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BONE MARROW


Two sisters of 10 and 11 years, suffering from congenital spherocytosis, both had a sudden onset of severe anemia, some days after they had caught an upper respiratory infection. The striking findings were the disappearance of the reticulocytes, the decreased bilirubinemia—in spite of the increasing paleness—and only minimal urobilinuria. In the bone marrow—absence of the normoblasts and appearance of giant proerythroblasts. A few days later again increased erythropoiesis in the bone marrow and reticulocytosis in the blood. The author supposes the trigger phenomenon of these aplastic crises to be the respiratory infection. The giant proerythroblasts result from a disturbance in the division of the immature proerythroblasts (stop between the K₁ and K₂ generation) which leads to a homoplastic-endomitotic multiplication of the K₂ generation.—C.G.


Ten year old boy, Mother asthmatic. Patient suffers from subsepsis allergica (septic temperature, transitory swelling of joints and repeated appearance of urticaria, rheumatoid heart, and palpable spleen). In the blood, leukocytosis with eosinophilia, high sedimentation rate. 10 weeks after admission the boy gets a hemorrhagic diathesis with thrombopenia, "Hemmkörper", and a positive direct Coombs-test with the red cells. At that time the reticulocytes disappeared from the blood, the normoblasts from the bone marrow, and a few giant cells (giant proerythroblasts) could be seen. A few days later the blood picture and the bone marrow were normal again. No anaemia followed the crisis as there was no congenital spherocytosis. In this child with an allergic constitution and a subsepsis allergica the acute erythroblastopenia is supposed to be due to unspecific antibodies which interfere with cell maturation.—C.G.

ATYPICAL HEMATOPOIESIS WITH MULTINUCLEATED GIANTFORMS IN A CHILD WITH HODGKIN’S DISEASE TREATED WITH 6-MERCAPTOPURINE. G. Sansone. From the Istituto di Clinica Pediatrica G. Gaslini, University, Genova, Italy. Minerva med. 45(2): 1407-1409, 1954.

In a 6 year old child, admitted for Hodgkin's disease, the bone marrow biopsy revealed, after 15 days of treatment with purinethol (100 mg. per day), the presence of atypical, giant erythroblastic cells, which reached the diameter of 50 micra. All maturation steps were
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represented, from the basophilic erythroblast to the mature erythrocyte. Multiple nuclei (6–7), nuclear rests, basophilic granulations were observed also. Multipolar Karyocynesis was detected as well. The giant erythroblasts in the bone marrow were not observed in the peripheral blood. After discontinuing the treatment, normoblastic evolution in the bone marrow took place. This finding is discussed in connection with similar findings in hematologic disorders (erythemia, erythroleukemia, etc.).—P.d.N.

CHRONIC HYPOPLASTIC NEUTROPENIA. Halley Pacheco Oliveira and E. Martins Garcia.

The chronic neutropenias are characterized by the extremely long course of the disease, its relative benign symptoms, a sort of rhythmic oscillation of the number of the neutrophilic cells, a familial occurrence, and a pathogenetic linkage to the spleen. Spaet and Dameshek, in 1952, published 4 cases of a similar entity differing from the common chronic neutropenias in that it lacked the cyclic and familial character and the splenic participation, but with the same clinical symptomatology. The first three patients were submitted to splenectomy without any result. Bone-marrow studies revealed a permanent hypoplasia of the granulopoietic neutrophilic cellular system, the hypoplasia being attributed to a specific defect of the granulopoietic system of unknown etiology. The patient described by the present authors was an old Portuguese woman followed for 16 months, presenting extreme degrees of neutropenia and occasionally complete agranulocytosis, slight anemia and normal platelets. Sternal punctures showed a severe myeloid hypoplasia, normoblastic erythropoiesis, and the presence of platelet-forming megakaryocytes. The clinical picture of weakness, anorexia, moderate fever and ulcerations of the mouth and pharynx mucosa resisted every therapeutic trial, including ACTH. This patient did not have the monoscytosis described in Spaet and Dameshek's cases. An investigation of two daughters revealed no hematologic disease.—M.A.J.


Cytometric investigations of erythroblasts were carried out in the bone marrow of 10 cases of chronic, acquired pancytopenia. Statistical evaluation of the obtained data was done. The results were as follows: (1) the mean cell diameter was significantly increased as compared with that of normal erythroblasts in all phases of maturation; (2) the mean cytoplasmatic diameter was increased as well, more evidently in the mature than in the immature cells; (3) the mean nuclear diameter was significantly increased in the proerythroblasts, but not in the basophilic, polychromatophilic and orthochromatic erythroblasts; (4) the nuclear diameter decreased normally in proportion with increasing maturation; the cytoplasmatic diameter was not modified after the phase of basophilic erythroblast. In conclusion it was assumed that the total cell diameter, as well as the cytoplasmatic diameter of erythroblasts in chronic pancytopenia are increased in all phases of maturation. Macroerythroblastosis in these conditions is particularly due to increase of cytoplasmatic diameter, while the nuclear diameter does not significantly influence such phenomenon, except in the proerythroblastic phase.—P.d.N.

