Hairy Cell Leukemia: B-Lymphocyte and Phagocytic Properties

By Peter D. Utsinger, William J. Yount, C. Randall Fuller, Marshall J. Logue, and Eugene P. Orringer

The diagnosis of hairy cell leukemia was made in three patients by phase-contrast microscopy and histochemistry of the abnormal peripheral blood cells. Both IgM and IgD surface immunoglobulins were resynthesized after these cells were trypsinized and cultured. Aggregate or Fc receptors were demonstrated on hairy cells. The ability to phagocytose latex was also a property of hairy cells; however, these cells did not demonstrate nonspecific esterase activity. Stimulation by phytohemagglutinin resulted in very low incorporation of tritiated thymidine. Cytofluorographic analysis of the phytohemagglutinin-stimulated cell population revealed less than 9% of the cells in an interploid or tetraploid state. The abnormal mitogen response was largely restored when purified T lymphocytes obtained from the peripheral blood of the patients were cultured with phytohemagglutinin. Hairy cells cultured with normal allogeneic mononuclear cells did not undergo blast transformation. These data strongly suggest that the cells of at least some patients with hairy cell leukemia are B lymphocytes with phagocytic capabilities.

Hairy Cell Leukemia, a neoplastic disease with manifestations in spleen, blood, lymph nodes, and bone marrow, is considered to be a rare type of chronic leukemia.1-3 The abnormal cells in this disease have been shown to have tartrate-resistant acid phosphatase and to lack lysozyme.4 Morphologically, a high percentage of the abnormal cells have a characteristic ribosome-lamella complex rarely seen in other human tumors.5 Nonetheless, the nature of the hairy cell has not as yet been clearly defined. Different investigators consider it to be a monocyte or lymphocyte, or a hybrid cell with properties of both monocytes and lymphocytes.6-15 We have studied the neoplastic cells of three patients with hairy cell leukemia and describe here our characterization of these cells. Our data strongly support the concept that at least in some patients these cells are of lymphocytic origin but have some features of monocytes.

MATERIALS AND METHODS

Mononuclear cell isolation. Mononuclear cells were separated from peripheral blood by Ficoll-Isopaque centrifugation.16 For the lymphocyte enumerations, only preparations with a mononuclear cell yield of greater than 70% were used. Cells from the interface, at a concentration of 1 x 10^6/ml, were then washed three times in 10% FCS-RPMI 1640 at room tem-

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Submitted April 26, 1976; accepted August 19, 1976.

Supported in part by USPHS Grants AI 10327, AM 15811, HL 03650; and Grants from the Arthritis Foundation, the Regional Medical Program, the Jefferson Pilot Foundation, and the University of North Carolina Cancer Center.

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Blood, Vol. 49, No. 1 (January), 1977 19
temperature. Viability was always assessed by trypan blue exclusion, and only preparations with a viability of greater than 90% were used.

**Monocyte identification.** Monocytes were identified by α-naphthyl acetate staining and latex phagocytosis. For the latex phagocytosis enumeration, a modification of the method of Zucker-Franklin was employed. One drop of a suspension of 0.81 μm latex (Dow Chemical Company, Midland, Mich.) was added to 1 × 10⁶ mononuclear cells in 1 ml RPMI 50% autologous serum, incubated 45 min at 37°C on a shaking table, and washed twice at 400 g at room temperature in RPMI. The α-naphthyl acetate staining was done according to the method of Yam. Cell smears fixed in buffered formalin were air dried and incubated in a medium of phosphate buffer, hexazotized pararosanilin, and α-naphthyl acetate in ethylene glycol monomethyl ether; washed in distilled water; counterstained with 1% methyl green; washed with distilled water; dried; and mounted for examination under light microscopy.

**Surface immunoglobulin-bearing cell enumeration (Slg-cell).** Lymphocytes, in a concentration of 1-2 × 10⁶ in 0.05 ml of 10% FCS-RPMI 1640, were incubated with 0.05-0.10 ml of fluorescein-conjugated purified F(ab')₂ fragments from polyvalent antihuman immunoglobulin and antisera specific for human μ, γ, κ, and λ chains in 10-mm x 75-mm glass tubes for 1 hr at 4°C, washed three times with a total of 10 ml of cold 10% FCS-RPMI 1640, and mounted on glass slides, as previously described. The cells were overlaid with a cover slip, and 1000 cells were counted by epi-illumination with a Leitz ultraviolet microscope equipped with a mercury arc HBO-200 lamp using BG 38 and 490-nm (FITC) exciter filters and a K510-nm barrier filter, and Plöem illuminator.

