ABSTRACTS

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ABSTRACTERS

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LEUKEMIA


The incidence of cutaneous manifestations during the course of leukemia is difficult to assess. Statistical records from hematologists do not include the numerous cases observed by dermatologists. Stated rates varying from one to ten per cent were artificially established. Those cutaneous manifestations raise problems of the greatest interest: presence in the skin of malignant reticulo-histiocytic proliferations (cutaneous reticuloses, fungous mycosis) possibly evolving towards leukemia (histio-leukemia, leukemia with monocytes) is demonstrative of the difficulty in discriminating these affections and determining exactly the starting point of the disease, whether in the skin, lymph-nodes or blood. In the present paper the authors describe the dermatologic aspects of cutaneous leukemia.—J.D.


Cutaneous lesions in leukemia are more frequent than appears from hematologic statistics, because they are chiefly observed by dermatologists. Most of these lesions, however, are suggestive of a diagnosis of hemoderma, such as erythroderma, infiltrations and tumors, but some of them are more banal, such as pruritus, eruptive erythemas, papules and vesicles. The dermatologic aspect is not always consistent with the histologic aspect. The infiltrated and tumorous lesions as well as most of the erythrodermal forms correspond to a leukemic infiltrate in the skin, but the other cutaneous manifestations may show no specific structure. Conversely, lesions that appear trivial may be histologically leukemic. A comparison of cells from histologic sections with cells from hemograms, myelograms and adenograms does not afford conclusive information. Much information is given by skin biopsies, but it is difficult, in the reticulo-histio-monocytic line, to discriminate a malignant-cell proliferation from a simple "reaction formula". There may be an association of obviously malignant cellular elements with histiomonoecytic pictures exclusively observed in the skin, blood, lymphnodes or bone marrow. A joint malignant proliferation of two types of cellular elements is difficult to ascertain. Thus it is impossible to ascribe a proper dermatologic aspect to such-and-such type of leukemia. No accurate classification can be established. It can only be stated that certain cutaneous forms are to be more frequently encountered in the course of lymphoid and monocytic, acute leukemias. What is the relationship of cutaneous leukemias to mycosis fungoides and malignant histiocytic reticulos? That is a nosologic and cyto-patho-genetic problem, which is not considered here by the authors.—J.D.
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CUTANEOUS, ACUTE LEUKEMIA WITH EROSIVE, PLURIOFICIAL ECTODERMATOSIS. A. Grana.

A case of acute leukemia with predominant cutaneous alterations was described in a 74 year old man. The skin alterations were characterized by: (1) erythematous infiltrative manifestations, resembling the plurifacial erosive ectodermatosis; (2) heliotrope color of the lesions; (3) deep infiltration into the muscular layers, as in dermatomyositis.—P.D.N.


This report discusses nine patients, most of whom were elderly, in whom chronic lymphocytic leukemia was present. In five of the patients, the disorder was asymptomatic and was found on routine blood counts; in four, lymph nodes were enlarged; in none of the nine were the presenting symptoms related to the leukemia. A few comments made by the author are unusual. Thus, he found myelocytes and normoblasts on the blood smears "from time to time", apparently in all the cases. The bone marrow, in addition to showing lymphocytosis of over 25 percent, showed "an increase in promyelocytic and myelocytic forms." Of interest is the observation in five cases that the lymph nodes showed no obvious leukemic changes when the peripheral blood and bone marrow pictures were already pathognomonic of chronic lymphatic leukemia. This finding is contrary to others in the literature which suggest that node biopsy is of diagnostic value in this disease.—S.E.

EARLY EXPERIENCE WITH p-(N,N-Di-2-chloroethyl)-AMINOPHENYLACETIC ACID (CB 1348), A NEW CHEMOTHERAPEUTIC AGENT EFFECTIVE IN THE TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA. S. J. Altman, A. Haul, G. E. Cartwright, and M. M. Wintrobe. From the Dept. of Internal Medicine, University of Utah College of Medicine, Salt Lake City, Utah. Cancer 9: 512-517, 1956.

