

phane to nicotinic acid as evidenced by the excretion of nicotinic acid and N'-Me by man. Rosen and Perlzweig¹² showed that indoleacetic acid had no effect on the excretion of N'-Me by rats receiving a basal diet alone or with tryptophane supplements. Others have also been unable to obtain depression of rat growth by inclusion of indoleacetic acid in the diet, although the addition of corn or protein low in tryptophane has retarded growth.¹⁰⁻¹³ The replacement of a portion of the wheat diet by corn products has been shown to decrease the excretion of N'-Me by man.^{7,14} This effect may be due to the lower tryptophane content of the corn as compared with the wheat or to the presence of an unidentified inhibitory agent in the corn.⁸

The increase in excretion of tryptophane compounds by man after the ingestion of indoleacetic acid may be due to the conversion of indoleacetic acid to a substance which has

tryptophane-like activity for *L. arabinosus*. It is also possible that indoleacetic acid may have some effect on tryptophane metabolism in man which is separate from the tryptophane-nicotinic acid relationship. In rats, indoleacetic acid cannot replace tryptophane as a growth stimulant, when added to a diet deficient in tryptophane and nicotinic acid.¹⁰⁻¹³

Summary. The addition of 25 to 200 mg of indoleacetic acid per day to a diet low in protein and nicotinic acid appears to have no significant effect upon the utilization of tryptophane and nicotinic acid by man as evidenced by urinary excretion studies.

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Changes in Circulating Eosinophils in Man Following Epinephrine, Insulin, and Surgical Operations.*

JOHN H. LARAGH AND THOMAS P. ALMY. (Introduced by Ephraim Shorr.)

From the Department of Medicine, New York Hospital, and the Cornell University Medical College, New York City.

Forsham and his associates¹ have reported that pituitary adrenocorticotrophic hormone (ACTH) produces a fall in circulating eosinophils which is dependent upon normal adrenal cortical function. Long and Fry² had previously demonstrated that epinephrine stimulates the adrenal cortex of the rat, and that this effect is mediated by the anterior pituitary. For these reasons we have studied the effects upon the circulating eosinophils of

epinephrine, and later of insulin and of surgical operations. Studies have been made upon healthy persons, patients with adrenal and pituitary insufficiency, and patients with "diseases of adaptation"³ such as essential hypertension and nonspecific colitis.

While this study was in progress, eosinopenia after intravenous epinephrine and insulin was reported by Godlowski,⁴ and Thorn and his associates⁵ reported that intravenous epinephrine reduced the eosinophil count in

* Aided by a generous gift from Mr. John L. Given.

¹ Forsham, P. H., Thorn, G. W., Prunty, F. T. G., and Hills, A. G., *J. Clin. Endocrinol.*, 1948, **8**, 15.

² Long, C. N. H., and Fry, E. G., *Proc. Soc. Exp. Biol. and Med.*, 1945, **59**, 67.

³ Selye, H., *J. Clin. Endocrinol.*, 1946, **6**, 117.

⁴ Godlowski, Z. Z., *Brit. Med. J.*, 1948, **1**, 46.

⁵ Recant, L., Forsham, P. H., and Thorn, G. W. Read at the thirtieth meeting of the Association for the Study of Internal Secretions, June 18, 1948.

Eosinophil Counts following Epinephrin, Insulin, Surgery

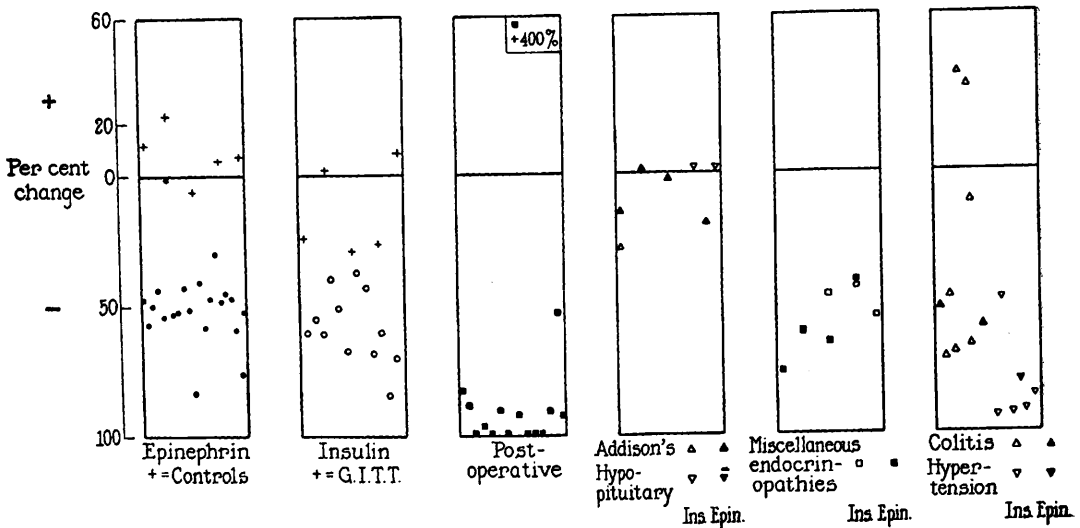


FIG. 1.

persons with normal adrenals. Gershberg and Long⁶ demonstrated that insulin stimulated the adrenal cortex of animals with intact pituitaries.

