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RE SYSTEM—THE SPLEEN


The physiologic activities of the spleen include storage of blood: in man the spleen is probably of little importance as a reservoir, but several mechanisms are potentially available whereby erythrocytes may undergo hemolysis. Yet the spleen is not an important organ of red cell destruction in normal circumstances. Other functions include hemopoietic activity, phagocytic and reticuloendothelial activities, hormonal functions in regulating the maturation and release of red cells, leukocytes and platelets from the marrow, and capacity to elaborate antibodies. From a group of about 40 patients subjected to splenectomy during a period of years, illustrative examples are given, and the ways in which the operation leads to improvement are discussed. Idiopathic acquired hemolytic anemia should be regarded as a primary disorder of the plasma protein- and antibody-forming mechanism. Idiopathic thrombocytopenic purpura should be regarded in at least a substantial proportion of cases as being immuno-allergic in origin. The success of splenectomy is probably chiefly due to the removal of a major thrombocytolytic site. In cases thought to be suffering from hypersplenism, successful splenectomy does not in itself justify the diagnosis or throw much light on the essential pathogenetic mechanism. The spleen might be overactive, but some extrasplicic factor might equally well be responsible by acting on cells in such a way as to prevent their maturation in the marrow and to render them susceptible to destruction by normal splenic activity in the peripheral blood. There is, however, no doubt that splenectomy may greatly benefit some patients with cytopenias who have an active bone marrow and splenomegaly, especially when the disease is primary, or, if secondary, when the underlying disorder is chronic and the hematologic features severe. Brief details are given of 11 such patients: splenectomy achieved some degree of success in every case. In contrast, splenectomy was unsuccessful in six patients with peripheral cytopenias but without appreciable splenomegaly and with marrow hypoplasia. In leukemia and myelosclerosis, when transfusion requirements are large, splenectomy may produce great improvement in the anemic state, especially if evidence of hemolysis is found. —R. H. G.

EXPERIMENTAL PORTAL HYPERTENSION. Tadahiko Suzuki. From the Department of Surgery, Osaka City Medical School, Osaka, Japan. Symposium on Hematology (Japan), Vol. 7: 99-120, 1954.

The author tried to produce portal hypertension in experimental animals by the method of sensitization with foreign protein. Saline extract of normal human spleen, Banti spleen or egg-albumin solution, respectively, was injected to rabbits intravenously. The injections were performed daily for 30 to 450 days. Approximately 30 days after the first injection...
usually splenomegaly and portal hypertension developed and sometimes anemia was observed. The results were listed as follows:

Type I. Cases with portal hypertension, showing histologically pseudolivercirrhosis, spleen with follicular atrophy and fibroadenosis: one typical case and 2 incomplete cases.

Type II. Those with unchanged portal pressure and unchanged liver and spleen: 13 cases.

Type III. Those with giant splenic tumor (f. i. 13.2 Gm.) and distinct anemia: 3 cases.

Type IV. Those with portal hypertension, but without evident change in liver and spleen: 16 cases. They were considered as a transitional form between types I and III.

The author interpreted the difference of results as due to individual constitutional difference of reaction in each animal. The portal hypertension was sometimes temporary.

There was no correlation between portal hypertension and histologic changes of liver and spleen.

The author performed some additional experiments. The existence of antischistosomal antibody was demonstrated serologically in the serum both of patients with Banti's syndrome and the animals in these experiments. Another experiment of obliterating the splenic vein showed a temporary portal hypertension only in the early stage.


On the basis of detailed investigations, 108 cases of chronic splenomegaly could be broadly divided into two groups. In group I, which consisted of as many as 100 patients, malarial infection and malnutrition appeared to be important etiologic factors. In advanced stages of this group, the liver showed evidences of parenchymatosus degeneration and hyperplenism was responsible for varying degrees of peripheral pancytopenia. Response to splenectomy was not encouraging in cases showing hepatic changes. In group II, which consisted of only 8 cases the basic pathology was portal obstruction, intrahepatic or extra-hepatic; neither malnutrition nor malarial infection contributed to the splenomegaly and associated changes.—J. B. C.

