ABSTRACTS

JOSEPH F. ROSS, M.D., Editor

ABSTRACTERS

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ANEMIA and POLYCYTHEMIA


The clinical and pathologic findings in a sporadic case of Fanconi's syndrome are reported in detail. Prominent features of the disease in this patient, an 11 year old girl, were pancytopenia, generalized olive-brown pigmentation of the skin, congenital skeletal anomalies, microcephaly, mental retardation, microphthalmos and enlarged breasts without other signs of sexual maturity. The clinical course was characterized by numerous hospitalizations for blood transfusions, antibiotic therapy for recurrent and severe staphylococcal infections, and a splenectomy which was of no apparent benefit. Of interest was the development of leukocytosis with the multiple infections during the last year of life.—H.W.B.

THE ANEMIA OF RENAL INSUFFICIENCY AS INDUCED BY BILATERAL NEPHRECTOMY OF THE RABBIT: WITH EMPHASIS ON ITS HEMOLYTIC NATURE. E. E. Muirhead, F. Jones and A. Grellman. From the Department of Pathology, Southwestern Medical School of the University of Texas, Dallas, Texas. J. Lab. & Clin. Med. 39: 505-517, 1952.

Ten rabbits were subjected to bilateral nephrectomy, one kidney being removed and about one week later the second kidney was removed. Ten animals were subjected to the same sham operation to act as controls.

The BUN, NPN, hematocrit, plasma volume and red cell volume; bile pigment in feces, serum bilirubin; serum iron, iron binding capacity of serum, tissue iron; leukocyte, platelet and reticulocyte counts were all determined at intervals in both groups of animals.

The results indicated a rapidly developing anemia as measured by hematocrit and red cell volumes. There was no evidence of external blood loss. The serum bilirubin, stool bile pigments, serum iron and iron content of the spleen all increased.

Although 5 animals showed a normal or normoblastic marrow there was no reticulocytosis, and neither leukocytes nor platelets were decreased.

These studies are in agreement with the findings of other workers that in humans with depressed renal function and azotemia there is evidence for a hemolytic component which is responsible in whole or in part for the "anemia of uremia."—T. R. T., Jr.


In a case of kala-azar, the authors found increased total urobilinogen excretion, shortened survival time of transfused compatible red cells and hyperplasia of the bone marrow. Treatment with hydroxyurea resulted in considerable reduction in the size of the spleen, improvement of the blood picture and decrease of the urobilinogen output. The effect of chemotherapy is considered as a further proof of the hemolytic nature of the anemia.—C.M.
THE ORAL USE OF COMBINED VITAMIN B12 AND FOLIC ACID IN TROPICAL SPRUE. F. D. Rivas, F. H. Morales and L. M. Meyer. From the Department of Clinical Medicine, University of Puerto Rico, School of Medicine, San Juan, Puerto Rico and the Department of Medicine, Kings County Hospital, Brooklyn, N. Y. Ann. Int. Med. 36: 1076-1085, 1952.

The article begins with a brief review of several papers on the apparent dosage requirements of folic acid and vitamin B12 in cases of sprue and pernicious anemia. Some of the details are given of 6 cases of tropical sprue treated with 1.67 mg. of folic acid and 25 µg. of vitamin B12 by mouth daily. Although the authors consider the hematopoietic responses to have been optimal, 5 of the 6 cases had macrocytosis at the time of the final observation reported. One patient did not have a reticulocyte peak until 23 days of therapy and one not until 17 days of therapy. Furthermore, one patient had a red blood cell count of only 2.94 million per cu.mm. after 30 days of therapy. Their final conclusion does not seem warranted at the present time. ""... in tropical sprue as in pernicious anemia there is a deficiency of both folic acid and vitamin B12 and that the mechanism of absorption and utilization of these two substances is similar in both diseases."—P.F.W.


