ABSTRACTS

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LEUKEMIA AND MALIGNANT LYMPHOMA

Behavior of Hodgkin's Disease Nodules Transplanted into the Anterior Chamber of the Rat's Eye.
It was known that Hodgkin's tissue transplants to the anterior chamber of the guinea pig eye failed to produce any "takes." Therefore, similar experiments were conducted on rats and it was found that this animal is also a poor host for the transplanted lymphoma. Errors in the technic of transfer were ruled out by the successful "takes" of homologous transplants of rat embryonic tissue. In general the rats developed a chronic inflammatory reaction of the iris to heterologous tissue.

This review article summarizes the experiences with a number of chemotherapeutic agents in various forms of tumor growth, including lymphomata and leukemias. Included for consideration are potassium arsenite in leukemia, urethane in leukemia, nitrogen mustards in Hodgkin's disease, stilbamidine in multiple myeloma, and aminopterin in acute leukemia; as well as several less well established experimental materials.

This report is a summary of the results of aminopterin treatment in 54 patients with acute leukemia. The general plan of therapy was to administer one milligram of aminopterin intramuscularly or by mouth daily until toxic manifestations appeared. A partial remission was defined as improvement in either the clinical condition or the bone marrow and blood of the patient. A complete remission represented improvement in both. Of 11 children with acute leukemia, complete remissions were observed in 5 and partial remissions in 5, or a total incidence of 48 per cent. Among 33 adults, only 3 showed partial remissions, 3 complete remissions, or a total incidence of 18 per cent remissions. The average duration of the complete remissions was two and one-half months. Toxic manifestations were frequent. Stomatitis was present in 29 of the 54 patients, enteritis in 15, alopecia in 8, deafness in 4, and a hemorrhagic rash in one. These results are quite similar to those reported by Farber and Dameshek. One may conclude that aminopterin is the most effective agent yet known in the production of remissions in acute leukemia.

THE INFLUENCE OF THE ADRENAL GLAND ON SOME OF THE CHANGES INDUCED IN THE ANIMAL ORGANISMS BY THE FOLIC ACID ANALOGUE, AMINO-TEROPTERIN. G. M. Higgins and K. A. Woods. From the Division
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The toxicity of the folic acid antagonist amino-teropterin in daily doses of 25-50 micrograms was studied in normal and adrenalectomized rats. The adrenalectomized animals showed histologically less severe bone marrow damage, reflected also in better maintained leucocyte levels in the peripheral blood. The adrenal enlargement in the treated animals might suggest that the overactivity of the adrenal gland played a part in the toxicity of the folic acid antagonist.

C. A. F.

LEUKEMOID REACTIONS IN CARCINOMAS. D. B. Hinshaw, and H. J. Hoxie. From the Department of Internal Medicine of the College of Medical Evangelists, Los Angeles, and the Glendale Sanitarium and Hospital, Glendale, Calif. California Med. 71: 300-301, 1949.

The authors report a case of severe leukemoid reaction associated with a bronchiogenic carcinoma which had metastasized to adrenal glands and bones. The leucocyte count reached as high as 144,000 with virtually all the cells relatively mature granulocytes.

W. N. V.


A study of the plasma proteins was made in 22 cases of multiple myeloma. The chemical estimations were made with two principal methods: (1) The salting out method, using an equimolecular mixture of mono- and bipotassic phosphates at pH 6.8 (three concentrations are utilized: 45 per cent, 54 per cent, and 63.5 per cent, giving three fractions very similar to the three main electrophoretic fractions; (2) the method described by Jayle is also used to isolate the glucose conjugate proteins (similar to the globoglycoids and seroglycoid of Hewitt).

With the first method, and in cases of γ myeloma, Delbarre finds a good relation between phosphate fractionation and electrophoresis. In cases of β myeloma, the increase in globulin is usually found in more than a single chemical fraction. With the Jayle method, if there is an increase of globoglycoids compared to the globulins, it is usually a β myeloma. If there is a relative decrease of globoglycoids the diagnosis of γ myeloma is to be presumed.

Delbarre reviews the nonspecific reactions (sedimentation rate, formol-gel reaction, Veltmann, Wunderly, Gros, Henry-Chorine reactions, Haptoglobin index). All these reactions are perturbed but differently, depending upon whether the case is one of β or γ myeloma.

