HEMATOPOIETIC TISSUES

Effects of Folic Acid Deficiency and a Folic Acid Antagonist on Chicks, E. Woll. From the Research Department, Lederle Laboratories, Pearl River, N. Y. Arch. Path. 46: 559-566, 1948.

Rapidly growing subjects like newly hatched chicks readily lend themselves for such purposes as the study of nutritional disturbances. It was for this reason that they were selected for experiments in folic acid deficiencies. About 200 one day old New Hampshire Red chicks were divided equally into the following six dietary groups: control; folic acid-free diet; folic acid-free diet plus folic acid by injection; regular diet plus 4-aminopteroylaspartic acid in the diet; regular diet plus 4-aminopteroylaspartic acid by injection; and folic acid-free diet for ten days, followed by same diet supplemented with a daily intraperitoneal injection of 0.1 mg. of folic acid. Changes in the folic acid-deficient birds and those in the birds treated with antagonist were essentially the same. Of the organs involved, the bone marrow and bowel showed the greatest departure from normal. The ultimate picture of the marrow was that of a severe aplasia with a myxomatous appearance of the connective tissue. In the distal third of the small bowel, there was an atrophy of the mucosa with the appearance of retention cysts and fibrous elements of the stroma. Folic acid will prevent these changes when injected into folic-acid-deficient animals.


Clinical response to the use of intravenous nitrogen mustard in diseases of the lymphatic tissue has been reported by various authors since 1944. In order to determine possible differences in lymph node architecture before and after therapy, 27 cases from a series of 53 were selected for study. The most surprising thing was the absence of a single criterion that could be said to exist in any two treated cases. The authors point out that it is difficult to rationalize the use of a drug, which primarily attacks the lymphocytes, in the treatment of a disease generally considered to be one of the reticuloendothelium.


By means of radioactive phosphorus (P32), the effects of lethal and sublethal continuous radiation were studied in chick embryos and developing chicks. There was an overall retardation of the growth of the birds, a marked retardation of bone growth, and especial sensitivity was noted in the cells of the testes and ovaries. In the present paper, the effects on bone marrow, lymphoid tissue, and peripheral blood are recorded.

In the bone marrow, the effects were the result of the heavy irradiation of marrow cells due to the concentration of P32 within the bones. Sublethal irradiation resulted in maturation arrest of the hemato-
poietic cells, and a reduction of mitotic activity, so that pancytopenia developed maximally in 1 to 2 weeks. In 2 to 3 weeks, recovery began, with an increase in mitotic activity and, later, maturation of the blood cells. When irradiation was lethal, there was a complete halt of mitotic activity and of maturation within 2 to 3 days after use of P32, with resultant hypoplasia of the marrow, fatty degeneration within the marrow, and progressive pancytopenia with death in 2 weeks. In both lethal and sublethal actions, the reticulo-endothelial cells were little affected, and tended to give rise to primitive blood cells during recovery.

In lymphoid tissue, P32 caused suppression of mitoses and a thinning out of the lymphocytes. This response was followed rapidly by prompt and marked regeneration of lymphoid tissue, with recovery being complete in most instances. Regeneration was excessive in amount.

In the peripheral blood, the lymphocytes fell rapidly and, with recovery, returned fairly rapidly to normal. The granulocytes fell more slowly; an agranulocytosis was present within 2 weeks; and the recovery phase was slower than for the other blood cells. The red cells fell quite slowly, following a lag period; and recovery was quite rapid, although slower than the return of the lymphocyte level to normal.


Eosinophils, Paneth cells and acidophilic plasma cells are usually more numerous in the lamina propria of the small intestine than they are in either the stomach or large bowel. Collections of acidophilic cells which are usually in the vicinity of cancerous growths seem to be a defensive response of the host. Acidophilic cells are seldom the source of primary neoplasm. There may be some relationship between the presence of these cells in the small intestine and appendix, and the infrequency of carcinoma or tendency slowly to metastasize there.

The Rate of Mitotic Activity in the Lymphoid Organs of the Rat. E. Andreasen and S. Christensen. From the Department of Anatomy, Faculty of Medicine, University of Copenhagen, Denmark. Anat. Rec. 103: 401-412, 1949.

In studies of mitotic activity with sectioned material of lymphoid tissue, the results have not been wholly reliable because of the irregular and capricious distribution of dividing cells. In an effort to determine the proportion of dividing cells visible in a population, suspensions of cell nuclei were made by treating finely divided tissue with 5 per cent citric acid for one-half to one hour. After a series of centrifugations, staining with gallocyanine, resuspensions in absolute alcohol and finally benzyl benzoate, ten thousand nuclei were counted in a Bürker-Türcck counting chamber. Mitotic phases before the disappearance of the nuclear membrane and after reconstruction of the nuclear membrane in telophase were rarely seen. Hence, the counts involved phases between these two extremes. Thymi, lymph nodes and spleens were examined from rats of three different age groups, i.e., 1 month, 3 months and 8-12 months old. The number of mitotic figures per thousand nondividing nuclei was consistently higher in the thymus than in either lymph nodes or spleen. There was a decrease with age, which was most noticeable in lymph nodes and spleen. Additional experiments were conducted to determine the source of lymphocytes in rats during restitution after starvation. The thymus reaches its normal mitotic activity 3-4 days after restitution while lymph nodes and spleen show no deviation from normal either at the end or during restitution.


