

ABSTRACTS

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ABSTRACTERS

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ANEMIA

L'ANÉMIE DES PRÉMATURÉS, SON TRAITEMENT PRÉVENTIF PAR LES TRANSFUSIONS DE SANG PRÉCOCES ET RÉPÉTÉES (ANEMIA OF THE PREMATURE INFANTS: ITS TREATMENT WITH REPEATED BLOOD TRANSFUSIONS). *A. Rossier and L. Poliron.* From the Centre des Prématurés de l'École de Puériculture. Paris, France. *Arch. franc. pédiat.* 9: 113-139, 1952.

Hematologic studies of the blood of each premature infant were made from birth to the end of the first year. Although almost normal at birth, the number, size of red cells and the hemoglobin concentration decreased until the third or fourth month. The anemia, which was first isochromic and macrocytic, may later on become hypochromic and microcytic.

The role of the superoxygenation in the incubator is discussed among other factors of anemia in the premature. It is suggested that the main cause is the impossibility for the infant to increase its hemopoietic capacities as fast as its growth.

A new therapeutic approach is proposed, using small repeated blood transfusions. Two series of prematures were compared: 120 nontransfused against 180 transfused. The results of the treatment as reported are very good not only as concerns the anemia, but also on the general state and growth.—*J. P. S.*

ACQUIRED HEMOLYTIC ANEMIA AS THE PRESENTING SYNDROME OF LUPUS ERYTHEMATOSUS DISSEMINATUS. *E. L. Dubois.* From the Department of Medicine of the University of Southern California, School of Medicine, and the Los Angeles County Hospital, Los Angeles, Calif. *Am. J. Med.* 12: 197-204, 1952.

Three patients with disseminated lupus erythematosus who initially presented a picture of acquired hemolytic anemia are discussed. A positive Coombs test was obtained in each case. Splenectomy, performed in 2 of the patients, failed to affect the hemolysis.

Certain blood abnormalities in lupus (anemia, leukopenia, thrombocytopenia) are not uncommon but reports of the occurrence of hemolytic anemia have been few.

Comment is made on the possibility that the hematologic disorders of lupus might be attributed to "hypersplenism." At the present time, however, there does not appear to be sufficient evidence to support the author's concept.—*H. W. B.*

HEREDITARY SPHEROCYTOSIS (CONGENITAL HEMOLYTIC JAUNDICE): PATHOGENESIS OF THE "HEMOLYTIC" CRISIS. *By J. D. Battle, Jr.* From the Cleveland Clinic Foundation, Cleveland, Ohio. *Am. J. M. Sc.* 224: 82-92, 1952.

In 1948, Owren reported a study of 6 patients in one family who had congenital hemolytic jaundice. In this he advanced the belief that the "hemolytic" crises of this disease are in reality "aplastic crises" due to transient aplasia of erythropoiesis with maturation arrest of granulopoiesis. Other workers found evidence for abnormal isoantibodies or increased fecal urobilinogen. These indicated that perhaps both "aplasia" and hemolysis play a part in the crisis.

The author reports on his observations of 3 brothers studied during crisis.

The initial blood studies showed profound anemia, reticulocytopenia, hypocellular marrow with decrease in late erythroblasts. There was slight granulocytopenia in the blood. Only one platelet count is recorded during crisis, and it was 450,000. There was no leukopenia which suggests a rise in lymphocytes as well as a fall in granulocytes.

After such an initial picture during crisis, there was a spontaneous rise in reticulocytes within a few days, with resumption of normal marrow activity.

The authors state that in view of this, splenectomy should be deferred until the crisis has passed.—*T. R. T., Jr.*

VITAMIN B₁₂ and FOLINIC ACID

TREATMENT OF SPRUE WITH FOLINIC ACID: REPORT OF NINE CASES. *C. A. Romero, R. Viscarrondo and R. Rodriguez-Molina.* From the Medical Service, Veterans Administration Center, San Juan, Puerto Rico. *Am. J. M. Sc.* 224: 9-22, 1952.

The authors report the results of a well done clinical study concerning the effects of folic acid (citrovorum factor) on 9 cases of well established sprue. All of the patients had macrocytic anemia with less than 2.5 million red cells per cu. mm. and a megaloblastic bone marrow as well as glossitis, weight loss, diarrhea and weakness.