J. P. S.

BLOOD PROTEIN EXAMINATIONS AND THEIR CLINICAL SIGNIFICANCE IN 60 CASES OF PLASMACYTOMA. F. Wuhrmann, Ch. Wunderly and F. Hugenholtz. From the University of Zurich Medical School, Department of Medicine. Deutsche med. Wchnschr. 16: 481, 1949.

Based upon 60 specimens of plasmocytoma-sera (verified cases of multiple myeloma) a disposition is presented with the α, β1, β2, and γ globulin subdivisions. The cases with α globulin show morphologically very immature and atypical plasmacells, and clinically an acute and unfavorable course. The cases with γ globulin exhibit the most mature plasmacell elements, and the prognosis is relatively better. Both of the subdivisions with β globulin in the serum stay between the α and γ cases as far as the clinical picture is concerned.

C. M.

BLOOD COAGULATION, BLOOD PLATELETS AND HEMORRHAGIC DISEASES

STUDIES ON THE INITIATION OF BLOOD COAGULATION. I. THE RELATIONSHIP OF PLATELETS TO THE CLOT-PROMOTING EFFECT OF GLASS SURFACES. R. C. Hartmann, C. L. Conley and J. S. Lalley. From the Clinical Microscopy Division, Department of Medicine, The Johns Hopkins University and Hospital, Baltimore, Md. Bull. Johns Hopkins Hosp. 8: 231-244, 1949.
Normal human plasma of varying platelet concentration was prepared without anticoagulants by centrifugation of blood in silicone treated apparatus. Essentially platelet-free plasma clotted relatively promptly after transfer to glass tubes, but in silicone-treated tubes coagulation did not occur. Under the experimental conditions of these studies the glass surface area and the platelet concentration could be varied independently. Crushed glass was more effective in shortening the clotting time of platelet-deficient plasma than was a suspension of macerated platelets. The action of crushed glass in promoting coagulation appeared to be independent of its action on platelets, and, since storage for relatively short periods of time prevented clotting by the addition of glass, the authors suggest that some labile plasma component is concerned in the phenomenon.

While platelets did not appear essential in these experiments for the initiation of clotting, the rate of conversion of prothrombin to thrombin in plasma in contact with glass was directly related to the platelet concentration. Prothrombin conversion was not appreciably affected by platelets when plasma was protected from contact with glass and similar surfaces. For rapid conversion of prothrombin both the surface factor and platelets were required.

W. N. V.


Ten patients receiving radiation therapy for various neoplastic conditions were followed at intervals. Blood coagulability curves were performed by adding increasing amounts of heparin to the patient's blood and determining the coagulation time. There was a progressive decrease in coagulability in the blood through the period of x-ray therapy. It is unfortunate in this study that no attempt was made to measure specific components of the blood coagulation mechanism.

C. A. F.


After a discussion of the principal properties of rutin (physico-chemical, pharmacologic, and therapeutic) the authors emphasize the inconvenience of the insolubility of this drug.

They describe a new compound, morpholyl-ethyl-rutoside, which is characterized by its great solubility in water, allowing injections of solutions at a concentration of 10 per cent or more, and its lack of toxicity for animals (as for rutin itself). In a clinical trial on 11 patients (3 cirrhosis, 3 purpura, 6 hypertension) the authors found good results, using a dosage between 0.08 and 0.12 gram a day.

Reports on the activity of rutin are rather conflicting, and in the abstracter's hands rutin has always been disappointing in numerous cases of hemorrhagic diseases with increased capillary fragility (except in one case of Rendu-Osler disease). Nevertheless and in spite of the small series here reported, it is believed that this new compound is worthy of trial and its great solubility perhaps makes it more active.

J. P. S.


According to Schwarz's previous articles on megakaryocytes, platelet formation is preceded by a granulopoiesis which starts as a monocentric process in the functional area. However, certain authors have described thrombocytopenic activity in the basophilic nongranular stage of megakaryocyctic development. Pseudopodia responsible for this so-called thrombocytopenia are actually produced by shearing and lacerating a layer of viscous material surrounding early megakaryocytes. The separation of excrescences simulates the production of thrombocytes which should rightfully be called pseudoplatelets or pseudothrombocytes. True thrombocytopenia is restricted to the granulated mature megakaryocyte.

