LEUKOCYTES AND LEUKOCYTIC DISEASES


In the presence of normal adrenocortical activity there is an almost complete disappearance of circulating eosinophils during the first twenty-four to forty-eight hours after a major operation. The finding of a normal or high eosinophil level during the first twenty-four to forty-eight hours after an operation suggests adrenocortical insufficiency. There is usually a sharp rise of the eosinophil level on the second to the fourth postoperative day, associated with clinical improvement. The response of the eosinophils to ACTH during the postoperative period provides a rapid and useful means of as-

saying adrenocortical reserve.—P.F.W.


Repeated determinations of the peripheral blood eosinophil count in a fatal case of adrenal hemorrhage were made during treatment with adrenal cortical hormone. The number of eosinophils rose initially but on therapy fell. Direct eosinophil counts are suggested as a supplementary diagnostic test for the Waterhouse-Friderichsen syndrome.—P.F.W.


II. SUR UNE ADIINOPATHIE REGIONALE SUBAIGUE ET SPONTANEAMENT CURABLE AVEC INTRA DERMORÉACTION ET LÉSIONS GANGLIONNAIRES PARTICULIÈRES. (A SUBACUTE REGIONAL ADENOPATHY, SPONTANE-


III. R. Laplane. (Discussion of the preceding communication, same reference.)


VI. IN NOUVEAU CAS DE POLYADNOPATHIE SUBAIGUE PARAISANT CONSECUTIVE À DES GRIFFURES DU
ABSTRACTS


The above references are a series of communications (under the general title, "A New Lymphatic Disease") concerning altogether 31 cases of a type of subacute adenopathy observed in children and adults. From the descriptions of the different authors the following characteristics can be ascribed to the disease:

The adenopathies involve one or a small number of lymph nodes in a single area, without becoming generalized. The usual sites are cervical or axillary. Sometimes, but seldom, an inoculation point is found. Usually fever is observed, often after a few days of the disease. Sometimes a transitory rash has been observed. Lymph nodes are painful, with inflammatory reaction and periadenitis. Suppuration is usual, and sometimes ends by fistula formation. Even in such cases, spontaneous healing is observed after a few weeks or months.

The blood data remains normal.

All the etiologic researches (bacteriologic explorations, Frei, Mantoux, Paul and Bunnell, Ducrey tests) are negative but the intradermal reaction with material obtained from lymph node aspiration (syndallised) is strongly positive in these patients. Often the cases are familial, sometimes a small cutaneous excoriation is found (cat scratch, or bite, or thorn prick).

In a great number of cases the cat seems to be the vector of the disease, but the animal itself seems not to be affected; it is rather its claws which are contaminated, perhaps by a bird virus (although all virus explorations remain, up to the present time, negative).

The histologic studies show an acute reticular hyperplasia with histiocytes and epithelioid cells, an inflammatory reaction of the peri-lymphoid tissues. Later disseminated foci of suppuration appear, and necrosis without preliminary polynuclear infiltration. Some giant cells can be observed.

In some observations, aureomycin was given and seems to have prevented suppuration of the lymph node and to have hastened cure.

The great similarity of these observations, and the clinical, biologic and histologic characteristics allow differentiation of this disease, which always heals spontaneously, from other affections such as Sodoku, Hodgkin's disease, lymphoreticulosarcoma, tularemia, lymphogranuloma, infectious mononucleosis, and above all tuberculous lymphadenitis.

Until now, the finding of a cat scratch, or a positive intradermal reaction with the specific antigen, are the best differential symptoms.

The histologic examination does not seem to be specific enough to make a diagnosis with the other infectious reticular hyperplasias.—J.P.S.


A study of 8 cases of acute leukemias is presented. Six patients among the 8 had characteristic modifications of the fundi; that is, hemorrhages oval-shaped, with a discolored bright white center. These hemorrhages are localized to the posterior pole, close to the papilla or the macula. They are inconstant, some disappearing in a few days, some multiplying.