Folinic acid was administered intramuscularly in doses of 100 to 400 units of folic acid per day for 12 days to 3 patients (one unit is stated to equal approximately 1 μ g. of pure citrovorum factor). All exhibited inadequate response both clinically and hematologically.

Six other patients received 1000 units for 12 days. The clinical response was rapid and adequate. The hematologic response was submaximal in 1 patient.

One patient exhibited a marked eosinophilic response to folic acid, but there were no other signs or symptoms of drug sensitivity.

The authors conclude that folic acid is qualitatively as effective as folic acid in the treatment of sprue. Weight by weight folic acid is ten to fifteen times more effective than folic acid in the treatment of this disease.—*T. R. T., Jr.*

OBSERVATIONS ON THE ETIOLOGIC RELATIONSHIP OF ACHYLIA GASTRICA TO PERNICIOUS ANEMIA. XIV. INTRINSIC FACTOR ACTIVITY OF DESSICATED AND DEFATTED HUMAN FUNDUS, DUODENUM, AND JEJUNUM. *E. Landboe-Christensen, L. Berk and W. Castle.* From the Thorndike Memorial Laboratory, Boston City Hospital, Boston, Mass. *Am. J. M. Sc.* 224: 1-8, 1952.

Although it had been demonstrated that an anti-anemic effect follows the administration of hog stomach, duodenum, ileum and colon, the evidence at hand indicated that in man no extragastric sources of intrinsic factor exist.

Results obtained with material from the human stomach have demonstrated a significant hematopoietic activity of preparations of desiccated and defatted human fundus and moderate activity of similar preparations of human pylorus.

Since no data existed for human duodenum or the remainder of the small intestine, preparations were made from human fundus, pylorus, Brunner gland (containing region of the duodenum) and proximal jejunum. The hematopoietic activity of these preparations was studied in 4 patients with Addisonian pernicious anemia either in relapse or without previous treatment.

The duodenum preparation caused a moderate response in two patients. The jejunum preparation caused no response in 2 patients, in each of whom subsequent treatment with the fundus preparation caused a definite hematopoietic response.

Beef muscle (which contains vitamin B₁₂) was added to each of the preparations before desiccation and defatting in order to make constant the amount of extrinsic factor. The amount added was concluded to contain an amount of vitamin B₁₂ which would be ineffective in the absence of intrinsic factor, and the positive results obtained with the fundus and duodenum preparations are therefore believed to be due to the presence of intrinsic factor.—*T. R. T., Jr.*

IRON METABOLISM

PLASMA IRON: NORMAL VALUES; RESPONSE FOLLOWING MEDICATION. *W. M. Fowler and A. P. Barer.* From the Dept. of Internal Medicine, College of Medicine, State University of Iowa, Iowa City, Iowa. *Am. J. M. Sc.* 223: 633-641, 1952.

The authors report the results of studies on plasma iron in normal subjects, in patients with achlorhydria, and in patients receiving iron in the form of (1) iron and ammonium citrates, (2) colloidal iron or "Ferropol," (3) ferrous sulfate.

The range of normal values from 20 to 265 $\mu\text{g.}$ per 100 cc. (The authors state "per 100 cc. of blood," but it is assumed that serum was the word intended.) This is a surprisingly large range, and exceeds that found by other workers. The reviewer can hardly avoid questioning this range, although the average value is in excellent agreement with reported data.

There was no significant difference in the plasma iron of 10 patients with achlorhydria from that of normals.

The daily variation was determined in 20 subjects and concluded to be not significant.

The plasma iron levels in 20 patients receiving iron and ammonium citrates, in 21 patients receiving Ferropol, and in 25 patients receiving ferrous sulfate were compared at 4 and 6 hours after oral administration of Gr. XV of each of these preparations. The amount of increase at 6 hours was (in the order given): approximately 67 $\mu\text{g.}$ per 100 cc., approximately 75 $\mu\text{g.}$ per 100 cc. and approximately 37 $\mu\text{g.}$ per 100 cc. It is of interest that the variations in the control group were about equal to the differences between the different iron preparations.

No gastro-intestinal disturbance was encountered from the use of Ferropol.

It is concluded that the response to Ferropol is as good as that obtained with other iron preparations.—*T. R. T., Jr.*

IRON ABSORPTION BY WOMEN: COMPARISON OF THREE FERROUS SALTS. *M. R. Gram and R. M. Leverton.* From the Human Nutrition Research Laboratory, Agricultural Experiment Station, Lincoln, Neb. *J. Lab. & Clin. Med.* 39: 871-873, 1952.