Eight patients with chronic lymphocytic leukemia received 11 courses of therapy with CB 1348, a synthetic aromatic mustard related to the nitrogen mustards. The recommended dose was 0.1 mg/Kg/day, or about 4 to 9 mg per day; and was used for 25 to 80 days. Treatment was continued until the white count approached 10,000 and, except in one case, no maintenance therapy was employed. All the patients felt better with therapy. The blood showed reduction in leukocytes, chiefly because of a reduction of lymphocytes. Usually there was also a reduction in granulocytes, and in the single patient in whom maintenance regime was undertaken, the fall in granulocytes continued. There was no change in the red count or hemoglobin, and there was no particular change in the level of platelets. Splenomegaly was diminished in some (but not all patients), and lymphadenopathy was reduced in some (but not all) patients. CB 1348 is considered a good drug for the treatment of chronic lymphocytic leukemia.—S.E.

LEUKEMIA IN CHILDREN


The author emphasizes the pronounced liability of the bone marrow and the peripheral blood in children in response to acute and chronic infections, intoxications, hemorrhage and other disorders; and notes the difficulty of establishing a diagnosis of leukemia in certain children suspected of having the disorder. Repeated examination of blood and marrow is stressed, as well as proper evaluation of normal variations in the hemogram of children. A graph records 44 children suspected of having leukemia, but who turned out to have other disorders. Of these, 26 had acute infections (including infectious lymphocytosis, infectious mononucleosis, pertussis, and upper respiratory infections), 4 had chronic rheumatoid
The onset of acute or chronic leukemia may be characterized by a rheumatoid symptomatology, which represents a rather unusual and only recently described pattern of the disease. In nine cases of leukemia out of 74, all aged below 11, the first symptoms were characterized by articular pain, as happens in rheumatic fever, and often accompanied by pectoral angina. The differential diagnosis of these forms is discussed. — P.d.N.


The authors calculate that, on the basis of coincidence, Mongolism might occur together with leukemia in perhaps one child in 10,000,000. Their observation, therefore, of four such cases in a period of a year, and a fifth presented as an addendum to their paper, suggested that the coincidence of the two disorders could not be attributed to chance. Personal communications from other investigators confirmed that other cases have occurred, too many to attribute to chance. They therefore suggest that there may be an etiologic relationship between Mongolism and leukemia, at least in these cases: perhaps some “toxic” substance or, conceivably, a virus, acting on the fetus at the 6th to 9th week of pregnancy, and causing widespread damage to mesenchymal tissue in the process of development and differentiation. The cases presented include two with congenital leukemia, in one of whom leukemia was found only after a considerable search for it, because of the presence of Mongolism at birth. — S.E.


Four additional cases are reported of acute leukemia and Mongolism. Leukemia was diagnosed at ages 10, 4, 3 and 2 years; Mongolism had been noted earlier, at age 6 weeks to 16 months. The authors discuss the possibility that whatever stress is responsible for the development of Mongolism also affects not only the brain, heart and skeleton, which are involved in Mongolism, but also the hematopoietic system, so that leukemia ultimately develops. — S.E.


Twenty-one children with acute leukemia have been treated with prednisone and the response is analyzed according to the “criteria for evaluation of response to therapy of acute leukemia” of the Cancer Chemotherapy National Service Center. The patients responded with complete remissions in 8 instances, 8 others showed a clinical remission and 12 partial remissions occurred. The remissions were similar in duration to those observed with cortisone but were associated with less severe adverse side-effects. The earlier in the course of the disease the drug was used, the better the response. Previous therapy appeared to affect the response to prednisone adversely. — N.J.S.


The authors prefer to use steroids in the initial therapy of acute leukemia in most cases, and to use antimetabolites (6-mercaptopurine in adults, antifols in children) if the steroids fail to cause response within two weeks. This regime is based on their belief that most acute leukemias are “lymphocytic” in type. In acute granulocytic and monocytic leukemia they
first try antimetabolites, adding steroids if no remission occurs in two to three weeks. They report that 25 per cent of children with acute leukemia have a complete clinical and hematologic remission by these measures, and that another 25 to 40 per cent have a partial remission.—S.E.


This lecture briefly summarizes current chemotherapy of acute leukemia of children. The author distinguishes "emergency" treatment, which is used when the patient is critically ill; and "nonemergency" treatment, which is used in more chronic cases. The emergency regime includes the use of intravenous infusions of corticotropin, the oral use of hydrocortisone or prednisone, and the ancillary use of blood transfusions, antibiotics, sedatives, fluids and electrolytes. Following subsidence of the emergency, the basis of therapy is the use of antimetabolites: amethopterin, aminopterin and azaserine are recommended. In addition, psychologic management of patient and family is important.