**SPLENOGRAM IN KALA-AZAR.** J. B. Chatterjea, and P. C. Sen Gupta. From the Department of Hematology and Kala-azar, School of Tropical Medicine, Calcutta. Bulletin Calcutta School of Tropical Medicine 4: 58, 1956.

The characteristic feature was increase of plasma cells and monocytes. In 2 out of 14 cases there were normoblastosis (2 and 5%) suggesting extramedullary erythropoiesis in spleen.—J. B. C.


Comparing the results of adrenalin test in 8 patients suffering from hypersplenism with a group of other diseases the authors draw the conclusion that this test cannot be used in the diagnosis of hypersplenism to such an extent as recommended by Doan’s school. The adrenalin test is positive both in hypersplenism and in other diseases to the same degree; therefore, this test cannot be used as an indication for splenectomy.—M. N.


The author reports his observation of tuberculosis of the spleen, the clinical course of which showed a huge splenomegaly with a small tumor of the liver, and hematologically a picture of panhematopenia and excessive anemia. The diagnosis was made at autopsy. The sternal puncture showed an obvious hyperplasia of the reticulum. Blood transfusion caused a rapid and prolonged rise of temperature and shivering on two occasions. An instantaneous
success of streptomycin therapy manifested itself by a sudden drop of temperature and cessation of shivering. A splenectomy could not have been performed because of the very serious condition of the patient.—M. N.


Two cases of splenoptosis with splenomegaly are described and discussed. The spleen in the first case appears to have been enlarged because it fell; in the second to have fallen because it was enlarged. The first case was associated with abnormality in rotation of the colon, and the spleen was the site of chronic passive venous congestion; the second spleen was enlarged by Gaucher's disease.—G. C. de G.

RE SYSTEM—PHAGOCYTOSIS AND ANTIBODY PRODUCTION


In the search for an efficient, readily available, and inexpensive plasma expander, many substances have been investigated. Relatively few have turned out to be acceptable. Polyvinylpyrrolidone (PVP), a synthetic polymer, has been shown to meet most of the requirements satisfactorily. However, the fate of the portion which is not excreted during the first few days has not been determined. When PVP is administered to mice intravenously, intraperitoneally, or subcutaneously, some of the colloidal particles are taken up by cells of the reticuloendothelial system, including macrophages of the liver. This results in the development of foam cells which is interpreted as presumptive evidence of PVP storage. Reticuloendothelial changes occurred only after a certain critical quantity of PVP was administered. Hepatic alterations involved the Kupffer cells and the histiocytes of the periportal connective tissue. The percentage of foam cells among the total number of sinusoidal lining cells of the liver was used as a criterion for evaluating the extent of histologic change. Foam-cell production is apparently a function of molecular size. The number of large molecules present in the injection determines the degree of storage.—O. P. J.

THE UPTAKE OF RADIOCOLLOIDS BY MACROPHAGES IN VITRO. A KINETIC ANALYSIS WITH RADIOACTIVE COLLOIDAL GOLD. R. E. Gosselin. From Division of Pharmacology, Department of Radiation Biology, University of Rochester School of Medicine and Dentistry, Rochester, N. Y. J. Gen. Physiol. 39: 625–649, 1956.

It has long been recognized that various foreign particles of submicroscopic size are extracted from extracellular fluid and stored within the cytoplasm of special tissue cells. These cells are known collectively as the reticuloendothelial system, and the process has been called colloidopexy or ultraphagocytosis. Closely related to the cells of the reticuloendothelial tissues are inflammatory macrophages. The latter can be obtained in large quantities from the peritoneal cavity of rabbits, and the isolated cells can be tested in vitro under carefully controlled conditions. Their ability to extract radioactive colloidal gold from solutions involves two phases: the reversible adsorption of gold on the cell surface and the subsequent irreversible removal of surface-bound colloids into the cell. The latter process (ingestion) appears to proceed at a rate which is proportional at any moment to the amount of gold attached to the cell surface; the latter in turn can be related to the concentration in extracellular fluid by a simple absorption isotherm. In terms of rate, therefore, ingestion is related to the extracellular gold concentration in the same way that many enzyme reactions are related to the substrate concentration. Although enzyme kinetics are useful in describing rates of ultraphagocytosis, there is no evidence that enzymes participate in either adsorption or ingestion or that metabolic energy is required of the macrophage. Exudative leukocytes of heterophilic series show little or no interaction.—O. P. J.
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One hour after intravenous injection of bacterial lipopolysaccharides (pyrogens) in rabbits, the plasma has the property of stimulating the phagocytic activity of human leukocytes in vitro. This phenomenon may be caused by a secondary endogenous factor, the origin of which in leukocytes is discussed. The bacterial lipopolysaccharide itself stimulates phagocytic activity of human leukocytes in blood in vitro in concentrations about 10^{-4}. It does not have this property in the concentrations used in the animals.—M. H. H.


