appears in normal fashion as the cartilage cell reaches its full stage of differentiation; as the cell persists, however, for reasons which are not clear at this time, the glycogen disappears. In the rachitic animals in which healing had not been induced, no deposition of inorganic material is present in the vicinity of the hypertrophic glycogen containing cells, or those from which glycogen has disappeared. When healing was instituted, it took place, as has often been noted both *in vivo*[9] and *in vitro*,[10] in the matrix adjacent to those cartilage cells which have most recently matured, that is, in the immediate vicinity of the cells which contain abundant glycogen and, in the early period of observation, not down farther in the matrix adjacent to the hypertrophic cells devoid of glycogen. There is thus a regional relationship between the presence of glycogen and deposition of inorganic elements as demonstrated by the von Kossa technic. It is, of course, impossible to determine any precise reciprocal relationship between the disappearance of glycogen and the appearance of inorganic materials since to follow the disappearance of one and the appearance of the other is not possible. It is hoped that quantitative methods[11] now available, using larger animals, can be applied to study this particular problem.

The glycogen content of rachitic cartilage has received little attention. Some years ago Suppes[12] reported observations on postmortem human material and concluded that rachitic cartilage did not contain glycogen. No mention was made of the presence of glycogen in the uppermost hypertrophic cells so that one suspects autolytic changes may have been a complicating factor.

The localization of glycogen in rachitic cartilage in the region where calcification first appears during healing is, of course, important in any theory of calcification which has the glycogenolytic cycle as its basis.[13] More precise localization of phosphorylase activity[6] as well as that of other enzymes which participate in the cycle will have to be carried out before such an hypothesis can be fully accepted.

Summary. Glycogen is present in rachitic cartilage only in the most recently matured hypertrophic cells. The broad zone of hypertrophic cells beneath is devoid of glycogen. This localization coincides with the area where inorganic elements deposit during the initial stages of healing and furnishes further evidence for the relationship of glycogen, and possibly the glycogenolytic cycle, to the calcification mechanism.

[9] McCollum, E. V., Simmonds, N., Shipley, P. G., and Park, E. A., *J. Biol. Chem.*, 1922, **51**, 41.

[10] Shipley, P. G., Kramer, B., and Howland, J., *Biochem. J.*, 1926, **20**, 379.

[11] Follis, R. H., Jr., *Fed. Proc.*, 1949, **8**, 480.

[12] Suppes. J., *Frank. Z. Path.*, 1922, **26**, 268.

[13] Gutman, A. B., Trans. Conf. on Metabolic Aspects of Convalescence, Josiah Macy, Jr. Foundation, 1946, **14**, 20.

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17218. Simultaneous Administration of Adrenal Cortical Extract and Desoxycorticosterone; Effects on Blood Pressure of Hypertensive Patients.*

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Previous studies[1] have indicated that the continued administration of an adrenal cortical extract may be associated with a decrease in the "resting" blood pressure of patients with

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[1] Pines, K. L., Perera, G. A., Vislocky, K., and Barrows, A. D., PROC. SOC. EXP. BIOL. AND MED., 1948, **68**, 286.

TABLE I.
Laboratory Data of 5 Hypertensive Patients Before and During Treatment with DCA and ACE.

Wt, k		Urine*			Serum							
		Vol. cc	Sodium milliequiv.	Chloride milliequiv.	Hematocrit % cells		Urea N, mg/100 cc		Proteins, g/100 cc		Na milliequivs./l	
A†	P†				A	P	A	P	A	P	A	P
65.5–66.0		1840–1580	96–64	85– 50	40.3–37.3		17–15		6.2–6.1		140.0–142.3	
65.6–66.3		1400–1400	57–42	69– 58	46.0–46.0		10– 8		6.4–6.4		139.3–138.3	
78.5–78.4		1460–1520	74–56	94– 75	—		—		—		136.3–137.4	
63.2–64.0		1540–1400	84–60	98– 72	45.0–44.1		12–10		6.6–6.5		138.9–138.6	
65.0–65.6		1620–1480	—	118–100	—		—		7.5–7.4		138.6–138.7	

Serum			
Cl milliequivs./l		K	
A	P	A	P
99.6–102.0		3.8–3.3	
102.2–100.2		4.7–4.2	
—		4.4–4.3	
99.2–100.0		3.9–3.1	
—		5.2–5.2	

* Mean daily values for week preceding and week of steroid administration.
† A = Start of treatment.
P = End of treatment.

uncomplicated hypertensive vascular disease. Inasmuch as the daily injection of desoxycorticosterone acetate has consistently produced at least a transitory and sometimes a sustained pressor response under comparable conditions,[2,3] the effect of both agents was observed when given in combination.