An edema of the papilla is often associated.—J.P.S.


The authors present a systematic study of the fundi in hematologic diseases. In the leukemias, they find (in good correlation with Bonnet's and Dollfus' description) hemorrhages with a very special shape: "canoe-like" (oval with a white center).

They successively describe the aspects found in pernicious and achreatic anemias, in polycythemia, in osteosclerotic anemia, in Hodgkin's disease and in thrombocytopenia, before and after splenectomy. (Twelve good colored plates illustrate the text.)—J.P.S.

ABSTRACTS

This is a report of data on a large group of cases treated with HN₂, including among others 27 cases of Hodgkin's disease. One-tenth to 0.36 mg. of HN₂ per kilogram body weight per day for four days were used intravenously. Subcutaneous or intramuscular injection of sodium amytil seemed the most effective means of reducing nausea. Benadryl was ineffective in combating gastro-intestinal symptoms. Focal lymph node Hodgkin's disease was controlled better by X-ray therapy than by HN₂. Four patients without clinically demonstrable lymph node or visceral involvement at the time of treatment with HN₂, but with persistent or recurrent fever, showed rather dramatic improvement. In this group of 52 patients treated with over 100 courses of HN₂, no instance was observed among the patients who died in which it was felt the fatality could be ascribed directly to the drug. Leukopenia (maximum eight to fourteen days after starting treatment) was not complicated by infection. The leukopenia resembled that seen following roentgen therapy but was more rapid in appearance and of shorter duration. An absence of marked depression of the white cell count was interpreted as evidence of inadequate dosage or of relative resistance to the drug. Thrombopenia was less frequent than leukopenia but was more persistent and usually the limiting factor in the continuation of treatment. In 4 cases, treatment was discontinued because of purpura. Radiation seemed the therapy of choice in patients with Hodgkin's disease relatively localized in peripheral, mediastinal or retroperitoneal regions with obstructive lesions about the spinal cord, biliary tract, ureters or great vessels, with bone involvement and with extensive fibrosis in the lesions.—P.F.W.


This is a careful study of 113 pathologically proved cases of Hodgkin's disease. Although there was an over-all five-year survival of 51 per cent, the importance of this figure is relatively insignificant in comparison with the correlations of certain clinical findings with prognosis. For example, the group of cases having only single lymph node regions involved at the time of admission had a survival of 88 per cent at five years and 79 per cent at ten years. In addition to the extent of involvement on admission there were four other factors apparently influencing the prognosis: the age and sex of the patient, the pathologic picture and the presence of constitutional symptoms on the first admission. The early age groups responded to therapy better than the later age groups. Hodgkin's disease of the female sex ran a more chronic course than that in the male. Although using a different terminology, the author adhered to the Jackson-Parker histopathologic classification, with the exception of placing some granuloma cases with the sarcoma cases in the 'late' group. Only 9 per cent of the 'late' group survived five years. It is suggested that early intensive irradiation of involved lymph nodes be combined with precautionary treatment to the proximal nodes. Institution of radiation therapy to recurrences as early as possible is also recommended.—P.F.W.

HEMORRHAGIC DISEASE


This is a vague and undocumented report on the effects of large doses of vitamin P (hesperidin) and vitamin C on the 'capillary fractility' of a heterogeneous group of patients with 'increased capillary fractility.' The 38 patients studied included diagnoses of hypertension, arteriosclerosis, anemia [sic], rheumatoid arthritis, gingivitis [sic], and obesity. The presence of increased capillary fractility was apparently deduced from an increased number of petechiae in a positive-pressure test. In addition to the normal regimens, these patients received 600 mg. each of vitamins P and C daily for six weeks, and 400 mg. each for an additional six weeks. In the 'majority' of patients, the authors state, there was improvement of the capillary fractility.

The suggestion is made that vitamin P is necessary for the utilization of vitamin C in the maintenance of the normal strength of the intercellular cement of the capillaries.