Endotoxins which are phospholipid-polysaccharide-protein complexes can be extracted from gram-negative bacteria. All toxic reactions produced by the bacteria themselves can be provoked by the isolated endotoxin. A previous nonlethal injection of one of the endotoxins protects the animals 24 hours later against several lethal doses of any other endotoxins. The mechanism of this protection is not clear. The role of the reticuloendothelial system was investigated in affording protection to white male mice. A single large dose of bacilli or endotoxin administered intravenously causes a transient depression of the phagocytic activity of the R.E.S. Multiple intravenous or subcutaneous injections bring about a very marked increase in phagocytic activity, and also a significant increase in the relative weights of the liver and spleen. At the same time the resistance of the animals to the toxic products of the bacilli is substantially increased. Cortisone greatly reduces the stimulating effect of the killed typhoid bacilli on the phagocytic activity of the R.E.S.—O. P. J.


The plasma cell and its precursor as well as macrophages have been considered responsible for the formation of antibody globulins. This activity has been reported at the local site of injection, in regional, homolateral and contralateral lymph nodes, and in remote organs like the liver, lungs, kidney and spleen. In order to correlate these findings with the ability of isolated tissues to synthesize specific antibody when incubated in vitro, 350-500 Gm. guinea pigs were injected once in the left foot-pad with 5 mg. of crystalline egg albumin in 0.2 ml. of a water-in-oil emulsion. Animals were killed 3 weeks after injection by inhalation of chloroform. The granuloma at the site of injection of the antigen mixture and the adjacent popliteal lymph node were composed mostly of macrophages and had a few antibody-containing plasma cells; they were relatively inactive in the synthesis of anti-ovalbumin in vitro. On the other hand, the highest activity was found in lymph nodes of the contralateral flank. Organs other than lymph nodes had low in vitro activity with the exception of the spleen and bone marrow. If this activity of the bone marrow were uniform throughout the red marrow of the whole animal it would be a major contributor to total antibody production.—O. P. J.


There has been a revival of interest in the local production of antibodies in response to stimulation by antigens present within the cavities of organs. It has been shown that a single
injection of diphtheria or tetanus alum-precipitated toxoid (A.P.T.) into the skin, fat, voluntary muscle or cornea of immunized rabbits results in the local production of the corresponding antitoxin in the injected tissue. Results of the present investigation show that local antitoxin production can be demonstrated in the mammary glands and spleen and in the walls of the uterus, vagina and appendix of immunized rabbits when diphtheria or tetanus A.P.T. is injected into the tissue or introduced into the lumen of the organ. No evidence has been obtained of local antitoxin production in the liver.—O. P. J.

LYMPHOMA—CLINICAL AND CYTOLOGIC MANIFESTATIONS


Analysis of the histologic features of follicular lymphomas revealed considerable variations in their cellular composition. They were subdivided into five groups according to cell type as follows: (1) Lymphocytic type, well differentiated; (2) Lymphocytic type, poorly differentiated; (3) Mixed type (lymphocytic and reticulum cell); (4) Reticulum cell type; (5) Hodgkin's type. They frequently, but not invariably, progressed into the diffuse lymphomas, usually of the corresponding cell type. The prognosis as to longevity could be correlated to a considerable extent with cellular composition and cellular differentiation. It could also be shown that within a certain cell group the presence of a follicular pattern is of prognostic significance. Follicular lymphoma is not regarded as a distinct disease entity, but as a variant of diffuse lymphoma of corresponding cellular composition.—H. R.


