

are present in low titer to the heterologous organisms. *L. donovani* and *T. cruzi*, responsible for systemic infections, produce higher

titers than *L. tropica* and *L. brasiliensis*, which have only cutaneous or mucocutaneous manifestations.

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Effect of Adrenocorticotrophic Hormone on Leucocyte Picture of Normal Rats and Dogs.*

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Experimental evidence is available which indicates that stimulation of the adrenal cortex by injection of adrenocorticotrophic hormone (ACTH) produces a marked decrease in the weight of the thymus and lymph nodes in the mouse¹ and in the rat.² Subsequent studies by Dougherty and White on the white blood cells in the mouse and rat³ and dog⁴ after such treatment have demonstrated a typical change in the leucocyte picture characterized by transient leukopenia with an absolute lymphopenia and an absolute polymorphonuclear leucocytosis. The reaction was thought to be specific in that the effects were not observed in the treated adrenalectomized animal, and were not duplicated by the injection of control substances. The same response, moreover, was produced by the injection of adrenal cortical extract into normal and adrenalectomized mice.

Certain of the above findings studied in this laboratory have been confirmed. Acute and chronic injections of purified ACTH in normal rats of the Long-Evans strain have resulted in the production of an absolute lymphopenia and

polymorphonucleosis. A typical experiment is presented. Purified ACTH⁵ was injected into normal 26-day-old male rats in doses IP (intraperitoneal) of 1 mg every 4 hours. Four hours after the second injection, leucocyte counts and differential counts were made from tail blood samples. The findings are presented in Table I. It is apparent that ACTH treatment is followed by a mild leukopenia with a definite absolute change in the ratio of polymorphonuclear to mononuclear cells.

Injections of ACTH were carried out on fasted adult normal dogs to ascertain the type of reaction which might be obtained in this animal form. Purified sheep ACTH was injected IP in dosages of from 10 to 100 mg. Duplicate white cell counts and differentials were made at 2-3-hour intervals until counts and differential percentages returned to normal control levels. Specimens of blood were obtained from the femoral artery in unanesthetized animals. Control experiments were carried out using similar amounts of purified lactogenic hormone,⁶ boiled (inactivated) interstitial cell stimulating hormone⁷ (ICSH), and boiled inactive pituitary gland residue. The experiments are summarized below. Peak leucocytoses were noted in all animals within a period of 5-10 hours. The white cell counts returned to normal within

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¹ Dougherty, T. F., and White, A., *Proc. Soc. Exp. Biol. and Med.*, 1943, **53**, 132.

² Simpson, M. E., Li, C. H., Reinhardt, W. O., and Evans, H. M., *Proc. Soc. Exp. Biol. and Med.*, 1943, **54**, 135.

³ Dougherty, T. F., and White, A., *Science*, 1943, **98**, 367.

⁴ White, A., personal communication.

⁵ Li, C. H., Simpson, M. E., and Evans, H. M., *Science*, 1942, **96**, 450.

⁶ Li, C. H., Simpson, M. E., and Evans, H. M., *J. Biol. Chem.*, 1942, **146**, 627.

⁷ Li, C. H., Simpson, M. E., and Evans, H. M., *Endocrin.*, 1940, **27**, 803.

TABLE I.
Effect of ACTH Injections on Leucocyte Picture in Normal Male Rats.

Exp.	No. of animals	Avg B.W. g	White cells per cmm	% Polymorphonuclear cells	% Mononuclear cells
ACTH treated	6	71	5800 (3850-7600) *	69 (63-79)	31 (21-37)
Control untreated	6	71	6875 (5400-8400)	24 (17-31)	76 (69-83)

* Figures in parentheses indicate ranges in the groups.

TABLE II.
Effect of Injection of ACTH on White Blood Cell Count in Normal Dogs.

Dog No.	Treatment (I.P. injection)	White cell/cmm		
		Initial	Peak	% Increase
1	ACTH 100 mg	12250	37075	
2	" 100 "	8950	29425	
3	" 100 "	10550	29400	
4	" 10 "	15500	36700	
	Avg			286
5	Boiled ICSH 100 mg	11375	19875	
6	" 50 "	9074	19800	
7	Lactogenic 100 "	15400	28400	
8	Inactive boiled residue 100 "	24000	47300	
	Avg			193

TABLE III.
Effect of Subcutaneous Injection of ACTH on Leucocyte Picture in the Dog.