O. P. J.

Periodic Disease: Periodic Fever, Periodic Abdominalgia, Cyclic Neutropenia, Intermittent Arthralgia, Angioedematous Edema, Anaphylactoid Purpura and Periodic Paralysis. H. A.
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To his previous report of a series of patients with cyclically recurring syndromes (J. A. M. A. 136: 239-244, 1948), the author adds a number of more recently observed patients who fall into the same curious category of "periodic disease." Depending upon the particular abnormality which occurs cyclically, the particular diagnosis is listed as periodic fever, abdominal pain, arthralgia, etc. Of especial interest are 16 cases of periodic neutropenia, sometimes with thrombocytopenia, sometimes with arthralgia; splenectomy in 4 cases afforded incomplete relief, in two others, no relief at all.

The author comments on the various hypotheses as to the nature of these syndromes, concluding that these are only hypotheses, and that, apart from an accurate description of these disorders, no advances in etiology or treatment are yet forthcoming. (See also Blood 4: 1109, 1949.)

S. E.


Blood sedimentation rate, red cells minimal sediment, plasma formol-gel test, Gros-Takata reaction and haptoglobin index, were followed in women during pregnancy and puerperium. The eighth day after a normal delivery, the colloidal balance of the plasma is only slightly modified. In cases of puerperal phlebitis, even clinically latent, humoral modifications are striking: the plasma gelification by the formol test is positive, as is the Gros-Takata reaction. A very marked increase in the haptoglobin index, and in the sedimentation rate is observed. The red cells minimal sediment is markedly diminished in severe cases. The peak of this humoral syndrome does not necessarily coincide with the clinical symptoms, and there is no close parallelism. The humoral syndrome seems, to the authors, to be the best guide to judge the evolution of a phlebitis. Above all the plasma gel test and the haptoglobin test seem the best indications to appreciate the development of the process; and when they both return to normal treatment may be stopped. Sedimentation test and Gros-Takata come back to the normal much later.

J. P. S.

HEMOLYTIC ANEMIA


A Negro mother and two daughters all with anemia, splenomegaly, elevated icterus index, reticuloctyosis, spherocytosis, increased urobilinogen excretion and increased saline fragility of the red cells are reported. In 1 of them, mother, aged 38, and daughter, aged 9, the disease was severe and accompanied by symptoms suggesting a hemolytic crisis and roentgen-ray changes in the bones of the skull. There was no evidence of the sickling trait. Splenectomy was not performed in any of the 3. Seven other members of the family were also studied. The authors conclude: "Three typical cases of congenital hemolytic jaundice were encountered in a Negro family consisting of 10 persons."

G. E. C.

Paroxysmal Cold Hemoglobinuria Associated with Dementia Paralytica. Report of Treatment with Penicillin. F. T. Nichols, Jr., and C. J. Williams. From the Department of Medicine, Grady Memorial Hospital, and Emory University School of Medicine, Atlanta, and the Clinic for Genito-infectious Diseases of the Georgia Department of Public Health, Atlanta, Ga. J.A.M.A. 140: 1322-1324, 1949.

This is the third description in the literature of the use of penicillin in the treatment of syphilitic paroxysmal cold hemoglobinuria. The authors' patient had primary syphilis at the age of 32, and was inadequately treated. At the age of 41, he first noted that exposure to cold was followed by chills, fever,
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nausea, dizziness, and the passage of dark urine; and, sometimes, subsequent transitory jaundice. Such episodes occurred every winter for the following seven years, but could be prevented if exposure to cold did not occur. At the age of 48, he developed confusion, forgetfulness, and emotional instability, and a diagnosis of early dementia paralytica was made after examination and spinal fluid studies.

The blood at this time showed, in addition to the positive Kahn reaction, a positive Donath-Landsteiner test. When a finger was bound with a ligature and placed into ice water, subsequent warming of the finger resulted in local hemoglobinemia (an in vivo Donath-Landsteiner test, called the 'Ehrlich test'). The serum showed no cold agglutinins.

