

Effect of Epinephrine on Blood Count and on Hematocrit Value.*

S. P. LUCIA, P. M. AGGELER, G. D. HUSSER AND M. E. LEONARD.
From the Division of Medicine, University of California Medical School, San Francisco.

The subcutaneous injection of epinephrine produces certain changes in the blood count.¹⁻⁴ These changes are not dependent upon the presence of the spleen.⁵ The leukocytosis that follows injection of epinephrine has been attributed to splenic contraction, hemoconcentration, stimulation of the bone-marrow, redistribution of formed elements of the blood, expulsion of leukocytes from lymph-nodes, and stimulation of the vegetative nervous system. Recently it has been reported that injection of epinephrine produces a rise in the serum potassium⁶⁻⁸ and that the action of potassium is responsible for the reactions ascribed to epinephrine.⁹

Human subjects were injected into the deltoid region with single doses of one cc. of a 1:1000 solution of epinephrine hydrochloride. The usual reactions of anxiety, palpitation, hyperidrosis, tremor and elevated blood-pressure occurred. Some of the patients who had diseases of the blood-forming tissues complained of soreness over the spleen and tenderness over the long bones.

In the first experiment all blood-counts were made from capillary blood (U. S. Bureau of Standards equipment). Differential blood-counts were made on cover-slip preparations stained by the Jenner-Giemsa method. Hemoglobin determinations, and erythrocyte, leukocyte, differential, and platelet counts were made before injection. Leukocyte and differential counts were made also 10, 20, 40, 60, and 100 minutes after injection.

In the second experiment the complete studies enumerated above, together with calculations of the mean corpuscular volume, were made on samples of venous blood withdrawn before injection and at

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the five stipulated intervals after injections. The Wintrobe tube was used for hematocrit determinations, and each sample was spun to constant volume at about 2500 revolutions per minute for 3 or more hours.

Results. Experiment I: In all but 4 of 68 patients studied, the majority of whom had diseases of the blood-forming tissues, the injection of epinephrine was followed by a definite leukocytosis. The blood of 8 patients who had undergone splenectomy showed a leukocytic response similar to that of patients whose spleens had not been removed. In 56 cases, the increase in number of lymphocytes was earlier and relatively greater than that of the other cellular elements; whereas the percentage of polymorphonuclear neutrophils decreased immediately after injection, and then gradually increased as the lymphocytes returned to normal values. In the remaining 12 cases there was no considerable change in the percentage of lymphocytes. Except in 2 cases (one of erythroblastic anemia and one of hemolytic icterus), immature cell-forms did not appear in the circulation in numbers sufficient to indicate stimulation of the bone-marrow.

Experiment II: In 10 patients studied, the injection of epinephrine was followed by an increase in the erythrocyte-counts. The maximum values were noted at 20 and 40 minutes after injection, following which there was a gradual decline to the pre-injection levels by the end of 100 minutes. The content of hemoglobin showed corresponding fluctuations. In all cases a leukocytosis occurred. The maximum leukocyte-count was noted at 10 minutes in 2 cases, at 20 minutes in 5 cases, and at 40 minutes in 3 cases. In all cases the percentage of lymphocytes first increased and then gradually decreased; whereas the percentage of polymorphonuclear neutrophils decreased immediately after injection and then gradually increased as the lymphocytes returned to normal values. In all instances, the volume of packed cells increased after the injection of epinephrine and gradually returned to normal levels. The maximum hematocrit value was found at 10 minutes in 4 cases, at 20 minutes in 4 cases, and at 40 minutes in 2 cases. In 5 cases the mean corpuscular volume was found to be increased, the maximum values occurring 10 minutes after injection (maximum variation 22 cubic micra); in 3 cases the volume was decreased and gradually returned to the pre-injection level (maximum variation 28 cubic micra); and in 2 cases, the volume fluctuated within wide limits (maximum variation 34 cubic micra). Tests for fragility of erythrocytes failed to show any alterations following the injection of epinephrine.

In 5 cases, the addition of epinephrine to samples of blood removed before injection was without effect.

Summary. Injections of epinephrine were found to produce the following reactions in patients with and without diseases of the blood-forming tissues, from whom samples of capillary or venous blood were withdrawn: 1. Tenderness over the spleen and long bones occurred in some of the patients who had diseases of the blood-forming tissues. 2. There was an increase in the erythrocyte and leukocyte counts regardless of whether or not the spleen was present. 3. The lymphocytes were the first blood-cells to increase in numbers following injection. 4. Immature cell-forms did not appear in numbers sufficient to indicate stimulation of the bone-marrow. 5. The hematocrit values were increased. 6. The mean corpuscular volume varied too greatly to be of significance. (The calculation of the mean corpuscular volume is at best only an approximation.) 7. The fragility of erythrocytes was not altered. 8. When added *in vitro* to whole blood, epinephrine did not produce significant changes. The results of these experiments are compatible with the hypothesis that the leukocytosis following injection of epinephrine is due to hemo-concentration.

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Local Irritation from Sodium Bisulfite as Preservative in Epinephrine Solutions.*

M. L. TAINTER, A. H. THRONDSOHN AND A. J. LEHMAN.

From the Departments of Pharmacology, Stanford University School of Medicine, and College of Physicians and Surgeons, School of Dentistry, San Francisco.

A large number of the epinephrine preparations on the market contain sodium bisulfite in a concentration of about 0.1%, to prevent the oxidation of the alkaloid. As far as we can determine, no studies have been made on the possible irritant properties of sodium bisulfite, so that its suitability for a therapeutic product does not seem to have been adequately established. We have, therefore, tested the material, to see whether irritant phenomena could be produced by this chemical, either in pure solution, or in the media in which it is used clinically in local anesthesia.

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