These substances will continue to be employed clinically in instances of 'increased capillary fractility'.
on an empiric basis, despite lack of definite evidences of effects on the status of the capillary strength—S.E.


Bismarsen was administered to a patient because of recurrence of lichen planus, which had responded without incident to the same drug eight years previously. The injection of the material on the second occasion was followed within a few hours by headache, nausea, and acute thrombocytopenic purpura, with bleeding from the gums and generalized petechiae and ecchymoses. Treatment with blood transfusion and BAL (2-3-dimercaptopropanol) was followed by rapid return of the blood values to normal, and cessation of the bleeding.—S.E.

**HEMOGLOBIN AND BILIRUBIN METABOLISM**


When the whole blood of subjects with sickle-cell anemia is incubated aerobically with N15-labeled glycine, labeled heme is formed. Such in vitro synthesis of heme from glycine is not observed when normal human blood is incubated under similar conditions. The present experiments demonstrate that the non-nucleated but immature rabbit erythrocytes are capable of synthesizing heme in vitro, whereas significant synthesis does not occur with normal mature rabbit erythrocytes. The data indicate that although elevated reticulocyte counts were associated with appreciable concentrations of N15 in heme there was no close correlation between the height of the reticulocyte count and the hemin isotope concentration. This suggests either that the capacity of reticulocytes for synthesis of heme may vary widely or that the synthesis may be performed not only by reticulocytes but by other immature erythrocytes. No significant synthesis of heme occurred under certain anaerobic conditions nor with cells hemolyzed by distilled water.—P.F.W.


Circulating red blood cells of the duck have been shown to synthesize heme in vitro. Four-tenths of one per cent of the heme was synthesized in the first day. The rate of synthesis was maximum initially. As thoroughly washed cells could carry on synthesis and acetic acid is necessary for heme synthesis, then the red cells must retain acetate or sources of acetate. Anaerobiasis inhibited heme synthesis. Destruction of the cell structure abolished synthesis ability as determined in these experiments. The red cell of the duck can incorporate histidine into cell proteins at the rate of the porphyrin synthesis. It is possible that globin as well as heme is made as required for hemoglobin synthesis.—P.F.W.


The administration of N15-labeled serine or acetylglycine to rats resulted in isotope concentrations of the hemin similar to those found after labeled glycine administration. However, after incubation of duck blood with labeled acetylglycine there was little incorporation of the labeled nitrogen in the hemin. When isotopic serine and large amounts of nonisotopic glycine were incubated with duck blood only small amounts of isotopic heme were formed. If isotopic glycine and large amounts of nonisotopic serine were incubated with duck blood, heme with a high concentration of N15 was formed. The authors suggest that serine and acetylglycine are precursors for the glycine subsequently utilized in hemin formation.—P.F.W.

**Metemalbumin. Interaction between Human Serum Albumin and Ferrisprotoporphyrin IX.** M. Rosenfeld and D. M. Surgenor. From the Department of Pharmacology and Experimental Therapeutics,
School of Medicine, the Johns Hopkins University, Baltimore, Md., and the Department of Physical Chemistry, Harvard Medical School, Boston, Mass. J. Biol. Chem. 183: 663-677, 1950.

Methemalbumin is an abnormal component of blood plasma in certain diseases associated with excessive hemolysis. No physiologic role has been assigned to it. This is a study of the characteristics of the interaction between crystallized human serum albumin and ferriprotoporphyrin. Spectrophotometric studies indicated the reaction was rapid with a maximum extinction occurring at 403 mm. within thirty minutes at 38 C. Although optical density studies at 403 mm. indicated 2 moles of iron porphyrin were bound by one mole of albumin when spectrophotometric titration of albumin with ferriprotoporphyrin was measured at 623 mm., the data indicated the binding of 4 moles of iron porphyrin per mole of albumin. The 3rd and 4th mole of ferriprotoporphyrin did not effect the Soret band, indicating their binding with the protein was by a different mechanism from the first two moles of ferriprotoporphyrin. Albumin alone, of the plasma proteins studied, interacted with ferriprotoporphyrin in the way described.—P.F.W.