Dog No.	Treatment	White cell count		Total lymphocyte count	
		Initial	After 6 hr	Initial	After 6 hr
1	ACTH 10 mg	11900	21025	2618	1051
2	" 10 "	12050	13025	964	390
3	" 10 "	9325	13625	1771	408
4	Lactogenic 10 mg	19500	22500	3120	3375
5	Boiled ICSH 10 "	12000	13250	2040	1987

24 hours after injection. The differential cell counts in the ACTH and the control treated animals did not differ significantly, there being an increase of polymorphonuclear leucocytes to approximately 90% in each group. The curves of the leucocyte counts were of the same character in ACTH and control treated animals, the only difference being apparent in the greater quantitative increase in leucocytes in the ACTH treated group.

Further experiments were carried out in dogs employing subcutaneous injections of purified ACTH and other anterior lobe preparations. In these experiments, 10 mg of the hormone preparation in isotonic saline were injected beneath the skin of the groin. Blood samples were taken from the femoral artery. The data obtained are presented in Table III.

The total lymphocyte counts in the ACTH treated animals returned to the original level 24 hours after injection of the hormone preparation. The lymphopenia here demonstrated on subcutaneous injection of ACTH in the dog confirms the findings of Dougherty and White⁴ for the same animal. It is probable that the marked polymorphonuclear leucocytosis evoked by intraperitoneal injection in the dog obscures the specific effect on the lymphocyte picture which is seen on subcutaneous injection in the absence of a clearcut leucocytosis.

The reported experiments on the effect of ACTH on the various tissues (thymus, lymph nodes, and white blood cells) suggest the employment of ACTH or adrenal cortical substances experimentally and clinically in the

treatment of conditions associated with overgrowth or neoplastic processes in the lymphoid tissues. Experiments in the transplantation of neoplastic tissues in rats either adrenalectomized or treated with ACTH or adrenal cortical substances by Murphy and Sturm⁸ give further support to the hypothesis that these tissues are under the hormonal influence of the adrenal cortex.

Summary. IP injection of adrenocortico-

⁸ Murphy, J. B., and Sturm, E., *Science*, 1943, **98**, 568; 1944, **99**, 303.

trophic hormone (ACTH) in the rat produces a transient leukopenia with decrease in number of lymphocytes and increase in the number of circulating neutrophils. Intraperitoneal injection of ACTH in the normal dog produces a marked neutrophilic leucocytosis which is qualitatively similar to but quantitatively greater than that produced by injection of other anterior lobe substances. Subcutaneous injection of ACTH in the dog produces a lymphopenia which is similar to that occurring in the rat after treatment with ACTH.

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Gravity Shock in Rabbits. III. Changes in Distribution of Phosphate and Chloride in Blood and Urine.

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The significant chemical changes occurring in the blood of rabbits suspended by their ears until unconsciousness occurs are: decreased blood pH, CO₂, venous O₂, increased blood lactate, pyruvate, plasma potassium, inorganic phosphate and non-protein nitrogen. Urine flow falls to zero or nearly so. The changes are considered to be the result of hypoxia caused by peripheral circulatory deficiency.^{1,2} To determine in part the source of the phosphate and whether or not a change in the chloride ratio occurs, studies have been made on the distribution of phosphorus and chloride in cells and plasma, and on the excretion of urinary phosphate in rabbits before, during, and recovering from gravity shock.

Methods. The animals used and the methods of producing shock, of withdrawing blood samples, of measuring pH, hematocrit and

chloride content have been previously described.² Inorganic and acid-soluble phosphorus were determined by the Fiske and Subarrow method as modified by Guest and Rapoport.³ Samples of blood were drawn just before suspension, just after unconsciousness, and from one to 2 hours after the animals had been returned to the horizontal position.

Results. The hematocrit during shock did not change consistently, but during recovery always decreased (Table I). Whether or not the rabbits had been fed preceding the experiment, the plasma and red cell inorganic phosphorus increased during shock, and was roughly correlated with the decrease in blood pH. The organic acid-soluble phosphorus in plasma usually increased during shock but in the cells it fluctuated around the control values. During recovery the plasma phosphorus compounds and the cell inorganic phosphorus tended to shift back towards control values, but the cell organic acid-soluble phosphorus increased significantly above control levels. Evidently the added inorganic phosphorus was not derived from food in the

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¹ Cole, W. H., Allison, J. B., and Boyden, A. A., *Proc. Soc. Exp. Biol. and Med.*, 1943, **54**, 215.

² Cole, W. H., Allison, J. B., Murray, T. J., Boyden, A. A., Anderson, J. A., and Leatham, J. H., *Am. J. Physiol.*, 1944, **141**, 165.

³ Guest, G. M., and Rapoport, S., *J. Biol. Chem.*, 1938, **124**, 599.