associated with histologic changes affecting the chromophobes and eosinophilic cells.

8755 P

Cytological Studies of Biopsied Pernicious Anemia Bone Marrow During Relapse.

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In the past we have reported that in pernicious anemia marrow during relapse there is a pathologic hemoglobiniferous series, the megaloblastic, which is not related to the normoblastic or definitive red cell series.[1] The only thing these two series have in common is their ancestral cell, the myeloblast. The present report deals with certain observations which were made while the above mentioned work was in progress and takes into consideration pathologically altered neutrophils and megakaryocytes found in pernicious anemia marrow.

The present investigation was carried out upon nine bone marrows from patients with pernicious anemia during relapse. Six were prepared by smearing freshly aspirated sternal marrow and three were dry imprints (abklatsch). All preparations were stained with May-Grünwald-Giemsa combination of Pappenheim. The best morphological detail of marrow cells was elicited by the dry imprint method, consequently these preparations were studied more intensively than films of aspirated marrow.

Studying large neutrophils (macropolycytes) revealed that their entire life history is quite different from that encountered in normal bone marrow. As early as the leukoblast stage the nucleus has assumed a polymorphic shape as indicated by peculiar protuberances and invaginations. During the promyelocyte stage the nucleus may be shaped like a giant "stab" form. In other words, nuclear development and maturation has preceded that of the cytoplasm to such an extent the large pathologic neutrophils have skipped myelocytes and metamyelocyte stages. This particular point has been previously mentioned by Tempka and Braun.[2] Generally the arrange-

1 Jones, O. P., *Anat. Rec.* (Suppl.), 1934, **58**, 23; *ibid.*, 1935, **61**, 57.

2 Tempka and Braun, *Folia Haematol.*, 1932, **48**, 355.

ment of chromatin is less compact than that of corresponding stages in the normal neutrophil. The cytoplasm of promyelocytes may contain either rarified areas of light hyaloplasm or distinct vacuoles. These cytoplasmic vacuoles tend to disappear as the pathologic neutrophils mature. When these cells have obtained their full complement of granules practically all the vacuoles have vanished. Besides these vacuoles in the cytoplasm there are holes in the nuclei. These commence as a single definitely circumscribed hole in the nuclear material which later tends to become drawn out into an irregularly shaped space. Single large holes are found in some myelocytes which give them the appearance of a "doughnut". Other pathologic neutrophils were found with three or more holes in the nucleus, each being separated from the other by a strand of chromatin material of varying thickness. It is by means of these holes in the nuclear material that the pathologic neutrophil ultimately attains the morphology of macropolycytes (II and III) described by Cooke.[3]

Tempka and Braun[2] have interpreted these findings to indicate characteristics of degenerative alterations of the neutrophil. Our interpretation is that they represent processes in the maturation and development of a pathologic neutrophilic series. It is by means of this precocious nuclear polymorphism along with the appearance of holes in the nuclear material that the bizarre-shaped nuclei of the pernicious anemia neutrophil (macropolycyte) develop. This finding agrees with the third hypothesis of Cooke's in which he assumes that "the polymorph is inherently abnormal owing to a defect in its parent, the hemocytoblast, or in its environment"[3]; for, it has been shown that these pathologic alterations commence as early as the leukoblast stage and can be traced through the subsequent promyelocyte and myelocyte stages to the pernicious anemia neutrophil of the circulating blood.

The megakaryocytic system is involved in some bone marrows, but not to the extent claimed by Tempka and Braun.[2] These authors found numerous megakaryocytic nuclei devoid of cytoplasm and believe this to be the result of the same process which effected the erythropoietic and leukopoietic systems. The type of pathologic megakaryocyte which we encountered was an intensely basophilic one with a polymorphic nucleus. The cytoplasm was devoid of azurophilic granules. Normally when the nucleus is polymorphic the cytoplasm contains azure granules and is not as basophilic as the pathologic ones. Here it seems that the nucleus is maturing

[3] Cooke, W. E., *J. Lab. and Clin. Med.*, 1934, **19**, 453.

while the cytoplasm shows no tendency to develop azure granules and form platelets The pathologic alteration of the megakaryocytes in some pernicious anemia bone marrows may account for the decrease in platelets occasionally found in cases of pernicious anemia.

From these observations upon the qualitative alterations of the marrow cells one must conclude that the lack of anti-pernicious anemia principle produces a panmyelopathy, in that three distinct cell lines are effected. The normoblastic or definitive series is inhibited while the pathologic red cell series, the megaloblastic, proliferates. The neutrophilic series is effected to the extent that there is developing in the marrow a pathologic series which gives rise to the abnormal pernicious anemia neutrophils (macropolycytes) of the peripheral blood. Also, in some cases the megakaryocytes are pathologically altered so that they are not producing platelets. This interpretation of the panmyelopathy in pernicious anemia is different from Tempka and Braun's[2] in that we do not believe the qualitative alterations in the neutrophils and megakaryocytes represent degenerative manifestations. The very fact that all of these above mentioned alterations disappear under adequate therapy and the marrow returns to normal favors our interpretation.[4]

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The Isolation of *Brucella abortus* from the Blood-Stream of Cattle.*

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Soule[1] has perhaps done the most extensive work on this subject. His method consisted of adding 50 cc. of whole blood to 450 cc. of glycerol-infusion-broth and then incubating under 10% carbon dioxide. More than 5000 ordinary "herd-run" cattle were studied. Two series of tests were made on each animal at intervals of approximately 6 months. In the first series of tests agglutinins were present in the blood of 2,237 of the animals but only 299 gave positive blood-cultures. In the second series agglutinins were present

4 Tochowicz, L., *Folia Haematol.*, 1934, **53**, 16; Braun, B., *ibid.*, 1934, **53**, 27.

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1 Soule, M. H., *Premier Congrés International de Microbiologie*, 1930, **1**, 606.