**T-cell enumeration.** Spontaneous cold sheep erythrocyte rosettes (E) were assayed as previously reported by a variation of the method of Ross. The method detects receptors for both C³b and C³d. E and EA controls were always done. E controls were always less than 2%, and EA controls always less than 5%.

**Aggregated (Fc) receptor-bearing cell enumeration.** The Fc receptor was identified as described by Dickler, employing the following modifications (Dickler HB: personal communication). The pelleted aggregated IgG was homogenized in a 7-ml Dounce homogenizer, and the pH was corrected with 0.1 N NaOH to 8.3, rather than 8.1, for maximum solubility of aggregated IgG. Just prior to use, aggregated material was centrifuged at 600 g at room temperature, not 4°C as originally described. Staining was carried out for 1 hr at pH 8.3 at room temperature, rather than 4°C. Under these conditions, a more uniform speckled staining pattern over the entire cell surface was noted.

**Mitogen stimulation.** RPMI 1640 with 10% pooled AB plasma supplemented with 200 mM glutamine, 100 units/ml penicillin, and 100 μg/ml streptomycin was the medium used in all cultures. Two types of cell suspensions were used: Ficoll-Hypaque separated hairy cell leukemia mononuclear cells and isolated T lymphocytes from hairy cell leukemia patients. In all experiments, lymphocyte viability by trypan blue exclusion was greater than 90%.

Quaduplicate cultures of 0.5 × 10⁶ mononuclear cells in 1 ml medium were made in 10- x 75-mm sterile capped plastic tissue culture tubes (Falcon) for each concentration of phytohemagglutinin (PHA) (Burroughs Wellcome, Research Triangle Park, N.C.). For each patient and controls, dose response of 1 μg, 5 μg, and 10 μg were carried out. Cultures were incubated at 37°C in a 5% CO₂ atmosphere for 2, 3, 4, 5, and 6 days. In the monocyte reconstitution experiments, 1 × 10⁵ mononuclear cells were cultured in 10% AB plasma-RPMI 1640 in flat-bottom sterile tissue plates (Linbro Chemical Co., New Haven, Conn.) in a total volume of 0.2 ml/well. One microcurie of tritiated thymidine (³H-TdR) (New England Nuclear, Boston) was added to duplicate tubes for the last 5 hr of culture. The trichloroacetic acid-insoluble radioactivity of cells collected on Millipore filters (HAMK) (Millipore Corp., Bedford, Mass.) was measured in a liquid scintillation counter. All data were expressed as the maximal difference between the counts per minute (cpm) in the stimulated culture and the cpm in the control culture. To determine the maximal difference in cpm, the difference in cpm for each day of culture and each concentration of mitogen was determined, and the largest (maximal) difference in cpm was then recorded. Thus the maximal differences in cpm represented the group mean derived from the maximal differences in cpm of each individual determination.

**Cell staining and cytofluorograph instrumentation.** Duplicate tubes of the PHA-stimulated
HAIRY CELL LEUKEMIA

Mononuclear cells were stained with ethidium bromide, a general nucleic acid stain, by the method of Göhde and Dittrich. For analysis of cellular DNA content, $1 \times 10^6$ cells were treated with 10 ml ribonuclease (Worthington, Freehold, N.J.) for 30 min at 37°C to hydrolyze RNA prior to ethidium bromide staining.

To $1 \times 10^6$ lymphocytes/ml, 10 ml of a solution containing 5 mg ethidium bromide (Calbiochem, San Diego, Calif.) and 100 mg 1.12% aqueous sodium citrate was added, incubated for 30 min at room temperature, and centrifuged at 400 g for 5 min. The supernatant was discarded and the cells resuspended in RPMI, recentrifuged at 400 g for 5 min, and the supernatant discarded. The cells were resuspended in distilled water for counting. All counting was done with a Bio-Physics Systems, Inc. (Mahopac, N.Y.) Cytofluorograf Model 4802A. This cytofluorograf has been described in detail elsewhere. Each stained cell, in suspension, passed in single file through a 488-nm argon ion laser beam. During transit through the beam, a stained cell generated a fluorescent light flash which was converted to an electronic pulse by a photomultiplier phototube. The light flashes were amplified and analyzed for intensity. The intensity distribution, which was directly proportional to the DNA content, was stored in a multichannel pulse-height analyzer, which could accumulate a record of the DNA content per cell of 10,000 cells in several minutes.