Method. The eosinophils of heparinized venous blood were enumerated in the Levy double depth counting chamber, using a modification of the method of Dunger.⁷

Results (see Figure). The normal range of eosinophil count was found to be 100-300 per cu mm.

Epinephrine. Epinephrine HCl, 0.5 cc of 1:1000 solution, was administered subcutaneously to 21 healthy subjects. In 20 of these subjects the eosinophil count dropped by an average of 56% in 2½ - 3 hours. Five subjects given 0.5 cc saline showed no significant drop in eosinophils.

Insulin. Regular insulin 0.1 unit/kg was given intravenously to 11 healthy subjects and to one patient with moderately advanced pulmonary tuberculosis who was on prolonged bed rest. In all these subjects the eosinophil count fell, the average change being minus 57.5%, four hours after injection. In all cases a blood sugar of 60 mg% or below was

attained. Five subjects were given standard glucose-insulin tolerance tests as controls. Two of these patients showed no significant change; the other 3 had slight drops (22 to 28%) but in these 3 we were unable to obtain neutral sugar curves.

Addison's Disease and Pituitary Insufficiency. In 4 cases of Addison's Disease and 2 cases of pituitary insufficiency the typical fall in eosinophil count after epinephrine and insulin did not develop. The largest change observed was a 28% fall, associated with sustained hypoglycemia in a patient with Addison's Disease.

Miscellaneous Endocrinopathies. In this group are 2 acromegalics, 2 cases of pituitary tumor, 1 of Cushing's syndrome, and 1 of possible Cushing's. This group all responded normally with an average drop of 55.2% after epinephrine or insulin.

Hypertension. Six patients with essential hypertension have been studied. Four showed an exaggerated response to insulin with an average drop in eosinophils of 90.4%. Blood sugar curves were similar to those observed in the healthy group. A fifth mild hypertensive dropped 79% after epinephrine and the sixth patient showed a 48% drop after insulin.

Colitis. Of 3 patients with severe ulcer-

⁶ Gershberg, H., and Long, C. N. H., *ibid.*

⁷ Dunger, A., *Munchen. Med. Wchnschr.*, 1910, 57, 1942.

tive colitis given insulin, 2 showed a rise in eosinophils (32%, 37%) and a third only a 12% drop. Five patients with milder ulcerative colitis showed a normal response.

Surgical Operations. Fifteen patients have been followed through the stress of major surgery. Following operation, 14 of these patients showed profound drops in their eosinophil counts, 6 falling to zero. In general the degree of fall varied directly with the magnitude of the operation. The peak of response occurred most commonly 3-8 hours after the beginning of the operation. The fifteenth patient, one with severe ulcerative colitis, showed a marked and progressive eosinophilia following an ileostomy.

Discussion. Epinephrine and insulin appear to exert similar effects on the circulating eosinophils of man, and our results suggest that this effect is mediated through the pituitary and adrenal cortex. The failure of response in a small number of cases of Addison's Disease and pituitary insufficiency leads us to anticipate that the eosinophil changes following epinephrine and insulin may be useful in the diagnosis of these conditions.

Browne and his associates⁸ have measured

⁸ Browne, J. S. L., Conference on Bone and Wound Healing, Josiah Macy, Jr., Foundation, December 11-12, 1942, pp. 45-47.

the changes in excretion of glycogenic corticoids and other indices of adrenal function following major surgery, and have interpreted these changes as part of the process of adaptation to non-specific stress. The occurrence of eosinopenia following operations may be construed as further evidence of the role of the adrenal cortex in the "alarm reaction" in man.

In view of the postulated role of the adrenal in the genesis of "essential" hypertension, the exaggerated eosinophil response in patients with this disorder is being studied further. The absence of an eosinophil response in three patients with severe chronic ulcerative colitis suggests that adrenal insufficiency may occur in such patients. This possibility is being investigated.

Summary. Significant eosinopenia has been observed following injection of epinephrine and of insulin. This change was exaggerated in patients with essential hypertension, and diminished or absent in patients with adrenal or pituitary insufficiency. Marked eosinopenia has been found after surgical operations.

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Electrophoretic Patterns After Dicumarol Medication.

SHEPARD SHAPIRO AND DAN H. MOORE.

From the Goldwater Memorial Hospital, the Department of Medicine, N. Y. University, College of Medicine, and the Electrophoresis Laboratory, College of Physicians and Surgeons, New York City.

Dicumarol induces prothrombinopenia by inhibiting the production of prothrombin, presumably in the liver. At dosage levels used for therapeutic purposes, its action is reversible and can be counteracted by vitamin K.¹⁻³ In order to determine whether or not protein components other than prothrombin were measurably altered by the drug, comparisons by means of electrophoresis of

human plasma before and after Dicumarol medication were made.

¹ Campbell, H. A., Smith, W. K., Roberts, W. L., and Link, K. P., *J. Biol. Chem.*, 1941, **138**, 1.

² Shapiro, S., Redish, M. H., and Campbell, H. A., *Proc. Soc. Exp. Biol. and Med.*, 1943, **52**, 12.

³ Cromer, H. E., Jr., and Barker, N. W., *Proc. Staff Meet. Mayo Clin.*, May, 1944, **19**, 217.