Macrofollicular lymphoma generally is considered to be a form of lymphoma which is easily recognized providing it can be distinguished from hyperplasia, and a condition which tends to be maintained for a long period, to terminate eventually as a malignant lymphoma of diffuse nonfollicular type. There has been considerable disagreement about the terms used to designate this condition, namely: giant follicular, macrofollicular or follicular-lymphosarcoma, lymphoblastoma, lymphadenopathy, reticulosis or hyperplasia. It is a disease of middle age, with no patient in a series of 136 cases under 25 years. The duration of symptoms before biopsy was 1 year or less in 95 cases. In 79 cases, two or more separate sites were involved and 6 patients had retroperitoneal tumors. The more common sites were neck and groins. A certain proportion of the patients with localized disease are cured and the rest experience spread to other sites.—O. P. J.


This disease was first recognized by Scott and Robb-Smith (1939), who described four cases of an invariably fatal condition characterized by fever, wasting, generalized lymphadenopathy and enlargement of the spleen and liver. Jaundice, purpura, anemia and leukopenia were common. Associated with these clinical features, there was a systematized proliferation of histiocytes in the lymphoreticular tissue, many of them being abnormal forms. Erythrophagocytosis was frequent. In the present paper 8 cases of histiocytic medullary reticulosis are described, with the clinical, laboratory and postmortem findings. These cases correspond essentially with those originally described by Scott and Robb-Smith and the condition is considered to be a distinct entity.—O. P. J.


The value of cytodiagnosis in 82 proven cases of malignant lymphoma was limited, since a positive diagnosis of malignancy was made in only 9 of these patients whose sputum,
bronchial secretions, or pleural or ascitic fluid were submitted for study. Of the nine diagnoses of malignancy, 4 were specified as “lymphoma”, and in 1 additional case lymphoma was suspected; in the others, only “malignancy” could be stated. Of the five cases in which “lymphoma” was diagnosed by cytology, leukemia ultimately developed in three. In none of three cases of Hodgkin’s disease could any diagnosis beyond “malignancy” be made on the basis of cytologic study. Although the yield from this method is small it is suggested that familiarity with more specimens will allow diagnosis in instances in which only equivocal diagnoses can be suggested at present.—S. E.

GASTRIC LESIONS IN HODGKIN’S DISEASE AND LEUKEMIA. H. R. Wahl and J. H. Hill. From the Department of Pathology, University of Kansas School of Medicine, Kansas City, Kans. Am. J. Path. 32: 255-261, 1956.

In leukemia and Hodgkin’s disease the stomach usually shows no gross lesions. However, in a few instances, characteristic infiltrations occur and should be recognized. In the present study, 16 cases out of 109 showed obvious gastric lesions. Evidences of gastric involvement may precede manifestations of other visceral involvement and a thorough postmortem examination with complete microscopic study almost always reveals wider dissemination. Gastric lesions are rarely, if ever, primary in the stomach.—O. P. J.


The authors illustrate, by means of personal cases, the difficulties in making a preoperative diagnosis of lymphosarcoma of the intestinal tract; and emphasize the potential prognostic importance of such a diagnosis as against carcinoma. X-irradiation of gastric lymphosarcoma allowed remission in some cases for as long as 7 years, and in small bowel lymphosarcoma for 9 years. The x-ray appearance of gastric lymphosarcoma was not pathognomonic, but rather suggested ulcer, carcinoma, or hypertrophic gastritis. In favor of the diagnosis, according to the authors, was marked flexibility of the lesion on fluoroscopic examination; and, perhaps, marked coarsening of the gastric rugae. In several cases, it was the gastroscopist who suggested that the tumor might be lymphosarcoma rather than carcinoma. With regard to intestinal lymphosarcoma, the x-ray appearance was again not diagnostic, but rather resembled that of regional enteritis, deficiency pattern, and motor dysfunction. Multiple nodular defects and “stiffening,” if present, suggested lymphosarcoma of the small bowel. Intensive x-ray therapy of the area, not necessarily preceded by surgical extirpation, was the mainstay of treatment, and sometimes led to apparent cures after 7 to 9 years.—S. E.