The percentage of diploid (2n) $G_1$ cells, tetraploid (4n) $G_2 + M$ cells, and interploid (2n > DNA > 4n) S phase cells were calculated from the DNA histograms. $G_1$ was defined as the first peak of cells in the histogram of the DNA spectra of the control (unstimulated) or stimulated cells. S-$G_2-M$ was defined as those cells outside the $G_1$ locus. Replicate determinations of 10,000 cells from the same sample were in agreement within 1.1%. Measurements on duplicate cultures had an error of less than 3.2% from the mean. Fluorescent microscopic examination of cell samples after stimulation with PHA failed to reveal any pairs of agglutinated cells, supporting the concept that the DNA content measured reflected individual cell DNA content.

Other studies. Trypsinization was done by a variation of the method of Preud'homme. T cells were purified by layering the Ficoll-Hypaque separated cells over sterile washed nylon wool columns (Fenwal Leukopak, Travenol Labs, Thetford, England) as described by Julius et al. The ratio of lymphocytes to milligrams of Leukopak column was predetermined to result in an effluent containing greater than 90% T lymphocytes. The method of Yam was used to detect tartrate-resistant acid phosphatase. Neuraminidase treatment of SRBC was performed by the method of Wiener. Monocytes were obtained from Ficoll-Hypaque-separated peripheral blood cells by adherence to the surface of plastic tissue culture wells; cells in 10% AB plasma-RPMI 1640 were added to flat-bottom sterile tissue plates, 0.3 ml/well, (Linbro Chemical Co., New Haven, Conn.). The cells were incubated for 2 hr in a 5% CO$_2$-95% air, 37°C incubator. Each well was then washed five times to remove nonadherent cells. Over 95% of the cells remaining in the tissue culture wells were monocytes by morphological examination (greater than 10 μm), phagocytosis (greater than 96%, phagocytosed latex), and by nonspecific esterase activity (greater than 95% stained with α-naphthyl acetate).

RESULTS

Neoplastic cells. The peripheral blood smears from all three patients showed typical large mononuclear cells, which on phase contrast microscopy exhibited numerous slender hairlike cytoplasmic projections. The diagnosis of hairy cell leukemia was made with certainty by demonstrating tartrate-resistant acid phosphatase isoenzyme in the cells. In each patient, greater than 75% of the mononuclear cells were hairy cells.

Cell surface markers. In all three patients, a large percentage of the hairy cells stained strongly for surface immunoglobulin, as outlined in Table 1. All three patients had a large percentage of cells staining with both IgM and IgD antisera. In contrast, there was minimal or no staining with antisera to IgA and IgG. Further documentation that the immunoglobulin present on the surface
### Table 1. Surface Markers on Normal Mononuclear Cells and Hairy Cell Leukemia Mononuclear Cells

<table>
<thead>
<tr>
<th>Cell Population</th>
<th>Mononuclear Cells No./cu mm</th>
<th>Ig*</th>
<th>IgG*</th>
<th>IgM</th>
<th>IgD</th>
<th>IgA</th>
<th>Fc (% ± SEM)</th>
<th>E (% ± SEM)</th>
<th>EAC (% ± SEM)</th>
<th>Latex Phagocytosis (% ± SEM)</th>
<th>Esterase Activity (% ± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (9 Subjects)</td>
<td>3,400 ± 652</td>
<td>10.8 ± 0.6</td>
<td>2.3 ± 0.2</td>
<td>9.7 ± 0.8</td>
<td>9.1 ± 0.7</td>
<td>0.8 ± 0.1</td>
<td>12.0 ± 1.0</td>
<td>71.6 ± 1.5</td>
<td>10.0 ± 0.8</td>
<td>21.7 ± 2.8</td>
<td>24.1 ± 1.6</td>
</tr>
<tr>
<td>Patient 1</td>
<td>2,460</td>
<td>73</td>
<td>0</td>
<td>79</td>
<td>75</td>
<td>0</td>
<td>72</td>
<td>14</td>
<td>ND*</td>
<td>59</td>
<td>4</td>
</tr>
<tr>
<td>Patient 2</td>
<td>4,890</td>
<td>74</td>
<td>1</td>
<td>82</td>
<td>81</td>
<td>1</td>
<td>86</td>
<td>9</td>
<td>ND*</td>
<td>74</td>
<td>2</td>
</tr>
<tr>
<td>Patient 3</td>
<td>10,740</td>
<td>81</td>
<td>0</td>
<td>92</td>
<td>84</td>
<td>0</td>
<td>89</td>
<td>8</td>
<td>90</td>
<td>78</td>
<td>3</td>
</tr>
</tbody>
</table>

*Antiser used were F(ab')2 anti-Ig and F(ab')2 anti-IgG.