Methods. Two men and 3 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.[4] All subjects were maintained on a constant dietary, fluid and sodium chloride intake. Following a 3-week baseline period, desoxycorticosterone acetate† (DCA) was administered subcutaneously in 5 mg doses twice daily, and adrenal cortical extract (Upjohn) (ACE) was given intramuscularly in 10 cc doses twice daily, both materials being injected for

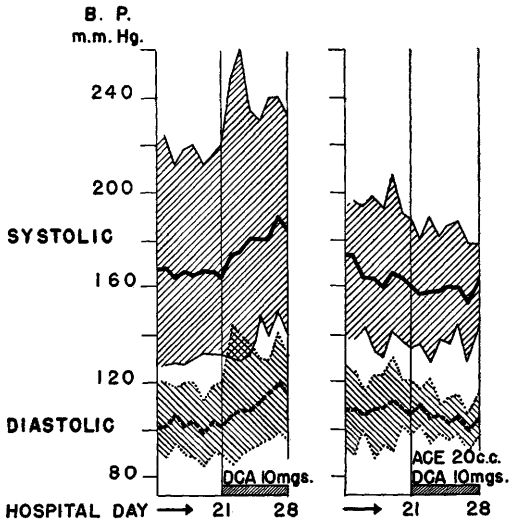

FIG. 1.
Maximum, minimum and mean systolic and diastolic blood pressures of 12 hypertensive patients given DCA and 5 given both DCA and ACE.

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

[3] Perera, G. A., PROC. SOC. EXP. BIOL. AND MED. 1948, **68**, 48.

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

† Desoxycorticosterone acetate (DOCA) was supplied through the generosity of Dr. K. W. Thompson of Roche-Organon, Inc., Nutley, N. J.

a period of a week. The results were compared to those previously obtained in 14 patients receiving only DCA,[2] two of whom being included in the present series after repeatedly demonstrating a prompt rise in blood pressure in association with this steroid given alone.

Results. The combination of DCA and ACE generally produced increases in weight, hemodilution, reductions in urinary volume, and sodium and chloride retention. These changes were similar to those observed after DCA alone. No consistent alterations in serum sodium or chloride values were noted, but reductions in serum potassium levels were again evident in the majority (Table I). In no instance was fever, leucocytosis, eosinophilia or rise in erythrocyte sedimentation rate produced by these agents. In all patients there were either minimal changes in "resting" blood pressure or an actual decline (Fig. 1).

Conclusions. In patients with hypertensive vascular disease, the simultaneous administration of an adrenal cortical extract appears to block the pressor effect of desoxycorticosterone acetate when used alone.

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17219. Effect of 11-Desoxycorticosterone Acetate upon Carbohydrate Utilization by the Depancreatized Rat.*

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In recent years it generally has been thought that only those steroids of the adrenal cortex which have an oxygen atom at the 11 position in ring C can directly influence carbohydrate metabolism. In particular, the synthetic compound 11-desoxycorticosterone, which has not even been demonstrated with certainty to occur in the gland and which is exceedingly potent in causing sodium retention, has been considered to have no carbohydrate action. However, Verzar and his co-workers have demonstrated[1] that this steroid may reduce glycogen synthesis in isolated diaphragm muscle and may prevent the increased glycogen formation produced in this tissue by insulin. Using glucose labeled with carbon 14, this observation has been confirmed and extended in this laboratory.[2]

Ingle[3] recently has found that in rats made diabetic by partial pancreatectomy, 11-desoxycorticosterone acetate caused a slight decrease in the level of urinary glucose when given in small doses, while large doses of the steroid led to a marked exacerbation of the glycosuria.

Our experiments were carried out in an attempt to find out if desoxycorticosterone would oppose the action of insulin in the diabetic organism.

Methods. Male albino rats of the Slonaker strain[4] were depancreatized at 6 weeks of age in the usual manner.[5] The rats were maintained on Purina Chow until 1 week before the start of the experiment at which time they were fed the following rather high carbohydrate diet: Sucrose 50, casein 18, yeast 10, salt mixture 4, C.L.O. 4, lard 14. After their diabetes was stabilized on this above diet, the animals were placed in individual metabolism cages. The rats were weighed and their food intake determined daily. The urine was

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1 Verzar, F., and Wenner, V., *Biochem. J.*, 1948, **42**, 35; 1948, **42**, 48.

2 Bartlett, G. R., Wick, A. N., and MacKay, E. M., *J. Biol. Chem.*, 1949, **178**, 1003.

3 Ingle, Dwight J., PROC. SOC. EXP. BIOL. AND MED., 1948, **69**, 329.

4 MacKay, L. L., *Am. J. Physiol.*, 1928, **86**, 215.

5 Pauls, Frances, and Drury, Douglas R., *J. Biol. Chem.*, 1942, **145**, 481.