

the vasodepressor mechanism is suggested as a possible mode of action of these compounds on the reversal of the vasodepressor response

and the potentiation of the vasopressor response to epinephrine and arterenol.

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Response of Circulating Eosinophils to Nor-Epinephrine, Epinephrine and Emotional Stress in Humans. (17884)

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The diminution of the number of circulating eosinophils after subcutaneous injection of epinephrine is believed to be due to an increased secretion of adreno-cortical glucocorticoids, elicited by a discharge into the blood of adrenocorticotrophic hormone(1,2) which, in turn, constitutes a typical reaction to injected or secreted epinephrine(3,4). On the other hand, it is becoming increasingly apparent that l-nor-epinephrine plays a prominent role in the manifestations of sympathetic stimulation as the specific chemical neuro-transmitter of the sympathetic system (5) and as a secretory by-product of the adrenal medulla(6,7). It seemed of interest therefore to investigate the following questions: (a) Does nor-epinephrine exert an analogous effect upon the pituitary-adreno-cortical system as its methylated homologue epinephrine? (b) Are the neurovegetative phenomena of emotional stress attributable mainly to discharges of epinephrine from the adrenal medulla or to neuro-secretory dis-

charges of nor-epinephrine?

Methods. Twelve patients with various disorders but not acutely ill, were tested to compare the response of the circulating eosinophils to equal amounts (by weight) of subcutaneously injected natural l-epinephrine* and synthetic l-nor-epinephrine† (0.25 mg of each). Blood samples from the finger tip were taken early in the morning for the initial eosinophil counts and the injections were administered immediately thereafter. Four hours later the eosinophil counts were repeated. No nourishment was taken preceding and during the tests. In 24 healthy medical students in the fasting state, finger tip blood samples for eosinophil counts were taken in the morning, 5 to 20 minutes before the students were to begin their mid-year examinations. Blood pressure and pulse rate were also recorded (after only a few minutes rest in sitting position). Several weeks later when no examinations were in sight the same students were again tested in the same manner. In all instances the direct eosinophil counts were carried out according to the method employed by Forsham *et al.*(2). However, the staining method of Randolph(9), as modified by Henneman *et al.*(10), was used in-

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* Adrenaline hydrochloride Parke & Davis was used, which contains besides l-epinephrine an estimated 10-19% admixture of l-nor-epinephrine(8).

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† We are indebted to Dr. M. L. Tainter of Sterling-Winthrop Research Laboratories for l-arterenol bitartrate (l-nor-epinephrine).

stead of the eosin acetone stain. The eosinophils were counted between 20 and 60 minutes after dilution of the blood samples.

Results. There was a striking difference between the effects of l-epinephrine and l-nor-epinephrine upon the eosinophil count in that the average decrease due to epinephrine was 61% (range: 41% - 84%) while analogous doses of nor-epinephrine caused an average fall of only 9% (range: 0% - 24%).

The average eosinophil count of the 24 students during a non-stress period was 128 per mm³. Under emotional stress before examination it was 66 per mm³. Thus, there was an average difference of -48%. Only in one case were the 2 counts identical. The greatest individual difference was -89%.

The average systolic blood pressure and heart rate were higher in the state of tension while the average diastolic pressure remained unchanged: 137/82 mm Hg and 96 beats as compared with 128/81 mm Hg and 82 beats.

Discussion. The relatively weak eosinophil-reducing effect of l-nor-epinephrine, in contrast to that of l-epinephrine, suggests a considerably weaker stimulating action of the former on the ACTH and gluco-steroid secretion. This assumption seems to be supported by recent animal experimentation: The doses of nor-epinephrine which were required to reduce the ascorbic acid content of the rat adrenal (criterion of gluco-corticoid secretion) (4) were found to be several times larger than the doses of epinephrine which sufficed to elicit an equal ascorbic acid depletion of the rat adrenal(11,12). As far as the marked eosinophil-reducing influence of emotional stress, demonstrated by the pres-

ent data, is concerned, this observation makes it probable that epinephrine discharges from the adrenal medulla are largely, if not entirely, responsible for the accompanying neurovegetative phenomena. This is also suggested by the fact that the emotional cardiovascular reactions follow the pattern of epinephrine action (elevation of systolic pressure; little, if any, participation of the diastolic pressure; cardiac acceleration and palpitations), while nor-epinephrine injection causes a marked rise of both systolic and diastolic pressures with bradycardia and only a minimum of subjective sensations(13,14, 15,16).

A simultaneous discharge of some nor-epinephrine from both the adrenal medulla and post-ganglionic sympathetic fibres during emotional stress cannot be excluded but the present observations do not supply any positive evidence for it.

Summary. In human subjects the effectiveness of l-nor-epinephrine in reducing the circulating eosinophils was found to be only about one-sixth of that of epinephrine.

A marked diminution of the eosinophil count was observed in students in a state of emotional tension. This and the pattern of the accompanying cardiovascular reactions suggest that the neurovegetative manifestations under emotional stress are essentially caused by a discharge of epinephrine from the adrenal medulla. However, a certain degree of participation of neuro-secretory nor-epinephrine discharges cannot be entirely excluded.

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