*ND, not done.

### Table 2. ³H-TdR Incorporation by PHA-stimulated Normal Mononuclear Cells and Hairy Cell Leukemia Mononuclear Cells (cpm) ± SEM

<table>
<thead>
<tr>
<th>Cell Population</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (9 Subjects)</td>
<td>24,341 ± 5,821</td>
<td>37,186 ± 6,506</td>
<td>35,736 ± 6,201</td>
<td>32,129 ± 6,100</td>
<td>27,065 ± 5,429</td>
</tr>
<tr>
<td>Patient 1</td>
<td>2,668</td>
<td>3,889</td>
<td>3,378</td>
<td>3,368</td>
<td>2,619</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1,421</td>
<td>1,508</td>
<td>2,145</td>
<td>1,604</td>
<td>821</td>
</tr>
<tr>
<td>Patient 3</td>
<td>2,252</td>
<td>3,025</td>
<td>3,287</td>
<td>3,357</td>
<td>2,681</td>
</tr>
<tr>
<td>Normal (17 Subjects, 98% T cells)</td>
<td>68,437 ± 11,241</td>
<td>66,595 ± 10,841</td>
<td>56,431 ± 9,879</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 1 (97% T cells)</td>
<td>41,251</td>
<td>38,591</td>
<td>36,421</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 2 (98% T cells)</td>
<td>30,821</td>
<td>27,494</td>
<td>22,592</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 3 (99% T cells)</td>
<td>52,821</td>
<td>46,531</td>
<td>44,374</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 3. Per Cent of Normal Mononuclear Cells and Hairy Cell Leukemia Mononuclear Cells in G₁, S, G₂, and M During Culture After PHA Stimulation (± SEM)*

<table>
<thead>
<tr>
<th>Cell Population</th>
<th>Day 0</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>92.0 ± 8.0</td>
<td>81.5 ± 7.9</td>
<td>28.5</td>
<td>62.8 ± 9.4</td>
<td>37.2</td>
<td>61.3 ± 8.9</td>
</tr>
<tr>
<td>Patient 1</td>
<td>93.6 ± 6.4</td>
<td>92.8</td>
<td>7.2</td>
<td>93.4</td>
<td>6.6</td>
<td>92.7</td>
</tr>
<tr>
<td>Patient 2</td>
<td>92.8</td>
<td>7.2</td>
<td>8.4</td>
<td>92.5</td>
<td>7.5</td>
<td>91.8</td>
</tr>
<tr>
<td>Patient 3</td>
<td>92.0</td>
<td>8.0</td>
<td>92.5</td>
<td>7.5</td>
<td>92.7</td>
<td>7.3</td>
</tr>
</tbody>
</table>

*This experiment outlines data obtained using 1 μg PHA. A lower percentage of patient cells were in S, G₂, M using higher concentrations of the mitogen.
of the cell was, indeed, produced by the cell was obtained in trypsinization experiments. For example, in patient 1, 79% of the mononuclear cells had IgM and 75% IgD; after trypsinization and culture, 73% of the cells bore IgM and 71% IgD, and 74% were stained with a polyvalent F(ab')2 fragment antiserum, providing strong evidence that the immunoglobulin molecules found on the surface of the cell were, indeed, synthesized by the cell. Additional evidence for the B-lymphocyte nature of the cells was obtained in patient 3, where 90% of the cells were EAC binding but only 4% were EA binding. Of interest, aggregate or Fc receptors were found on a large percentage of hairy cells. Significant numbers of T lymphocytes were not found immediately or after 1 hr of ice incubation. Even 12 hr of ice incubation and neuraminidase treatment of the sheep red blood cells prior to incubation with the patient's lymphocytes did not increase the low percentages of T lymphocytes found. Large percentages of the lymphocytes showing properties of hairy cells phagocytized latex, as outlined in Table I. A very low percentage of these cells demonstrated nonspecific esterase activity using a-naphthyl acetate staining.

