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LEUKEMIA


The author has reviewed the pathologic findings in the brain and meninges of untreated patients with acute leukemia. Involvement of the meninges and cerebral parenchyma was not unusual but clinical evidence of such involvement was infrequently noted. In recent years the advent of treatment with chemotherapeutic agents and steroids has altered this situation to a striking degree. During an 18-month period 25% of children being treated for acute leukemia developed signs and symptoms of increased intracranial pressure. In those patients studied at autopsy, meningeal involvement is the most striking finding with marked thickening of the meninges being responsible for the increased intracranial pressure. Cerebral masses of leukemic tissue are also found.

Available evidence suggests that 6 mercaptopurine and methotrexate fail to cross the blood brain barrier in adequate amounts to control the leukemic process in the central nervous system while controlling the process elsewhere in the body. Symptomatic relief has been obtained with roentgen therapy; 250-500 r in a 7-10 day period. Similar clinical experience has been noted in many clinics throughout the country. The early recognition of symptoms should result in prompt therapy with irradiation and greatly to the comfort of these patients. Roentgen therapy has been used minimally in the past in acute leukemias; however, in dealing with intracranial lesions it is most helpful and without disastrous side effects.—N. J. S.


Changes in the long bones in childhood leukemia are well known. In the present report, the author seeks to emphasize the less commonly reported leukemic changes which occur in the vertebral bones. Such changes are reported in 15 children aged 6 months to 14 years: diffuse demineralization of the vertebral bodies, compressional deformities, and horizontal radiolucent zones at the upper and lower margins of the vertebrae.—S. E.

Autopsy findings in a case of chronic myeloid leukemia dying of spontaneous rupture of spleen are described.—J. B. C.


An instance of chronic myeloid leukemia in a 3½-year-old male child is described. Treatment with deep x-ray resulted in a remission—J. B. C.


The author presents 2 cases of weakness, pallor, hemorrhagic tendency, and pancytopenia in whom no definite diagnosis could be made at the onset of the illness despite blood, marrow, and ancillary studies. In each case, it was only after a period of 3 to 4 months that a diagnosis of leukemia could be established by the usual criteria. In line with other recent reports of "preleukemia," the author points out the difficulties in diagnosis despite the high index of suspicion of leukemia.—S. E.


The 17-ketosteroids and the reducing keto corticoids were studied in 10 cases of acute leukemia and 20 cases of chronic myeloid and lymphatic leukemia. Low levels of urinary steroids and quantitative alterations of the chromatographic fractions of 17-ketosteroids were observed. The involvement of gonades and adrenals in leukemia are discussed in this respect.—P. d. N.


Seventeen acute leukemia patients were submitted to treatment with 1.0 Gm. daily of prednisone. Twelve cases were children and five adults. The criteria used for evaluation of the results were those of the Cancer Chemotherapy National Service Center, U.S.A. presented by Bisel in his letter to the Editor of Blood, July 1956, p. 676. The mean duration of complete remission observed was 64 days. The maximal duration of complete remission was of 210 days. The mean survival time was of 165 days, the maximal survival being of 450 days. The steroid has specific action upon the leukemic cells, stimulating erythropoiesis, granulopoiesis and platelet production. No toxic effects were registered, even in the electrolytes serum concentrations. Prednisone seems indicated, specially in these high doses, in the severe acute cases where is no time to wait the lag of response of other agents, like mercaptopurine and the folic acid antagonists.—M. A. J.


The Langdon-Brown Lecture was delivered at the Royal College of Physicians in November 1957. There is some foundation for the view that malignant behavior of the cancer cell depends upon the chemical structure of its genes and that this is demonstrably different from that of analogous normal cells. If the metabolism of cancer cells differs sufficiently from that of healthy tissues it should be possible to find a substance that will block some
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metabolic pathway essential to the survival of the first, but unimportant to the second, and it is logical to regard nucleic acid metabolism as the most promising target for attack.

The drugs considered in the lecture are:

**Cytotoxic Drugs**

a) Alkylation agents
   1. the nitrogen mustards
   2. the ethyleneimines
   3. the methanesulphonyloxy alkanes.

b) Others
   1. urethane
   2. colchicine derivatives
   3. actinomycins

**Antimetabolites**

a) Folic acid antagonists
b) Purine antagonists
c) Others such as pyrimidine antagonists, and antagonists of methionine, cystine and glutamine.

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One hundred patients with malignant disease have been treated with E₃₉₆, an alkylating agent. Sixty-two had chronic malignant blood disease, and thirty-eight had other kinds of neoplasm. A daily intravenous dose of 10 mg. was used and was generally well tolerated. After a total dose of about 200 mg. a fall in the leukocyte count often occurred; this was reversible, either by spacing the dosage, or by the addition of prednisone without altering the dose.

E₃₉₆ offers a considerable advance in the chemotherapeutic treatment of lympho- and reticulosarcoma and sarcomatosis (seventeen out of twenty cases were sensitive) and in cases resistant to radiotherapy or previous chemotherapeutic agents. E₃₉₆ was less frequently of benefit than previous agents in Hodgkin's disease. If it is of use in chronic lymphoid or myeloid leukaemia, it probably should not replace either chloraminophenylbutyric acid or 1-4 dimethanesulphonyloxybutane.—J. D.


In previous reports the authors have shown that cell-free filtrates from transplantable mouse tumors are able to produce myelocytic leukemia in mice. Their present work deals with the antigenic qualities of the leukemogenic filtrate. They demonstrate that the filtrable leukemogenic agent from the mouse tumor Sa I (Landschütz) has a distinct antigencity following heterogenous immunization with rabbit anti-Sa-serum. The leukemogenic action of the agent is almost completely destroyed by specific rabbit antisem. Rabbit antisem directed against normal mouse tissue does not show any inactivating effect against the leukemogenic agent. Homologous immunization does not produce antisem against the filtrate.—M. H. H.


