The Persistence of Extramedullary Leukemic Infiltrates during Bone Marrow Remission of Acute Leukemia

By BOYD A. NIES, GERALD P. BODEY, LOUIS B. THOMAS, GEORGE BRECHER and EMIL J. FREIREICH

FOLLOWING the successful treatment of a patient with acute leukemia, evidence of residual leukemia by bone marrow, peripheral blood, or physical examination is often absent. Invariably, however, infiltration of the bone marrow by leukemic cells recurs. Whether a few undetectable leukemic cells remain during remission or whether leukemic cells are reinduced by a persisting etiologic agent is not known. Skipper has shown in the L1210 mouse leukemia model system both that a single leukemic cell will eventually cause death, and also that "cure" can be accomplished only in those animals in which there is a statistical possibility of having eliminated all leukemic cells.1 These observations suggest that, in mice, recurrences are due to survival of a few leukemic cells. In order to explore this problem in man, patients with acute leukemia dying during bone marrow remission were studied to determine if leukemic cell infiltrates were present in their organs and tissues.

MATERIALS AND METHODS

The clinical records of 380 patients with acute leukemia (60 per cent were classified as having acute lymphocytic leukemia and 39 per cent acute myelogenous leukemia) who were autopsied at the Clinical Center of the National Institutes of Health from December, 1953 to August, 1963, were studied to select those patients who died in apparent complete bone marrow remission. The last bone marrow specimen obtained from each of the patients before death was examined to verify the presence of complete remission. The criteria for "complete bone marrow remission" were the presence of normal hemopoietic elements and the absence of marrow replacement by leukemic cells. In addition, smears were searched for small numbers of leukemic cells. In some cases even rare abnormal cells could be identified as leukemic in view of the previously established diagnosis. Patients with such marrows were excluded from the present study. The criteria for "complete bone marrow remission" were thus more stringent than those of the Cancer Chemotherapy National Service Center Leukemia Group as modified by Acute Leukemia Cooperative Group B. Nevertheless, the diagnosis, "complete bone marrow remission," implied only that no leukemic cells could be identified by the morphologic means now at hand but not that such cells were completely lacking from the entire marrow. Fourteen patients met these criteria. An additional 2 patients in whom the last bone marrows were inadequate for complete evaluation were also included in the present study since previous bone marrows had shown complete remission and no leukemic cells had subsequently appeared in the peripheral blood. In all of these 16 patients, the autopsy marrow sections were examined. One patient with antemortem remission marrows had abnormal cells in the bone marrow at autopsy, and was excluded from the study. This left 15 of 380 patients who had no evidence of leukemic infiltration of the bone marrow at...
Table 1.—The Distribution of Leukemic Cell Infiltrates at Autopsy in 10 Patients with Acute Leukemia Dying during “Complete Bone Marrow Remission”

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Liver</th>
<th>S. Bowel</th>
<th>L. Bowel</th>
<th>Kidney</th>
<th>Testes</th>
<th>Arach.</th>
<th>Brain</th>
<th>LN</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>x</td>
<td>x</td>
<td></td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

The autopsy material from each of these 15 patients, most of whom died of either infection or liver failure, was reviewed to ascertain whether leukemic cells were present in histologic sections of any organs or tissues. In deciding whether leukemic cells were present, only definite infiltrates of immature cells were recorded. It was easier to recognize leukemic cells in parenchymal organs such as liver and kidney than in hematopoietic organs such as spleen and lymph nodes. No infiltrate which consisted of only a few cells was recorded as leukemic.

RESULTS

Of the total of 15 patients without evidence of bone marrow involvement at time of death, 10 had evidence of leukemia elsewhere on postmortem examination (table 1). The kidney was involved in 6 patients, the liver in 5, the testes in 3, the lung and bowel in 2, and the arachnoid, brain and lymph nodes in 1 case each. In 2 patients leukemic infiltration was demonstrated only in the liver, whereas in 1 patient 5 organs were involved. The remaining 7 patients had leukemic cell infiltrates demonstrated in either 2 or 3 organs. Some of the leukemic cell infiltrates observed in these patients are illustrated in figures 1–3.