The patient was given 4.8 million units of aqueous penicillin G at the rate of 60,000 units every 3 hours. He showed definite clinical improvement; and six months after therapy his mental symptoms had cleared, his spinal fluid was normal except for a positive Kolmer reaction, and he had had no further bouts of hemoglobinuria. At this time, the Donath-Landsteiner test was still positive, although possibly a little weaker (it required lower temperature for its demonstration than previously). The Ehrlich test was still positive. Immersing hands and feet into ice water, however, caused no clinical reaction (negative Rosenbach test). It was felt that there had been definite improvement following penicillin treatment.

S. E.

Acute Hemolytic Anemia due to Naphthalene Poisoning: A Clinical and Experimental Study.


Four cases are described of acute, fulminating hemolytic anemia in young children following the ingestion of moth balls (pure naphthalene). All patients were approximately 2 years of age. The clinical symptoms began with malaise and anorexia, were followed by vomiting and gastrointestinal distress, and continued with pallor and hemoglobinuria. Icterus, however, was not notable; nor was enlargement of the spleen. Recovery occurred in all cases within a few days of hospitalization, usually with symptomatic therapy, sometimes together with blood transfusion.

It was noteworthy that a history of naphthalene ingestion was not volunteered by the patients or family, but was obtained only on direct questioning. In only one case was naphthol found in the urine after hospitalization. Dogs fed naphthalene responded in typical fashion: on the second day, Heinz bodies appeared in the erythrocytes; on the next day the hemoglobin began to fall; then there were fragmentation of the erythrocytes, leukocytosis and reticulocytosis, and subsequent return to normal of blood and subject. The hemolytic action of naphthalene (moth balls consist of pure naphthalene) was thus indisputable. In the children, all other causes for a hemolytic anemia were ruled out; and questioning invariably revealed that the child had sucked on or eaten moth balls in the days before the illness.

Exact diagnosis of this form of acute hemolytic anemia becomes important since spontaneous recovery, with proper care, was the rule.

S. E.


Eleven reports on the association of both chronic neurologic involvement and chronic hemolytic process are gathered by the authors from the literature and from five personal observations.

Among the neurologic manifestations were 5 cases of spasmodic familial paraplegics, 2 of Friedreich diseases, one of cerebellar ataxia of the Pierre Marie type, 2 of degenerative myelosis and one patient was an isolated spasmodic paraplegic.

The hemolytic process was given in five reports, a familial hemolytic anemia, in two a chronic non-familial hemolytic anemia. In four instances the hemolytic process was described as 'spleenic anemia.' In all but 3 cases, hematologic signs of increased hemolysis were present.

The association of chronic hemolytic anemia and chronic neurologic involvement in spite of its rarity and in spite of the dissimilarity of the observations reported by the authors, seems worthy of report. Unfortunately, the Rh factor was not studied in these cases.

J. P. S.

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In 9 of 17 infants with erythroblastosis fetalis, skeletal survey by x-ray showed transverse lines of increased density at the metaphyseal portions of the shaft ends. These findings were present at birth and in the first few days of life; were more marked the more severe the erythroblastosis; and were most prominent at the sites of the most active growth (e.g., the distal ends of the radius, ulna, tibia, fibula). Such findings were never seen in normal infants, but occurred also in premature infants, in syphilitic infants, and, after the first few days of life, in a large variety of disorders unrelated to erythroblastosis fetalis. Their diagnostic value after birth is superfluous; the possibility of their demonstration in utero, however, is of theoretic interest for further work.

HEMATOPOIETIC TISSUES

Chemical Composition of Normal Bone Marrow. A. A. Dietz. From the Toledo Hospital Institute of Medical Research, Toledo 6, Ohio. Arch. Biochem. 23: 211-221, 1949.

There is a direct linear correlation between the water and lipid-free solids and an inverse linear correlation between these two components and the lipid content of marrow from guinea pigs, rats, cats, beef, hogs and rabbits. High concentrations of total sulfur, phosphorus, nonprotein nitrogen and inorganic sulfate and phosphate are found in the active marrow of rabbits, but somewhat lower values for these constituents do not necessarily indicate a less active marrow. The variations found may be due to differences in the rate of manufacture and liberation of cellular elements.