This report deals with 4 patients with Hodgkin’s disease in whom the ingestion of alcohol was associated with the onset of severe pain. The pain occurred during or within minutes after the drinking of small amounts of beer or cocktails. In each case, remission of the disease by therapy was associated with elimination of this symptom. The pain was located in regions of Hodgkin’s granulomatous infiltration. A report on the same subject appeared in New England Journal of Medicine 252: 608-609, 1955.—S. E.

THALASSEMIA


Plasma hemoglobin was estimated in 90 subjects: 25 normals, 22 patients with Cooley’s anemia, 13 cases with Cooley’s trait and 30 cases of anemia due to other causes. In Cooley’s anemia mean plasma hemoglobin was 26.28 mg. per 100 ml. (range 4.3 to 56.50). In other
groups, including normals, the plasma hemoglobin levels varied from 0.69 to 4.35 mg. High level of plasma hemoglobin in Cooley’s anemia suggests, as already pointed out by Crosby and Dameshek (J. Lab. & Clin. Med. 39: 829, 1951), that intravascular hemolysis plays a significant role in the pathogenesis of the anemia.—J. B. C.


A 6 month old female baby suffering from severe Cooley’s anaemia (Hb. 2.9 Gm; fetal Hb. 27.6%; R.B.C. 0.87 mill.) was a transfusion problem owing to the absence of suitable veins. Nine blood transfusions 50 ml. each, given mostly by the intratibial route, raised the hemoglobin and R.B.C. levels to 4.93 Gm. and 1.89 mill. respectively and reduced the fetal Hb. to 16 per cent. At this stage an exchange transfusion was carried out in which 571 ml. of blood was introduced and 482 ml. withdrawn. Following exchange transfusion maximum levels of Hb. and R.B.C. attained were 12.47 Gm. and 3 mill. respectively, recorded 72 hours after the transfusion when the fetal hemoglobin was 4.85 per cent.—J. B. C.


Incidence of Rh(D) negatives in Indians in different states varies from 2 to 10 per cent. In a series of 43 patients with Cooley’s anemia the incidence of Rh(D) negatives was 20.9 per cent. The incidence of Rh(D) negatives were 13.6 per cent in the fathers and 13.04 per cent in the mothers of the above patients.—J. B. C.


Mechanical fragility of red cells was only slightly increased in Cooley’s anemia (mean 5.39%; range 3.33 to 9.0%) and nutritional macrocytic anemia (mean 5.16%; range 2.3 to 9.1%). Mean normal values were 3.38 per cent and the range of variation was from 2.32 to 4.80 per cent.—J. B. C.


Routine radiologic investigation done to study the bony architectural pattern revealed an unsuspected fracture in the middle of the shaft of the right radius in a male child aged 2 years. The fracture united well with proper immobilization for four weeks. This was the first case of spontaneous fracture encountered in a series of 56 cases of Cooley’s anemia investigated radiologically.—J. B. C.


Cytochemical studies on bone marrow cells showed PAS-positive material in the cytoplasm of some of the intermediate and late normoblasts of Cooley’s anaemia. The findings, which confirmed the observations of Astaldi (Acta Hematol. 12: 146, 1954), indicate a defect in the synthesis of carbohydrates by the normoblasts of Cooley’s anaemia.—J. B. C.

Preliminary results show that while two patients with "tropical splenomegaly" as well as a control patient were susceptible to induced infection with P. vivax, the two patients with thalassemia were resistant.—J. B. C.

INVESTIGATIONS ON THE BLOOD COAGULATION PICTURE IN COOLEY'S DISEASE. S. Li Mok and D. Funarola. From the Istituto di Clinica Mediatrica and the Istituto di Patologia Generale, University, Bari, Italy. La Pediat-ria 64: 54-64, 1956.