Response to mitogens. Table 2 outlines the minimal incorporation of 3H-TdR by the patients' mononuclear cell populations after stimulation by 1 μg PHA. Even lower incorporation was found with higher mitogen concentrations. To eliminate the possibility that the low incorporation of 3H-TdR was due to an abnormality in thymidine transport, cytofluorographic analysis of the cells' DNA content was performed (Table 3). In every experiment, less than 9% of the cells entered an interploid or tetraploid state after PHA stimulation. Greater than 91% of the cells stayed in a diploid or G1 state after PHA stimulation. In contrast, a mean of 33% of the lymphocytes of normal age- and sex-matched controls entered an interploid or tetraploid state after PHA stimulation. To eliminate the contention that PHA responsiveness was impaired because of an abnormality in the monocytes of patients with hairy cell leukemia, 3-, 4-, and 5-day stimulations were performed using patient mononuclear cells reconstituted with allogeneic monocytes. In these experiments, a similar impairment in blastic transformation was documented.

To investigate the possibility that a dilution of T lymphocytes by the proliferating neoplastic cells was responsible for the impaired PHA response, T lymphocytes from three patients were purified by passage of the cells over Fenwal Leukopak columns. Greater than 97% of the lymphocytes were T lymphocytes. As shown in Table 2, the incorporation of 3H-TdR by the purified T lymphocytes cultured on normal allogeneic monocytes was less than the incorporation of 3H-TdR by age-matched normals, on all days cultured.

DISCUSSION

Three patients with hairy cell leukemia were studied. Our patients exemplified the key clinical features of the entity. All were male adults with splenomegaly, fever, and no lymphadenopathy. Two were pancytopenic. Strong evidence for B-cell characteristics of their neoplastic cells was provided by the presence of both IgM and IgD on freshly drawn neoplastic cells, and by the resynthesis of both IgM and IgD after trypsinization. Although monocytes and other mononuclear cells have an Fc or aggregate receptor, resynthesis of immuno-
globulins by trypsinized cells documented by F(ab')2 fragment antisera made aggregate receptor binding of immunoglobulins highly unlikely.

Further evidence for features of B cells was provided by the finding of a large percentage of neoplastic cells bearing complement receptors in the one patient studied. However, a significant percentage of cells in all patients also phagocytized latex. In this respect, hairy cell leukemia differs from the B-cell leukemia most analogous to it, chronic lymphocytic leukemia, in which latex-phagocytic cells are found in low percentages. Among mononuclear cells, latex phagocytosis is generally considered to be a property of monocytes, macrophage precursors, or macrophages. However, in our patients, a second property of monocytes, nonspecific esterase activity, was not present. Thus, it seems reasonable to conclude from these data that hairy cells most closely resemble B lymphocytes.

The phagocytic function demonstrated by these cells may result from a malignant proliferation of a small subpopulation of B lymphocytes with phagocytic capabilities. The presence of such cells has been intimated by Zucker-Franklin. On occasion, we have seen surface immunoglobulin-producing, EAC-bearing peripheral blood lymphocytes, and lymphoblastoid cell lines which, under phase contrast microscopy, have phagocytosed latex even after xylene (which dissolves extracellular latex) has been added, (Utsinger: unpublished observation). We have also observed morphological characteristics of macrophages in a small percentage of cells in a cloned lymphoblastoid cell line which has characteristics of B cells, including surface λ chains, EAC receptors, and Fc receptors (T5-1 clone of PGLC33H). This preliminary observation in a cell line derived from a single clone suggests the possibility of transition of differentiated properties. Alternatively, the latex phagocytosis exhibited by the hairy cells of our patients may represent a function acquired during malignant transformation.

The conflicting evidence that the hairy cell is a lymphocyte or monocyte seemingly cannot be fully explained by technical differences. Evidence from other studies points strongly toward a B-cell nature of these cells. Fu et al. studied four patients. Only one class of surface light chains was found; two patients had IgD heavy chains alone, and two had IgD and IgM heavy chains. However, these cells were also capable of phagocytosing latex. Rubin and co-workers found synthesis of IgD and A molecules by peripheral blood cells of one patient. Debusscher and colleagues used a radioimmunodiffusion technique to demonstrate both synthesis and secretion of IgM type λ chains in one patient. Catovsky and co-workers demonstrated surface-bound IgM and IgD immunoglobulins in two patients and IgM in one patient. One of these patients also had a large percentage of hairy cells with complement receptors.