For a period of four weeks ferrous gluconate was given daily to 27 normal women, ferrous lactate to 29 and ferrous sulfate to 27. The doses in the order given were 99 mg., 102 mg. and 101 mg. per day.

Complete fecal collections were made during the third and fourth weeks of medication and hemoglobin determinations in duplicate were made for two consecutive days before medication. Weekly thereafter the iron content of the stools was carefully measured.

The mean daily iron absorption given ferrous gluconate was 9 mg., ferrous lactate 13 mg. and ferrous sulfate 11 mg. There was no significant difference between the groups. The standard deviations were 18.9, 13.2 and 10.0.

There was no change in hemoglobin values during the period of medication.—*T. R. T., Jr.*

BLOOD COAGULATION and HEMORRHAGIC DISEASE

THROMBOTIC THROMBOCYTOPENIC PURPURA. *B. R. Gendel, J. M. Young and A. P. Kraus.* From the General Medicine and Hematology Section of the Medical Service and the Laboratory Service, Veterans Administration Medical Teaching Group, Kennedy Hospital, Memphis, Tenn. *Am. J. Med.* 13: 3-11, 1952.

The authors add 2 cases to the small but recently expanding group of patients with thrombotic thrombocytopenic purpura reported in the literature. One of their patients showed the characteristic clinical picture of hemolytic anemia, thrombocytopenic purpura and transitory focal neurologic signs. The other, however, failed to exhibit hemorrhagic manifestations and a thrombocytopenia of significance. The clinical course suggested instead disseminated lupus erythematosus and at autopsy a nonbacterial verrucous endocarditis was found. L.E. cells were not demonstrated, the microscopic findings of lupus were lacking, and the discovery of the typical vascular lesions of thrombotic thrombocytopenic purpura made the diagnosis clear only after death. This case brings up again the

possibility of a relationship between thrombotic thrombocytopenic purpura and disseminated lupus.

The various manifestations of this disease are reviewed and many of the controversial aspects of its pathogenesis discussed with reference to the findings in these 2 cases.—*H. W. B.*

LA PROCONVERTINE (PROCONVERTIN) *P. A. Owren*. From the Rikshospitalet, Oslo, Norway. *Rev. d'hémat.* 7: 147-155, 1952.

LE FACTEUR VII. SA FONCTION DANS LA COAGULATION. SON IMPORTANCE CLINIQUE. (FACTOR VII, ITS FUNCTION IN THE COAGULATION, ITS CLINICAL IMPORTANCE). *F. Koller, A. Loeliger and F. Duckert*. From la clinique Médicale de l'Université de Zurich, Switzerland. *Rev. d'hémat.* 7: 156-167, 1952.

AC-GLOBULINE ET SPCA: DEUX FACTEURS PLASMATIQUES DE LA CONVERSION DE LA PROTHROMBINE. ÉTUDE ET REVUE CLINIQUES ET BIOLOGIQUES. (AC-GLOBULIN AND SPCA, TWO PLASMATIC FACTORS OF THE PROTHROMBIN CONVERSION. CLINICAL AND BIOLOGICAL STUDIES). *B. Alexander*. From the Yamins Research Laboratory, Beth Israel Hospital, and the departments of Medicine, Harvard Medical School, Boston, Mass. *Rev. d'hémat.* 7: 168-228, 1952.

These three studies are gathered in the second special issue of the *Revue d'Hématologie* for 1952, devoted to blood coagulation problems. The authors of each article agree on the similarity between the factors they have independently described.

Proconvertin of Owren, Factor VII of Koller, SPCA of Alexander thus seem to be a single factor. Differences arise about the best methods for testing this new factor and about its function.

For Koller and Alexander it is an accelerator of the prothrombin conversion, but for Owren it is only a converting factor, which is in an inactive form in the plasma, and activated by thromboplastin into active convertin.—*J. P. S.*

THE EFFECT OF QUANTITATIVE VARIATIONS OF ANTICOAGULANT SOLUTIONS UPON PROTHROMBIN TIME. *B. W. Volk and S. Losner*. From the Division of Laboratories, Jewish Sanitarium and Hospital for Chronic Diseases, Brooklyn, N. Y. *Am. J. M. Sc.* 224: 27-33, 1952.

