ABSTRACTS

HEMATOPOIETIC TISSUE

OLIVER P. JONES, Ph.D.


For many years papers have been published regarding the erythrocytogenic power of endothelium and the nature of the vascular channels in avian and mammalian bone marrow. Several authors (Jordan, H. E., and Johnson, E. P.: Am. J. Anat. 71: 71, 1935; McDonald, J. G.: Am. J. Anat. 65: 251, 1939) have discredited the presence of intersinusoidal capillaries as described by Doan et al. (1925). Instead, they have reported stromal or interlipocellular tissue spaces lined by histiocytic elements. Regardless of this controversy, Doan et al., Jordan and Johnson, McDonald, Peabody, Ringoen, Sabin and Miller, etc., have observed and described the openings of these structures directly into the sinusoids. In the present paper, which is based on a study of marrow obtained from a single patient—before and after the intravascular infusion of 3000 ml. of fresh blood plasma—the author claims that the "conical openings" are closed to the general circulation. This offers no restraint to the entering corpuscles because the author first assumed (without bibliographic reference) that cellular elements pass through the sinusoidal wall after they "have reached a certain physico-chemical state of their colloidal envelopes." Structures originally called intersinusoidal capillaries or stromal and interlipocellular tissue spaces are now designated intraparenchymal sinuses by Schleicher. He has presumed that these structures were produced by loss of fluid from fat cells. However, such minute changes in cellular contour may very well have been due to fixation artifacts—a thing which should have been ruled out.


One of the hematological problems which has intrigued many workers in the past as well as the present is the nature of the barrier between hematopoietic organs and the peripheral blood. Besides this, there is also the problem of determining the regulatory mechanism which maintains blood cells at relatively constant levels. Since published works on the action of pituitary adrenotropic hormone and extract of suprarenal cortex indicated that lymphocytes were under hormonal rather than nervous control, Yoffey and Baxter undertook certain experiments to confirm these findings. Although their group of test animals was small (16 Wistar rats), the results were so definite that they could be considered as being significant. The administration of pituitary adrenotropic hormone caused a marked diminution of lymphoid tissue of the nodes after 4 weeks and the administration of extract of suprarenal cortex produced the opposite effect to the extent that the nodes were more active than normal. When animals were given both of these substances simultaneously, Yoffey and Baxter undertook certain experiments to confirm these findings. Although their group of test animals was small (16 Wistar rats), the results were so definite that they could be considered as being significant. The administration of pituitary adrenotropic hormone caused a marked diminution of lymphoid tissue of the nodes after 4 weeks and the administration of extract of suprarenal cortex produced the opposite effect to the extent that the nodes were more active than normal. When animals were given both of these substances simultaneously, the effects seemed to be neutralized. One of the most interesting observations was the finding that cortical extract produced a lymphopenia in face of hyperactive lymph nodes. Hence, in the absence of degenerative changes, it would seem that the rate with which lymphocytes left the blood was the determining factor in these cases. These authors were unable to produce a significant change in the blood lymphocytes of 2 rabbits after daily subcutaneous injections of cortical extract for 16 and 22 days respectively.


Since very little is known about the age changes of laboratory animals, Andrew undertook a study
of the spleen as a part of a general program sponsored by The Wistar Institute. In addition to studying a pedigreed stock of rats, human spleens from 43 individuals were also studied to see what comparisons could be made. Spleens from the rats were divided into 5 groups according to their age. The most immature animals were 2.1 days old and the senile group included rats over 726 days old. The human spleens were from unselected autopsy specimens ranging in age from newborn to 91 years. All material was analyzed for: (1) appearance of malpighian follicles, (2) nature of red pulp, (3) amount of pigment, (4) appearance of pigment-containing cells, (5) relative numbers of plasma cells and eosinophils, and (6) the condition of the megakaryocytes. All of the youngest rats had a reticular type of red pulp whereas 77 per cent of the senile group had a sinusoidal type. Reaction centers (germinal) were not present in the most immature group but made their appearance in the group having an age range of 50-150 days.