RED CELL APLASIA. Marvin J. Sakol. From the Division of Hematology, Department of Medicine, University of Louisville School of Medicine. Louisville, Kentucky Arch. Int. Med. 94: 481–488, 1954.

Red cell aplasia is characterized by a severe refractory normochromic normocytic anemia in which there is no reduction in the numbers of leucocytes or platelets. The bone marrow shows either a considerable number of primitive red cell forms or complete absence of red cell precursors. In both types the aspirated bone marrow appears cellular since granulopoiesis and megakaryopoiesis appear to be normal. Nine acceptable and four doubtful cases are reviewed from the literature and an additional case is reported. In the latter the
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Sternal marrow showed normal granulopoiesis. Megakaryocytes were plentiful but there was complete absence of erythropoiesis. This patient was followed for only three months; his condition remained unchanged. Some patients have been maintained with blood transfusions as long as five to six years. Spontaneous remissions can occur.—H.R.


A male aged 48 and a female aged 62 had pure red cell anaemia associated with thymomas. One had myasthenia gravis. Both were subjected to thymectomy, splenectomy and ACTH therapy and recovered. The anaemia was severe and normochromic. White cell and platelet counts were normal; the marrows showed a severe diminution of all forms of erythroblasts. The first patient did not respond to thymectomy or splenectomy alone, but has been well for two years after a short course of ACTH. In the second patient, ACTH was ineffective until thymectomy and splenectomy had been done, but maintenance therapy with the hormone was required.—R.H.G.


A 53 year old woman with chronic discoid lupus erythematosus was treated intermittently for two and a half years with mepacrine. She developed a bleeding tendency and was found to have anaemia, granulocytopenia and thrombocytopenia. There was no response to antibiotics or corticotrophin. At necropsy the diagnosis of aplastic anaemia was confirmed. The condition was attributed to the mepacrine therapy.—R.H.G.

THE BONE MARROW IN KALA-azar: P. C. Sen Gupta. From the Kala-azar Research Department, School of Tropical Medicine, Calcutta. Bulletin Calcutta School of Tropical Medicine. 1: No. 4: 17–19, 1954.

Cellularity was in general normal or increased. Proliferation of reticuloendothelial cells was a constant feature. Varying number of these cells was filled up with L. D. bodies. There was no definite correlation between the degree of parasitization and activity of the hematopoietic cells. Erythropoiesis was active and was characterized by normoblastic hyperplasia; transitional cells were present in 4 out of 12 cases in which these cells were specially searched for. Granulopoiesis appeared to be decreased in the majority of cases; occasional giant stab or metamyelocytes were seen in 5 out of 12 cases. Plasma cells were increased in most of the cases. Megakaryocytes were normal in number or increased; platelet formation was normal in 8 cases and significantly decreased in 4. The changes in the bone marrow were in many respects similar to those seen in hypersplenism.—J.B.C.

PLASMACYTOSIS OF BONE MARROW. Helen Clark and E. E. Muirhead. From the Department of Pathology, Southwestern Medical School of the University of Texas. Arch. Int. Med., 94: 425–432, 1954.

An increased percentage of plasma cells in the bone marrow cannot be considered by itself as diagnostic of multiple myeloma. Among 50 cases with an increased percentage of plasma cells in the bone marrow, 13 had more than 10 per cent (up to 21%), 14 ranged from 7 to 10 per cent, and 24 from 5 to 7 per cent. Hyperglobulinemia was present in 31 patients and cryoglobulinemia in 6. Bence-Jones proteinuria was not found and skeletal x-ray films did not reveal osteolytic lesions attributable to multiple myeloma. In some instances a few immature plasma cells were present, in contrast to multiple myeloma where immature forms are usually numerous. Plasmacytosis of bone marrow may be associated with a variety of clinical conditions: (1) sensitivity to drugs or antigens, (2) "collagen diseases", (3) infections, predominantly chronic and frequently of granulomatous type, (4) cirrhosis of the liver, and (5) disseminated malignant neoplasms.—H.R.
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A peculiar mutation occurs in the house mouse, characterized in the heterozygous type by white spotting of the fur and in the homozygous type by a lethal anemia, due to a gene named W. The lethal effect, described by Little (1915) is due to a severe and progressive anemia initiated in intra uterine life and followed by death some days after birth. The anemia was first recognized by Detlefsen (1923). The author presents histologic studies which suggest that this anemia is an aplastic one due to hypoplasia of the organs of red cell production (liver and spleen) and of granulocyte production (bone marrow).

The homozygous animals also have a gonadal atrophy with almost complete lack of sexual cells.—M.A.J.


