ABSTRACTS

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ABSTRACTERS

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ERYTHROCYTE MORPHOLOGY and PHYSIOLOGY


This is a report of a very detailed study based on the extensive experience of the author, and incorporating a comprehensive review of the literature, concerning the cyto logic aspects of the erythrocytic series during its development in pernicious anemia during relapse and in various stages of remission. The observations recorded have been made with great care and the conclusions reached after careful thought; the impression is left that the conclusions must remain a highly individualized matter. An extract of the author's own summary follows:

"The primitive erythroblasts (erythrogones, proerythroblasts) of pernicious anemia are all of the same general type but vary in size, in basophilia of cytoplasm, and in size and character of nucleoli. Differences between them and the corresponding cells of normoblastic hyperplasia are no greater than between individual proerythroblasts of pernicious anemia. The most immature erythroblasts from both types of marrow can, therefore, be assumed to be identical. Both are derived from reticulum without going through a myeloblast stage, as in normal hemopoiesis."—T.R.T.


In healthy people the mean blood pyruvic acid levels were 0.76 ± 0.18 mg. per 100 ml. of blood in the fasting state and 0.92 ± 0.17 and 0.94 ± 0.20 mg. per 100 ml. at 60 and 90 mins. after a loading dose of glucose. In three patients with subacute combined degeneration, the levels before vitamin B12 therapy were, respectively, 0.55, 0.75, and 0.83 mg. per 100 ml. However, 90 minutes after glucose they were, respectively, 1.70, 2.60, and 1.77 mg. per 100 ml. Vitamin B12 therapy resulted in a return towards normal figures. Estimation of the blood α-ketoglutaric acid level showed that this was not raised.—R.H.G.


Many of the substances with activity similar to that of vitamin B12 are probably not pure substances. In this paper are discussed the possible causes of activity of pseudo-vitamins B12, and B12b, factor A, vitamin B12m, B12t factor WR, factor B and factor C.
The vitamin B₁₂ activity for micro-organisms of extracts of gut contents and feces is contributed in varying proportions by five substances, viz. factors A, B, and C, pseudovitamin B₁₂, and vitamin B₁₂ itself. In natural materials these compounds may exist in both free and combined forms.

As these vitamin B₁₂ active compounds are formed by microbial synthesis in the rumen or large intestine or both, it is probable that the relative amounts of each that appear in gut contents depend on the composition of the microbial flora. This will vary with the nature of the diet.—R.H.G.


There are several compounds related to vitamin B₁₂ but not in the cobalamin series. Using paper chromatography, factor A, vitamin B₁₂m and pseudo-vitamins B₁₂ and B₁₂b could not be separated with the solvents usually employed. The ionophoresis of these substances was tested. Results with veronal/acetate buffer were not helpful, but where 0.5 N acetic acid was used, with 0.01 per cent potassium cyanide, five substances could be distinguished. These, with their mobilities expressed as cm² V⁻¹ sec⁻¹ were: factor A (vitamin B₁₂m), 3.9 × 10⁻⁴; factor B, 5.0 × 10⁻⁴; factor C, -1.4 × 10⁻⁴; pseudo-vitamin B₁₂, 1.5 × 10⁻⁴; vitamin B₁₂, zero mobility.

The growth activities of these and other factors for micro-organisms were compared, B. coli (tube assay), B. coli (plate assay), and L. leichmannii being used. Factor A and vitamin B₁₂m have similar properties, as have pseudo-vitamins B₁₂ and B₁₂b. The two groups differ markedly in microbiologic activities and there are further differences with factors B, WR, and C. Factor WR is probably a mixture that includes inhibitors for the growth of B. coli.—R.H.G.


The Jews of Yemen have lived in isolation for nearly two thousand years. Among one hundred and four unrelated Yemenite Jews there was no evidence of a sickle cell trait.

Their Rh chromosome cDe had a frequency of 1.4 per cent, compared with about 2 per cent in Europe and more than 50 per cent in negroes. Their chromosome cDe had the high frequency of 20 per cent: only in the Touaregs of Agades (North Africa) has a comparable frequency been reported.—R.H.G.