Pulmonary function studies utilizing some of the newer technics were carried out on 5 patients, believed to have polycythemia vera, before and after treatment with phlebotomy. Alterations in ventilation and gas exchange resulting in marked anoxia and respiratory center damage were observed in some instances. Since these changes were not reversible in all cases, the importance of early and adequate phlebotomy is stressed. On the basis of their findings the authors present the possibility that polycythemia vera may be a heterogeneous disease and that in some patients the polycythemia is a response to primary respiratory centre damage of unknown etiology.—H.W.B.

HEMOCHROMATOSIS


"Three patients with hemochromatosis treated by repeated phlebotomies have exhibited ability to mobilize the excess tissue iron, tremendous capacity to regenerate red blood cells and hemoglobin, pronounced subjective improvement, diminution in size of the liver, improvement in liver function and in carbohydrate metabolism, and considerable decrease in the concentration of iron in the liver as shown by repeated biopsy sections of the liver."—T.R.T., Jr.

LEUKEMIA

LEUKAEMIA IN CHILDREN. C. L. Rodgers, W. L. Donohue and C. E. Snelling. From The Hospital for Sick Children and the Departments of Pathology and Paediatrics, University of Toronto, Toronto, Ont. Canad. M. A. J. 65: 548-552, 1951.

The records of 148 children with leukemia seen prior to 1948 were analyzed for purposes of comparison with groups of leukemic children treated subsequently with the folic acid antagonists and with ACTH and cortisone (see articles in this same journal). Pertinent clinical and laboratory findings have been summarized briefly. Emphasis is laid on duration of life and, for practical purposes, the group is classified according to the acuteness of the disease. Thus, in this series, 139 patients with acute leukemia had an average survival of 2.9 months from the onset of symptoms; 11 "subacute" cases survived between 9 and 24 months with an average duration of 12.4 months; and 2 chronic cases, both granulocytic, lived 50 and 53 months respectively (date of death unknown in 6 cases). There was no evidence that the various forms of treatment employed (blood transfusions and in a few in-
stances radiation, urethane and pent-nucleotide) effectively prolonged the life of any of these patients.

A word of caution is injected regarding the evaluation of any new specific therapy without taking into consideration that small group of patients, usually those with normal or low total white cell counts, who fall into the classification of so-called subacute leukemia.—H.W.B.

**Folic Acid Antagonists in the Treatment of Leukaemia in Children.** B. Laski, J. M. M. Darre, C. E. Snelling and W. L. Donohue. From The Hospital for Sick Children and the Departments of Paediatrics and Pathology, the University of Toronto, Toronto, Ont. Canad. M. A. J. 65: 556-560, 1951.

Fifty-three children with leukemia were treated with the folic acid antagonists, aminopterin and a-methopterin. Although in 16 of these patients the therapy was used either prior to or subsequent to treatment with ACTH or cortisone, response to treatment was evaluated here only on the basis of the patient's reaction to the folic acid antagonist. Of interest, however, was the lack of correlation between a patient's response to the two types of specific therapy. The development of a refractory state to one did not preclude the possibility of a remission with the other type of therapy.

Approximately 25 per cent of the group responded to the folic acid antagonists with a complete or partial remission. Despite the fact that remissions were usually short and subsequent relapses not as amenable to treatment, there was a definite prolongation of life in the responsive group compared to those who received no specific therapy (see previous paper in this journal).—H.W.B.


Complete but temporary remissions resulting in some prolongation of life occurred in approximately 50 per cent of 37 children with leukemia treated with ACTH and/or cortisone. The percentage of remissions was higher and the remissions more complete and obtained with fewer toxic effects than in a similar group of children treated with the folic acid antagonists (see article same journal). Yet, in view of the shortness of remissions and the comparatively small number responding to retreatment, it cannot be concluded that the steroid hormones offer more than the folic acid antagonists in the practical control of this disease.—H.W.B.


Nine patients with acute leukemia (predominantly adult) were treated with ACTH and/or cortisone. This constituted the only treatment in three of these patients whereas the others received supplementary transfusions and penicillin and in 4 cases, folic acid antagonists. Other than a transitory clinical improvement during the actual period of therapy, little benefit as shown by hematologic and autopsy changes or by prolongation of life could be attributed to the hormones alone.—H.W.B.