Table 2 summarizes the clinical features of all 15 patients. The 5 patients in whom no leukemia was demonstrable at autopsy (Group II) were all females. Six of the 10 in whom leukemic infiltrates were present at autopsy (Group I) were females. The age distribution and the types of drugs used to induce remission were similar in the 2 groups. Acute lymphocytic leukemia predominated in both groups, comprising 3 of 5 patients in Group I and 8 of 10 in Group II. Two patients with acute myelogenous leukemia were present in each group. In all 4 patients methyl-glyoxal-bis-guanylylhydrazone (Methyl-GAG) had been used to induce the remission. The length of remission prior to death was somewhat shorter in Group II (median 15 days) than in Group I (median 50–54 days). In 8 of the 15 patients the bone marrow remission was accompanied or followed by return to normal of peripheral blood values and by clinical recovery until the terminal illness (Cases, 1, 2, 3, 6, 7, 9, 10, and 15). Leukemic cell infiltrates were present in 7 of these...
EXTRAMEDULLARY LEUKEMIC INFILTRATES

Fig. 1.—(04-98-67) Fourteen-year-old female with acute lymphocytic leukemia who had been in “complete bone marrow remission” for 49 days prior to death. Definite infiltrates of leukemic cells were present in the portal tracts of the liver. Leukemic cell infiltration was also found in postmortem sections of the kidneys and the lung. Hematoxylin and eosin. Mag. x 400.

8 patients. In the remaining 7 patients who died early in the course of remission prior to clinical and peripheral blood recovery, leukemic cell infiltrates were found in only 3. Of the 8 patients who had complete clinical and peripheral blood remissions, 7 received a combination of 6-mercaptopurine and methotrexate for remission maintenance. Most of the patients died during their first marrow remission. Death was due primarily to infection in 10 and to severe liver disease in 3 (Cases 7, 9, and 10). The remaining 2 patients (Cases 3 and 6) had extremely complicated terminal illnesses. One patient had high fever, seizures, bronchopneumonia, and evidence of gastrointestinal bleeding at autopsy. The other had high fever, hypomagnesemia, and seizures. At autopsy a hemorrhagic pineal cyst obstructing the aqueduct of Sylvius was found. During the terminal illness an absolute granulocyte count of 1500 or less was present at least 50 per cent of the time in 11 of the total group of 15 patients and in 9 of 10 patients who died of infection. In those patients who died of severe liver disease, granulocytopenia was not present. A platelet count of 50,000 or less occurred in 10 of the 15 patients, whereas the hemoglobin was less than 10 Gm. in 11 of 15 at least 50 per cent of the time during the terminal illness. There was no striking clinical difference when patients with single organ involvement were compared to the patient who had leukemic involvement of 5 organs.
Fig. 2.—(04-26-88) Ten-year-old female with acute lymphocytic leukemia in "complete bone marrow remission" for 75 days prior to death. Leukemic cell infiltration of the kidney is illustrated. Leukemic cell infiltrates were also found in the liver, arachnoid, small and large intestine. Hematoxylin and eosin. Mag. x 240.

DISCUSSION

In previous reports, extramedullary leukemic infiltrates during periods of bone marrow remission have been largely confined to the meninges. In a series of 25 patients with meningeal leukemia previously reported from this institution, 4 were in unequivocal complete hematologic remission. The relatively frequent occurrence of meningeal leukemia during remission has been attributed to the inability of antimetabolites to cross the blood brain barrier in effective quantities.

The hypothesis that the meninges are the primary reservoir of residual leukemia cells seemed logical since only 3 well documented reports of leukemic infiltrates appearing elsewhere in the body during a period of bone marrow remission have been noted in the literature. Anderson and Roberts have reported a case of acute monocytic leukemia in which chloromatous tumors were present at autopsy in the breast, subdurally in the left frontal pole, and extradurally in the region of the sixth through tenth vertebrae despite a normal bone marrow at that time. In another report, massive leukemic infiltration in the gastrointestinal tract was found at autopsy in a patient whose bone marrow examination 9 days prior to death showed a complete remission. Smaller leukemic infiltrates were present in the lung, liver, and spleen. Unfortunately, however, the result of the postmortem bone marrow
EXTRAMEDULLARY LEUKEMIC INFILTRATES

Fig. 3.—(03-92-94) Twenty-seven-year-old male with acute lymphocytic leukemia in "complete bone marrow remission" for 16 days prior to death. Leukemic cells can be seen infiltrating the intertubular tissues of the testes. Hematoxylin and eosin. Mag. x 400.

examination was not reported and therefore infiltration of the bone marrow at the time of death cannot be ruled out. In addition, Dameshek and Gunz have recently reported a 6-year-old boy with acute leukemia who developed leukemic infiltrates of the testes and kidneys at a time when the peripheral blood and bone marrow appeared to be normal. The occurrence of testicular infiltration by leukemic cells and of bone and joint symptoms during periods of peripheral blood remission has been reported by other authors. These cases, however, are not germane to the present discussion, since normal peripheral blood values do not rule out the presence of leukemic cells in the bone marrow.