Lymph node hyperplasia is a common occurrence in some blood dyscrasias and under certain experimental conditions. Attention has been generally directed toward structural changes of the lymphatic tissue and not of the capsule. In order to study the latter, experimental hyperplasia was produced in hamsters and rats by injecting Eberthella typhosus vaccine. Hyperplastic mediastinal and bronchial lymph nodes from calves with acute bronchopneumonia were obtained from the slaughter house. In
hamsters and rats hyperplastic nodes had a portion of the cortex extending through areas deficient in capsule because of a previous rupture. Maximal peripheral expansion of these nodes was observed in the hilar region. The degree of extracapsular migration of lymphatic tissue into the perinodal areolar tissue increased with the length of the postinjection period. In the hyperplastic calf's lymph node the capsule did not rupture because of its thickness.

O.P.J.


The author uses agar for embedding particles after fixation. This procedure reduces the forceps trauma and permits a single block easily to be carried through subsequent steps.

O.P.J.

ERYTHROCYTE PHYSIOLOGY


The hormonal control of erythropoiesis has been investigated in the mammal and bird but not in the amphibia. The adult frog normally has hypoplastic marrow during hibernation, so that perhaps the posthibernation erythroplasia may be the result of participation by the endocrine system. Adult frogs of both sexes were kept in refrigerators at a constant temperature of 4-6°C before and during the experiments. Four groups of test animals received 2.0 injections of sesame oil, thyroxine, testosterone propionate and estradiol benzoate respectively. The animals were sacrificed 4 days after start of injections. The results indicate that there is some relationship between the endocrine system and hemopoiesis but further study is necessary in order to understand the mechanism.

O.P.J.

ON THE NATURE AND SIGNIFICANCE OF STIPPLING IN LEAD POISONING WITH REFERENCE TO THE EFFECT OF SPLENECTOMY. A. J. S. McFadean and L. J. Davis. From the University Department of Medicine, Royal Infirmary, Glasgow, Scotland. Quart. J. Med. 18: 57-72, 1949.

In both human patients and in guinea pigs with lead intoxication, stippling is demonstrable in the bone marrow in normoblasts as well as in the non-nucleated erythrocyte in marrow and peripheral blood. A positive reaction for iron is exhibited by a variable proportion of the granules and there is often associated evidence of defective hemoglobinization in the affected cells. It is of interest that in the experimental guinea pigs employed in these studies splenectomy ameliorated or prevented the anemia of lead intoxication as well as increased the relative proportion of stippled cells in the circulation and the frequency of a positive reaction for iron in the granules. The suggestion is made that lead interferes with hemoglobin synthesis with partial failure in the incorporation of iron into the protoporphyrin ring. Removal of the more defective cells by the spleen could thus explain the hemolytic component of lead intoxication and the beneficial effect of splenectomy on experimental lead induced anemia. It is possible that a similar mechanism may explain the beneficial results of splenectomy in a peculiar acquired hemolytic anemia, previously described by the authors, in which iron containing inclusion bodies were demonstrated in the erythrocytes (Glasgow M. J. 28: 237, 1947).

W.N.V.


In previous studies on the human red cell, the loss of K increases with time until the K concentration inside the cell is approximately the same as that in the medium outside in systems containing lysins. When no lysin has been added, the losses are rapid at first and they tend to slow down so that a new steady state remote from equilibrium is reached. The present experiments concern four such kinds of
systems. (1) Washed red cells in saline at 4 C, (2) washed red cells in saline at 25 C, (3) washed red cells in saline at 37 C, and (4) washed red cells in systems at 4 C, 25 C, and 37 C, containing hypotonic saline, glucose, or a number of other substances. In order to prevent bacterial contamination and thereby possibly introduce a hemolysin, all of the experiments were conducted under aseptic conditions based on the method used by Osgood for marrow culture.

**O.P.J.**


Since the work of Overton, it has been widely accepted that compounds soluble in lipid solvents penetrate cells by reason of their solubility in the lipids of the cell surface. A new method was devised to measure the relative rate of penetration of the lower fatty acids into mammalian erythrocytes. This method, a chemical one, depends upon the fact that oxyhemoglobin loses some of its oxygen when placed in an environment containing an increased hydrogen ion concentration. The relative rates of penetration of the fatty acids investigated were found to be (a) for beef cells: caprylic < heptylic < caproic = valeric < butyric > propionic > acetic = formic; (b) for human cells: caprylic = heptylic < caproic < valeric < butyric > propionic > acetic > formic. The rates of hemolysis by these acids were determined and found to be (a) for beef cells: caprylic > heptylic > caproic > valeric < butyric > propionic > acetic > formic; (b) for human cells: caprylic > heptylic > caproic < valeric < butyric > propionic > acetic < formic.

