method except that barium hydroxide was substituted for sodium hydroxide in the protein precipitation.[4]

Values for nonfermentable reducing substance have been expressed in terms of glucose-equivalents and have, therefore, only relative significance.

Results. The results of whole blood and plasma determinations of nonglucose reducing substances are shown in Table I, as well as the standard error of their means. The difference between the levels of nonglucose reducing substances of normal and hypertensive subjects, when subjected to statistical analysis, cannot be regarded as significant. The variance between our results and those of Holden[1] can possibly be accounted for by the fact that he was using Somogyi's earlier copper reagent which employs a carbonate-bicarbonate buffer mixture and contains KI. The reagent we used contains a phosphate buffer system and no KI.

Summary and Conclusions. The nonglucose reducing substances remaining after a Somogyi protein precipitation[4] were determined in blood and plasma.

The blood or plasma concentration of these nonglucose reducing substances was not significantly different in hypertensive subjects as compared to normals.

16458 P

Effect of Adrenal Cortical Extract in Hypertensive Subjects.*

KERMIT L. PINES, GEORGE A. PERERA, KATHERINE VISLOCKY, AND ANN D. BARROWS.

From the Department of Medicine, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital, New York City.

Following studies on the pressor activity of desoxycorticosterone acetate,[1] suppression of adrenal cortical function was considered as a possible means of decreasing the blood pressure in essential hypertension. Observations were therefore undertaken on the effects of prolonged administration of an adrenal cortical extract on the arterial tension, circulatory physiology, electrolyte and fluid balance of patients with this disorder.

Methods. Four women with uncomplicated hypertensive vascular disease were studied on the metabolism ward of the Presbyterian Hospital. The criteria in selection of patients and the methods employed were identical to those previously described.[2] All subjects were maintained on a constant dietary fluid and sodium chloride intake and were afebrile throughout the experiment. Following a 3-week baseline period, adrenal cortical extract (Upjohn) was administered intramuscularly in 10 cc doses twice daily for 20 days; then, in 3 patients, 3 times daily for an additional 10 days. The remaining patient (No. 3) developed a moderately severe headache after 6 days on the increased dosage so that the schedule of 2 injections was resumed for 9 additional days. During the final week of the preliminary period and for one week after the extract was discontinued, each patient received intramuscular injections of glucose in distilled water or of 10% alcohol twice daily as well as the advice that this medication was producing a beneficial effect.

Results. Slight weight gain relative to the baseline trend appeared during the period of adrenal cortical extract administration in all instances, together with minimal evidence of salt and water retention. In 3 subjects a decrease in "resting"[2] blood pressure was observed, with a rapid return to baseline values

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1 Perera, G. A., and Blood, D. W., *Ann. Int. Med.*, 1947, **27**, 401.

2 Perera, G. A., and Blood, D. W., *J. Clin. Invest.*, 1947, **26**, 1109.

TABLE I.
Effects of Adrenal Cortical Extract on Blood Pressure and Laboratory Data in 4 Patients with Hypertensive Vascular Disease.

	Patient	Wk before ACE	Final wk of ACE	Wk after ACE
Mean B.P. (mm Hg)	1	169/95	151/81	175/93
	2	183/109	155/91	174/105
	3	182/100	167/90	181/100
	4	167/78	173/82	157/78
Min., Max. Systolic and Diastolic	1	156–180	130–160	164–190
Values		88–108	76–90	86–100
	2	172–198	146–166	166–180
		104–118	84–96	98–114
	3	170–190	158–180	170–196
		94–108	86–96	94–104
	4	158–176	164–180	146–170
		74–82	78–84	70–84
Serum Sodium, meq./l	1	139.6	137.0	140.4
	2	138.6	142.1	139.1
	3	142.4	141.8	141.0
	4	143.5	142.4	144.0
Serum Potassium, meq/l	1	4.1	3.6	4.1
	2	5.2	4.5	4.8
	3	4.7	4.3	4.6
	4	4.5	4.7	4.2
Serum Chlorides, meq/l	1	100.9	97.2	104.1
	3	97.8	101.4	101.6
	4	102.0	97.8	104.6
Serum CO_2 Content, meq./l	1	28.2	30.3	28.7
	3	32.1	29.5	29.6
	4	28.9	30.1	27.5
Urine Sodium, meq./24 hrs	1	48	45	46
	3	43	49	56
	4	38	55	60
Urine Potassium, meq./24 hrs	1	65	63	53
	3	65	59	58
	4	41	45	51
Urine Chlorides, meq./24 hrs	1	45	44	66
	3	64	59	63
	4	42	58	55
Serum Proteins, g/100 cc	1	7.4	7.3	7.3
	2	7.5	7.2	7.5
	3	6.5	6.9	6.8
	4	7.0	6.5	6.4
Serum Vol., cc	1	2530	2640	—
	2	3220	3300	—