Despite the paucity of reports in the literature, the pathologic findings of the present study indicate that sites other than the meninges are often involved with leukemic infiltrates during bone marrow remission. Additional support for these findings is provided by recent clinical observations in 4 patients who have developed peripheral evidence of leukemia other than meningeal leukemia during periods of "complete bone marrow remission." In a 4-year-old girl with acute myelogenous leukemia, reddish purple intradermal tumors composed of immature cells were noted seven months prior to the reappearance of abnormal cells in the bone marrow. In a 10-year-old boy with previously diagnosed acute lymphocytic leukemia, testicular en-
Table 2.—Clinical Features of 15 Patients with Acute Leukemia Dying during “Complete Bone Marrow Remission”

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Unit Number</th>
<th>Age</th>
<th>Sex</th>
<th>Type L</th>
<th>Inducing Drug(s)</th>
<th>Maintenance Drug(s)</th>
<th>Length of Remission (Days)</th>
<th>Interval Last Marrow Decline (Days)</th>
<th>No. of Remissions</th>
<th>Length of Terminal Illness (Days)</th>
<th>PMN &lt;1500 (% of Days)</th>
<th>Platelets &lt;50,000 (&lt;10 Gm. %)</th>
<th>Hg. (%)</th>
<th>Cause(s) of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1* 04-39-29</td>
<td>13 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>6-MP</td>
<td>6-MP, MTX</td>
<td>82</td>
<td>13</td>
<td>1</td>
<td>27</td>
<td>88%</td>
<td>80%</td>
<td>88%</td>
<td>Pseudomonas septicemia</td>
</tr>
<tr>
<td>2* 04-07-42</td>
<td>8 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>6-MP</td>
<td>6-MP, MTX</td>
<td>54</td>
<td>3</td>
<td>1</td>
<td>10</td>
<td>100%</td>
<td>0%</td>
<td>100%</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>3* 04-26-88</td>
<td>10 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>6-MP</td>
<td>6-MP, MTX</td>
<td>75</td>
<td>10</td>
<td>1</td>
<td>25</td>
<td>67%</td>
<td>25%</td>
<td>58%</td>
<td>GI hemorrhage, broncho- pneumonia, seizures of unknown etiology</td>
</tr>
<tr>
<td>4 03-02-04</td>
<td>27 M</td>
<td></td>
<td></td>
<td>ALL</td>
<td>MTX</td>
<td>MTX</td>
<td>16</td>
<td>16</td>
<td>2</td>
<td>45</td>
<td>53%</td>
<td>63%</td>
<td>59%</td>
<td>Ventricular fibrillation secondary to plasma myocarditis</td>
</tr>
<tr>
<td>5 04-45-64</td>
<td>23 M</td>
<td></td>
<td></td>
<td>AML</td>
<td>GAG</td>
<td>None</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>30</td>
<td>97%</td>
<td>100%</td>
<td>88%</td>
<td>Klebsiella septicemia</td>
</tr>
<tr>
<td>6* 04-08-67</td>
<td>14 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>V, P</td>
<td>6-MP, MTX</td>
<td>49</td>
<td>6</td>
<td>1</td>
<td>16</td>
<td>50%</td>
<td>50%</td>
<td>50%</td>
<td>Hemorrhage into pineal cyst, fever of unknown etiology</td>
</tr>
<tr>
<td>7* 04-81-97</td>
<td>8 M</td>
<td></td>
<td></td>
<td>ALL</td>
<td>V, P</td>
<td>6-MP, MTX</td>
<td>50</td>
<td>5</td>
<td>1</td>
<td>10</td>
<td>0%</td>
<td>0%</td>
<td>29%</td>
<td>Acute viral hepatitis, pulmonary edema</td>
</tr>
<tr>
<td>8 04-89-79</td>
<td>46 M</td>
<td></td>
<td></td>
<td>AML</td>
<td>GAG</td>
<td>None</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>30</td>
<td>100%</td>
<td>95%</td>
<td>87%</td>
<td>Pseudomonas septicemia, disseminated candidiasis</td>
</tr>
<tr>
<td>9* 03-30-55</td>
<td>8 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>V</td>
<td>OH-urea, P</td>
<td>61</td>
<td>3</td>
<td>3</td>
<td>90</td>
<td>0%</td>
<td>100%</td>
<td>0%</td>
<td>Hypoglycemia secondary to hepatic failure</td>
</tr>
<tr>
<td>10* 01-88-14</td>
<td>3 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>Pred.</td>
<td>6-MP, MTX</td>
<td>215</td>
<td>22</td>
<td>1</td>
<td>5</td>
<td>0%</td>
<td>0%</td>
<td>100%</td>
<td>Acute yellow atrophy</td>
</tr>
</tbody>
</table>