These centers persisted throughout all the remaining groups but were markedly decreased in the senile group. Warren believes that the term ‘germinal center’ is a misnomer and that Hellman’s term ‘reaction center’ explains more accurately the function of this structure. Macrophages were not observed in the youngest rats but increased rapidly from 50 days on to 726 days and then decreased somewhat in the senile group. The incidence of megakaryocytes was greatest in the youngest group with a decrease to about one-third in the senile group. Andrew believes certain observations indicate that megakaryocytes may arise by a fusion of smaller cells; however, a few cells were found which supported a hypertrophy of single cells into megakaryocytes. Comparison of the rat spleens with the human spleens showed in general similar things due to age changes. There was a loss of reaction centers, a variable destruction of the pulp architecture, and a change in red pulp from a reticular type to a more sinusoidal type.


Although it is customary to divide erythropoietic activity into two main categories, viz., normoblastic and megaloblastic, it has been recognized for some time that giant erythroblasts and erythrocytes exist in normal bone marrow. By using several staining technics on a group of normal and pathologic bone marrows, Schwarz carefully studied the morphology and occurrence of gigantism in hematopoiesis. The clue to the nature of this gigantism was first found by observing giant leukocytes with two normal and independent nuclei. A graded series of these cells in transitional stages could be traced back to a binucleated myeloblast. In the case of erythroblasts, giant forms were found to arise from unicellular erythroblasts which had completed karyokinesis but not cytokinesis. Such cells doubled their cytoplasmic mass, number of centrioles and chromosomes (tetraploid). This process did not interfere with nuclear maturation and hemoglobin formation. While plurinucleated erythroblasts are present in normal bone marrow, they were found to be more numerous in megaloblastic marrows than in hyperplastic normoblastic ones. Since the greatest number of nuclei found was 8, it was suggested that three succeeding divisions apparently exhaust the mitotic activity of an erythroblast (used in the general sense). It is interesting to note that such a condition does not obtain in megakaryocytes, for Japa (Brit. J. Exp. Path. 26: 111, 1945) has counted 31 nuclei in these cells. In some cases, after cytokinesis had been suppressed for a while, it appeared that an attempt had been made to resume segmentation. The factor responsible for the suppression of cytokinesis and the production of giant erythroblasts is still unknown.


Numerous clinical reports as well as the results of experimental hypophysectomy have shown that the pituitary gland has a regulatory effect on erythropoiesis. Since the exact mechanism of the resulting anemia has not been explained satisfactorily, Crafts has attempted to show why this anemia develops in a well controlled group of Long-Evans adult female rats. Hypophysectomy produced a marked drop in the erythrocyte and hemoglobin values after 10 days and then an even greater decrease between 30 and 40 days following the operation. Wright's stained films showed a severe hypochromasia and microcytosis. The bone marrow was definitely hypoplastic. Injections of ferrous sulfate into hypophysectomized rats maintained normal erythrocyte levels for 30 days and hemoglobin values for 20 days before each of these gradually decreased. Intraperitoneal injections of ferrous sulfate and cupric sulfate produced results similar to the administration of iron alone, with the exception that hemoglobin values were maintained for 30 instead of 20 days. Subcutaneous injections of thyroxin maintained the erythrocyte
count at an approximately normal level while the hemoglobin values gradually decreased but not to the level obtained in the untreated hypophysectomized rat. The last group of animals was treated simultaneously with iron, copper, and thyroxin. The erythrocytes were maintained at a normal level but hemoglobin values decreased markedly. At the end of 30 days doses of iron and copper were increased, and after 30 more days it was found that hemoglobin values had risen but not to the normal level. This treatment almost completely prevented hypochromia and microcytosis in addition to producing a hyperplastic bone marrow. These data indicate that the anemia induced by hypophysectomy is perhaps due to a faulty metabolism and that iron may be involved.

Leukopenia and Inflammation. The Presence of a Leukopenic Factor in Inflammatory Exudates.


For a number of years, Menkin has been interested in the dynamics of inflammation and as a result he focused his attention on the nature of exudates. By using various methods of extraction, fractionation, and purification he was able to isolate from the exudate of an acute inflammatory process substances which would produce cellular damage and necrosis, fever, leukopenia, and leukocytosis. Two substances have been isolated in a relatively pure form and have been called necrosin and pyrexin. The present article reports the results of an investigation to determine the nature of the leukopenic factor. Purified necrosin administered to dogs fails to reduce the absolute number of leukocytes. On the other hand pyrexin not only produced fever but also a marked leukopenia. By subjecting pyrexin to incomplete hydrolysis it was possible to dissociate the leukopenic factor from the pyrogenic factor. Further studies will be necessary to determine whether or not the leukopenic factor is a separate substance or a separate factor in pyrexin.