Twenty cases of acute leukemia in remission have been studied by various bone marrow punctures (sternal, iliac, vertebral, tibial). On 17 occasions the aspect of the marrow was the same, twice slightly different, and once completely different. In 15 cases before treatment there was one slight and marked disparity (between iliac and sternal marrow).
The authors draw the following conclusions: A single normal bone puncture, cannot rule out definitely acute leukemia, or affirm a complete remission. Possibility of disparity between marrow punctures seems to prove that acute leukemia may have a localized beginning.—J.P.S.


A case is reported of fatal reticuloendotheliosis in a 16 month old infant who, in addition to most of the more commonly reported findings, presented emphysema of the lungs, mediastinum and subcutaneous tissues; bone marrow cysts; and clinical and pathologic signs of meningeal involvement.—H.W.B.

BLOOD COAGULATION and HEMORRHAGIC DISEASE

HEMOPHILIA: CLINICAL AND LABORATORY OBSERVATIONS RELATIVE TO DIAGNOSIS AND INHERITANCE. A. J. Quick and C. V. Hussey. From the Department of Biochemistry, Marquette University School of Medicine, Milwaukee, Wis. Am. J. Med. Sc. 223: 401-413, 1952.

The authors state: “there is emerging a fairly general agreement concerning the broad fundamental facts” of the problem of coagulation: At least five primary agents are indispensable for the formation of thrombin. These are prothrombin, calcium, labile factor, thromboplastinogen, and a platelet constituent.

Labile factor is also known as factor V, Ac-globulin, and thromboplastin co-factor.

Thromboplastinogen is probably the same as the antihemophilic globulin of Minot et al. and the prothrombokinin of Lenggenhager.

Evidence is accumulating to show that these five basic factors react or interact stoichiometrically to form thrombin. A lack of any one decreases the amount of thrombin produced and if the reduction is sufficiently marked, defective hemostasis results.

In hemophilia, a lack of thromboplastinogen is now rather well established as the basic coagulation defect. This is measured by the prothrombin consumption test, which the authors describe. Also described is the “thromboplastinogen activity test,” in which heated rabbit brain extract is used (and apparently behaves like a platelet extract). Thus, hemophilia can be readily differentiated from thrombocytopenia or thrombasthenia.

In discussing the diagnosis of hemophilia it is pointed out that the triad of a bleeding tendency, a prolonged clotting time, and the hereditary pattern may not be reliable or specific. A normal clotting time does not exclude the diagnosis of hemophilia. However, the two tests listed above have given far more reliable results and the thromboplastinogen activity test promises to be the more sensitive and specific.

Finally, the authors demonstrate that the hemophilic defect appears to remain unchanged throughout the life of the individual, and indicate that within any given family (viz. siblings) there is a quantitative as well as a qualitative similarity.

This presents much of the available data in clear form.—T.R.T., Jr.


Three siblings with a hemorrhagic tendency are described. They are 3 of 10 siblings in a family whose family tree shows 6 others with a hemorrhagic tendency, 5 of whom died as a result of bleeding. The hereditary features of the condition are described and it is suggested that the bleeding tendency is inherited either through a recessive gene or through a dominant gene with poor penetrance.

The deficient factor in the coagulation mechanism of the patients studied is shown to be associated with prothrombin activation. The children of the affected individuals, though
without symptoms, are shown to have a mild coagulation defect of the same type. The data indicate that the plasma concentration of prothrombin is normal but that the labile factor of Quick (Ac-globulin of Seegers; factor V of Owren) is lacking.

Fresh plasma is effective in reducing the prothrombin time and in controlling bleeding. It is concluded that the deficient factor acts like a catalyst. No regular effect on the prothrombin time is noted following the administration of vitamin K, protamine sulfate, or aminophylline.—C.E.R.