GROUP II (No Leukemic Cell Infiltrates at Autopsy)

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Unit Number</th>
<th>Age</th>
<th>Sex</th>
<th>Type L</th>
<th>Inducing Drug(s)</th>
<th>Maintenance Drug(s)</th>
<th>Length of Remission (Days)</th>
<th>Interval Last Marrow Decline (Days)</th>
<th>No. of Remissions</th>
<th>Length of Terminal Illness (Days)</th>
<th>PMN &lt;1500 (% of Days)</th>
<th>Platelets &lt;50,000 (&lt;10 Gm. %)</th>
<th>Hg. (%)</th>
<th>Cause(s) of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 03-02-56</td>
<td>48 F</td>
<td></td>
<td></td>
<td>AML</td>
<td>GAG</td>
<td>None</td>
<td>48</td>
<td>14</td>
<td>3</td>
<td>60</td>
<td>80%</td>
<td>100%</td>
<td>100%</td>
<td>Miliary tuberculosis</td>
</tr>
<tr>
<td>12 00-25-96</td>
<td>46 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>6-MP, MTX</td>
<td>6-MP, MTX</td>
<td>15</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>Disseminated candidiasis, klebsiella septicemia</td>
</tr>
<tr>
<td>13 04-75-45</td>
<td>9 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>V, P, 6-MP, MTX</td>
<td>None</td>
<td>9</td>
<td>2</td>
<td>1</td>
<td>17</td>
<td>100%</td>
<td>85%</td>
<td>50%</td>
<td>Disseminated candidiasis, Acute hepatic necrosis</td>
</tr>
<tr>
<td>14 04-19-60</td>
<td>58 F</td>
<td></td>
<td></td>
<td>AML</td>
<td>GAG</td>
<td>GAG</td>
<td>12</td>
<td>12</td>
<td>1</td>
<td>5</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>Pseudomonas septicemia</td>
</tr>
<tr>
<td>15* 04-44-78</td>
<td>2 F</td>
<td></td>
<td></td>
<td>ALL</td>
<td>6-MP</td>
<td>6-MP, MTX</td>
<td>38</td>
<td>5</td>
<td>1</td>
<td>7</td>
<td>100%</td>
<td>0%</td>
<td>80%</td>
<td>Severe interstitial pneumonia</td>
</tr>
</tbody>
</table>

*Complete peripheral blood and clinical recovery following demonstration of bone marrow remission until terminal illness.

V = Vincristine
P = Prednisone
6-MP = 6-Mercaptopurine
MTX = Methotrexate
GAG = Methyl GAG
OH urea = Hydroxyurea
EXTRAMEDULLARY LEUKEMIC INFILTRATES

139

largement due to leukemic cell infiltration was noted in September 1963, during a period of bone marrow remission which continued until March 1964. Cervical lymph node enlargement due to leukemic replacement occurred in a 17-year-old boy with acute lymphocytic leukemia in whom marrow relapse did not occur until 4 months later. Finally, leukemic infiltration in the submandibular gland was demonstrated in a 4-year-old girl with acute lymphocytic leukemia on December 4, 1963, during a bone marrow remission which continued to her death in March 1964. In view of these findings, the relatively frequent recognition of leukemic infiltration of the meninges during marrow remission when compared to other organs may have been due more to the ease of cerebrospinal fluid examination, than to a truly higher incidence of involvement by leukemic cells.

The high frequency of leukemic infiltrates in our patients dying in “complete bone marrow remission” is strong evidence that leukemic cells are not completely eliminated during treatment. The theory that relapse occurs because of persistent leukemic cells is thus supported by our data. The failure to detect residual infiltrates in 5 of the 15 patients is best explained by the difficulty in recognizing small numbers of leukemic cells in individual sections and also by the limitations inherent in microscopic examination of large masses of tissue. This explanation may also hold for the rare cases of acute leukemia in which absence of leukemic infiltration was noted at autopsy. It is best explained by the difficulty in recognizing small numbers of leukemic cells in individual sections and also by the limitations inherent in microscopic examination of large masses of tissue. This explanation may also hold for the rare cases of acute leukemia in which absence of leukemic infiltration was noted at autopsy. In each of these cases marrow remission, usually associated with marrow aplasia, occurred without specific chemotherapy.