Twenty cases of Cooley's disease were investigated with respect to the coagulation mechanisms. The following results were pointed out: (1) the bleeding time, the clotting time, the retraction time, the tourniquet test and the platelet count were normal; (2) prothrombin and factor VII were usually normal; (3) in two cases a slight prolongation of the recalcification time was observed; (4) normal thrombelastographic values (see Blood 11: 71, 1956), except in two cases in which a slight prolongation of "t" was detected. In two cases, which were characterized by a particularly severe clinical picture, the signs of a latent hemorrhagic diathesis were observed, as indicated by thrombocytopenia, prolongation of the bleeding time and clotting time, hypoprothrombinemia.—P. d. N.


Thalassemia has not been described in a Scottish family. It is now reported in a family in which both parents (Mr. and Mrs. A.) were born in Dundee, Scotland. The condition occurred in the mother and her son, and in her daughter and the daughter's son. Blood grouping showed that it was impossible for Mr. A to be the daughter's father. There was no history of Mediterranean ancestry (but Dundee is a port!).

The clinical manifestations included anemia, mongoloid facies, epicanthic folds, jaundice and enlargement of the spleen. The red cells showed poikilocytosis, polychromasia, microcytosis, macrocytosis, target cells and basophilic stippling. Nucleated red cells were found. There was an increased amount of alkali-resistant hemoglobin, presumably identical with hemoglobin F.—R. H. G.

AUTOIMMUNE DISEASE


Serologic studies in a case of quinine thrombocytopenia revealed that the patient's serum contained a factor which in the presence of quinine was able to agglutinate platelets, fix complement, and reduce clot retraction. Various studies seemed to show that quinine acts as a link between the platelets and the serum factor. It is reasonable to assume that the thrombocytopenia was due to antibody formation following repeated administration of quinine, in a similar way as described in allergic thrombocytopenia induced by sedormid (Ackeroyd), quinidine and other drugs. It is stressed that, whenever possible, serologic studies in vitro should replace in vivo experiments in the clarification of the etiology of drug-induced thrombocytopenia.—M. S.
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In the serum of a 26 year old woman with lupus erythematosus, it was possible to detect leukocyte- and platelet-agglutinating antibodies. The antibodies were different, as indicated by adsorption tests. Cortisone treatment reduced the leukocyte-agglutinating antibodies and, to a lesser degree, the platelet-agglutinating antibodies. This finding seemed to be independent from the L.E.-cell phenomenon, which was not modified by the cortisone treatment.—P. d. N.


A case of pyridamidon agranulocytosis is reported in which the lowest leukocyte counts were reached 18–24 hours following oral application of the drug. The leukocyte antibodies reached their maximum not before 72 hours. To exclude leukocyte agglutination it is necessary to perform serologic examinations on subsequent days following drug application.—M. H. H.


This is the report of a case in which symptomatic hemolytic anemia was associated with hepatomegaly, generalized adenopathy, autoagglutination of red cells and absence of reticulocytes in the circulating blood. The bone marrow showed normal development of platelets and granulocytes, but reduced numbers of erythrocytes. A lymph-node biopsy was reported as “consistent with Hodgkin’s disease.” Cortisone was given without response. Nitrogen mustard was then given. There was then reticulocytosis, reduction of the serum bilirubin to normal, and “hypererythropoiësis” in the bone marrow. Six months later, the patient showed fatigue, but showed no clinical or hematologic abnormalities. The erythroid hypoplasia described in this case parallels that described in crises of familial spherocytosis and sickle cell anemia; its occurrence in association with acquired hemolytic anemia, apparently secondary to Hodgkin’s disease, is extremely unusual. A hibernoma which was removed from the patient during remission does not seem relevant.—S. E.

SYMPTOMATIC HEMOLYTIC ANAEMIA IN DERMOID CYST OF THE OVARY. J. Procházka. From the 1st Medical Clinic, Palacký University in Olomouc, Czechoslovakia. Vnitrní Lékařství 2: 240–244, 1956.

In a female, aged 40, suffering from hemolytic anemia, splenectomy was performed. After an improvement of short duration there was a recurrence and the hemolysis disappeared only following the removal of a dermoid cyst of the ovary. Atypical incomplete antibodies confirmed by the Coombs test disappeared within two weeks after the operation, while the antibodies acting at a temperature of 4 C disappeared more slowly.—M. N.

The Other Journals of Hematology

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