The prevention of leukemic meningitis in childhood acute leukemia by prophylactic cranial radiation with intrathecal methotrexate has been established.1 Indications for prophylaxis against central nervous system (CNS) complications in adult acute leukemia have not been adequately studied. Wolk et al.2 demonstrated a 27% incidence of leukemic meningitis based on autopsy or spinal fluid evaluation of adults with acute myelogenous leukemia following response to chemotherapy. This author felt that as the survival of adults with acute leukemia increased the incidence of leukemic meningitis would approach the frequency seen in childhood leukemia. Experimental evidence for this was suggested by Thomas.3 He demonstrated that mice inoculated with L 1210 leukemia at autopsy demonstrated a marked increase in the frequency of arachnoidal leukemic infiltration if given subcutaneous methotrexate to prolong their lives by several days. The occurrence of leukemic meningitis has often been a late complication of acute leukemia.4 The Southwest Cancer Chemotherapy Study Group found the median duration from onset of disease to the moment of leukemic meningitis to be approximately 9 mo.5 The rarity of this syndrome in adults may therefore be due to their prior short survival.

Within the past 9 mo we have seen three adult patients with leukemic meningitis at Sinai Hospital of Detroit.

Case 1. M.L., a 48-yr-old white female, was diagnosed 2/26/74 as having acute myelogenous leukemia. Bone marrow demonstrated greater than 90% blasts with a peripheral leukocyte count of 46,800, consisting of 50% blasts. The patient was given induction therapy with vincristin, ARA-C, and prednisone, consisting of two courses, after which she developed a remission marrow. She was maintained on vincristin, ARA-C, and prednisone on a monthly basis. On 8/13/75 the patient complained of cephalgia and right orbital pain of 3 wk duration. Spinal fluid revealed 7,450 cells mostly mononuclear with some blasts and a protein of 545 mg/100 ml. Peripheral blood findings along with bone marrow aspirate and biopsy indicated a remission marrow. The patient was treated with intrathecal methotrexate 15 mg every 3 days with 2,000 rads of cranial radiation with clearing of the spinal fluid and loss of symptomatology.

Case 2. S.W., a 27-yr-old white female, was diagnosed as acute myelogenous leukemia 1/15/75 with a peripheral leukocyte count of 189,000 with 90% blasts. Bone marrow biopsy and aspirate revealed 95% blasts. She was treated with vincristin, ARA-C, and prednisone

To the Editor:

The prevention of leukemic meningitis in childhood acute leukemia by prophylactic cranial radiation with intrathecal methotrexate has been established.1 Indications for prophylaxis against central nervous system (CNS) complications in adult acute leukemia have not been adequately studied. Wolk et al.2 demonstrated a 27% incidence of leukemic meningitis based on autopsy or spinal fluid evaluation of adults with acute myelogenous leukemia following response to chemotherapy. This author felt that as the survival of adults with acute leukemia increased the incidence of leukemic meningitis would approach the frequency seen in childhood leukemia. Experimental evidence for this was suggested by Thomas.3 He demonstrated that mice inoculated with L 1210 leukemia at autopsy demonstrated a marked increase in the frequency of arachnoidal leukemic infiltration if given subcutaneous methotrexate to prolong their lives by several days. The occurrence of leukemic meningitis has often been a late complication of acute leukemia.4 The Southwest Cancer Chemotherapy Study Group found the median duration from onset of disease to the moment of leukemic meningitis to be approximately 9 mo.5 The rarity of this syndrome in adults may therefore be due to their prior short survival.

Within the past 9 mo we have seen three adult patients with leukemic meningitis at Sinai Hospital of Detroit:

Case 1. M.L., a 48-yr-old white female, was diagnosed 2/26/74 as having acute myelogenous leukemia. Bone marrow demonstrated greater than 90% blasts with a peripheral leukocyte count of 46,800, consisting of 50% blasts. The patient was given induction therapy with vincristin, ARA-C, and prednisone, consisting of two courses, after which she developed a remission marrow. She was maintained on vincristin, ARA-C, and prednisone on a monthly basis. On 8/13/75 the patient complained of cephalgia and right orbital pain of 3 wk duration. Spinal fluid revealed 7,450 cells mostly mononuclear with some blasts and a protein of 545 mg/100 ml. Peripheral blood findings along with bone marrow aspirate and biopsy indicated a remission marrow. The patient was treated with intrathecal methotrexate 15 mg every 3 days with 2,000 rads of cranial radiation with clearing of the spinal fluid and loss of symptomatology.

Case 2. S.W., a 27-yr-old white female, was diagnosed as acute myelogenous leukemia 1/15/75 with a peripheral leukocyte count of 189,000 with 90% blasts. Bone marrow biopsy and aspirate revealed 95% blasts. She was treated with vincristin, ARA-C, and prednisone.
without response and given a second course of induction with cyclophosphamide, vincristin, ARA-C, and prednisone with only a partial remission. She was readmitted 7/3/75 with cephalgia and blurred vision of 1 wk’s duration. Spinal fluid revealed 921 mononuclear cells, many being blast forms with a protein of 480 mg/100 ml and a glucose content of 36 mg/100 ml. Peripheral leukocyte count was 286,000, mostly blasts. She was treated with one course of cyclophosphamide, vincristin, thioguanine, and ARA-C with intrathecal methotrexate every 3 days. Spinal fluid cleared but she developed severe leukopenia and subsequently had multiple complications consisting of fungal pneumonia, small bowel obstruction, and subsequently expired.

Case 3. J.D., a 43-yr-old white male, was diagnosed acute undifferentiated leukemia on 1/9/75 with 90% blasts in the marrow and peripheral leukocyte count of 95,000 mostly blast cells. He was treated with two courses of cyclophosphamide, vincristin, ARA-C, and prednisone with remission occurring. The patient was given ARA-C and thioguanine for maintenance therapy monthly. The last dose of ARA-C and thioguanine was given 5/12/75. He was readmitted 6/4/75 for evaluation of swelling of the scrotum and frequent cephalgia. Physical examination at that time demonstrated a moderate swelling of the testes; the rest of the physical examination was negative. Peripheral leukocyte count was 3,600 with a normal differential and bone marrow biopsy and aspirate demonstrated hypercellular marrow with 2% blasts compatible with a remission marrow. Spinal fluid revealed 2,160 mononuclear cells, a protein of 92 mg/100 ml, and a glucose content of 14 mg/100 ml. A right orchiectomy and left testicular biopsy demonstrated bilateral leukemic infiltrations. The leukemic meningitis was treated with intrathecal methotrexate 15 mg every 3-4 days with 2,000 rads of radiation to the cranium. The patient subsequently had clearing of the spinal fluid and loss of symptomatology and maintenance of a remission marrow.

There is evidence to support prophylactic treatment to prevent leukemic meningitis in the adult group responding to chemotherapy. We feel that the instance of leukemic meningitis in the adult group will parallel the increasing response to therapy and strongly recommend that prophylactic CNS therapy be included in acute leukemic protocols.

STEVEN GOLDFARB, D.O.
ARNOLD R. AXELROD, M.D., F.A.C.P.
Department of Medicine
Sinai Hospital of Detroit
Detroit, Mich. 48235

REFERENCES

Letter: Leukemic meningitis in acute leukemic adults

S Goldfarb and AR Axelrod