Cytogenetic Studies in Non-African Burkitt Lymphoma

By Edwin C. Douglass, Ian T. Magrath, Elaine C. Lee, and Jacqueline Whang-Peng

A particular translocation between chromosomes 8 and 14 has been found repeatedly in cytogenetic studies of Burkitt lymphoma, both of African and non-African origin. We report here our findings in cytogenetic studies of direct tumor preparations from 18 non-African Burkitt lymphoma patients, 9 of whom also had cell lines available for study. A t(8;14) was found in direct tumor material in 10 of the 18 patients. Seven of the 9 cell lines had a t(8;14). A total of 15 patients had either a t(8;14) or a 14q+ present in tumor material and/or cell lines. In addition, 8 patients had a peculiar marker chromosome 1. The t(8;14) was not found in every malignant cell and, where present, it was rarely the sole karyotypic abnormality. The relationship of the t(8;14) to the evolution of the tumor is discussed.

KARYOTYPIC abnormalities occur frequently in malignant disease. When a consistent abnormality is present, it may provide insight into the nature of the disease and even be of diagnostic importance, e.g., the Philadelphia chromosome (Ph') of chronic myelocytic leukemia.

Abnormalities of chromosome 14 have been found frequently in various lymphoid malignancies and immunodeficiency disease. A particular translocation between chromosomes 8 and 14 [t(8;14)] has been found repeatedly in cytogenetic studies of Burkitt lymphoma. Previous reports have dealt primarily with preparations made directly from tumors of African Burkitt lymphoma (ABL) and cell lines derived from ABL and non-African Burkitt lymphoma (NABL). We have found only one previous report of cytogenetic findings in a direct preparation of NABL. In this article, our findings in karyotypes derived from direct preparations of tumor material obtained from 18 patients with Burkitt lymphoma treated at the National Cancer Institute from 1976 through 1979. Cytogenetic findings of cell lines established from tumor material of 9 of these patients are also included in this report.

MATERIALS AND METHODS

Patient Population

The patient population consisted of 18 patients referred to the National Cancer Institute with a pathologic diagnosis of Burkitt lymphoma. Thirteen were previously untreated and 5 were relapsing patients referred for intensive chemotherapy. These 18 patients were derived from a larger group and represented all of those who had tumor material available that was adequate for cytogenetic analysis. In all except 2 patients a single sample of tumor material was available. Patient D.H. was treated at the National Naval Medical Center. All patients were white. All were Americans except for C.A. (Cuban) and N.I. (Italian).

The patients were clinically staged according to the system of Ziegler and Magrath.1 stage A, single extraabdominal site; stage B, multiple extraabdominal sites; stage C, intraabdominal disease with single extraabdominal site; stage D, same as C with multiple extraabdominal sites; and stage AR, >90% resection of tumor mass.

Surface immunoglobulin was detected with fluorescein-isothiocyanate conjugated anti-human immunoglobulins. All tumor material and cell lines tested were positive (11 of the 18 patients were tested). One patient (L.E.) has been previously reported.2

Except for patient J.A., all tumors were negative for Epstein-Barr virus nuclear antigen (EBNA). This will be reported more fully elsewhere.3

Derivation and Culture of Continuous Cell Lines

Tumor cells obtained from bone marrow cells, effusions, or finely minced pieces of solid tumor were suspended in RPMI 1640 medium containing penicillin (100 U/ml), streptomycin (100 µg/ml), and 20% fetal calf serum. The suspensions were then cultured at 37°C in a 5% CO2 atmosphere. Cells were subcultured after the development of a continuous cell line (in many cases proliferation began immediately after explantation) by diluting 3-4-fold with the above medium every 3-4 wk. Full details of the characteristics of these cell lines will be provided elsewhere.1

Chromosome Preparation

Solid tumors and lymph nodes were finely minced in medium containing colchicine (0.1 µg/cc). The resulting suspension and cells were incubated in colchicine for 1-2 hr at 37°C, washed, and incubated for 10 min in hypotonic solution (0.075 M KC1). One percent sodium citrate was used for hypotonic incubation of bone marrow. The cells were then fixed in Carnoy's solution (3 parts absolute ethanol to 1 part glacial acetic acid), air dried,4 and stained with both the conventional Giemsa stain for screening and with trypsin-Giemsa for banding.5 More recent chromosome preparations were incubated in colchicine for a total of 15-30 min, which resulted in less contracted chromosomes with better banding.

