constant in all of the animals. No differences in the excretion of water as related to the presence and absence of the adrenal glands and to cortisone were observed. The amounts of amino nitrogen in the urine were negligible. It seems probable that the amino acids of the plasma would move freely with water lost into the extracellular fluid of the tissues, but this is uncertain. The average increase in concentration of plasma amino acids caused by treating adrenalectomized-eviscerate rats with cortisone was over 60 per cent. If this change were due to a relative loss of diluent, there should have been a significant change in the hematocrit and in the concentration of hemoglobin. Such was not observed. The factors responsible for the effects of adrenal cortical hormones upon the concentration of plasma amino acids remain to be fully elucidated, but we suggest that it probably represents an extra-hepatic effect of the hormones upon protein metabolism.

Summary. Male rats were eviscerated and eviscerated-adrenalectomized. All of the animals received continuous intravenous infusions of saline with glucose and insulin for 24 and 48 hours. The administration of cortisone acetate in doses of 5 and 10 mg per 24 hours to one rat of each pair caused significant increases in the concentration of plasma amino acids above the values for untreated animals. It is postulated that the observed change represents an extra-hepatic effect of cortisone upon protein metabolism.

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Marked Acute Hyperglycemic Response of Depancreatized Chicks to Adrenal Cortical Extract (ACE).* (18349)

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Neither pancreatectomy nor alloxanization effects a persistent hyperglycemia in chicks. Birds chronically surviving these procedures exhibit normal blood glucose levels and glucose tolerance curves(1-6). The reasons for this remain obscure. Previously, Golden and Long demonstrated that adrenal cortical extract (ACE) elicits gluconeogenesis in normal chicks; moderate hyperglycemia supervenes (2). These workers did not study the response of pancreatectomized birds to ACE.

The possibility presents itself that ACE-induced hyperglycemia may be enhanced in depancreatized birds due to a relative insulin lack present despite normal control plasma glucose levels(7). Since such a finding would throw light on the metabolic relationships prevailing in pancreatectomized birds, we undertook to study their glycemic responses to ACE.

Methods. A total of 9 depancreatized and 8 unoperated (control) cockerels were used.

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TABLE I. Four Hour Hyperglycemic Responses of Depancreatized and Control Chicks to a Single 5 cc Injection of ACE.

Control birds				Pancreatectomized birds			
	Plasma glucose	Plasma glucose	ACE-induced		Plasma glucose	Plasma glucose	ACE-induced
Chick No.	Pre-ACE mg%	Post-ACE* mg%	Glucose Δ+ mg%	Chick No.	Pre-ACE mg%	Post-ACE* mg%	Glucose Δ+ mg%
1	218	250	+32	6	252	256	+4
2	250	250	0	7	235	332	97
3	243	272	29	8	237	330	93
4	178	260	82	9	202	342	140
5	152	230	78	10	203	273	70
1	200	238	38	11	200	301	101
2	239	277	38	6	286	346	60
3	224	262	38	7	190	251	61
				8	228	343	115
Mean	213	255	+41.9 ± 9.4†	Mean	226	308	+82.3 ± 13.1†
Range	152-250	230-277	0-82	Range	190-286	251-236	4-140

* 4 hr response.
+Δ is rise in plasma glucose conc.
† 9.4 and 13.1 are standard errors(9).

Pancreatectomy was performed via an abdominal incision under sodium pentobarbital anesthesia. All experiments were done at least 10 days after pancreatectomy, some several months thereafter. All birds exhibited normal feed intake, growth and development and exhibited no overt signs of abnormal metabolism. All birds in paired experiments were approximately the same age and weight. Completeness of pancreatectomy was confirmed postmortem; in 2 of the birds, small pancreatic remnants were found. Two series of experiments were done. In the first, a single 5 cc injection of adrenal cortical extract‡ was given and the 4 hour plasma glucose response analyzed. In the second, hourly ACE injections (1 cc) were given for 10 hours. Blood for plasma glucose analysis was drawn from an alar vein 1, 20 and 40 hours after the last ACE injection. Glucose was determined by the Somogyi-Shaffer-Hartman method§(8).

Results. The findings in the first series of experiments are summarized in Table I. In accord with other workers(2), we found that ACE induces a hyperglycemic response in normal chicks. Further in accord with previous results(1-6), the depancreatized chicks exhibited pre-ACE control plasma glucose levels within the normal range. Depancreatized chicks responded to a single 5 cc injection of ACE with a 4 hour rise in plasma glucose levels that was significantly greater than in the control cockerels (Table I).

This phenomenon was demonstrated far more clearly by the experimental procedure utilized in the second series (Table II). Thus 1 hour after the last of 10 hourly 1 cc injections of ACE, the depancreatized chicks showed a rise in mean plasma glucose from 234 to 617 mg% (controls: 223 to 403 mg). One operated bird exhibited a plasma glucose of 745 mg% at this time, an increment of 502 mg%. The rise in plasma glucose persisted in the pancreatectomized birds, as revealed by 20 and 40 hour analyses, whereas it was transitory in the controls (Table II). These differences are statistically significant(9).

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TABLE II. Hyperglycemic Responses of Depancreatized and Control Chicks to 10 Hourly Injections of ACE (1 cc).

Pancreatectomized birds

Chick No.	Plasma glucose pre-ACE, mg%	Plasma glucose 1 hr post-ACE,* mg%	1 hr Δ mg%	Plasma glucose 20 hr post-ACE, mg%	20 hr Δ mg%	Plasma glucose 40 hr post-ACE, mg%	40 hr Δ mg%
12	212	630	+418	450	+238	260	+ 48
13	248	475	227	440	192	243	— 5
14	243	745	502	700	457	495	+252
Mean	234	617	+382	530	+296	333	+ 98
Range	212-248	475-745	227-502	440-700	192-457	243-495	—5 - +252

Control birds

Chick No.	Plasma glucose pre-ACE, mg%	Plasma glucose 1 hr post-ACE,* mg%	1 hr Δ mg%	Plasma glucose 20 hr post-ACE, mg%	20 hr Δ mg%	Plasma glucose 40 hr post-ACE, mg%	40 hr Δ mg%
15	217	390	+173	228	+11	205	—12
16	207	405	198	228	21	205	— 2
17	245	415	170	298	58	185	—60
Mean	223	403	+180	251	+30	198	—25
Range	207-245	390-415	170-198	228-298	11-58	185-205	—2 - —60

* After last of 10 consecutive hourly inj.

Discussion. Injection of ACE into depancreatized chicks results acutely in a hyperglycemia significantly greater in degree and longer in duration than that exhibited by unoperated control birds. This response corresponds to that observed in partially depancreatized rats given ACE(7). The plasma glucose levels in our operated, ACE-treated chicks are in the diabetic range. These findings supervene although the depancreatized chicks have normal pre-ACE plasma glucose levels and glucose tolerance curves. They indicate a relative insulin lack and a latent diabetic tendency (subdiabetes), in depancreatectomized birds(4,7,10-14).

Summary. Injection of ACE into depancreatized cockerels induces a marked acute hyperglycemic effect, significantly greater in degree and longer in duration than in unoperated control birds.

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