The author compares his results with those previously reported when no treatment was used. Of 208 cases without treatment, 50 per cent were alive 3.9 months after diagnosis; and 10 per cent were alive 11 months after diagnosis. These figures were obtained from the literature. Of 174 cases seen at Memorial Center from June 1952 to March 1955, 50 per cent were alive after 12 months, and 10 per cent after 20 months.—S.E.

METABOLIC AND CYTOCHEMICAL CHANGES PRODUCED BY 6-MERCAPTOPURINE IN HUMAN ACUTE LEUKAEMIA. R. P. Heany and L. P. Eliel. From the Cancer Research Section, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma. Cancer 9: 252-261, 1956.

Metabolic studies were made in a 3 year old child with acute lymphoblastic leukemia during treatment with 6-mercaptopurine. The urine showed increased excretion of nitrogen, phosphorus and potassium in ratios approximating the content of these elements in the destroyed leukemic tissue. The nitrogen and phosphorus balance remained positive; therefore, it was concluded that there was continued anabolism of most nonleukemic protoplasm. That is, the anabolism of normal tissue is immune to 6-mercaptopurine, presumably because its metabolism is different from that of leukemic tissue. Cytotoxic studies were also made in this patient and in a second child with acute lymphoblastic leukemia. The whole-cell phosphorus fell, and there was a fall in nuclear nitrogen, phosphorus, and potassium. The conclusion was made that there was a decrease in the nucleic acids in the neoplastic tissue.—S.E.


Lyophilized platelet material (LPM) was administered to 10 patients with hemorrhagic phenomena associated with secondary thrombocytopenia, (leukemia, malignancy, aplastic anemia). Using the clotting time, thromboplastin-generation test, and prothrombin-consumption time only those patients were treated whose in vitro studies could be normalized by the addition of platelets. In 24 of 29 observations the LPM appeared responsible for correcting the prothrombin-consumption test. In only 5 of 10 patients did hemostasis result, however. The lyophilized platelet material administration was not associated with any thromboembolic phenomena and the material has been shown to retain the antihem, antifibrinolytic and thromboplastin-generating effects of normal, intact platelets. The possible sensitizing potential of the material is briefly referred to. These encouraging reports demand further experiments to define the practical effectiveness of this readily prepared and easily handled material which might be useful in management of thrombocytopenia.—N.J.S.
COAGULATION


By the technic of recalcified clotting time of oxalated plasma, small amounts of glass powder produced acceleration whether the glass was removed from the system prior to recalcification or allowed to remain. With large amounts of glass, further acceleration resulted only if the glass was allowed to remain. Two hours of contact gave no greater effect than 2 minutes, and the glass effect was similar at temperature ranges from 2 to 42 C. The method of plasma decalcification was immaterial except that plasmas prepared with ion-exchange resins were already activated and showed no further response on contact with glass. Washed platelets were unaffected in glass. However, clot-promoting activity was developed by glass in hemophilic plasma rendered free of proaccelerin, fibrinogen and the factors adsorbed on barium sulfate. No anticoagulant could be eluted from glass that had been exposed to plasma, and a specimen of glass did not lose its clot-promoting properties with exposure to successive plasma aliquots. It is suggested that glass affects a factor differing from those presently recognized. A possible effect on Hageman factor or on the initial formation of fibrin strands is also considered.—T.H.S.


By means of ultrasonic treatment, almost complete disruption can be achieved of platelets suspended in saline or in plasma. The clot-promoting and vasoconstrictor properties of the platelet fragments are retained and in some cases augmented, but the ability to promote clot retraction is destroyed. Hemophilic platelets behave normally. Ultrasonic energy produces deterioration of coagulant activity in rabbit-brain thromboplastin. It appears to reduce the AHG content of normal plasma and induce anticoagulant activity. Prothrombin, fibrinogen, serum accelerator activity, and thrombin are inconstantly affected or not at all.—T.H.S.

OCCURRENCE AND MODE OF ACTION OF ENDOGENOUS CIRCULATING ANTICOAGULANTS. M. Verstraete and J. Vandenbrouck. From the Physiopathology Laboratory, Department of Medicine, University of Louvain, Belgium. J. Lab. & Clin. Med. 48: 673-689, 1956.