The immediate cause of death of patients dying during remission deserves further comment. The principal cause of death in the majority of cases was either infection or liver failure. In 7 of the 15 cases, complete hematologic and clinical recovery following the appearance of a bone marrow remission did not occur and the death of these was therefore due to complications of cytopenia during therapy. However, in the remaining 8, all except 1, in whom pre-existing liver disease was present, enjoyed a period of asymptomatic complete remission. Each of these patients was being treated with the combination of 6-mercaptopurine and methotrexate for remission maintenance at the time the terminal illness began. In 3 of these patients, no significant fall in the WBC count occurred with the terminal illness. These patients died of liver disease, which presumably was of viral origin in 2. The other 5 died either of infection or of a combination of infection and other factors. Peripheral granulocyte counts were significantly low in all of these 5 patients during the terminal illness. However, the granulocytopenia followed rather than preceded the clinical onset of the terminal illness. This suggests that the combined therapy not only lowered bone marrow reserves, but also increased the likelihood of fatal infections with relatively avirulent pathogens. The known depressant effect of 6-mercaptopurine and methotrexate on immune response, inhibition of other host defenses, or a combination of these factors may have been involved.

Summary

Leukemic cell infiltrates were found at autopsy in the tissues of 10 of 15
patients with acute leukemia dying during “complete bone marrow remis-
sion.” The kidney was the most common site of leukemic cell infiltrates
followed by the liver, testes, bowel, lung, central nervous system, and lymph
nodes.

These findings indicate that leukemic cells are not completely eradicated
by current chemotherapy even in patients in whom no leukemic cells can be
identified in the bone marrow.

The distribution of residual leukemic cells demonstrates that the central
nervous system is not the only reservoir of leukemic cells in patients during
bone marrow remission.

**SUMMARIO IN INTERLINGUA**

Infiltratos de cellulas leucemic esseva trovate al necropsia in le tissus de 10
de 15 patientes con leucemia acute qui habeva morite durante “un complete
remission del signos del morbo in le medulla ossee.” Le ren esseva le sito le
plus commun del infiltratos de cellulas leucemic, sequite del hepate, del
testes, del intestinos, del pulmon, del systema nervose central, e del nodos
lymphatic.

Iste constatationes indica que le cellulas leucemic non es completemente
eradicate per le currente modalitates chimotherapeutic mesmo in patientes in
qui nulle cellulas leucemic pote esser identificate in le medulla ossee.

Le distribution del residue cellulas leucemic demonstra que le systema
nervose central non es le sol reservoir de cellulas leucemic in patientes qui
se trova in remission quanto al medulla ossee.

**REFERENCES**

1. Skipper, H. E., Schabel, F. M., Jr., and Wilcox, W. S.: Experimental evalua-
tion of potential anticancer agents. XIII. On the criteria and kinetics as-
associated with “curability” of experimental leukemia. Cancer Chemo-

2. Bisel, H. F.: Criteria for the evaluation of response to treatment in acute leu-

leukemia: a syndrome resulting from increased intracranial pressure in pa-


thecal amethopterin in neurological manifestations of leukemia. Arch. In-

plete remission and death from subsequent development of chloromata.

infiltration of the gastrointestinal tract during apparent remission in

8. ——: Personal communication.

9. Dameshek, W., and Ganz, F.: Leu-

10. Stegagno, G. A., Digilio, C., and Felici, W.: Testicular location of tumoral in-
filtration as the first sign of relapse in treated leukemic children. Arch.

11. Delger, J. R., and Curuchet, E.: Si-
multaneous bilateral testicular acute
EXTRAMEDULLARY LEUKEMIC INFILTRATES


Boyd A. Nies, M.D., Formerly, Clinical Associate, National Cancer Institute, National Institutes of Health, Bethesda, Md. Present address: Stanford University Hospital, Palo Alto, Calif.

Gerald P. Bodey, M.D., Clinical Associate, National Cancer Institute, National Institutes of Health, Bethesda, Md.

Louis B. Thomas, M.D., Head, Surgical Pathology and Post Mortem Service, National Cancer Institute, National Institutes of Health, Bethesda, Md.

George Brecher, M.D., Chief, Hematology Department, Clinical Center, National Institutes of Health, Bethesda, Md.

Emil I. Freireich, M.D., Head, Leukemia Service, Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Md.
The Persistence of Extramedullary Leukemic Infiltrates during Bone Marrow Remission of Acute Leukemia

BOYD A. NIES, GERALD P. BODEY, LOUIS B. THOMAS, GEORGE BRECHER and EMIL J. FREIREICH