Karyotypes were analyzed according to the Paris Conference.6 M1 is used here to designate a marker chromosome 1 with a duplication of its long arm [dup 1q(12-31) or 1q(21-31)]. 14q+ indicates additional material on the long arm of chromosome 14, and 8q− indicates missing material from the long arm of chromosome 8.

RESULTS

The 8:14 Translocation

The numerical and structural aberrations found in specimens from the 18 patients reported here are listed...
| Pt. | Source | Date | # Cells | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | X | Other |
| CA  | AF     | 4/76 | 3       | M₂  | 2† | 6q(-11) | +10q(-3) | -13(2) | 14q(-2) | -20(2) | -X(11) |
|     | AF-TC  | 5/76 | 1      | M₁  | 8q(-) | +10q- | -14q(-) | +15 | -18 | -20 | +dic |
| J A | AF     | 2/78 | 4      | 1p+1(3) | -3(2) | -5(3) | +6(4) | +7q(-11) | 8q(-13) | -11(2) | 14q(14) | +15q(11) | -17(2) | -22(1) | +Cₘ₅₄(4) |
|     | FF-TC  | 6/78 | 5      | 6p- | 8q(-) | -10qα(-13) | 14q(12) | +15q(-12) | -17(2) | -18(2) | -19(2) | -22(1) | +Cₘ₅₄(4) |
|     | BM-TC  | 6/78 | 4      | 10qα(-1) | 14q(-11) | +17(1) |
| K B | AF     | 7/78 | 4      | 6p- | 8qα(-2) | 10qα(-11) | 14q(-11) | +17(1) |
| B B | LN     | 7/78 | 8      | M₃(6) | 3p- | -6q(-5) | +8(2) | +14(4) | +15(2) | -17(2) | +18(3) | -21(5) | -22(2) |
| M B | PF     | 8/77 | 1      | 7q+ | 14q+ |
| T E | BM-11%* | 7/77 | 1      | -10 | 14q(-) | +21 |
|     | BM-100%* | 3/78 | 3      | 1p- | +2(11) | +2(11) | 4q(-11) | -13(1) | 14q(-1) | +15qα(-11) | -22(1) |
|     | BM-TC₁ | 4/78 | 3      | M₁(3) | +2p- | -3q- | 4q(-3) | +6q- | +7(1) | 14q(2) | -17(2) | -18(2) | -19(2) | -22(1) |
|     | BM-TC₂ | 4/78 | 5      | M₁(5) | +2p- | +4p- | 4q(-3) | -14q(-3) | 14qα(15) | 15qα(3) | -18(3) | -18(3) |
| L E | AF     | 6/76 | 4      | 12q- | +14q(6) | +16qα(1) | +20(11) |
| R F | BM-100%* | 6/77 | 3      | 14q(-) | +16(1) |
| K G | BM-100%* | 1/77 | 4      | +1q- | +14(2) | +15(1) | +16(1) | +17q(-1) | +21(1) |
| D H | BM-60%* | 2/77 | 4      | -4(2) | 13qα(1) | +14q(4) | +15qα(-1) | +19(1) | +21(3) |
| N I | BM-60%* | 2/77 | 6      | M₁(1) | 1pα(2) | 8q(-3) | +14q(4) | +16qα(1) | +20(11) |
| J L | AF     | 9/77 | 2      | -2(11) | +3(11) | +6q- | 8q(-12) | -13(1) | 14q(12) | +15qα(-12) | +16qα(2) | +18(1) | +19(2) | +21(1) | -22(1) | +Cₘ₅₄ |
|     | PF-TC  | 11/77 | 3      | 7q(-1) | 8q(-15) | +9(15) | +11(11) | 14q(11) | 14q(17) | -15qα(-11) | -15qα(-12) | +18qα(2) | +21(1) | -21(1) | +Cₘ₅₄ | +Gₘ₅₄ |
|     | FF-TC  | 4/78 | 7      | M₁(3) | +3(5) | 7q- | 9q(-15) | +10qα(-3) | 14qα(11) | 14qα(17) | -15qα(-11) | -15qα(-12) | +18qα(2) | +21(1) | -21(1) | +Cₘ₅₄ | +Gₘ₅₄ |
| Tod R | AF     | 9/76 | 3      | M₁(3) | 8qα(-13) | +10(2) | -13(1) | -14(1) | +16(1) | +17(1) | +18qα(1) | +21(1) | +21(1) | +21(1) | +22(1) |
| Tan R | AF     | 2/78 | 4      | 2p- | 3p- | -5(3) | +7 | -8(3) | -12 | -13 | +14(3) | -17(2) | +22(1) | +Cₘ₅₄ |
|     | AF-TC  | 6/78 | 1      | 2p- | 3p- | -5(3) | +7 | -8(3) | -12 | -13 | +14(3) | -17(2) | +22(1) | +Cₘ₅₄ |
| D S | BM-TC  | 9/78 | 5      | -7(1) | -9(1) | -10(1) | -11(2) | -14(1) | +14q(2) | -20(11) |
|     | TUM    | 9/78 | 5      | 8q(-3) | -9(11) | 14qα(4) | +11(1) | +15qα(11) | +19(1) | +21(1) |
|     | BM-64%* | 11/78 | 5      | 1q- | -9(11) | 14qα(4) | +11(1) | +15qα(11) | +19(1) | +21(1) |
|     | Perf   | 1/79 | 2      | mar(122) | +5p(11) | +10q(11) | -11(11) | +13q(11) | 14q(22) | -16(2) | +21(1) | +21(1) | -Xq(2) |
|     | PB-TC  | 2/78 | 4      | mar(321) | +6(11) | 8q(-11) | -10qα(-11) | +13q(11) | 14q(22) | -16(2) | +21(1) | +21(1) | -Xq(2) |
|     | LW-TUM | 8/78 | 4      | mar(12) | +5q(-11) | 8q(-14) | +12(2) | +13(3) | 14q(13) | +18(2) | -19(1) | +22(2) |
|     | BM-0%* | 10/78 | 3      | mar(12) | +5q(-11) | 8q(-14) | +12(2) | +13(3) | 14q(13) | +18(2) | -19(1) | +22(2) |
| D W | PF     | 11/78 | 8      | M₁(6) | +3p(11) | 8q(-16) | 14q(18) |
|     | FF-TC  | 6/78 | 1      | 8q(-16) | 14q(18) |
| J D | AF     | 2/79 | 9      | M₁(6) | 7q(3) | 14q(-16) | 13q(13) | 14qα(17) | -16(2) |