during the final week of placebo therapy. A small increase in blood pressure took place in one patient (No. 4) in whom "resting" diastolic values had fallen to normal limits shortly after hospital admission (Table I).

Decreases in serum potassium levels (of 0.7

milliequivalents per liter or less) were noted in 3 cases, but no significant change could be detected in hematocrit, carbon dioxide content, chloride, sodium, protein or urea nitrogen concentration of the serum. There was no major alteration in the excretion of sodium, potassium or chloride in the urine. Determinations of serum volume with the blue dye T. 1824 were carried out in 2 subjects before and at the end of the period of extract injection with no significant change. Ballistocardiographic tracings were unaltered in one patient who exhibited a drop in blood pressure. Toward the close of the extract period there was no leucocytosis, eosinophilia or rise in erythrocyte sedimentation rate; no effect on the electrocardiogram or teleroentgenogram; and the patients complained of no symptoms during the treatment period other than the headache previously mentioned.

Discussion. In the dosage employed, the continued administration of adrenal cortical extract was associated with a decrease in "resting" blood pressure in 3 of 4 hypertensive patients. The changes in arterial tension could not be ascribed to alterations in serum volume, fluid or electrolytes, or apparent change in cardiac action.

The results suggest the possibilities that the fall in blood pressure may reflect suppression of adrenal cortical function or represent counteraction of a desoxycorticosterone-like pressor hormone. The adrenal cortex may possess a homeostatic group of substances concerned with blood pressure regulation.[3] However, one cannot exclude the possibility that the decrease in tension observed in this study may have been the result of some non-specific component contained in the extract. Further search for depressor materials is indicated among purified products of the adrenal cortex.

Summary. The continued administration of an adrenal cortical extract for one month, to four subjects with uncomplicated hypertensive vascular disease on a constant regimen, was associated with a decrease in "resting" blood pressure in 3 instances, a small rise in arterial tension in one.

[3] Soffer, L. J., *Diseases of the Adrenals*, Lea & Febiger, Philadelphia, 1946.

16459

Influence of pH on Growth of Bone in Tissue Culture.*

GEORGE H. PAFF.

From the Department of Anatomy, Long Island College of Medicine, Brooklyn, N.Y.

Although a great amount of work has been done on the general subject of bone growth, the exact actions of the factors involved are poorly understood. The problem of bone growth and pH is a case in point. With little or no experimental evidence the idea is widespread that the calcification which accompanies bone growth occurs because of a local change to a more alkaline pH. To ascertain whether or not this speculation was correct we undertook to grow bones in tissue culture at two levels of pH, namely 7.0-7.3 and 7.8-8.0.

The pertinent literature on the problem traces largely from the work of Robison and his co-workers. Following Robison's discovery[1] of phosphatase in bone the theory was advanced that this enzyme played an important role in ossification. Further work revealed that in the test tube phosphatase was most active between pH 8.4 and 9.4 when glycerophosphate was employed as the substrate.[2] Robison then postulated that osteo-

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[1] Robison, R., *Biochem. J.*, 1923, **17**, 286.

[2] Robison, R., and Soames, K. M., *Biochem. J.*, 1924, **18**, 740.