Two patients are reported whose blood displayed striking anticoagulant activity. One of these was a patient with established AHG deficiency in whom the anticoagulant developed following transfusions but spontaneously disappeared; the other patient had no previous hemorrhagic history. In plasma specimens from both patients there was interference with normal recalcified clotting time and whole blood prothrombin consumption when 10 per cent or more of the abnormal plasma was used; and 5 per cent was sufficient to cause impairment of normal reagents in the thromboplastin generation test. The anticoagulants were effective in the thromboplastin generation test only when present in the initial reacting mixture containing AHG, serum and calcium ion, but not if added after these reagents were allowed to pre-incubate (i.e., form “product I”). They displayed mutual neutralization with Cohn’s fraction I, but not with PTC concentrate. They were less potent in serum, were storage-stable in the frozen state, were partially inactivated at 70 C., were not adsorbed on barium sulfate or removed by dialysis. They moved as gamma globulin with paper electrophoresis. Patients’ sera gave positive precipitin tests against a variety of reagents containing AHG, but failed to react with specimens in which the AHG had been inactivated. The authors feel that their data support the view favoring identification of the anticoagulants as antibodies.—T.H.S.

Technics are described for the purification of the reagent in human plasma that is activated by staphylocoagulase. The basic steps involve separation by column chromatography and subsequent precipitation with ammonium sulfate. The coagulase-reacting factor (CRF) so obtained migrates between beta and gamma globulin on zone electrophoresis and gives two peaks in the ultracentrifuge. Human prothrombin purified by the Seegers method was activated by staphylocoagulase. However, it migrated between alpha-2 and beta globulin and in the ultracentrifuge differed from CRF. When this prothrombin was treated with calcium ion and platelet factor 3, prothrombin activity disappeared but CRF persisted. The authors suggest that CRF is not prothrombin itself, but probably a derived protein analogous to the autoproteins.-T.H.S.


Fibrinolytic and fibrinogenolytic properties were demonstrated in a number of snake venoms and proteolytic enzymes from other sources. The fibrinolytic activity of snake venoms was found to be less susceptible to inhibition by serum than presently available fibrinolytic agents, suggesting possible clinical value. However, the snake venoms displayed undesirable effects such as thrombic activity, thromboplastic activity and hemolytic properties. The authors suggest that the toxic effects might be separable from the fibrinolytic by fractionation.-T.H.S.


The plasma cofactor which blocks thrombin formation in the presence of heparin has been studied. This cofactor has the same properties as antithrombin. Both are thermolabile, adsorbed by alumina gel or tricalcium phosphate and destroyed by chloroform. Both are consumed during the inactivation of thrombin both are found in the same fraction and at the same concentration. The authors think that heparin acts by increasing the speed of inactivation of thrombin by antithrombin and by so doing prevents the autocatalytic action of the thrombin.-J.D.


The antithrombin cofactor of heparin is concentrated in the Cohn Fraction IV-1. The cofactor has been adsorbed from this fraction with alumina gel and eluted with disodium phosphate. After several adsorptions and elutions a product has been obtained from bovine plasma which was found to be a hundred times more active than the original plasma. It is an α2 lipoprotein. Antithrombin and heparin cofactor are identical.-J.D.


An evident clearing effect was observed in the plasma of twenty normal subjects after administration of a gastric mucoprotein from pigs. The intensity of the effect was of about three per cent of that of heparin and lasted for about two hours.—P.D.A.
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IRON


Spectrophotometric methods now used for the determination of total iron-binding protein are inaccurate when cloudiness or jaundice is present in the serum. In the method described, an excess of iron as ferric ammonium citrate, is added to a 1 ml. serum sample. The excess unbound iron is removed by the addition of an iron-binding resin, Amberlite IRA 410, and the serum sample is then analyzed for serum-iron concentration. The resin removes the nonprotein-bound excess iron with a 96 per cent efficiency. This is a simple method which eliminates the problem of extraneous color in the serum and which gives values comparable to those obtained by other previously described methods.—W. N. J.


In this method for the determination of serum iron, complete extraction of iron from fresh and frozen serum specimens was obtained by the addition of 0.2 N HCl and thioglycolic acid to the specimen prior to precipitation of the plasma proteins with trichloracetic acid. The iron in the protein-free supernatant was then determined by the measurement of color intensity after the addition of sodium acetate and an alcoholic solution of bathophenanthroline. The advantages of this method, as compared with others, are the simplicity of the procedure, the greater color intensity produced by the bathophenanthroline-iron complex and the more complete extraction of iron afforded by the use of thioglycolic acid. Recovery experiments gave a mean value of 101.5 per cent ± 0.48 per cent. Reproducibility of the method was good, and the mean value for normal sera was 119.7 micrograms per 100 ml.—W. N. J.