The author describes nine of his patients with gout, splenomegaly, and immature cells in the circulating blood; five of these had polycythemia at some stage in their illness. Four had gout before any symptoms or signs of disorder of the blood-forming system were found. Eight of the patients had autopsies performed, but the final diagnoses are not clear from the data given.—R.H.G.

ANEMIA

ABSTRACTS

Hemolytic anemia is defined here as "an anemia that results when the average survival time of the red cells is so short that the maximum erythropoietic effort of an uninhibited bone marrow is unable to maintain a normal volume of red cells in the circulation."

Two patients with hereditary hemolytic anemia of moderate severity were studied by means of the Ashby method and related technics in order to ascertain the limits of erythropoietic capacity under stress of chronic hemolytic disease. It was found that the marrow reaches its limit to compensate when the average red cell survival time is reduced to about fifteen to twenty days. At this point the marrow is able to produce 6 to 8 times the normal mount of red cells and hemoglobin or, in terms of hemoglobin production, 0.60 to 0.65 Gm. per Kg. of body weight per day compared to the normal estimate of 0.09 Gm. per Kg. per day. Anemia was present in the two patients studied because the average life span of their red cells was reduced to about twelve days or one tenth of normal. Figures were given to indicate that hemoglobin output may be less in other types of chronic hemolytic anemia.

The discrepancy between the rate of hemolysis and excretion of urobilinogen is discussed in some detail. The finding of a cyclic variation in urobilinogen excretion in one patient, in whom long periods of determinations were carried out, is of interest and for the present unexplained.—H.W.B.


A male patient aged 63 had hemolytic anemia with a direct positive Coombs' test and autohemagglutinins most active in the cold. There was no response to 25 mg. of ACTH intramuscularly every six hours for three days followed by 40 mg. every six hours for two days, but a temporary response followed 1.1 Gm. of cortisone given over a week. Two further short courses of cortisone gave temporary benefit. Splenectomy gave more lasting improvement, despite wound rupture and arterial hemorrhage from the wound. These complications may have been due to the cortisone.—R.H.G.

LEUKOCYTES and LEUKOCYTIC DISEASES


Interest in B-glucuronidase has been aroused because of the fact that its activity is high in primary malignant neoplasms of the breast, uterus, ovary, stomach, and colon, and in their metastases to other organs and to the lymph nodes. Other workers have found a high percentage of activity in the leukocytes and negligible activity in the platelets and red cells; consistent variations from the normal were found in the leukocytes from patients with chronic lymphocytic leukemia and in chronic and acute myelocytic leukemia.

This report is concerned with a study of the B-glucuronidase activity in the leukocytes of normal subjects and patients with diseases or abnormalities of the leukocytes. The results of the present study indicate that the lymphocytes contain less activity than the neutrophils and that the pathologic lymphocyte of leukemia is metabolically different from the normal lymphocyte.

No correlation of B-glucuronidase activity to prognosis in chronic myelocytic leukemia could be established. The eosinophil appeared to have at least a normal, or slightly high, content of B-glucuronidase. In patients with various diseases receiving cortisone in large doses, the activity was not outside the normal range.

At present these data are descriptive and cannot yet be subjected to functional interpretation.—T.R.T.

CHANGES IN WHITE BLOOD CELL COUNTS AFTER ADMINISTRATION OF CORTISONE ACETATE TO HEALTHY AMBULATORY INDIVIDUALS. H. J. Kowalski, W. E. Reynolds, and D. D.

The interpretation of previously existing data led the authors to conclude that: (a) intramuscular injection of cortisone acetate has usually been followed by an increase in the neutrophil count, and, inconstantly, by a decrease in the lymphocyte and eosinophil counts; (b) cortisone acetate probably exerts its effect on white blood cell counts less promptly after intramuscular than after oral or intravenous administration.

In order to confirm these observations, single doses of oral cortisone acetate (50 mg.), intramuscular cortisone acetate (50 mg. in 2 ml.) and aqueous vehicle (2 ml.), were each given on successive occasions to eight healthy ambulatory medical students at intervals of at least forty-eight hours.

After the injection of the aqueous vehicle, the neutrophil count remained near the initial level until a slight increase occurred at seven and one-half hours. Lymphocytes did not change significantly. However, eosinophils dropped from an average of about 120 to 80 at seven and one-half hours.