1Marker No. 1 with reduplication (see text).
2† = no. of cells with abnormality.
3% = no. of cells with abnormal chromosome.
4** = extra long 14q+.

AF--ascites, TC--tissue culture, PF--pleural fluid, BM--bone marrow, Perf--pericardial fluid, TUM--tumor.
PB--peripheral blood, dic--dicentric, mar--marker, min--minute, i--isochromosome.
Dates refer to time of harvest of tissue cultures or preparation of tumor material.
cells with a 14q+. Bone marrow (64% tumor cells) studied 10 wk after diagnosis contained 5 of 5 cells with a 14q+. Three of these cells had an identifiable 8q−. A preparation of pericardial fluid obtained immediately postmortem contained 2 analyzable cells, both with a 14q+ (one of these cells had an identifiable 8q−). Tissue culture of peripheral blood (leukemic phase) done after 1 mo in culture contained 3 of 4 analyzable cells with a t(8;14).

Only one patient (R.F.) had a t(8;14) as the sole chromosomal rearrangement. Three other patients (N.I., D.W., and J.D.) had the t(8;14) accompanied only by a duplication marker 1 (see below). The remaining patients reported as having a t(8;14) had other chromosomal rearrangements as well.

Abnormalities of Chromosome 1

Our patients with NABL also have a high frequency of chromosome 1 abnormalities. Fourteen of 18 patients (77%) had some rearrangements of chromosome 1. Especially notable is the similarity of a 1 marker chromosome that was seen in 8 patients (44%). This marker chromosome apparently involves a duplication of 1q12–31 or 1q21–31 and is designated here as M1 (Fig. 2). It was present in a majority of the cells examined wherever it was found. It was seen in 5 direct tumor or bone marrow preparations (C.A., B.B., N.I., D.W., and J.D.) and 3 tissue cultures (T.E., J.L., and To.R.). A summary of 8q−, 14q+, and M1 found in direct material and cell lines is presented in Table 2; also included is the time of cytogenetic study and the modal chromosome number that showed little variation from 46.

