tion and purification of precipitates is almost totally neglected.

The section on systematic analysis includes general information which should be useful for reference purposes.

There are a number of aids for the student and the instructor: question and problem sets following each chapter; a plan of the course; and an appendix containing sample report forms, a division on the literature of analytical chemistry, a division on reagents and supplies, density tables, gravimetric factors and a table of five-place logarithms.

The experiments are well chosen and conveniently arranged, if a bit old-fashioned, but the book suffers from an attempt to cover too much ground in too short a space with a resultant dearth of specific information. However, the material included could serve as good basis for a course in quantitative analysis if properly expanded in the accompanying lectures.

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## THE CHEMICAL FORMULARY

*The Chemical Formulary.* Vol. VI. By H. BENNETT, editor-in-chief. xx + 636 pp. Brooklyn, N. Y.: Chemical Publishing Company, Inc. 1943. $6.00.

THIS is the sixth volume of the series, and as in previous volumes the editor-in-chief has had the assistance of an editorial board of about fifty specialists in industrial and educational organizations. A footnote to the preface states that all the formulae in volumes I to VI are different except for a few typical cases used in the introduction to illustrate directions and advice for new users of the volumes.

The fields covered in the present volume include Adhesives, Beverages, Emulsions, Inks, Paints and Varnishes, Paper, Pyrotechnics and Explosives, Rubber, Plastics, Detergents, Textiles, etc. A timely section is included on special formulae of military interest.

Another section which may be of value to many users is devoted to substitutes for scarce or priority materials. A perusal of this section would seem to indicate that many of the suggested substitutes would be far from universally adaptable but might be useful for certain specific applications.

A directory of sources of chemicals and supplies is included. This will prove of value to users of the volume, since many of the substances mentioned in formulae throughout the book are trade-marked or copyrighted "trade names" and could not be secured on the open market either by reason of their compound nature or secret composition. The editor feels justified in including such substances, since without them many ideas and processes offered in formulae of specialty producers would have been automatically eliminated.

Tables of weights and measures, a list of foreign sources of chemicals and an index of some 2,400 entries complete the present volume. Previous volumes have been widely reviewed in technical and trade publications such as *American Dyestuffs Reporter, Electrochemical Society Bulletin, Modern Plastics, Rubber Age,* etc., and have received most generous and favorable comment. The present volume is a worthy addition to the series and will doubtless find wide acceptance among chemists and technologists throughout the industry.

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# SPECIAL ARTICLES

## INFLUENCE OF ADRENAL CORTICAL SECRETION ON BLOOD ELEMENTS[1]

THE marked decrease of lymphoid tissue produced by augmented adrenal cortical secretion[2] has led to an examination of the changes in blood elements resulting from adrenal cortical stimulation. The availability of purified pituitary adrenotropic hormone,[3] the normal physiological regulator of adrenal cortical activity, makes possible the study of fundamental phenomena resulting from adrenal cortical secretion. The establishment of these data should be of significance in the elucidation of changes following stimulation of the adrenal cortex by a variety of agents.

It is the purpose of this communication to indicate the striking alterations in blood elements which result in normal, approximately fifty-day old, mice of both sexes (CBA strain, Strong) within a few hours following a single subcutaneous injection of pituitary adrenotropic hormone (1.0 mg in 0.5 ml solution). Blood analyses have been conducted at intervals after hormone injection, using groups of mice at each time interval, rather than successive determinations on the same animals. The blood picture observed is characterized by the following: (a) decrease in total leucocyte count, (b) decrease in absolute number of lymphocytes, and (c) increase in absolute number of

[1] This investigation has been aided by grants from the International Cancer Research Foundation, the Fluid Research Fund, Yale University School of Medicine and the Committee on Therapeutic Research, Council on Pharmacy and Chemistry, American Medical Association.

[2] T. F. Dougherty and A. White, *Proc. Soc. Exp. Biol. Med.*, 53: 132, 1943.

[3] G. Sayers, A. White and C. N. H. Long, *Proc. Soc. Exp. Biol. Med.*, 52: 199, 1943.

polymorphonuclear cells. These alterations in the leucocyte elements are evident three hours following hormone injection, and the maximum effect, which is characterized by an extreme lymphopenia, is observed at nine hours after injection. Shortly thereafter the leucocyte picture tends to return to normal. These changes are depicted in Fig. 1.