The conclusions of the author are as follows: Prothrombin determinations alone do not give security. They need to be associated with a test of the overall coagulability of the blood (as the in vitro heparin tolerance test). The prothrombin level needs to be decreased until hypocoagulability is obtained. If, in spite of a decrease of the prothrombin below 10 per cent, the blood is still hypercoagulable, dicumarol therapy should be exchanged for heparin. This more accurate control affords the best guarantee against hemorrhage and guarantees against further thrombosis.—J.P.S.


In 30 cases of cyanotic cardiac malformations, a delayed Quick prothrombin time was observed. The increased globulin makes it difficult to evaluate the exact recalcification time of the plasma, but even with different calcium concentrations, it is impossible to bring back the Quick time to normal. Fibrinogen is often decreased but not sufficiently so, it is said, to interfere with the Quick prothrombin time. This delayed prothrombin time seems to explain certain hemorrhages following surgery of patients with congenital cardiac malformations.

These facts are very interesting, but the authors do not give proof that the delayed Quick time is really due to a prothrombin deficit. It would be necessary to exclude the deficit of other factors interfering with the Quick time (accelerators) and above all, since there is a decrease in fibrinogen, to study the lytic mechanism. Proteolytic activity is able to decrease the fibrinogen and the clotting factors at the same time. Both Fiehrer and Soulier as well as the authors, have observed a delayed Quick time in polycythemia vera which indicates that this is not peculiar to the cardiac hyperglobulinemia.—J.P.S.


The authors own summary is given: "Forty-two transfusions of polycythemic or normal blood without anticoagulant were given to thirty-five thrombocytopenic individuals by means of multiple silicone-coated syringes."

"Such transfusions were found to be effective in temporarily raising the platelet counts and in causing cessation of spontaneous bleeding in thrombocytopenic individuals."

"Transfused platelets remained in the circulation for five to six days in patients with bone marrow aplasia. This period was taken as the normal life span of transfused platelets in this study."

"Rapid destruction of transfused platelets occurred in acute thrombocytopenia and in thrombocytopenia with massive splenomegaly. In chronic idiopathic thrombocytopenia
platelet destruction also occurred but was less rapid. Transfused platelets survived normally in two cases of pancytopenia with normal bone marrow and in one case of acute leukemia."—T.R.T., Jr.


Dextran sulfates of different molecular weights and with differing numbers of sulfate groups per glucose unit, were prepared and the anticoagulant properties tested. Maximum anticoagulant activity was attained when the number of sulfate groups exceeds an average of 1.3 per glucose unit, whereas toxicity was determined by molecular weight.

Evidence is presented that may lead to the development of a useful anticoagulant drug. A discussion is presented of the present status of our knowledge concerning the chemical structure of heparin.—T.R.T., Jr.

**Contribution to the Pathogenesis of the Hemorrhagic Capillarotoxicosis (Henoch’s and Schoenlein’s Allergic Purpura).** J. Karpiček. From the State Hospital in Praha, Czechoslovakia. Časop. lék. česk. 90: 791, 1951.

A woman, age 59, suffering from asthma and hemorrhagic capillarotoxicosis died in a severe hemorrhagic attack. The autopsy revealed diffuse collagenous degeneration of the capillaries of the lungs with massive bleeding and glomerulonephritis with focal necrosis of the glomerular arterioles and wire-loop lesions. Chronic empyema of sphenoidal sinus was found to be the focus.—M.N.

**Technical Methods**


The authors describe a method for counting cell suspensions, (especially red cells) utilizing the bending phenomenon of light rays. Comparison with the counting chamber method showed an accuracy of the new method of 2 per cent. The whole process does not take more than two seconds and a single reading is sufficient. The same apparatus (construction of Fritz Hellige, Freiburg, Germany) also allows leukocyte counting and hemoglobin measurements.—C.M.


A study was made of the factors responsible for variations in the hematocrit, and correlations are presented for erythrocyte count and hematocrit. The article should be in the hands of all laboratory personnel.—T.R.T., Jr.


This is an extremely careful study, well reported. The technical methods employed are too detailed for review, but appear to be sound.