On the other hand, conclusive evidence has been provided that some hairy cells, at least those from the spleen, are truly more closely related to monocytes. King et al. have described a patient whose splenic hairy cells were capable of glass adherence and latex phagocytosis. Hairy cell staphylocidal activity was similar to that of normal cells. Fc receptors, but not complement receptors, were found. Surface immunoglobulin staining was thought to be due to binding of antisera to the Fc receptor. Jaffe et al. studied two patients, both of whom demonstrated complement and Fc receptors, characteristics shared
with normal monocytes. Although splenic macrophages may differ from peripheral blood macrophages, the failure to find EA(IgM)C among these splenic neoplastic cells suggested that they were not lymphocytes.

Thus, hairy cell leukemia could be considered to be in reality two diseases. In some patients, a malignant proliferation of monocyte–histiocyte-like cells has been documented and in others proliferation of B-lymphocyte-like cells. Alternatively, hairy cell leukemia may involve malignant proliferation of a hypothetical subpopulation of B lymphocytes with phagocytic potential. The stage of maturation of the B-lymphocyte subpopulation at the onset of malignancy would then determine the presence of EA(IgM)C receptors and surface immunoglobulin.

The impaired PHA responsiveness noted in hairy cell leukemia from our patients has been previously documented but has not been uniformly found. Although it is tempting to ascribe differences in results to the percentage of responder T lymphocytes found in the whole mononuclear cell population, our data do not fully support such a contention. While the PHA responses in our patients greatly increased when T lymphocytes were purified, they were still less than responses seen in age- and sex-matched controls. Part of this impaired response may be due to the fact that these patients were febrile or clinically ill. In other diseases, an impairment in T-cell transformation has been noted to be a concomitant of disease activity. None was taking aspirin or other drugs known to interfere with lymphocyte transformation. The possibility that serum factors, which interfere with cell transformation by PHA, such as has been described in chronic lymphocytic leukemia, is currently under study. Alternatively, an intrinsic abnormality in the T lymphocytes may be present, such as the elevated levels of adenosine deaminase found in T lymphocytes in chronic lymphocytic leukemia. To eliminate the possibility that defective monocytes were responsible for the impaired transformation, we reconstituted the patients’ purified T lymphocytes on normal allogeneic monocyte monolayers. No improvement in responsiveness was noted, making it unlikely that monocyte dysfunction alone accounted for the impaired lymphocyte transformation.

Cytofluorography, in addition to thymidine incorporation, was used because lymphocytes themselves are not auxotrophic for thymidine and to document percentages and absolute numbers of cells capable of a PHA response. An intracellular pool of thymidine monophosphate as a DNA precursor exists; it is produced by synthetic reactions from simple precursors such as aspartic acid. Thymidine added to a culture system uses an unknown transport system to enter the cell. The relative contribution of these two metabolic pathways to the pool of thymidine monophosphate is usually not known, and discrepancies between incorporation of labeled thymidine into DNA and the actual rate of DNA synthesis have been observed in several systems. This study strongly supports the contention that, in hairy cell leukemia, there is an absolute decrease in the number of lymphocytes capable of responding by DNA synthesis to mitogen stimulation.

The prognosis of patients with hairy cell leukemia is generally very good, and frequently chemotherapeutic agents are not required for extended periods. This observation suggests that the cell type involved may represent a malig-
nancy of a more differentiated and very minor subpopulation of B lymphocytes. Further studies to identify the counterpart cell in normal populations of lymphocytes are indicated. The definitive identification of the cellular features described herein may herald a more benign prognosis. However, prospective, collaborative studies will be needed to determine more fully if functional capabilities and surface markers on the mononuclear cells of hairy cell leukemia patients will have prognostic value and reflect a low-grade malignancy of a minor B-cell subpopulation with phagocytic characteristics.

In summary, some patients with hairy cell leukemia have a malignant proliferation of B lymphocytes. These lymphocytes are unusual in that they have phagocytic capabilities. Mitogen transformation is abnormal and does not seem to be due solely to decreased T-lymphocyte numbers nor to abnormal monocyte function.

ACKNOWLEDGMENT

The authors are grateful to Brenda Cherry for expert secretarial assistance, The North Carolina Memorial Hospital Immunobiology Laboratory, and physicians participating in the North Carolina Regional Medical Program.

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