for sugar frequently. At the end of experimental periods percutaneous renal biopsies revealed normal kidneys in both dogs.

Results. The effects of glucagon (HGF) on glomerular filtration rate (GFR), renal plasma flow (RPF) and filtration fraction (FF) are summarized in Table I. GFR and RPF increased after or during HGF administration in every experiment. Mean increases were statistically significant ($p<0.001$). Although GFR and RPF usually increased progressively after HGF, the 3 to 5 post-HGF periods were averaged and compared to the 3 pre-HGF control periods. HGF had no consistent effect on the FF ($p>0.5$). Route of administration, the vehicle, and rate of infusion of HGF within the limits tested did not appear to affect the results. All types of experiments, therefore, were considered to be a single group. Arterial plasma glucose invariably increased after HGF. In some experiments, however, plasma glucose increase was not sufficient to result in glycosuria. GFR increased as much in these experiments as in those in which glycosuria developed. Likewise, HGF increased GFR in those experiments in which marked glycosuria was already present due to glucose infusion. In control studies neither glucose nor saline infusions at 8 ml/min. affected GFR significantly ($p>0.1$). RPF did increase in each of 4 control experiments but the data were too few to establish statistical significance.

The effects of HGF on Tm_G were studied in 11 experiments in 7 dogs. In all experiments

† Lot No. 258-234B-54-2, supplied through courtesy of Dr. W. R. Kirtley, Eli Lilly Research Laboratories, Indianapolis, Ind.

TABLE II. Effect of Daily Administration of Glucagon (HGF) on Renal Functions in 2 Dogs.

Dog No.	Wk of HGF	GFR (ml/min.)	RPF (ml/min.)	FF (%)	Tm_G (mg/min.)	Tm_G/GFR
1	0	62.4*	235†	29.9†	284	4.8
	6	74.7			470	6.3
	10	55.6	184	30.2	274	4.7
	12	59.8			258	4.3
	16	56.6			258	4.0
	17	52.2	155	33.7		
2	0	69.3†	190	39.4	162	2.5
	8	64.3			261	4.1
	10	62.2			243	3.9
	11	71.1			310	4.5
	16	52.9	176	30.1		

* Mean of 5 control studies. † Mean of 2 control studies. All other data represent one study.

plasma glucose levels were maintained sufficiently high to insure filtered glucose load to Tm_G ratios greater than 1.5, which is generally accepted to be adequate(12). Again, GFR invariably increased after HGF (mean control GFR = 57.4 ml/min., mean GFR after HGF = 69.1 ml/min). Because the plasma glucose also invariably increased, glucose filtered at the glomerulus increased markedly after HGF. Despite this, mean Tm_G increased in 4 experiments (4, 7, 29, and 42%), did not change in one, and decreased in 6 (17, 22, 24, 31, 33 and 37%). The effect of HGF on Tm_G was not statisticaly significant ($p > 0.2$ by paired comparison). However, the Tm_G/GFR ratio decreased in 9 (9, 25, 24, 28, 30, 33, 44, 44 and 46%) and increased in only 2 experiments (7 and 21%). The mean decrease in the ratio after HGF was statistically significant ($p < 0.005$). In a single control experiment in which Tm_G was measured for 8 fifteen minute periods, the mean Tm_G for the first 4 periods was 162 mg/min. and for the last 4 periods was 211 mg/min. Tm_G/GFR ratios were 2.6 and 3.6 respectively.

In 2 dogs treated with daily doses of HGF for 140 and 145 days respectively, GFR, RPF, and Tm_G did not change when measured 24 hours after a HGF dose (Table II). No tolerance to HGF developed, however, in that increased plasma glucose and GFR were observed after individual doses of HGF throughout the experiments.

Attempts to inactivate HGF by heating to 100°C for 1 or 12 hours failed, in that such preparations produced hyperglycemia and increased GFR in 3 experiments.

In a single experiment, HGF increased cardiac output (measured by the Fick principle) from 0.333 to 0.720 liter/min.

Discussion. HGF appears to increase GFR transiently but invariably in the dog. The increase is great enough to account for the increased electrolyte excretion observed by others(2), although other mechanisms of action of the hormone on renal electrolyte excretions are not excluded. We have no explanation for the failure of others to observe an increase in GFR after HGF, although variations in the preparation of HGF used perhaps might account for the difference (HGF lot numbers quoted by other investigators differed from ours). We are satisfied that various infusion rates, vehicles for HGF, hyperglycemia, glycosuria, or analytical errors do not account for the increased GFR observed in our experiments. HGF also increased RPF but did not significantly alter FF. The increased RPF after HGF is not surprising in view of the increased hepatic blood flow reported after this material(6) and the increased cardiac output we observed in a single experiment.

The effect of HGF on Tm_G was not consistent nor statistically significant in 11 experiments. However, in 6 of the 11 experiments, Tm_G decreased by more than 15% after HGF. Moreover, because of a consistent increase in GFR, Tm_G/GFR ratio was decreased significantly after HGF. Although by no means certain, these data are consistent with the possibility that the decreased Tm_G and Tm_G/GFR ratio observed after insulin

(13) might in part have been due to contamination of the insulin with HGF.

Summary. HGF increases GFR and RPF consistently but transiently in the dog, does not affect FF, at times decreases Tm_G. Tolerance does not develop during long term daily HGF administration nor does this regimen increase the basal renal functions.

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Received September 14, 1959. P.S.E.B.M., 1959, v102.

Electrophoretic Studies of Bovine Serum. IV. Differences in Serum Glycoproteins Due to Age and Sex.* (25369)

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Presence of protein-bound carbohydrates of the hexose variety in serum proteins has long been recognized, although very little is known concerning their physiological significance. Only recently has attention been focused on the clinical significance of these glycoproteins in human medicine(1,2) and to a limited extent in experimentation with small laboratory animals(3-5) and swine(6). It has been demonstrated that concentrations of serum glycoproteins are abnormally elevated in many pathological and physiological conditions(7-9) either as a result of tissue destructive(7,9) or proliferative processes(8,9). Limited data on glycoproteins in parasitic infestations in small laboratory animals have been published(10). In these cases significant alterations were not found. A study of serum glycoproteins of the bovine species has not been reported. Mention has been made that the albumin, alpha-, beta-, and gamma-globulins have some glycoprotein associated with each fraction as determined by paper electrophoresis(11). Due to our interest in various diseases of cattle, and the possible significance of serum glycoproteins in formulation of mechanisms of disease processes, an investigation was made of glycoproteins in normal bovine serum. This report presents information on the relative and absolute concentrations of glycoproteins associated with serum proteins. Values are also given with respect to age and sex differences.

Materials and methods. Cattle: Serum glycoproteins from 3 dairy herds of single and mixed breeds managed under southern Louisiana conditions were studied. Two herds consisted of 232 females ranging in age from 1 month to 13 years. The third herd consisted of 35 stud bulls ranging in age from 2 to 15 years. All animals were considered to be normal and appeared to be free from any apparent physiological or pathological disturbances. Blood was collected individually in early

* Supported in part by grant from Nat. Inst. of Allergy and Infect. Dis.