ON THE PRESENCE OF FERRITIN IN THE PERIPHERAL BLOOD OF PATIENTS WITH HEPATOCELULAR DISEASE. K. R. Reissmann and M. R. Dietrich. From the Department of Medicine, University of Kansas School of Medicine, Kansas City, Kansas. J. Clin. Invest. 35: 588, 1956.

Measurements of serum ferritin iron in patients with a variety of diseases and in normal individuals were made by an immuno-chemical method. Human ferritin antibody was developed in rabbits by the injection of crystallized apoferritin-ferritin and this was used to precipitate ferritin from human serum. Chemical determinations for iron were then performed on the precipitate. Serum hemoglobin iron and beta-globulin bound iron did not interfere with the serum ferritin iron determinations. Concentrations of less than 20 μg per cent of serum ferritin iron were not reliably detected by this method. In normal people and in those patients who had elevated serum iron levels not associated with hepatic disease, serum ferritin iron was not detected. Ferritin iron in the serum was found only in patients with acute hepatocellular disease and in 6 patients with Hodgkin's disease and hepatic involvement. The appearance of detectable levels of ferritin iron in the serum is attributed to the release of ferritin from disintegrating hepatic cells.—W. N. J.

BLOOD VOLUME STUDIES IN NORMAL AND ANEMIC SWINE. J. A. Bush, W. N. Jensen, G. E. Cartwright and M. M. Winifred. From the Department of Medicine, University of Utah College of Medicine, Salt Lake City, Utah. Am. J. Physiol. 181: 9-14, 1955.

The chief purpose of reviewing this article is to draw attention to simultaneous studies of plasma volume in normal and anemic swine performed by means of Pθ and Feθθ techniques. Plasma volumes when determined by the Feθθ method were somewhat higher than those estimated by the Pθ method. It is shown in one of the charts that the difference between
the Fe⁹⁵ and the P³² plasma volumes varied from −40 to +50 per cent. The authors state that it is possible that a portion of the iron leaves the plasma immediately after injection inasmuch as the difference was particularly great in animals with anemia associated with an accelerated rate of plasma iron turnover.—T.R.T.


In hemopoiesis induced by cobalt in small doses the body depot iron is mobilized first. With higher dosages of cobalt (3 to 6 mg. per kg.) increased ferritin iron formation takes place in the intestinal tract. High toxic dosages produce hemosiderosis of the spleen. If iron is given simultaneously the hemosiderosis is prevented. At higher dosages of cobalt with or without iron injuries of the liver parenchyma are observed. The physiologic iron uptake was increased if iron was given orally.—M.-H.H.


Results of treatment with an intravenous preparation containing 100 mg. saccharated oxide of iron with 5 mg. of cobalt indicate that the combination is safe. The author thinks that such a combination may work better than iron alone.—J.B.C.


Combination of saccharated iron oxide with cobalt given intravenously appeared to work better than saccharated iron alone.—J.B.C.

SERUM IRON, IRON-BINDING CAPACITY OF SERUM AND IRON ABSORPTION IN KALA-AZAR. C. R. Das Gupta, J. B. Chatterjea, S. K. Ghosh and P. C. Sen Gupta. From the Departments of Hematology and Kala-azar, School of Tropical Medicine, Calcutta. Bull. Calcutta School of Tropical Med. 4: 106–107, 1956

In 29 cases of untreated Kala-azar the serum iron was usually low, iron-binding capacity depressed and iron absorption decreased. After specific anti-kala-azar treatment, the binding capacity and absorption patterns improved but the serum iron was still low in many cases.—J.B.C.

The Other Journals of Hematology


Vol. 20, No. 3-Suppl. (Congress Number) July 1957. General Secretary, S. Amano, University of Kyoto. This number contains the proceedings of the XIX general meeting of the Japan Hematological Society. Three symposiums are included: Symposium I. Immunohematology. Symposium II. Inflammation and blood components. Symposium III. Blood pictures in healthy and occupationally irradiated Japanese and in atomic bomb survivors.