THE HYPERBILIRUBINEMIC EFFECT OF SODIUM NICOTINATE. M. Stefanini. From the Department of Internal Medicine, University of Roma, Rome, Italy and the Department of Biochemistry, Marquette University School of Medicine, Milwaukee, Wis. J. Lab. & Clin. Med. 2039-2048, 1949.

The intravenous injection of 30 mg. of sodium nicotinate into normal subjects is followed by a rise of the serum level of indirect reacting bilirubin which reaches a maximum after about ninety minutes, then slowly returns to the initial value within six to eight hours. Almost immediate stimulation of the secretion and excretion of bile (bilirubin) occurs and there is an increased elimination of urobilin which reaches a maximum two to three hours after the injection and returns to normal values in about twenty-four hours.

The authors suggest that the ascending part of the hyperbilirubinemia curve might be due to increased reabsorption of mesobilirubin from the bile. The descending part seems to be in direct relationship to the bile-excreting function of the liver. Because of the vasodilatory, cholagogic and choleretic effects of sodium nicotinate the authors believe that the increased elimination of urobilin is very likely due to the increased reabsorption of urobilinogen.—G.E.C.


The authors report a patient with recurrent episodes of severe abdominal pain, constipation, mental depression, and polyneuritis, in whom a diagnosis of porphyria was ultimately established. They discuss the nature and possible pathogenesis of the gastro-intestinal symptomatology of this disease, especially abdominal pain, and suggest that this may be the result of the hypomotility and distention of segments of the intestinal tract, which in turn are the results of a toxic effect on the autonomic system of the porphyrins in the disease. Therapy was of no avail in their patient.—S.E.


A case of acute porphyria in a 42 year old white woman who had recurrent episodes of acute abdominal pain and constipation, pain in the extremities with one attack of ascending paralysis, and red urine containing uroporphyrin (type not determined) is presented. The family history was interesting in that there were two other probable cases of porphyria as well as numerous congenital abnormalities.—H.W.B.

PORPHYRIA. J. S. Marietta. From the Department of Internal Medicine, Southwestern Medical College, Dallas, Texas. South. M. J. 42: 958-965, 1949.

Porphyrin metabolism and the clinical syndromes associated with a marked idiopathic increase of porphyrin excretion are briefly discussed. Two cases of porphyria, illustrating the chronic and acute forms respectively, are presented.—H.W.B.
FOLIC ACID AND VITAMIN B₁₂


Folic acid exists in yeast largely in the form of hexaglutamyl conjugate, the glutamic residues of which are presumably joined by peptide linkage. The data, based chiefly upon microbiologic assays with L. casei after enzymatic hydrolysis, can be interpreted as indicating the association of folic acid hexaglutamate with the proteins released by autolysis of the yeast cell. The results of ammonium sulfate fractionation of yeast autolysates, supplemented by electrophoretic studies, indicate the presence of a specific FA-protein complex.—P.F.W.


Binkley first demonstrated the occurrence in yeast extract of an antianemic principle, different from pteroylglutamic acid, but releasing that substance after acid or enzymatic hydrolysis. Pfiffner isolated this compound and named it vitamin B conjugate. In 1947, Schweigert and Pearson studied the folic acid content of both plasma and corpuscles in mammals and fowls, before and after treatment with an enzyme. The enzyme, takadiastase, released folic acid from its microbiologically inactive forms. They found minute amounts of free folic acid but significant amounts of B conjugate. Folic acid is set free after incubation with plasma for two hours at 37°C, the pH of the digestive mixture being 4.5. Good results were also obtained from baker's yeast from which 0.7 µg folic acid in one hour at 37°C. No significant differences were found in pernicious anemia patients or in other pathologic conditions except for a decrease in asystolic patients.—R.C.C.


