between small and large, but not between small and medium dogs. No sex difference was found within any single weight group of adult animals. Although the number of senile animals was small, their relative hypophysis size was distinctly (33.8%) and significantly less than that of adults.

No significant differences were found in water content of the hypophysis (range, 82.25% to 83.88%).

Discussion. The observations of relative hypophysis weights in pups and in adults, as far as sex difference is concerned, confirm those of other workers. Hypophysis weight seems subject to gonadal influence, being increased in the female by estrus(11), pregnancy(10), and the injection of chorionic gonadotrophin, theelin and theelol(12). The hypophysis of the male is not influenced, however, by the administration of testosterone. It would be expected, therefore, that the female hypophysis would be heavier.

Constancy of water content of the hypophysis in the several groups suggests that fluid shifts into and out of the gland are not important effects upon its relative weight. It would be of interest to study water content of the hypophysis in estrous females.

Summary. 1. It is confirmed in the dog, as has been shown for other species, that the relative weight of the hypophysis is greater in adult females than in adult males, and that this difference does not exist before maturity. 2. The hypophysis weight-body weight ratio of puppies is greater than that of adult dogs, and in adult dogs decreases significantly with increase in body size. 3. Relative hypophysis weight was smaller in senile than in adult animals. 4. No sex difference in hypophysis weight existed within any weight-group of adult animals. 5. No differences between groups could be detected with respect to water content of the hypophysis.

11. Andersen, D. H., PROC. SOC. EXP. BIOL. AND MED., 1933, v30, 657.

12. Leiby, G. M., PROC. SOC. EXP. BIOL. AND MED., 1933, v31, 14.

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Effect of Insulin Hypoglycemia on Eosinophiles and Lymphocytes of Psychotics.* (18048)

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The adrenal glucocorticoids, essentially the 11-17-oxysteroids, produce a fall in the circulating eosinophiles and lymphocytes(1,2). Eosinophile and lymphocyte counts have been utilized to evaluate the functional state of the adrenal cortex under various conditions of stress. Insulin hypoglycemia is one notable form of stress. An antagonism exists between insulin and adrenal glucocorticoids(3). Insulin hypoglycemia liberates epinephrine(4,5), which is an effective anterior pituitary-adrenal cortical activator(6,7).

The present report is a study of the effect of insulin hypoglycemia on the eosinophiles and lymphocytes of schizophrenic patients.

* The psychotic patients were made available through the cooperation of Dr. Jack R. Ewalt, Director, Galveston State Psychopathic Hospital.

1. Forsham, P. H., Thorn, G. W., Prunty, F. T. G., and Hills, A. G., *J. Clin. Endocrinol.*, 1948, v8. 15.

2. Dougherty, T. F., and White, A., *Endocrinology*, 1944, v35, 1.

3. Soskin, S. Z., *Medicine*, 1949, v28, 392.

4. Cannon, W. B., McIver, M., and Bliss, S. W., *Am. J. Physiol.*, 1924, v26, 46.

5. Heibrun, G., and Libert, E., *Endocrinology*, 1939, v25, 354.

6. Long, C. N. H., and Fry, E. G., PROC. SOC. EXP. BIOL. AND MED., 1945, v59, 67.

7. Recant, L., Hume, D. M., Forsham, P. H., and Thorn, G. W., *J. Clin. Endocrinol.*, 1950, v10, 187.

TABLE I.

No.	Age and sex	No. insulin injections	Insulin given I.M., units	Initial blood glucose (mg %)	Lowest blood glucose determined hr*	Lowest blood glucose determined mg %	Maximum % fall hr*	Maximum % fall Eos.	Maximum % fall hr*	Maximum % fall Lym.	Remarks
1	42 F	17	110	105	4	21	8	79	6	60	Drowsy
2	16 M	18	130	110	4	22	8	69	6	38	"
3	29 F	28	235	212	2	15	4	86	4	50	"
4	36 F	19	140	88	2	33	6	79	6	56	Coma
5	38 M	14	145	97	2	8	6	96	6	60	"
6	29 F	17	250	99	2	13	6	96	6	70	"
7	27 F	25	90	134	2	21	6	93	4	52	"
		27	90	122	1	65	2	37	2	16	Glucose†
8	38 F	12	340	120	7	51	4	27		‡	Glucose†
		17	250	—	2	23	6	75	6	64	Coma & EST
		22	250	122	4	18	6	87	6	47	"

* No. of hr after insulin administration.
† Glucose given concurrently with insulin.
‡ Lymphocytosis up to 39% at the end of 12 hr.

Eight schizophrenic patients were chosen at random for this study. They were hospitalized and had been receiving insulin treatment for varying periods of time. The essential clinical data are shown in Table I. Capillary blood samples were obtained from the finger. The blood glucose was estimated by the method of Folin and Malmros(8). Eosinophile counts were made with the Randolph direct method (9). Lymphocytes were calculated indirectly from the total white and differential counts of 400 or 500 cells. Control counts were obtained just before insulin was given. Additional counts were made every 2 hours for 12 hours.