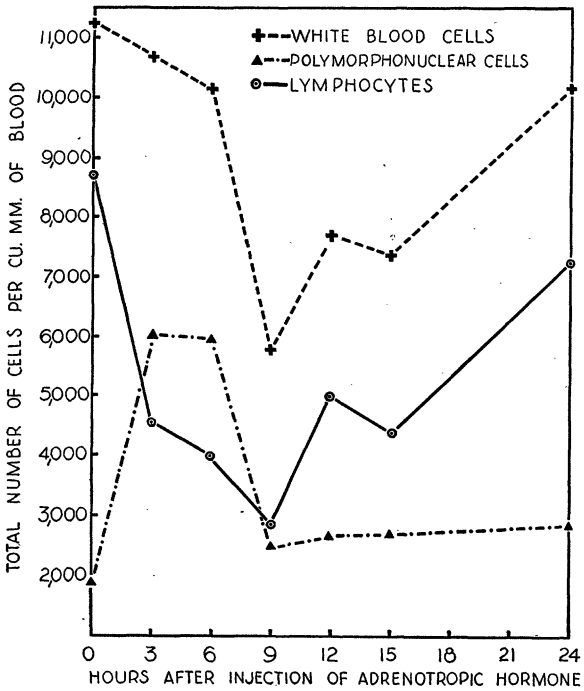


FIG. 1. Alterations produced in the total leucocyte, lymphocyte and polymorphonuclear blood counts of normal mice receiving, at zero time, a single, subcutaneous injection of 1.0 mg of pituitary adrenotropic hormone. The points on each curve at 3, 6, 9, 12, 15 and 24 hours after hormone injection are, respectively, the averages of data for groups of 5, 5, 7, 6, 7 and 5 animals. A total of 35 animals were employed.

An initial increase in hemoglobin and red blood cell count was generally observed within three to six hours after a single injection of adrenotropic hormone. This effect, however, did not persist in other animals injected daily with the hormone. The increase in hemoglobin concentration was not due to hemoconcentration.

In order to determine whether the change in leucocyte picture might be due to a non-specific protein effect, mice of the same age and strain were injected with 2 mg of prolactin[4] and blood determinations made on animals sacrificed at 3-, 6- and 9-hour intervals following the hormone administration. Other mice received subcutaneously 2 mg of serum gamma globulin (human) or one unit of posterior pituitary pressor principle (Parke-Davis). Injection of prolactin or pitressin produced an initial increase of polymorphonuclears, but no significant decrease in total leucocytes or lymphocytes. In contrast to the adrenotropic hormone injected animals which showed the maximum alteration in blood picture (lymphopenia) nine hours after hormone injection, mice given prolactin or pitressin had a normal leucocyte count at this time. Serum globulin injection produced no alteration in blood leucocytes. This would suggest that the results with prolactin are not attributable to a non-specific protein effect, but are likely the result of contamination of the prolactin preparation with posterior lobe principle.[5] The latter may initially stimulate the adrenal cortex.

Evidence that the effect of adrenotropic hormone on the leucocyte picture is mediated through the adrenal cortex is seen from the following summary of other experimental results which have been obtained:

(1) The injection of adrenotropic hormone, prolactin or pitressin into adrenalectomized mice does not produce a decrease in total leucocyte or lymphocyte counts.

(2) The injection of 0.5 ml of adrenal cortical extract (Wilson) in normal and in adrenalectomized mice produces a fall in total leucocytes, an absolute lymphopenia and an absolute polymorphonuclear leucocytosis. The blood changes produced by adrenal cortical extract administration in both normal and adrenalectomized mice are identical in degree with those occurring after adrenotropic hormone injection (Fig. 1). However, the time relationships are somewhat different in that the maximum leucocyte changes in mice given cortical extract occur at an earlier time.

Changes in the blood elements, identical with those presented in Fig. 1, have been observed in 250 to 300 gram male rats (Sprague-Dawley strain) given single injections of either 5 mg of adrenotropic hormone or 5 ml of adrenal cortical extract (Upjohn).[6]

A group of 25 mice were given daily injections of 1 mg of adrenotropic hormone for 15 days and blood determinations made on groups of 5 animals at 3-day intervals. Throughout the entire injection period, the animals did not show consistent changes in total leucocyte count, but exhibited an absolute lymphopenia and an absolute polymorphonuclear leucocytosis. Similar groups of mice injected chronically with 2 mg of prolactin each day showed a normal blood picture throughout the experimental period.

[4] A. White, R. W. Bonsnes and C. N. H. Long, *Jour. Biol. Chem.*, 143: 447, 1942.

[5] Assay of the prolactin preparation used showed it to have a pressor activity (cat) equivalent to 0.6 unit pitressin (Parke-Davis) per mg.

[6] The experiments in rats have been conducted in collaboration with Mr. C. U. Lowe.

