ABSTRACTS
JOSEPH F. ROSS, M.D., Editor

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ERYTHROCYTIC DISEASE


A man, aged 31, with Gaucher's disease and a grossly enlarged spleen with severe anemia, leukopenia and thrombocytopenia did not improve satisfactorily with blood transfusion but responded dramatically to splenectomy. A man, aged 66, with gout had an enlarged spleen and a blood picture similar to the above. The survival time of red cells transfused into the patient was shortened. The marrow is reported as showing myelosclerosis but as being very cellular. Splenectomy produced some improvement.

In a woman, aged 58, a similar peripheral blood picture was associated with myelosclerosis. Splenectomy did no harm. The authors consider that splenectomy should be used as a last resource in myelophthisic anemia where there is evidence of rapid cell destruction.

—R.H.G.


A woman aged 69, another aged 48, and a man aged 51 had polycythemia with splenomegaly. After four, twelve and five years, leuko-erythroblastic anemia developed. In two cases marrow biopsy showed myelofibrosis and in the third necropsy revealed osteosclerosis. The authors consider that myelofibrosis is caused by the same stimulus as that causing extramedullary hemopoiesis.—R.H.G.


The authors report a case of fatal aplastic anemia in a man 43 years old. The outstanding clinical picture was fever and severe anemia without jaundice. Blood findings were compatible with panmyelopenia. Bone marrow showed very poor cellular marrow with almost complete absence of the erythrocyte and megakaryocyte series, but the granulocytes showed a very marked left deviation with the myeloblast as the predominant element, without any other leukemic signs. Autopsy findings, however, showed miliary tuberculous nodules in lungs, liver, spleen, kidneys, and B.M. The authors reviewed the field of refractory and myelophthisic anemias and suggested the T.B. infiltrations of B.M. as one of the causes of this kind of anemia.—C.F.M.
LEUKOCYTES and LEUKOCYTIC DISEASE


Experiments were designed to investigate the mode of action of penicillin and terramycin on an otherwise fatal pneumococcal skin infection in rabbits. In order to assess the contribution of cellular and humoral defences, rabbits were infected after their granulocytes had been to a large extent eliminated by repeated injections of benzene. Rabbits were infected intradermally with virulent type I pneumococcus. Lesions in the normal animals became sterile after treatment for forty-eight hours, and those in the leucopenic rabbits after treatment for thirty-four to sixty-six hours. In neither normal nor leucopenic rabbits were the lesions sterile after twenty-four hours' treatment. It is possible that under certain conditions granulocytes can assist antibiotics to eliminate virulent organisms, but in the present experiments, using large doses of penicillin and terramycin, such an effect was not observed. It is concluded from these experiments that large doses of penicillin and terramycin, administered systemically, can exert a completely bactericidal action in vivo, without the aid of cellular and humoral defences of the animal.—O.P.J.


Three cases of acute infectious lymphocytosis (A.I.L.) are described. Its individualization has been carried out by peroxidase method (the author's original) which offers security in differentiating the cellular species. Hematologically there is a definite separation between A.I.L. and infectious mononucleosis. In the latter disease there is monocytosis which accompanies the lymphocytosis. Differential hematologic diagnosis with lymphoid leukemia is sometimes very difficult. Clinical facts and the benign evolution of A.I.L. are the keys to the diagnosis.—C.F.M.

PLASMOCYTOMAS PRODUCING PARAPLEGIA. L. Rogers. From the Surgical Unit, Welsh National School of Medicine, the Royal Infirmary, Cardiff, Wales. Brit. J. Surg. 16: 54-56, 1953.

Four patients developed paraplegia from extrathecal compression of the spinal cord by plasmocytoma. One patient was a female aged 37 years. The others were men aged 47, 61, and 68 years respectively. In one instance the tumor appeared to be a solitary plasmocytoma, but ten months after operation there developed evidence of multiple myelomatosis.

—R.H.G.


Four patients with osteosclerosis and five with myelosclerosis but no x-ray bony changes are considered, and postmortem findings are given for eight. Seven had x-ray treatment either to the spleen alone or to the spleen and long bones. Five had relief of abdominal symptoms and improvement in general health as a result.—R.H.G.