**O.P.J.**

**CRYPTOGENIC METABOLISM OF ERYTHROCYTES.** L. Heilmeyer and Th. Eilers. From the Medical Clinic of the University of Heidelberg. Schweiz. med. Wschr. 78: 973-76, 1948.

In an investigation of the metabolism of hemoglobin in pernicious anemia, the quantity of eliminated urobilin was found to be essentially higher than the reticulocyte level would indicate. By adding Giemsa stain for 8-11 hours in the refrigerator to the usual staining of reticulocytes with brilliant cresyl blue, pathologic reticulocytes of crescent form and containing many vacuoles are brought in evidence. These forms are not visible when the smears are stained in the usual way. They are more frequently found in smears from the spleen than in the peripheral blood. These reticulocytes are believed to be destroyed particularly fast within 1 to 48 hours. Even if they do not contain the final hemoglobin, they possibly represent prestages causing the increased metabolism of urobilin.

**C.M.**


It has long been recognized that centrifugal methods do not completely separate corpuscles from plasma. Attempts to measure the amount of fluid left in the sediment have not given constant results. These measurements have usually been based on some application of the principle of serum or plasma dilution. The present study was done on whole beef blood. Relative corpuscle and serum volumes were estimated by 12 different applications of the serum dilution principle. These results were then compared with those obtained by centrifugation. Mean differences between centrifugal and dilution results varied with the method from 2.0 ± 1.1 to 17.9 ± 10.8 per cent of the packed cell volume. Most dilution procedures are not well adapted to accurate serum volume estimates. The authors conclude that correction of conventional hematocrit results by a constant factor based on dilution methods is not justified.

**R.C.C.**

**BLOOD GROUPS**

ABSTRACTS

Theoretically, fetal damage from ABO maternal isoimmunization may result when the concentration of A or B factor in the child's body fluids is not sufficiently great to neutralize A or B maternal agglutinins.

Two hundred and eighty mentally deficient children were studied to determine the incidence of mother-child ABO incompatibility and the secretor status of the child. One hundred and fifty-seven of these had clinically defined mental deficiencies such as mongolism and were used as controls, whereas the remaining 123 were classified as undifferentiated congenital amentia of unknown origin. Evidence is presented to show the unreliability of the study of a single undiluted specimen of saliva or gastric juice, and in this study secretor status was determined only after both gastric juice and saliva were simultaneously examined and titrated.

There were 2 children who showed ABO maternal incompatibility and a nonsecretor status. The incidence of incompatible nonsecretors was greater in the group of undifferentiated mental deficiency (23 per cent) than in the control group (3 per cent), and it is suggested that ABO isoimmunization may be an etiologic factor in a small proportion of children classified as undifferentiated congenital deficiencies.

Even if confirmatory evidence were forthcoming, it would be necessary to conclude, from the significant clinical differences pointed out by the authors, that the mechanisms responsible for cerebral damage in ABO and Rh incompatibility are not similar. One wonders, because of the variable nature of secretor status, whether the concentration of A or B factor in body fluids later in life is a valid measurement of that present in the prenatal and neonatal states.

H.W.B.

IMMUNIZATION OF BLOOD DONORS WITH SALIVA. V. Bydlenský. From the State Health Institute, Prague, Czechoslovakia. Čas. lék. čes. 87: 725, 1948.

Immunization of blood donors with diluted saliva of A and B secretors, performed according to Wiener's proposal, increased the titer of hemagglutinins in 80 per cent of cases; the hemagglutinin titer rose on an average eight times and was constant even after nine months. Better results of immunization were obtained in persons under the age of 45.

M.N.


These four papers deal briefly with the current views on the genetics of the Rh-Hr factors, the medico-legal application of our knowledge of the several known blood types, the methods of detection of isoimmunization by the Rh factor, and the management of erythroblastosis fetalis.

The author of the second paper proposes the use of the basic locus symbol Rh with the letters C D E as superscripts to clarify further the nomenclature introduced by Fisher and Race. The two genetic hypotheses to account for inheritance of Rh-Hr blood types (e.g., the 8 allele hypothesis and the 3 locus hypothesis) are discussed by the same author from the point of view of serologic evidence, cross-over results, and evidence obtained from gene, genotypic and phenotypic frequency analyses.

H.W.B.


Two cases are reported, one of fatal erythroblastosis in first and second pregnancies of an Rh negative patient previously immunized by transfusions, the other of a major hemolytic transfusion reaction in an Rh negative male patient previously immunized by a single transfusion of Rh positive blood. These serve further to point up the necessity of administering Rh negative blood only to Rh negative patients. The second reaction was notable in that while laboratory evidence of complete hemolysis of a pint of blood within two hours of transfusion was dramatic, clinical symptoms of a major reaction were virtually absent.

W.N.V.