Other Abnormalities

There were numerous other structural abnormalities found (see Table 1). Those that appeared to be clonal (found in 2 or more cells) were: 2p− (2 patients), 3q− (2 patients), 6p− (2 patients), 7q+ (2 patients), and 10q− (2 patients).

Chromosomal losses or gains occurring in 2 or more cells in 2 or more patients include: +3 (2 patients), +14 (3 patients), +15 (3 patients), +16 (2 patients), +18 (2 patients), and −17 (5 patients). These abnormalities were also found sporadically.

Clinical Data

Clinical data are presented for each patient in Table 3. Survival data are given, but comparisons are probably not valid because of the mixture of relapse and primary patients and the different therapies given.

Fifteen of our 18 patients were stage D at the time of diagnosis. Two more patients (N.I. and L.W.) subsequently suffered bone marrow relapses. The high
incidence of stage D patients in our series most likely resulted from the greater availability of their tumor material for cytogenetic analysis and explantation for tissue culture. Stage A, B, C, and AR patients were usually biopsied or resected before referral to NIH, and no additional tumor material was available for study.

**DISCUSSION**

Tumor-derived material from all of the 18 patients in this study had an abnormal karyotype, including the specimens from the 13 previously untreated patients. Our results demonstrate the high frequency of abnormalities of chromosome 14 and, as in ABL, of 8;14 translocations. In addition, an abnormality of chromosome 1, apparently not previously observed in banding studies of ABL and NABL, was a frequent finding in our patients.

**Abnormalities of Chromosome 1**

Abnormalities of chromosome 1 have been reported frequently in many types of hematologic malignancy as well as various solid tumors, such as breast, lung, and cervical carcinoma. These abnormalities include

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**Table 2. Modal Chromosome Number and Cytogenetic Markers**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Cytogenetic Study</th>
<th>M1</th>
<th>8q</th>
<th>14q</th>
<th>Modal Chromosome No.</th>
<th>M1</th>
<th>8q</th>
<th>14q</th>
<th>Modal Chromosome No.</th>
</tr>
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<tbody>
<tr>
<td>C.A.</td>
<td>R</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>45</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>45</td>
</tr>
<tr>
<td>J.A.</td>
<td>D</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>46</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>46</td>
</tr>
<tr>
<td>K.B.</td>
<td>D</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>46</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Not done</td>
</tr>
<tr>
<td>B.B.</td>
<td>D</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>49</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M.B.</td>
<td>D</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>46</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T.E.</td>
<td>D and R</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>46</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>46</td>
</tr>
<tr>
<td>L.E.</td>
<td>D</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>46</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R.F.</td>
<td>R</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>46</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>K.G.</td>
<td>R</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>46</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D.H.</td>
<td>D</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>46</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N.I.</td>
<td>R</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>46</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J.L.</td>
<td>D</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>50</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>46-47</td>
</tr>
<tr>
<td>Tod.R.</td>
<td>D</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>47</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tam.R.</td>
<td>D</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>46</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>46</td>
</tr>
<tr>
<td>D.S.</td>
<td>D and R</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>45-46</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>46</td>
</tr>
<tr>
<td>L.W.</td>
<td>D</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>46</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>46</td>
</tr>
<tr>
<td>D.W.</td>
<td>R</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>46</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>46</td>
</tr>
<tr>
<td>J.D.</td>
<td>D</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>45-47</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>45-47</td>
</tr>
</tbody>
</table>

D, diagnosis; R, relapse.
Reduplications, trisomies, rearrangements, and iso- 
chromosomes and usually involve the long arm, lq, 
almost always including the q21–25 or q25–32 
region.  

We have observed very frequent abnormalities of 
chromosome 1 in our NABL patients. These include 
a similar marker chromosome (M,) in 8 of our 18 
patients, which is apparently formed by a duplication 
of 1q12–31 or 1q21–31. This marker was present in 
cells with a t(8;14) in 5 of these 8 patients and with a 
14q+ in 1 patient. In the other 2 patients, neither a 
14q+ nor a t(8;14) was present. The marker in one 
patient (T.E.) contains 2 reduplications of the same 
segment of 1q. Similar reduplications of 1q are noted 
by Oshimura et al. to have been reported in gastric 
carcinoma, sideroblastic anemia, acute lymphoblastic 
leukemia, myelomatosis, malignant melanoma, and 
chronic myelocytic leukemia. 