LEUKEMIA AND LYMPHOMA


The following diseases are discussed: Hodgkin's disease, lymphosarcoma, mycosis fungoides, plasma cell myeloma, polycythemia vera, acute and chronic leukemias. A clinical classification is presented, to be applied at the time of diagnosis and modified as necessary during further changes in the patient's condition. Class I: disease limited...
clinic to single locus with no constitutional signs or symptoms. Class II: disease limited regionally, with or without constitutional signs and symptoms. Class III: generalized disease with constitutional signs and symptoms.

On the basis of this classification, various forms of treatment are evaluated and recommendations made for their correct use.

A concise summary in tabular form is also presented. — T. R. T.


This report covers a two year period during which time thirty-eight patients with Hodgkin’s disease, lymphosarcoma, leukemia, or neoplasms not originating in the reticuloendothelial or hemopoietic systems were treated with TEM. In fourteen cases of Hodgkin’s disease the average duration of disease was estimated at forty-eight months. Eleven had been treated previously with roentgen rays or nitrogen mustard. First evidence of improvement was noted on an average of nine days after the first dose of TEM. The duration of improvement was thirty days after each course of TEM therapy. The average total dose was only 30 mg. The responses to therapy of the patients with Hodgkin’s disease in this series were quite variable.

One patient with follicular lymphoblastoma showed a favorable response to TEM therapy. One patient with lymphocytic lymphosarcoma and another with chronic granulocytic leukemia showed acute changes in their clinical picture and died soon after the institution of therapy. Of four patients with chronic lymphocytic leukemia and treated with TEM one responded in an excellent manner, two favorably, and one showed no benefit. One patient with bronchogenic carcinoma of the lung with vertebral metastases experienced relief of thoracic nerve root pain for four weeks following only 10 mg. of TEM.

Careful observation is necessary in the administration of this therapy to avoid severe depression of the bone marrow. Its oral administration and the lack of vomiting following its use are two advantages in its comparison with nitrogen mustard therapy. — P. F. W.

**Coagulation**


It has been established previously that there is an inverse relationship between Lee-White clotting time and environmental temperature. The authors recently described a procedure in which the clotting time is determined after the addition of suboptimal concentrations of anticoagulant solutions to venous blood. In the present study, “citrate clotting time” refers to the use of 1 cc. of venous blood to 1 cc. of 0.003 molar sodium citrate.

“Heparin clotting time” refers to the use of 1 cc. of venous blood after addition of 4 μg. of heparin in 0.1 cc. of saline solution. Determinations were carried out in thirty normal individuals and thirty patients receiving Dicumarol, in whom the mean prothrombin time was 18.2 seconds.

It was found that the pattern of inverse relationship between environmental temperature and Lee-White clotting time is followed by the heparin clotting time but not by the citrate clotting time, which increases at temperatures higher than 22 C. The latter is more sensitive to the reduction of the prothrombin level than the heparin clotting time. It is suggested that heparin may be less effective in febrile patients. — T. R. T.


The plasma of most animals examined has been found to contain profibrinolysin and antifibrinolysin. The present paper is involved with the presence of antifibrinolysin in the
formed elements, mainly the platelets. Bovine materials were used in this experiment. Platelets were obtained by differential centrifugation procedures, and a suspension in saline solution was made. This suspension contained 30 times more platelets than were found in cow blood. Platelet suspension was frozen and subsequently thawed, a procedure which liberates materials found in platelets. The assay for antifibrinolysin content of this platelet preparation showed that it contained 2310 units of antifibrinolysin per ml. Simultaneously, oxalated bovine plasma was found to contain 222 units of antifibrinolysin per ml. The authors calculated the distribution of antifibrinolysin activity in plasma and platelets. The platelet compartment contained approximately 70 per cent as much antifibrinolysin as was obtained from the plasma of the same sample of blood. The authors point out, however, that this cannot be regarded as an exact quantitative statement but rather as an order of magnitude concept. The authors also point out that there is no way of knowing whether the antifibrinolysin of platelets is the same substance as that of the plasma from this experimental work.—R.C.