The day-to-day constancy of the increase in polymorphonuclear leucocytes and the decrease in lymphocytes in animals injected daily with adrenotropic hormore and the lack of any leucocyte changes in prolactin treated animals emphasize the significance of the adrenal cortex in the phenomena which are being reported.

The changes which have been observed in the leucocyte picture following adrenotropic hormone injection are essentially those which have been described for a variety of circumstances, some of which may now be directly attributed to adrenal cortical stimulation. For example, inanition stimulates adrenal cortical activity and produces a similar leucocyte picture.[7] It is not unlikely that other agents and experimental procedures which affect the adrenal cortex, and lymphoid tissue, are accompanied by these leucocyte changes. These possibilities are being subjected to experimental study.

The experiments summarized here will be published in detail elsewhere.

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## THE NATURAL OCCURRENCE OF RIBOFLAVIN DEFICIENCY IN THE EYES OF DOGS[1]

OBSERVATION of malnourished persons for thirteen years has convinced me that the natural development of dietary deficiency diseases is slow; the onset insidious and difficult to recognize. Long before the nutritive failure can be diagnosed as pellagra, beriberi, scurvy, riboflavin deficiency or some one clear-cut syndrome, the afflicted persons have had months or years of ill health. Often they are unbelievably weak, listless and able to do little if any work. In the carefully selected case, the rapid improvement following intensive and persistent nutritive therapy leaves no doubt that the tissues function at a higher level soon after the missing substances are provided in sufficient amounts. Although the whole matter is very complex, comprehensive study over a period of several years has given us some valuable information. Since members of a family living together tend to eat a similar diet, we have adopted the policy of studying the entire family. That is to say, whenever a diagnosis of deficiency disease is made, we extend our studies to include the family. All members of the family are asked to report to the clinic for observation. Dietary surveys on the patient and on each member of his family are made by frequently visiting the homes. During such visits, we have observed that the family pets often appear emaciated and weak. Realizing that these animals usually subsist on scraps from the family table, it was natural for us to think that they, too, might have nutritional deficiencies. Examination of the dogs showed that black-tongue was not uncommon. (This spontaneous canine black-tongue responds as quickly to nicotinic acid as does pellagra in human beings.) Still more recently we have observed eye symptoms in dogs which appear similar to the ocular lesions of riboflavin deficiency in persons. These lesions respond as dramatically to riboflavin therapy as do those in human beings.

This communication is concerned primarily with such lesions in the eyes of four dogs belonging to families on which we were making laboratory and clinical studies. As these findings give an idea of the far-reaching effect of inadequate nutrition they seem worthy of separate publication at this time.

The dogs were emaciated, weak, sluggish, apathetic and held their heads much lower than the rest of their bodies. They refused food and all efforts to coax them to eat were without avail. Each dog had diarrhea characterized by frequently watery, foul-smelling stools. Saliva drooled continuously from their mouths. Examination of the mouth revealed the oral mucous membrane lesions characteristic of black-tongue.[2] While examining these animals lacrimation was observed. Even the light from a small flashlight in their eyes enlisted photophobia. In general the eyes appeared similar to those of persons with riboflavin deficiency which I have described,[3,4] and this suggested to me that these dogs had not only black-tongue, but riboflavin deficiency as well. A careful examination of their eyes showed pronounced injection of the sclerae and conjunctiva of both eyes. The vessels were unusually dilated and tortuous. There was a suggestion of rotary nystagmus. The animals did not keep their eyes still enough to carry out satisfactory slit lamp examinations. However, clinically the process appears similar to that in human beings, although in each of these dogs it was more extensive than I usually have seen in persons.

[7] C. F. Shukers and P. L. Day, *Jour. Nutrition*, 25: 511, 1943.

[8] Fellow of the International Cancer Research Foundation.

[1] University of Cincinnati Studies in Nutrition at the Hillman Hospital, Birmingham, Alabama. From the Department of Internal Medicine, University of Cincinnati. The expenses of this study were defrayed by funds given by the Nutrition Foundation for the study of earlier methods of diagnosing deficiency states and by the Abbott Laboratories.

[2] Garfield G. Duncan, "Diseases of Metabolism," 489 pp. Philadelphia: W. B. Saunders Company. 1942.

[3] Tom D. Spies, William B. Bean and William F. Ashe, *Annals of Int. Med.*, 12: 1830–1844, May, 1939.

[4] H. D. Kruse, V. P. Sydenstricker, W. H. Sebrell and H. M. Cleckley, *Public Health Reports*, 55: 157–169, January 26, 1940.