Neither the frequent presence of chromosome 1 
abnormalities nor the occurrence of this 1 marker has 
received comment in previous reports of the cytoge-
netics of either ABL or NABL. Since most previous 
reports have dealt with ABL, this marker may in fact 
be more common in NABL. The karyotypic evolution 
of a cell line containing this marker from patient J.D. 
is currently under study. 

Other Abnormalities 

Three of the patients in this report had a 6q– 
chromosome. Deletions of 6q have been previously 
reported in non-Burkitt lymphoma. Four patients 
had a 10q– chromosome, which was similar in ap-
pearance to the 10q– reported by Mark et al. of a 
10;14 translocation in a histiocytic lymphoma. All 4 of 
our patients with a 10q– also had a 14q+. However, 
the amount of material translocated to chromosome 14 
was more nearly equivalent to that missing from the 
8q–, which was also present in these patients; there-
fore, they were considered to have a t(8;14). 

The most common numerical aberration was 
trisomy 15, which was present in 6 patients, 4 of whom 
had a 14q+. A trisomy 14 was present in 2 of the 3 
patients who had no 14q+. 

The 8;14 Translocation 

A 14q+ chromosome is the most frequent chromo-
somal abnormality found in lymphoid malignancies. 
Fukuhara and Rowley found a 14q+ in 17 of 27 
patients with non-Burkitt lymphomas, including 
histiocytic lymphoma, mixed cell lymphoma, poorly 
differentiated lymphoma, Hodgkin disease, and myco-
sis fungoides. It has also been reported in chronic 
lymphocytic leukemia (CLL), Hodgkin’s disease, 
acute lymphoblastic leukemia (ALL), multiple 
myeloma and plasma cell leukemia, and B-cell 
ALL. A 14q+ has been found in 3 of 28 mycosis fungoides 
patients studied by banding in this laborato-
ry. A 14q+ resulting from a 14;22 translocation with 
formation of a 22q– (Philadelphia chromosome) was 
reported in a 34-yr-old patient with ALL. 

The t(8;14), however, has been found infrequently 
in diseases other than Burkitt lymphoma. It has been 
reported in two cases of CLL, one case of a “lympho-
sarcoma” derived cell line, and one case each of
hiocytic lymphoma, mixed cell lymphoma, and mycosis fungoides. A t(8;14) has been reported from a histologically uninvolved lymph node of an African patient with EBV-positive nasopharyngeal carcinoma. This was cited as preliminary evidence for the presence of this chromosomal abnormality before the actual development of malignancy. Chromosome 14 abnormalities, especially a 14q+ translocation are characteristic of ataxia-telangiectasia, and this translocation has been shown to persist in the malignant cells of patients who subsequently develop hematologic malignancies. Recently, a t(8;14) cell line arising after in vitro infection with EB virus of an ataxia telangiectasia-derived cell line has been reported, the first instance of an induced 14q+ abnormality in karyotypically normal lymphocytes.

A 14q+ marker chromosome was first observed in ABL by Manolov and Manolova in 5 of 6 biopsies and 7 of 9 cell cultures. A 14q+ was also found in 7 of 7 ABL cell lines studied by Jarvis and her colleagues, but this abnormality was not found in 31 infectious mononucleosis cell lines or in cord blood lymphocyte lines transformed by EBV. The 14q+ abnormality was first reported in NABL by Philip et al. in 1976. They observed it in 40% of the cells (8 of 21 abnormal karyotypes) in a direct preparation of tumor packed bone marrow from a 17-year-old Danish patient. Zech and her coworkers were the first to describe an 8q− present in the same cells as the 14q+ in 10 of 10 biopsies and 3 of 4 cell lines from ABL patients, and they suggested that the 14q+ represented a translocation of material from chromosome 8 to chromosome 14. This same t(8;14) has been found in 2 NABL cell lines studied by Kaiser-McCaw et al. in 1976. They suggest that the translocation is t(8;14) (q23;q32). Most recently, Manolova et al. have demonstrated the reciprocal nature of the t(8;14) by a detailed analysis of the sub-bands of prometaphase chromosomes from 5 ABL cell lines and have localized the breakpoints to 8q24.1 and 14q32.5. They have also pointed out the altered morphology of the 8 segment, which is translocated to 14, resulting in apparent increased length of the translocated segment.