A hemophilic patient had interstitial hemorrhage into the tongue and floor of the mouth, giving rise to respiratory obstruction. The patient was transfused, a nasal tube was passed blindly into the trachea, and a vertical midline submental incision was made. The nasotracheal tube was left in place for four days, and penicillin was given. The authors consider that tracheotomy should not be attempted except when tracheal intubation fails.—R.H.G.


The local Shwartzman reaction in rabbits was completely inhibited by the administration of heparin at frequent intervals sufficient to maintain a level of prolonged coagulation time. The same doses of heparin did not influence the pyrogenicity of the bacterial toxins, nor did it alter the systemic manifestations of the toxicity of these materials. Histologic studies showed that the thromboses and hemorrhages common to the early Shwartzman reaction were inhibited by the heparin injections. The absence of hemorrhages in the presence of an essentially incoagulable blood suggests that thrombosis is a fundamental process in the development of the local Shwartzman reaction.

These findings are in agreement with those of Good and Thomas. J. Lab. & Clin. Med. 40: 804, 1952.—C.E.R.

IMMUNOHematology


The chimera of classical tradition was a creature made up of the parts of several different vertebrate species. The patient described here was found to have 61 per cent of group O cells in her circulation: the rest were of group A. She was a survivor of twins and it is assumed that one set is the consequence of vascular communication with her twin. The O cells are kk, Jk (a + b +): the A cells are Kk, Jk (a – b +). In their other groups they do not differ. The serum contains anti-B, but no detectable anti-A. The patient secretes O (H) antigen in her saliva, but not A antigen. It appears that the genetic control of salivary secretion of the blood group substance does not operate through the red cell at any stage of the cell's existence.—R.H.G.

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In searching for Rh antibodies in pregnancy it is customary to examine the maternal serum upon the mother's first or second visit to the antenatal clinic and, if no antibodies are found, to repeat the test during the seventh or eighth month of pregnancy. In some instances Rh antibodies are very weak and difficult to detect, even on this second examination. Occasionally, weak antibodies may give rise to severe hemolytic disease in the infant. This report deals with two hundred cases in which Rh antibodies were detected. The author describes a slide technic with papain-treated test cells as a screening method for the detection of these antibodies, especially the very weak Rh antibodies. The other tests used were the agglutination tests in saline and albumin and the Coombs' test. In all the positive cases, at least two of the four tests gave positive results. The enzyme-treated cell test was most constantly positive; a few false positive results were found.—R. H. G.

ERYTHROBLASTOSIS FETALIS. N. M. Abelson. From the School of Medicine, University of Pennsylvania and the Children's Hospital, Philadelphia, Pa. M. Clin. North America 609-620, 1953.

The clinical picture is described from the points of view of the obstetrician, the pediatrician, and the general practitioner. From the viewpoint of the obstetrician, it is important to know that the disease is due to a sequence of isosensitizing events: (1) maternal isosensitization by fetal antigen; (2) passive transfer of maternal antibody to susceptible fetus; and (3) destruction of fetal tissue (and particularly red blood cells) resulting from antibody transfer.

Tests to detect the first include trypsinated red cell and saline-albumin technics with a panel of test cells representing the commoner antigens. Since these tests do not disclose certain unusual antigens, specimens from women with poor obstetric histories are also tested by the indirect Coombs test with cells representing the less common antigens. Whenever possible the husband's blood is included in the testing panel. The differential diagnosis of the disease in the delivery room may be difficult, and must include congenital abnormality, maternal diabetes, maternal hemorrhage, inclusion disease, prematurity, syphilis, fetal anoxia, and maternal hepatitis. Therefore, serologic tests must be done and must satisfy three criteria: (1) mother and fetus should be proved incompatible; (2) maternal antibodies to fetal antigen must be found; and (3) adsorption of maternal antibodies by fetal red cells should be demonstrated. No one of these tests alone is diagnostic.

From the point of view of the pediatrician, it is important to recall that edema, jaundice, hepatosplenomegaly, anemia, or hemorrhage may or may not be present in the critical period immediately after birth. Serologic data as outlined above are, therefore, of crucial importance.

Treatment includes exchange transfusions, simple transfusion, and certain general measures. It is emphasized that a trained team should be available for the care of these infants. Exchange transfusion should be given within the first four hours of life and should be repeated if indicated. Babies past seventy-two hours and mildly affected infants may be given simple transfusion merely to correct anemia.