In inbred white RFH-mice (spontaneous susceptibility rate to leukemia 1:500) the onset of myelocytic leukemia (leukemic and aleukemic myelosis) was observed in 15% of the animals within 6 months following the injection of indol (20 mg. per animal).
Other animals of the same group showed extensive extramedullary hematopoiesis in various organs, and occasionally amyloidosis. In another group of mice treated with whole body x-ray radiation of 300 r/l or 6 x 50 r/l respectively, and subsequent indol injections (20 mg per animal), the leukemia rate did not rise significantly in comparison with the first group treated with indol only. In both groups extensive myeloic infiltrations were seen in the spleen, the liver and partly in the kidneys and lungs. According to the results of the experiment indol has to be regarded as a leukonogenic agent. – M. – H. H.

PERNICIOUS ANEMIA


Three patients, two with normal hemoglobin levels, had glossitis. The marrow showed intermediate erythroblasts. The serum vitamin B₁₂ level was below the limits of normal in two of the cases. The glossitis improved with cyanocobalamin therapy, but the more anemic patient's blood counts (Hb 82% ; RBC 4.31 M) did not respond. The value of gastric aspiration and bone marrow biopsy in the detection of vitamin B₁₂ deficiency in nonanemic patients is emphasized. No steps were taken to exclude the diagnosis of idiopathic steatorrhea, and there is no mention of whether the patients could have been given preparations containing folic acid before the investigations were done. – R. H. G.


Of 16 cases of pernicious anemia, 4 had gastric atrophy and 2 had atrophic gastritis, four of the former having minor inflammatory changes. Four patients with megaloblastic anemia of pregnancy had normal mucosa; of 3 with megaloblastic anemia of idiopathic steatorrhea, 2 had atrophic gastritis and one had normal mucosa.

An abnormal gastric mucosa was almost invariable in histamine-fast achlorhydria associated with causes other than pernicious anemia, and in the majority the lesion, which could be superficial gastritis, atrophic gastritis or gastric atrophy, was severe. – R. H. G.


In 46 patients aged 50 or more with histamine-fast achlorhydria and what is described as “mild anemia but no manifest pernicious anemia” (mean Hb level 68%, mean red cell count 3,360,000 per cu. mm.), 7 had partial megaloblastic change in the bone marrow. The serum iron level in these cases gave a mean level of 56 µg./100 ml., as compared with 54 µg./100 ml., in the remaining 39 cases.

In a further comparison of 10 patients with “total” and 10 with “partial” megaloblastic erythropoiesis, the serum iron level was raised in males with total or partial megaloblastic erythropoiesis, but low in the females, apparently because of complicating iron deficiency. The plasma vitamin B₁₂ level was constantly low in total megaloblastic erythropoiesis, and sometimes so in partial. The serum ascorbic acid level was low in some patients in both groups.

It is important to remember the possibility of dimorphic anemia because the two deficiencies may neutralize each other in some hematologic data. Serial marrow punctures and plasma vitamin B₁₂ studies are important. – R. H. G.
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PERNICIOUS ANEMIA OF PREGNANCY

PREGNANCY AND ADDISONIAN PERNICIOUS ANEMIA. J. F. Adams. From the University Department of Medicine, Royal Infirmary, Glasgow, Scotland. Scot. med. J. 3:21-25, 1958.

Six patients who subsequently became pregnant were considered to have pernicious anemia because of a macrocytic anemia, megaloblastic marrow and histamine-fast achlorhydria with response to parenteral cyanocobalamin or to oral cyanocobalamin with intrinsic factor: additionally two had normal fat balances, two had a neuropathy and two had low serum vitamin B₁₂ levels. During the pregnancy and puerperium, cyanocobalamin was given by injection or together with intrinsic factor by mouth. Iron was also given. There was a fall in the blood counts in pregnancy, and the serum vitamin B₁₂ levels, which were done in three patients, were low, though there was clear demonstration of a progressive fall of serum vitamin B₁₂ in only one instance. This patient was receiving the oral cyanocobalamin preparation. It is claimed that this indicates an increased need for vitamin B₁₂ and the significance of this is discussed.

In the two instances investigated the infants had low normal serum vitamin B₁₂ levels at birth, but by the age of 7 and 9 weeks these had risen strikingly. Oral cyanocobalamin with intrinsic factor should not be used in treating pregnant patients with pernicious anemia.—R. H. G.

STUDIES ON THE BONE MARROW PICTURE IN PERNICIOUS ANEMIA OF PREGNANCY. Thoshio Nozuhara. From the Dept. of Internal Medicine, School of Medicine, University of Kumamoto, Kumamoto. J. Kyushu Hemato. Soc. 7:171-215, 1957.

Twenty one cases of pernicious anemia of pregnancy were observed from 1951 to 1954, and the bone marrow pictures were studied. The megaloblasts found in those cases were more mature than those in Addisonian pernicious anemia. It was considered that the status of these anemias was in general similar to that of Addisonian anemia which had been treated with some liver preparations. It was well understood from this fact that some cases of pregnancy anemia could get better without any treatment after the delivery.—K. M.


In all, 19 cases were given folinic acid: 17 were diagnosed antenatally, but 4 went into labor before treatment could be followed for any length of time. In 13 of the cases a low dosage regime was followed: on the first day of treatment 12 mg. was given by intramuscular injection, and then 6 mg. daily until the reticulocyte peak was reached. This usually occurred when just over 50 mg. had been administered. No further treatment was given and yet the patients continued to improve without relapsing during the pregnancy or in the puerperium. It is suggested that the action of folinic acid is catalytic.—R. H. G.