Although a 14q+ was found in 15 of our 18 patients, only 2 patients (L.E. and D.H.) with more than 2 analyzable cells had 100% occurrence of the 14q+ abnormality in direct tumor material. In the other patients, there were always cells with karyotypic abnormalities consistent with a malignant origin but with two normal-appearing 14 chromosomes. Philip et al. had similar findings in a previously reported patient with NABL in whom only 20% of the abnormal cells contained a 14q+. The presence of an 8q− and a 14q+ in the same cell is referred to as a t(8;14) in this article, we have found only 1 patient (R.F.) in whom the (8q−, 14q+) was the sole detectable rearrangement. Three others (N.I., D.W., and J.D.) had the t(8;14) and a single additional marker (M). The remaining 9 patients who are reported here as having a t(8;14) had other chromosomal rearrangements (2p−, 6p−, 10q−, etc.).

A 14q+ may be found in NABL without an accompanying 8q−, as in our patients M.B. and T.E. Both 8 chromosomes may be normal or the quality of the preparations may make them unanalyzable. The 14q+ may result from other translocations; either identifiable ones such as the t(12;14) in 2 cells from patient L.E., or other translocations that remain undetectable.

Studies of cell lines from both NABL and ABL as noted above and work in progress in this laboratory indicate a higher percentage of these lines containing a 14q+ or t(8;14) than we have found in direct preparations of tumor material from NABL. Furthermore, the cell lines that we report here have a higher percentage of cells with a 14q+ or t(8;14) than the tumor material from which they were derived. This may be due to the larger numbers of better analyzable mitoses obtained from tissue culture and/or it may be due to a clonal advantage or selection both in vitro and in vivo of cells containing a 14q+ or t(8;14). Because of the high frequency of 14q+ abnormalities in tumor cells examined directly, and the fact that we have identified a 14q+ abnormality in continuous cell lines where it was not detected in the original tumor in 3 cases, we cannot rule out the presence of a 14q+ in a subpopulation of cells in every Burkitt lymphoma. However, this population may be only a small percentage of the total population of malignant cells.

The t(8;14) has been cited as a disease-specific chromosomal abnormality much like the Philadelphia chromosome [Ph1, t(9;22)] of chronic myelocytic leukemia (CML). However, from our series of patients, we have observed the following differences. (1) Unlike the t(9;22) in CML, the t(8;14) is not necessarily present in every malignant cell of a given tumor, although it may be in some cases such as J.D. (2) The t(9;22) is usually the sole chromosomal rearrangement found in CML prior to blast crisis. In our patients with NABL, the t(8;14) was frequently accompanied by various other rearrangements and aberrations. However, these other abnormalities may be less frequent in less advanced disease.

The frequent presence of a t(8;14) in NABL is highly suggestive of an etiologic similarity between it and ABL, despite their differences with regard to primary anatomic site (facial in ABL, abdominal in
NABL) and presence of EBV nuclear antigen (positive in ABL, usually negative in NABL). However, this peculiar translocation is not necessarily present in every malignant cell in NABL. It may occur with increased frequency in advanced disease (our patients were all stage D or relapse).

The translocation may not be an essential requirement of malignant differentiation in NABL. If it is present in the primary malignant cell (or cells), later clonal diversification without its presence is certainly possible. Conversely, if it is not present during the malignant origin of the tumor, it may instead be a frequent “epiphenomenon” of the disease with a peculiar growth advantage such that its presence becomes increasingly evident with continued progression of the disease or growth in tissue culture. We are currently attempting serial cytogenetic studies of new NABL cell lines (and where possible, serial examinations of patient material) in an attempt to define further a possible evolving predominance of cells containing a 14q+ or t(8;14).

Further cytogenetic studies in lymphomas and leukemias, especially with regard to the immunologic characteristics of the tumor, may help to clarify the relationship of the 14q+ to the development of malignancy. Such studies eventually may point to specific gene defects and thus provide more understanding of the development and behavior of these tumors.

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