From the viewpoint of the general practitioner, it should be kept in mind that anemia may persist for two or three months and that the sparing use of blood is the only means of correcting it. Frequently, neurologic sequelae do not become manifest until after two or three months.

This article has succeeded in presenting all of the essential information concerning erythroblastosis fetalis while at the same time retaining remarkable clarity and conciseness.—T. R. T.

COAGULATION


Venous blood from normal humans and from hemophiliacs was collected with glass and with silicone-coated syringes and distributed into both glass and silicone-coated coagulation tubes at 37 C. The samples were incubated with sodium citrate for varying times and
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calcium chloride was added, the coagulation time then being measured. Normal blood incubated with sodium citrate in glass tubes for periods up to 15 minutes had its coagulation time accelerated compared with the untreated whole blood. In siliconed tubes the acceleration was not seen, and hemophilic blood behaved less uniformly than normal human blood.

The results are taken to show that normal blood plasma contains a soluble precursor of the thromboplastin complex which in contact with glass at calcium ion concentration as low as $10^{-4}$ M. becomes activated. This seems to be the first step in the chain of the clotting process. No breakdown of platelets occurs in this phase. Possibly the glass surface acts as a kinase, activating prothromboplastin to thromboplastin.—R.H.G.


A one-stage prothrombin time estimation was carried out with Russell-viper venom as a source of thromboplastin in eight persons after an ordinary ward diet containing 12 to 30 Gm. of fat, five patients after a breakfast containing 65 Gm. of fat and six persons after a meal containing 85 Gm. of fat. There was a marked increase in the prothrombin times at the height of the lipemia in the second and third groups.

The blood clotting time was then measured in silicon-coated tubes after an ordinary ward diet and after a meal containing 80 to 85 Gm. of fat. An increase of clotting time occurred where there was macroscopic lipemia after the meal.

The authors consider the possibility that lipemia, by leading to increased coagulability, produces fibrin deposits which are incorporated in the arterial wall and lead to atherosclerosis.—R.H.G.


The authors recently reported that the clotting time of whole blood added to a suboptimal concentration of sodium oxalate, or particularly sodium citrate, varied synchronously with the respective prothrombin level.

This study was undertaken in order to investigate the effect of a variable single dose of heparin upon the clotting time of venous blood added to a suboptimal concentration of sodium citrate.—T.R.T.


It has become evident that the conversion of prothrombin to thrombin does not occur merely with the aid of thromboplastin and calcium. In addition to Owren's factor V, workers have shown the existence of another factor which influences this conversion.

In this report the term labile factor (L.F.) is used for Owren's factor V and the term stable factor (S.F.) for the more recently discovered accelerator. These terms define resistance to storage. It is generally agreed that L.F. is the same as proacelerin, plasma accelerator globulin, and prothrombin accelerator, in addition to factor V. S.P. is a synonym for serum prothrombin conversion accelerator (SPCA), factor VII, co-thromboplastin, and convertin. Owren's parahemophilia is due to L.F. deficiency.

The purpose of the study reported here is well described by the title.

Although several cases of parahemophilia have been reported, only three detailed published reports of S.F. deficiency have been made.

The question whether L.F. or S.F. act as accelerators or stoichiometrically is not settled, but additional information is added. A deficiency of S.F. resulted in delayed con-
version of prothrombin, but the final yield of thrombin was normal if sufficient time was allowed for complete conversion. This was interpreted to mean that prothrombin conversion was defective in respect to time and not in respect to quantity. Also, the consistent effectiveness of S.F. contained in normal serum even several days after spontaneous coagulation suggested that S.F. was used to a small extent, if at all, during clotting. These facts strongly suggest that S.F. is a true accelerator (or catalyst) of prothrombin conversion.

This report confirms the familial incidence of a hemorrhagic diathesis due to deficiency of S.F. and it is suggested that cases of idiopathic hypoprothrombinemia should be re-evaluated in order to determine possible deficiencies in S.F. or L.F.

It is also stated that commercial thrombin contains enough S.F. as a contaminant to correct the delayed prothrombin conversion in this case.—T.R.T.