The mechanism of the effect was further studied in Cases 7 and 8 by preventing hypoglycemia by oral and intravenously administered glucose. Four grams of glucose per unit of insulin were given within 4 hours of insulin administration and blood glucose was estimated at half hour intervals. Eosinophile and lymphocyte counts were also made when Case 8 received a combined insulin and electric shock treatment.

A uniform and significant decrease in both eosinophiles and lymphocytes was observed in all cases of insulin hypoglycemia. The eosinopenia amounted to 69 to 96% fall; and the lymphocytopenia 38 to 70% fall. The lowest blood glucose value obtained at 2-hour intervals occurred 2 to 4 hours after the administration of insulin. The maximal eosinopenia occurred 4 to 8 hours after insulin administration and 2 to 4 hours after the lowest blood glucose occurred. The maximal lymphocytopenia occurred 4 to 6 hours after insulin administration and 2 to 4 hours after the lowest blood glucose occurred.

The number of previous injections of insulin, the dosage of insulin and the age of the patient did not influence the magnitude of the decrease of either eosinophiles or lymphocytes. Nor did it seem that the clinical status was related to the extent of fall in this mixed group of improved and unimproved cases.

An added electric shock, which also causes eosinopenia(10) and lymphocytopenia(11) did not intensify the drop in Case 8 when electric shock was given during the period of insulin shock.

When glucose was given concurrently with insulin in Cases 7 and 8 and hypoglycemia prevented, the eosinopenia (37 and 27% fall respectively) was below the minimal 50% fall produced by 25 mg ACTH or 0.2-0.3 mg of epinephrine(12). There was also no signi-

8. Folin, O., and Malmros, H., *J. Biol. Chem.*, 1929, v83, 115.

9. Randolph, G. H., *J. Allergy*, 1948, v15, 89.

10. Altschule, M. D., Parhurst, B. H., and Tillotson, K. T., *J. Clin. Endocrinol.*, 1949, v9, 440.

11. Mikkelsen, W. R., and Hutchens, T. T., *Endocrinology*, 1948, v42, 394.

12. Thorn, G. W., and Forsham, P. H., *Recent Progress of Hormone Research*, v. 4, Academic Press, N.Y., 1949, 265.

ficant change in the lymphocytes (16% decrease in Case 8 and 39% increase in Case 9).

We have found no reports on eosinopenia following insulin hypoglycemia in either psychotics or normal individuals. Godlowski(13) demonstrated, however, a similar significant decrease in eosinophiles of eleven allergic patients with eosinophilia after the subcutaneous administration of 100 units of insulin. The period during which maximal eosinopenia occurred was 6 to 8 hours after the administration of insulin in his series. This is comparable to our results of 4 to 8 hours after intramuscular administration of insulin.

Lymphopenia following insulin hypoglycemia in psychotics has been observed by Katzenelbogen(14) and Parsons(15). The period during which maximal lymphocytopenia occurred in Parsons' series was 4 to 6 hours after intramuscular insulin administration, which is identical with our findings.

As mentioned above, insulin hypoglycemia causes an outpouring of epinephrine(3,4), which stimulates the production of ACTH by the anterior pituitary(6,7). It is probable therefore that the adrenocortical activation in insulin hypoglycemia depends on the liberation of epinephrine from the adrenal medulla. The quantitative and qualitative similarity of the falls of eosinophiles following insulin and epinephrine in allergic subjects, as observed by Godlowski(13), and the same similarity of the falls of lymphocytes following insulin and epinephrine in psychotics, as observed by Parsons(15), support this view. The delayed occurrence of eosinopenia and lymphocytopenia following insulin as compared with epinephrine and electric shock(13, 15) can be explained by the time interval required for the hypoglycemic effect of insulin and the subsequent output of epinephrine from the adrenal medulla to take place. When hypoglycemia was prevented by glucose (Cases 7 and 8) no significant eosinopenia and lymphocytopenia occurred. This also supports our belief that epinephrine is the cause of adrenocortical activation in insulin hypoglycemia.

Further studies, including the concurrent employment of adrenolytic drugs during insulin hypoglycemia, are in progress.

Summary. Insulin hypoglycemia causes in schizophrenics a significant eosinopenia and lymphocytopenia, which is considered to be indicative of adrenocortical stimulation. Insulin does not produce such changes if hypoglycemia is prevented.

13. Godlowski, Z. Z., *British Med. J.*, 1948, v1, 47.

14. Katzenelbogen, S., *Am. J. Psychiatry*, 1939, v95, 793.

15. Parsons, E. H., Gildea, E. F., Ronzon, E., and Herbeit, S. Z., *Am. J. Psychiatry*, 1949, v105, 573.

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Culture of Brown-Pearce Carcinoma in the Embryonated Egg. (18049)

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The Brown-Pearce carcinoma is commonly maintained by rabbit inoculation. Since the tumor may regress or die out during the summer months, and because of obvious economic and experimental advantages, we have investigated the feasibility of maintaining the growth in the developing egg. The present experiments show that the Brown-Pearce carcinoma may be cultured readily on the chorioallantoic membrane of the chick, and that it retains its capacity for growth and metastasis in the rabbit. Data are also presented on some conditions conducive to an optimal number of "takes" on the chorioallantoic membrane.

Materials and methods. Brown-Pearce tissue was obtained from female Dutch rabbits inoculated by the intra-uterine technic of