In the determination of prothrombin time, calcium interacts with the anticoagulant (sodium oxalate or sodium citrate) at the moment of addition of calcium chloride. A relative excess of anticoagulant would therefore have to exert an influence upon the required concentration of calcium.

In order to examine this hypothesis the authors studied the effect of concentration of anticoagulant solution upon prothrombin time of normal plasma as well as the effect of concentration of anticoagulant solution upon prothrombin time of hypoprothrombinemic plasma.

Their results indicate that prothrombin times of normal plasma are influenced by the concentration of the anticoagulant solution. If the "optimum prothrombin time" is defined as the shortest prothrombin time obtainable by using varying strengths of calcium chloride solution then it is shown that as the concentration of anticoagulant rises the optimum prothrombin time increases.

In the studies of hypoprothrombinemic blood, it was observed: (1) that less anticoagulant was required to keep the whole blood from clotting; (2) the optimum prothrombin time decreased correspondingly with a lower molar concentration of anticoagulant solution, and the magnitude of this reduction was not related to the degree of hypoprothrombinemia.

Thus it can be concluded that in the determination of one stage prothrombin not only is the concentration of calcium important, but equally important is the concentration of anticoagulant. Inaccurate measurement, particularly a reduction of the quantity of anticoagulant solution, may result in a false shortening of the prothrombin time in hypoprothrombinemic blood.—*T. R. T., Jr.*

A CRITICAL EVALUATION OF THE ANTITHROMBIN TEST FOR VENOUS THROMBOSIS. *J. McLachlin, R. Paul and J. C. Paterson.* From Westminster Hospital, Department of Veterans' Affairs, and from the Departments of Biochemistry and Medical Research, University of Western Ontario, London, Canada. *Surg., Gynec. & Obst.* 94: 297-301, 1952.

A decrease in blood antithrombin levels in patients who developed clinical signs and symptoms of thromboembolism has been reported by several investigators. In this study, using the test of Kay and Ochsner (*Surgery* 28: 24, 1950), serial antithrombin determinations in seriously ill patients were compared with the presence or absence of venous thrombi, revealed by a complete postmortem dissection of the lower extremities, in the 19 patients who came to autopsy. No correlation was found between the results of this test and the autopsy findings. In fact, the patients with definite venous thrombi almost always had had a "safe" antithrombin level during life. The authors, therefore, do not recommend this procedure for the prediction or diagnosis of venous thrombosis.

While the validity of this method of measurement might certainly be challenged, there is as yet no evidence that any other method of determining antithrombin will accurately reveal a predisposition to thromboembolism.—*H. W. B.*

STUDIES ON PLATELETS. V. OBSERVATIONS ON THE REMOVAL BY THE PULMONARY CIRCULATION OF PLATELETS INJECTED INTO PATIENTS WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA. *M. Stefanini, J. B. Chatterjea, and W. Dameshek.* From the Joseph H. Pratt Hospital, Boston, Mass. *J. Lab. & Clin. Med.* 39: 865-870, 1952.

Two patients with idiopathic thrombocytopenic purpura (ITP) were given direct transfusions of polycythemic blood into an antecubital vein. This caused a rise in platelet count (1) from 34,700 to 237,800 in one case and (2) from 18,000 to 169,200 in another case. These samples were taken from the opposite antecubital vein.

Arterial samples were taken simultaneously from the carotid artery. There was no significant difference between venous and arterial platelet counts.

There was a drop in platelet count of about 5,000 per minute which, if this is caused by removal in the lung, is too small to permit measurement between arterial and venous counts of this magnitude.

Thus the authors conclude that although this evidence suggests that there is no precipitous removal of platelets by the lung, further studies must be undertaken before such removal can be proved or disproved.—*T. R. T., Jr.*

NEOPLASTIC and COLLAGEN DISEASE

THE EFFECT OF CORTISONE IN HODGKIN'S DISEASE. *B. Straus, A. S. Jacobson, S. A. Berson, T. C. Bernstein, R. S. Fadem and R. S. Yalow.* From the Medical Service and Radioisotope Unit of the Veterans Administration Hospital, Bronx, N. Y. *Am. J. Med.* 12: 170-189, 1952.