As early as December, 1948, Berk et al. demonstrated vitamin B₁₂ functions as extrinsic factor when administered simultaneously with gastric or intrinsic factor by mouth to patients with pernicious anemia in relapse. This is a report of observations on 13 cases receiving vitamin B₁₂ and lyophilized duodenal extracts, lyophilized duodenal mucosa, and extracts of gastric mucosa from swine, as well as pooled human gastric juice. The authors conclude that vitamin B₁₂ requires for effective utilization a potentiating agent (intrinsic factor of Castle) available in hog stomach and duodenum as well as in gastric juice of normal human beings.—P.F.W.

BLOOD SPECIFIC GRAVITY


A simple technic is described in detail for measuring the specific gravity of plasma, serum or whole blood. The method depends on the fact that a drop of plasma or blood falling into a solution of copper sulfate of similar gravity is instantly encased in a sac of copper proteinate and that the drop remains discrete and without change in gravity for about ten seconds. Several sources of possible error in technic are mentioned and the methods of avoiding them are described.—P.F.W.

ABSTRACTS


Equations have been derived for the determination of grams of protein per 100 ml. of plasma from plasma specific gravities. They are: $p = 373 (G. - 1.0070)$ for normal plasma and $p = 365 (G. - 1.0070)$ for 'pathologic' plasma from miscellaneous hospital cases without an elevation of sugar or urea concentration above 100 mg. per 100 ml. Variations in plasma lipides had little effect on the calculated results. The 'pathologic' plasmas had on the average 0.98 as much nitrogen-calculated protein per 100 ml. as normal plasmas of the same specific gravity. These data are comparable to those observed in subjects with malnutrition. The difference could be due to either a lower specific volume or lower nitrogen content of the proteins of the 'abnormal' plasmas.—P.F.W.


From specific gravity determinations of blood and plasma by the copper sulfate method, hemoglobin concentrations have been calculated. The standard deviation of the gravity determined from gasometric hemoglobin was ±0.15 Gm. per 100 ml. of blood in the normal bloods and ±0.26 Gm. in the 'abnormal' (mostly anemic). A nomogram is presented for rapid calculation of both plasma protein and blood hemoglobin concentrations from specific gravities.—P.F.W.

BONE MARROW


This report is a summary of an investigation undertaken during 1944-45 at Takorade, Gold Coast, into the value of examination of the bone marrow by sternal puncture in the diagnosis of malignant tertian (falciparum) malaria. The author found that in acute malignant tertian malaria the parasites were found in slightly greater numbers in thick films of peripheral blood than in thick films of bone marrow. He concludes that in the diagnosis of acute falciparum malaria sternal puncture is not a justifiable procedure in that interpretation is difficult and time-consuming and the information obtained not commensurate with the effort involved.—W.N.V.

Metastases in Bone Marrow and Myeolophtic Anemia from Carcinoma of the Prostate. R. W. Rundles and U. Jonsson. From the Department of Medicine, Duke University School of Medicine, and the Hematology Laboratory, Duke Hospital, Durham, N. C. Am. J. M. Sc. 218: 141-150, 1949.

Tumor cells were demonstrable by aspiration in the sternum or iliac bone marrow in 17 of 30 patients with carcinoma of the prostate gland. Twenty-one had roentgen-ray or pathologic evidence of metastases. Implantation appears to occur primarily in the hemopoietic rather than in the osseous tissues. Anemia in the absence of azotemia occurred only in those who had metastases. Gross infiltration of the bone marrow was associated with severe anemia. Immature granulocytes and nucleated red blood cells became prominent in the circulating blood when the hemoglobin was reduced to 7.5 Gm. or below. Following castration and estrogen therapy, the anemia regressed as the amount of tumor tissue demonstrable in the bone marrow decreased, or became more severe as tumor growth progressed in spite of therapy.—G.E.C.

Kala-azar. With Special Studies of Bone Marrow and Lymph Nodes. W. J. Senter, H. Satter, and H. E. Garver. From the Medical Service, Lawson Veterans Administration Hospital, and the Department of Medicine, Emory University School of Medicine, Atlanta, Ga. Am. J. Med. 7: 694-698, 1949.