Chemical Composition of Irradiated Bone Marrow. A. A. Dietz and B. Steinberg. From the Toledo Hospital Institute of Medical Research, Toledo 6, Ohio. Arch. Biochem. 23: 222-228, 1949.

Marrow, following 3000 r of x-rays, was analyzed at intervals up to thirty-two days after irradiation and compared with nonirradiated marrow of the same animals. The irradiated marrow showed an increase in lipid content and a decrease in water, lipid-free solids, nonprotein sulfur fractions, and total, lipid and nonprotein nitrogen. The changes in composition were greatest in marrow normally most active. A relatively greater amount of water was associated with the lipid-free solids of irradiated marrow.


The migration of lymphocytes into epithelium of the esophagus, intestine, trachea, various glands and their ducts, uterus, vagina, ureter and bladder has been reported by various authors. In the present study, the authors have studied the cell type which first enters the epidermis and later changes from a clear cell to an ordinary epithelial cell. From this and previous studies the authors believe that lymphocytes actually contribute to the formation of the epidermis. Although these cells are coming from tissues of a different germ-layer origin, it is felt that the multipotential characteristics of the lymphocytes makes this possible. Hence, the replacement of desquamated cells seems to be from two different sources, viz., mitosis of epidermal cells and transformation of lymphocytes.


The technic and diagnostic application of sternal puncture are discussed. The author considers the sternum an ideal and, in qualified hands, a safe site for puncture even in infants and young children. He includes a worthwhile and practical discussion of the development and anatomic relations of the sternum. The common hematologic disorders are briefly reviewed from the point of view of the value of sternal puncture in their diagnosis and prognosis.
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METHODOLOGY


A comparator block and accessory equipment for measurement of urobilinogen in urine and stool are described. This equipment has the advantages of commercial availability and simplicity and should find wide use in hospital laboratories. The Will Corporation (Rochester, New York) is now in a position to supply the entire unit.

G. E. C.


A method is described of measuring total body water in man by the intravenous injection of one gram of antipyrine. The distribution of antipyrine between plasma and red cells is equal. Its concentration appears to be slightly lower in edema fluids than in plasma. There are slight differences in certain tissues as well. The excretion of antipyrine is negligible and its transformation in the body occurs at about 6 per cent per hour. Comparison of measurements by antipyrine and deuterium oxide show agreement within 10 per cent. Specific gravity methods check equally well. This would appear to be a useful method of measuring total body water.

C. A. F.


This is a detailed, most comprehensive investigation of the plasma and total blood volumes of healthy infants and children from the age of 3 months to 13 years. Both congo red and Evans blue technics were used, and the technical details of procedure given correlate the two methods. The following conclusions are reached: as the age increased, the plasma and blood volumes also increased. Weight was more closely related to plasma and total volume than height or surface area, as determined by statistical relationships. The plasma and blood volumes in boys at these ages tended to be greater than those of females.

Detailed tabulations are included as to the blood and plasma volumes at each age studied, in each case.

S.E.

ESTIMATION OF BLOOD OXYGEN BY THE MICROMETHOD OF ROUGHTON AND SCHOLANDER. Z. Fejfar and J. Brod. From the Medical Department of the State Hospital in Prague-Motol and from the 1st Medical Clinic, Charles University, Prague. Časop. lék. čes. 87: 1045, 1948.

Over 500 estimations of the oxygen saturation of the blood have been performed with the micro-method of Roughton and Scholander. The method is advantageous for clinical use, as it requires only a minimal quantity of blood and can be performed within seven to eight minutes; it is very proper for serial work, can be performed with capillary blood and carried out at the bedside. The necessary equipment is very cheap and the reagents are stable.

The difference between duplicate samples of the same blood was 0.16 vol. per cent (average value); the comparison with the Van Slyke method gave a maximum difference of only 0.1 per cent between simultaneous estimations.

M.N.


Gower's solution, recommended by some authors, proved not to be suitable for the photoelectric determination of the red cell count because it produced a fine flocculation of plasma which gradually intensified. In using Müller's solution, the flocculation was still more pronounced. The photoelectric method is undoubtedly influenced by several variable factors of which probably the most important are size, hemoglobin content of the erythrocyte and the flocculation due to the diluting liquid.

M.N.