Observations made on 10 patients with rapidly progressive Hodgkin's disease treated with cortisone are reported in detail. In no instance was there a remission comparable to that usually obtained with nitrogen mustard or x-ray therapy. Seven patients exhibited some clinical improvement but this was of a transient nature and limited almost entirely to a reduction in fever, pain, anorexia and sedimentation rate. Lymph node regression was noted in only 1 patient. The addition of nitrogen mustard therapy prior to the termination of a second course of cortisone in 6 patients produced no observable additive effect.

Rather numerous collateral studies (total body potassium, plasma sodium and potassium, radioiodine uptake by the thyroid gland, tissue culture studies, etc.) were made. Of these the serial bone marrow observations were perhaps of most interest. All patients, including those with hypoplastic marrows, showed stimulation of marrow elements and a marked increase in cellularity. While the marrow changes were not always reflected in the peripheral blood, it was pointed out that few transfusions were necessary in this group following cortisone therapy. Blood eosinophilia (1 patient) was unaffected by cortisone.

From this report and the observations of others it would appear that cortisone has a very limited use in the treatment of Hodgkin's disease.—*H. W. B.*

SOME SUPRAVITAL OBSERVATIONS ON THE "L.E." PHENOMENON. *R. J. Rohn and W. H. Bond.* From the Department of Experimental Medicine, Division of Hematology, Indiana University Medical Center, Indianapolis, Ind. *Am. J. Med.* 12: 422-432, 1952.

The authors have reviewed the current literature on the L.E. cell phenomenon and pointed out the lack of agreement concerning the derivation of the L.E. cell inclusion body and the type of leukocyte capable of phagocytic activity in L.E. cell formation. Using the supravital technics routinely employed in their laboratory (described in detail), interesting observations were made on the formation of the L.E. cell in the peripheral blood and bone marrow of 5 patients with acute disseminated lupus erythematosus. In these cases the L.E. cell inclusion body was invariably a mature autolyzed polymorphonuclear neutrophil and the phagocytic cell a mature polymorphonuclear neutrophil, eosinophil or basophil with the neutrophilic leukocyte predominating. Bone marrow examination was considered a more reliable means of demonstrating the L.E. phenomenon than was the utilization of peripheral blood.

The supravital technic offers a direct method of L.E. cell demonstration and has the obvious advantage of more accurate cell identification by virtue of the opportunity afforded for following an individual cell throughout the entire phenomenon. Unless supravital technics are employed frequently in a laboratory by trained observers, however, this method would hardly seem practical for diagnosis of the occasional case of lupus erythematosus seen in most hospitals.

While there is no reason to doubt the validity of these observations, this series of patients is too small to definitely exclude the possibility that cells other than those noted by these investigators can, and under certain conditions do, participate in the L.E. phenomenon.—*H. W. B.*

BLOOD TRANSFUSION

EFFECTS AND CLINICAL SIGNIFICANCE OF BACTERIAL CONTAMINANTS IN TRANSFUSED BLOOD. *A. I. Braude, J. P. Sanford, J. E. Bartlett and O. T. Mallery, Jr.* From the Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, Mich. *J. Lab. & Clin. Med.* 39: 902-916, 1952.

Bacterial contaminants were isolated from 38 (2.24 per cent) of 1,697 pints of blood cultured before leaving the blood bank. Organisms most frequently isolated were nonpathogenic staphylococci.

The only febrile reaction among recipients of contaminated bloods was caused by very heavy growth of diphtheroids. No observable harm to the patient resulted.

The low rate of reaction was explained by: (1) the bactericidal or bacteriostatic action of about 50 per cent of the bloods, (2) the long lag phase preceding multiplication of bacteria in blood not possessing bactericidal or suppressive power, (3) infrequent growth of bacteria in the refrigerator and (4) small size of the bacterial inoculum.

The contaminants were inoculated into human blood in order to observe the changes created. Marked hemolysis, increased fragility and clotting due to consumption of citrate were frequently caused by gram negative bacteria but seldom by staphylococci.

When these same strains were inoculated into rabbits it was found that staphylococci and diphtheroids invariably produced fever but no harm. *A. aerogenes* was both pyrogenic and highly toxic and lethal.

It is concluded that harmful effects resulting from transfusion of contaminated blood probably occur clinically only under conditions which permit contamination of banked blood by gram negative bacteria in numbers large enough to shorten materially the lag phase and to overcome the bactericidal and suppressive actions.—*T. R. T., Jr.*