The conclusion is reached that “the error of the hematocrit reading, due to incomplete cell packing, is not in excess of 2 per cent for normal human blood spun at 2,080 g. for thirty minutes in Wintrobe hematocrit tubes.”

(The 2,080 g. was measured at the tip of the tubes. Many reports make this calculation based on measurements to the center of the packed red cell column.)—T.R.T., Jr.
Liver and Spleen Visualization by a Simple Roentgen Contrast Method. S. Zelman.

Following oral administration of Seidlitz powder and rectal introduction of air into the colon postero-anterior and left oblique x-ray pictures of the abdomen are made. By such a method sharp outlines of the spleen and liver may be obtained. This study revealed a poor correlation of clinical palpability with what apparently was actual enlargements of liver and spleen.—P.F.W.


Suitably absorbed serum containing weak albumin-agglutinating antibodies is freeze-dried and then made up to its original volume in 20 per cent bovine albumin. Sera treated in this way and used for preparing in tubes or on a slide as with saline agglutinating antibody, have been found satisfactory for routine rhesus grouping.—S.T.C.


The authors report the results of detailed experiments, indicating that if the full potential use of the antiglobulin test is to be realized, then serum should be considerably more potent than that which is now commercially available.—T.R.T., Jr.

Hemagglutinins and Hemolysins for Erythrocytes Sensitized with Tuberculin in Pulmonary Tuberculosis. W. H. Hall and R. E. Manion. From the Veterans Administration Hospital and the Department of Medicine, the Medical School, University of Minnesota, Minneapolis, Minn. J. Clin. Investigation 30: 1542-1546, 1951.

The results of 1,000 tests on serum of over 100 patients having active tuberculosis and a similar number of adults not having active tuberculosis indicate to the authors that neither the hemagglutinin test utilizing tuberculin-sensitized sheep cells nor the anti-hemolysin test are sufficiently reliable for widespread use in detecting the presence of active tuberculosis unless rigidly controlled by other accepted diagnostic criteria.—R.B.C.


It had been shown that the enzyme responsible for the depolymerization of thymonucleic acid is present in the serum of guinea pig, rabbit, mouse, and dog but not in man. This enzyme was named "desoxyribonuclease" by McCarty. The present study was carried out to determine whether the addition of magnesium ion to human serum would reveal any desoxyribonuclease activity and, if so, to study this activity in normal individuals and in patients with cancer and noncancerous disease. It showed that the addition of magnesium ion in a final optimal concentration of 0.003M to human serum leads to distinct and readily measurable desoxyribonuclease activity. The average value of this activity in a group of 50 patients with cancer was significantly lower than the average value in a group of 34 patients, of comparable age, with noncancerous disease. Both values were lower than that of a normal group.—R.B.C.
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IMMUNOHEMATOLOGY


The results of this study “indicate a general downward trend in agglutinability from twenty to sixty-five years of age associated with individual variation in the sensitivity of cells, not related to age.”—T.R.T., Jr.

SENSITIVITY OF SERUM ENZYME INHIBITORS TO A VARIETY OF CANCER CHEMOTHERAPEUTIC AGENTS. F. W. Ellis and P. M. West. From the Veterans Administration Hospital, Long Beach, Calif. and the School of Medicine, University of California at Los Angeles, Calif. J. Clin. Investigation 30: 547-557, 1951.

It has been shown that the serum concentration of proteolytic enzyme inhibitors is influenced by pathologic processes, including malignant disease. Two of these substances, chymotrypsin inhibitor and rennin inhibitor, are of value in following the course of certain malignant diseases under treatment with various chemotherapeutic agents. Usually the chymotrypsin inhibitor is maintained at 5 units or less per day and the rennin inhibitor titer is elevated, if a remission has taken place in the pathologic disease process. Representative cases of a variety of malignant processes are here studied. Data reported suggest that this method for following the effect of various agents in the therapy of malignant disease may possess practical value in following the course of neoplastic disease.—C.E.R.