Oral administration of cortisone produced a prompt increase in neutrophil count and distinct declines in lymphocyte and eosinophil counts. By ten and one-half hours the neutrophil count had returned to the initial level. The lowest eosinophil count was 49 at seven and one-half hours. Cortisone acetate intramuscularly produced an increase in neutrophil counts at seven and one-half hours, which was maintained beyond fourteen and one-half hours after the injection. The lymphocyte count showed little change and the eosinophil counts declined from an average of 130 to 61 at ten and one-half hours. All of the subjects had discomfort at the site of injection of cortisone acetate, which lasted about ten hours before subsiding.

Although the authors state that there are no significant changes in lymphocyte and eosinophil counts after the injection of cortisone acetate, whereas the reverse is true after an oral dose of 50 mg. of cortisone acetate, it is postulated that the prompt changes in white blood cell counts after the intramuscular injection are due not only to pharmacologic effects but in part to mechanical irritation at the site of injection.—T.R.T.


Nucleotidase is described as the phosphatase concerned in the degradation of a constituent part of the nucleic acid molecule. It is an acid phosphatase with a pH optimum of 4.0; it acts upon adenosine-5-phosphate, adenosine-2-phosphate, or adenosine-3-phosphate. The nucleotidase activity of the granulocyte is 10 times that of the lymphocyte.

The authors have found that other phosphatases such as pyrophosphatase and adenosine triphosphatase have similar degrees of activity in the lymphocytes and granulocytes.

AN INHIBITOR OF DESOXYRIBONUCLEASE IN HUMAN WHITE BLOOD CELLS AND BONE MARROW CELLS AND ITS RELATIONSHIP TO CELLULAR MATURITY. H. H. Hensnell and R. I. Freedman. From Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, Calif. Science 115: 357-358, 1952.

Inhibitors of the enzyme desoxyribonuclease have been found in yeast, in the crop gland of the pigeon, and in various normal and cancerous human tissues.

In the present work the authors studied the content of this inhibitor in blood cells and in bone marrow. The amount was found to vary with the degree of maturity—the more mature the cell, the more inhibitor contained. This substance was found in the white cells only. In leukemic patients, the cells being more immature, the amount of inhibitor was decreased. In treated leukemic patients, the inhibitor content was normal.—R.C.C.
THE EFFECTS OF CORTISONE AND HEPARIN ON EOSINOPHILS IN DEFIBRINATED HUMAN BLOOD. R. C. Muehrcke, J. L. Lewis, and R. M. Kark. From Department of Medicine and Research and Educational Hospitals, College of Medicine, University of Illinois, Chicago, Ill. Science 115: 377-378, 1952.

It is a well-known fact that injections of ACTH or cortisone will induce an eosinopenia. During the past three years these authors have attempted to reproduce these effects in vitro by incubation of human blood with cortisone. The authors were not successful. In the present experiment defibrinated blood from fifteen patients ill with various diseases associated with eosinophilia were incubated for 4 hours at 37.5 C. No effects were obtained on the eosinophil count. On the other hand, when a suspension of cortisone acetate or pure crystalline cortisone acetate was mixed with the defibrinated blood, the absolute eosinophil counts were significantly reduced after 4 hours incubation. The authors found that this effect of cortisone on the eosinophil count could be blocked by adding heparin to the defibrinated blood before introducing the cortisone.—R.C.C.


Relatively small doses of ionizing radiation have been found to increase the incidence of bilobed nuclei in the lymphocytes. An incident which occurred at this laboratory is a good example. While the cyclotron was running, two machinists started out the back door of the shop in the laboratory building toward the building housing the cyclotron. The men had reached a point about 50 feet from the cyclotron building before they realized their mistake and hastily retraced their steps. It was estimated that they were outside the shop for only a few minutes. The two men developed slight transient leukopenia during the week following exposure and showed a definite increase in lymphocytes with bilobed nuclei for about three weeks after exposure. Seven control smears from the two men before the incident contained no lymphocytes with bilobed nuclei. By contrast eleven of forty smears made during the first three post-exposure weeks were positive for binucleate lymphocytes. The incidence in terms of lymphocytes was 1.1 per thousand lymphocytes. This substantiates experimental work on dogs where similar effects have been found and re-emphasizes the importance of caution in working with ionizing radiation.—R.C.C.