A case is reported of kala-azar in a 18 year old veteran of World War II campaigns in the Mediterranean theatre who had recurrent episodes of chills, fever and generalized aching, pigmentation of the skin, weight loss, and marked enlargement of the liver and spleen. The patient had been treated elsewhere as a case of malaria for over two years before the diagnosis was made by the demonstration of Leishmania donovani in the bone marrow and lymph node biopsies. Laboratory findings before and after institution of treatment with Neostibosan are given. Particular attention is paid to the study of the bone marrow, in which the most striking abnormality was the increased number of plasma cells and the high degree of parasitization of macrophages and neutrophils.—H.W.B.
LYMPHOID TISSUE AND ITS RELATION TO SO-CALLED NORMAL LYMPHOID FOCI AND TO LYMPHOMATOSIS. I.

Birds do not have lymph nodes but possess widely scattered foci of lymphoid tissue in various organs. Lymphomatosis of the avian leukosis complex involves lymphoid tissue of the body and appears clinically as ocular, neural, visceral and osteopetrotic forms. In the present study, pancreatic lymphoid foci were studied in 332 birds from an original population of 1123 Single-Comb White Leghorn females. The reasons for section of the pancreas rather than the liver for study were lymphoid foci could be measured readily, the pancreas is not normally hematopoietic, and its size and shape make comparable sections possible. In no case was the pancreas diagnosed as positive for lymphoblastoma on gross examination. Lymphoid foci arose either from occluded vessels or perivascular areas. It was practically impossible to separate histologically lymphoid proliferations as hyperplastic and neoplastic reactions.—O.P.J.

HEINZ BODY PHENOMENON IN ERYTHROCYTES
CRITICAL REMARKS

By M. G. Good, M.D. (London, England)

Doctor Stewart H. Webster has published a very illuminating and exhaustive review of the Heinz body phenomenon (Blood 4:479, 1949). I feel that the following remarks to the problem in question may be worth making.

Chemical nature of Heinz bodies. It is worth emphasizing that the findings of Hartwich1 made it appear very likely that the Heinz bodies contain a lipoprotein. But Kunkel2 has proved conclusively, in our opinion, that they contain a phosphatide, a basic protein (histone) and a small amount of cholesterol, but no hemoglobin. These findings are not disproved by the results of the other authors quoted by Webster. The lipid nature of the Heinz body was confirmed by the staining methods of Gutstein and Wallbach3 as well as by those of Hess and Mueller.4 Webster quotes Kiese and Seipel5 who were led to believe that the Heinz bodies contain denatured proteins derived from the erythrocyte membrane. This conjecture, however, does not contradict the lipid nature of the bodies since, according to Gutstein,6 the membrane of the erythrocytes contains lecithin, probably in the form of a lecitho-proteid.

Pre-existent theory of Heinz bodies. Schilling originally claimed the existence of four different bodies in normal erythrocytes. For the demonstration of these structures he used various methods. Some of his results were probably on the basis of artifacts. Gutstein and Wallbach used 5 different staining methods together with viral staining with Nile blue sulfate for their studies. In addition they succeeded in staining hemoglobin and the "inner body" simultaneously in contrasting colors in the erythrocytes of mammals. Further, these authors showed that in the nucleated erythrocytes of birds, the new staining methods allowed the demonstration of nucleus and hemoglobin in the same way as in mammals.

The results and conclusions of Gutstein and Wallbach are objected to by Webster on the ground that "the special technic used to produce these structures in normal erythrocytes requires somewhat severe and rough processes, and great artifacts may result . . . ." These objections are hardly in accordance with the facts. The technic consisted in fixation, mostly with Susa fluid; the staining was done with 1 per cent watery solutions of acid or basic dyes. Hence, the technic used required neither 'severe' nor 'rough' processes. It is noteworthy that all the new staining methods evolved by Wallbach and myself have led to the same results, i.e., the demonstration of a nucleus-like central body in normal erythrocytes. In this con-