By means of the phase contrast microscope, the authors demonstrate that sensitization of rabbits by typhoid-paratyphoid vaccination leads to a drop-like dark granulation in the plasma cells of the spleen. With the moment of the appearance of antibodies in plasma the described cell alterations decrease. The observed granules are similar to those found in multiple myeloma cells and are considered to be in connection with the production of a globulin (here, antibody) formation. ACTH and cortisone injected similarly with the re-vaccination did not show any change of the granule formation, but started 8 days before a marked decrease occurred.—C.M.

BLOOD DESTRUCTION IN THE POLYCYTHEMIA INDUCED BY HYPOXIA. K. A. Reissmann, W. L. Burkhardt and B. Hoelscher. From the Departments of Physiology and Internal Medicine, U.S.A.F. School of Aviation Medicine, Randolph Field, Texas. Blood 7: 337-349, 1952.

The mechanism of red cell destruction after production of polycythemia by exposure to reduced barometric pressure was studied in dogs. Animals were exposed to gradually decreased pressures in a decompression chamber until simulated altitudes of 20,000 ft. were obtained. For the study of total bile pigment excretion, bile fistulas connecting the gallbladder and the renal pelvis were surgically produced. Total circulating hemoglobin was determined by means of blood volume measurements with T 1824.

It was found that bile pigment excretion increases during the first weeks of exposure to hypoxia. On return to normal atmospheric pressures there was an early rise in bilirubin excretion and a later rise thought to reflect the destruction of those red cells rapidly formed in the second and third weeks of exposure to reduced pressure. It is concluded from these balance studies of hemoglobin and bilirubin that the major loss of red cells in the postaltitude period is due to suppression of normal erythropoiesis and that increases in bilirubin excretion following exposure are dependent only on the fact that, the life span of red cells being about 110 to 120 days, there will be such an increase at the end of the interval of 110 days, after the rapid formation of new cells in the second and third weeks.
BOOK REVIEW


Selye's large volume on Stress with its 8000 or so bibliographic references makes rather formidable and at times weary reading. For the most part, it is a compilation of reference upon reference culled from the author's reprint library, probably the world's finest. There is little in that opus to give one an impression of Selye's dynamic personality; the present volume goes far to make up for that deficiency. Aptly labeled a "story," it presents Selye in his own highly personal style, but from the wire recorder, giving a series of seven lectures on the Adaptation Syndrome. The resultant book of 225 pages, interspersed with the well known Selye diagrams, and interlarded with philosophical remarks on such matters as research, critics, tributes to co-workers, etc. is one of the most entertaining, yet withal most informative volumes it has been our pleasure to read. That it can be perused in the rarified and occasionally stressful atmospheres of high-speed plane travel is a tribute to the author's ability to impart his facts, speculations and enthusiasm so simply and well. One can actually hear the author give these lectures as he has done so abundantly and in so many languages throughout the Western world.

The subjects of Stress and the Adaptation Syndrome are developed historically beginning with the first glimmer of the idea, through the early experiments and the early nomenclature to the final rather complex data and diagrams representing the present status of the subject. One may disagree with Selye on various aspects of his hypotheses, but there can be no doubt that many of his ideas have proved extremely valuable, particularly in giving one a unified theory of the pathogenesis of such conditions as arthritis, peptic ulcer, periarteritis nodosa and the like. According to Selye, these are the end results of continued stress and the body's over-reaction to this phenomenon, mediated through the anterior pituitary and the adrenal cortex.

That it remained for others than Selye to introduce ACTH and cortisone into clinical practice is a little sad, although it must be conceded that in some ways, his work seemed to point in a direction away from the use of the steroid hormones as therapeutic agents. Meanwhile others, notably Kendall and Hench, were the first to show the remarkable effects of Compound E (cortisone) in arthritis. In any event, since that time, Selye's ideas have become extremely popular, and his every appearance at medical lectures is greeted by huge crowds and boundless enthusiasm. This little book, beautifully printed in large type with diagrams and marginal annotations, should become a classic. It deserves close reading by medical students, young and old.—William Dameshek.
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