A deficiency of dietary protein or certain of its amino acid constituents results in anemia, leukopenia and a decrease in blood volume. Changes which occur in the bone marrow to bring about these peripheral effects have not been thoroughly studied. In order to discriminate between the effects of protein inanition and general inanition, 37 male Sprague-Dawley albino rats were divided into 3 groups and fed diets containing no protein, restricted protein and normal protein. The experiments were terminated after 41 days and the animals sacrificed. In addition to peripheral blood studies, thin pencils of bone marrow were fixed, sectioned at 8 microns and stained with hematoxylin eosin-azure II. Differential counts were made and the cells per cu. mm. computed. Protein deficiency resulted in a more severe depression of normoblasts than did general inanition. Homoplastic production of erythroblasts was reduced; however, general inanition permitted a greater heteroplastic formation of erythroblasts. General inanition apparently had a more severe and different effect on heterophil granuloctytopoesis than did protein deficiency. General inanition resulted in a depression of the plasma cell population to 33 percent of normal, a complete lack of dietary protein caused a reduction to 8 per cent of normal. The inability of the protein-depleted animal to produce specific antibodies is due not only to insufficient amounts of material from which to form them, but also to a reduction in the quantity of tissue in which they are formed. Reticular cells resisted the effects of general or protein inanition.—O.P.J.


Some minor stimuli, such as blood collection and intraperitoneal injection of glucose solution, were studied with reference to alterations of the white blood cells. There was regularly observed a decrease of eosinophils, neutrophilia and lymphopenia, without any definite change in the total number of white cells. Adrenalectomy did not interfere with the neutrophilia and lymphopenia, but the eosinophilic decrease was no longer observed.—M.A.J.

MEGALOBLASTIC ANEMIA


In two complex and highly technical papers the Cambridge workers describe a crystalline nucleotide-free degradation product of vitamin B_{12}, and their collaborators put forward evidence for the existence of a new type of ring system within the vitamin B_{12} molecule. The original papers should be consulted.—R.H.G.

Microbiologic assays of "free" and total vitamin B12 concentration in serum by use of Euglena gracilis were performed on varied groups. The mean vitamin B12 serum concentration of the normal individuals was 532 ± 161 μg/ml. Patients with pernicious anemia in relapse had a mean of 39 ± 26 μg/ml. Patients with such diverse abnormalities as hepatic cirrhosis, achlorhydria, folic acid deficiency, neurologic disease and pernicious anemia in remission had serum B12 serum concentrations which did not differ significantly from those observed in the normal individuals. Five of the 29 subjects with hepatic cirrhosis, who had not received antecedent vitamin B12 therapy, had serum vitamin B12 concentrations greater than 1000 μg/ml. Patients with pernicious anemia in relapse were found to have no free vitamin B12 (B12 available to support Euglena gracilis growth prior to dilution and heating), whereas all normal individuals possessed free B12 activity in their sera. In vitro studies showed that the sera from normal subjects and from patients with pernicious anemia possess approximately the same ability to bind added B12 and thus render it incapable of the support of growth of Euglena gracilis. An interesting observation was that sulfonamide derivatives inhibit growth of Euglena gracilis. This inhibition was reversed by PABA, whereas, folic acid and citrovorum factor failed to reverse the inhibition by sulfonamides.—W.N.J.


The effect of a clinically active intrinsic factor concentrate on the absorption of Co60 labeled vitamin B12 in rats was studied. The animals were divided into two groups, one of which received a diet deficient in vitamin B12; the other was supplemented with a high level of vitamin B12 for a period of 35 days prior to the administration of Co60 labeled vitamin B12. Each of these two groups were divided into subgroups which received either 0.42 μg. or 4.2 μg. of the radioactive vitamin with or without the intrinsic factor. Four days following the oral Co60 Vitamin B12 administration, each animal received an intraperitoneal injection of 20 μg. of non-radioactive vitamin B12. Excretion of the labeled vitamin as well as renal and liver concentrations in the 8 groups of 4 animals each were compared.

The Co60 B12 content in liver and spleen as well as excretion was decreased in the groups of animals that received labeled vitamin and intrinsic factor as compared to the groups that received labeled vitamin alone. The ratio of liver to spleen Co60 B12 concentration in the groups prepared with a low vitamin B12 diet was 1.5. This may be compared to a ratio of 4.6 to 7.5 observed in the groups which received supplementary vitamin B12. The authors conclude from this study that the rat is not a suitable experimental animal for an assay of the ability of intrinsic factor to increase absorption of vitamin B12.—W.N.J.


The cellular defect in pernicious anemia appears to be of nucleic acid metabolism. The deep basophilia of the cytoplasm of early megaloblasts is due to the presence of ribonucleic acid, and the mean amount of ribonucleic acid phosphorus (RNAP) per cell is much greater in megaloblastic marrows than in normal ones. The mean desoxyribonucleic acid phosphorus (DNAP) per cell has also been claimed to be greater.

In the present investigation, chemical estimations of nucleic acids have been done on suspensions of blood and bone marrow cells. The mean cellular content of RNAP was 18.53 × 10⁻² μg. per cell in pernicious anemia marrows (18 patients examined) and in marrows showing normoblastic erythropoiesis (9 patients) it was 10.69 × 10⁻² μg. per cell. In the two groups there were approximately equal amounts of DNAP, the figures in each case being about 150.
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per cent of the values for blood leukocytes. It is considered therefore that the high cellular DNAP of the pernicious anemia marrow is not due to a specific abnormality of mitosis, but to the prevalence in the marrow of cells of proliferative type. The cells are engaged in building up DNA in preparation for mitosis.—R.H.G.

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