This brief presentation includes the author's concept of the coagulation defect in hemophilia and many practical points of interest to the internist in the diagnosis and management of this disease.—H.W.B.

PLATELETS and PLATELET DISEASE


In contrast to the popular conception that platelets are fragile cells, the author introduces this report with the statement that they are hardy and that they can be preserved for a period of time far in excess of either red cells or white cells. This has been accomplished by application of knowledge concerning nonwettable surfaces.

Platelets used in these experiments were separated from fresh donor blood which had been passed over nonwettable surfaces. Anticoagulation was effected either by use of cation exchange resin or by standard ACD solution in plastic bags. Isolation of platelets was then done by any of three methods: (1) elution from the resin beads; (2) concentration of platelets from resin-plasma by falling film centrifuge; (3) concentration from ACD plasma after preliminary spontaneous red cell sedimentation. Blood was chilled promptly after leaving the donor's vein, by use of a heat exchange column at 4 C. Platelets were found to survive in many different media. Simple saline preserved morphology for one to two weeks. Usually they retained better morphology in a protein-containing media and one which was hypertonic. Gelatin gave good results as a colloid, at concentrations of 1.5 to 2 per cent. Sodium acetate was added, 0.2 Gm. per 100 ml., to prevent clumping. Forty ml. of final solution was used for the platelets derived from 500 ml. of blood. The composition of the media was as follows: glucose 5.0 Gm., NaCl 0.85 Gm., sodium acetate 0.2 Gm., sterile gelatin 2.0 Gm. (all per 100 ml. of solution).

The viability of platelets can be assayed only by morphologic, physiologic, or survival after transfusion characteristics. These factors were studied.

Normal morphology is exhibited longest in platelets originally collected into plastic bags containing ACD, and next longest in those from resin-plasma. The normal morphology under phase microscopy shows many tenuous filaments.

No apparent correlation exists between morphology and function. Studies with a two-stage prothrombin conversion system indicated that platelets alone would convert prothrombin to thrombin. This ability was greatly reduced if platelets were carefully washed three times in saline before preservation, so that contaminating plasma may have been responsible for this phenomenon.

Clot retraction was studied in a few instances, and there was always marked reduction in the ability of the platelets to fulfill this function.

Three patients were given transfusions of preserved platelets, with good evidence that bleeding tendencies due to thrombocytopenia were temporarily corrected.

The evidence is that the respiratory rate of platelets is 1/100 or less that of leukocytes.

—T.R.T.
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Thrombocytopenic purpura occasionally follows ingestion of the hypnotic Sedormid (allylisopropylacetylurea). One previously described in vitro test for sensitivity to the drug is to measure clot retraction of whole blood or plasma in the presence of Sedormid. If the test is positive, clot retraction is reduced.

Of six such patients this test was positive in two. Patch tests were negative in all, and even the administration of test doses of Sedormid to two patients did not produce further purpura.

The author considers that sensitivity to Sedormid may be of short duration and that in vitro tests should not be delayed but should be carried out at the height of the purpura.

—R.H.G.

ANNOUNCEMENT

A few changes may be noted in our Editorial Board. Dr. Leon O. Jacobson of Chicago has been elected an Associate Editor, and Lt. Col. William H. Crosby of the Army Medical College in Washington, D. C. and Dr. Richard H. Vilter of the University of Cincinnati Medical School have been elected Contributing Editors. All of these men are well-known for their hematologic investigations, and their specialized knowledge will be of great value in the review of manuscripts submitted to the Journal. It is a very unusual paper indeed that does not receive some very valuable constructive criticism at the hands of the various referee editors. These are recruited not only from the ranks of the Editorial Board, but from other sources as well. We should like to take the present opportunity to thank these “outside” referees for their unselfish and anonymous efforts. During 1953, we have had invaluable assistance from Drs. Joseph Beard, Lawrence Berman, John Bittner, Roger Crafts, Lloyd Craver, Charles W. Emerson, William H. Fishman, Malcolm T. Hargraves, R. G. Maefarlane, Martin Rosenthal, Milton Sacks, Karl Singer, Cyrus Sturgis, I. Snapper, Richard Wagner, and Abraham White.