We identified seven new recurring translocations among 483 cases of acute lymphoblastic leukemia (ALL) with adequate chromosome banding studies. Four were apparently balanced \([t(1;3)(p34;p21), t(7;9)(p15;p23-p24), t(12;13)(p13;q14), t(17;19)(q22;p13)]\), while three were unbalanced with the formation of a dicentric chromosome \([dic(7;9)(p13;p11), dic(7;12)(p11;p12), and dic(12;17)(p11;p11-p12)]\). One translocation was observed in five cases, two in four cases, and the remaining four in two cases each. The modal chromosome numbers in these 21 cases were 45 (n = 11), 46 (n = 9), and 47 (n = 2). Eight of the 11 cases with a dicentric chromosome had a modal number of 46. Only a single translocation was found in 14 cases (67%), representing the sole structural abnormality in six cases. In three of the seven translocations identified, the blast cells were consistently of B lineage (pre-B, early pre-B, or both); in all others, they represented both the B and T lineages. The small size of these subgroups prevented definitive clinical correlations, although it may be important that two of the four cases with a \(t(17;19)\) and an early pre-B-cell immunophenotype had disseminated intra-vascular coagulation, an event usually observed in acute promyelocytic leukemia or T-cell ALL. These findings add substantially to the existing list of nonrandom chromosomal translocations in childhood ALL and may help to explain the genetic alterations leading to the loss of normal growth control mechanisms in this disease.

**The Identification** of recurring chromosomal translocations in leukemic cells can provide clues to cellular events with biologic and often clinical significance. Many of these chromosomal changes are consistently associated with either myeloid or lymphoid leukemias, and may correlate with specific morphologic or immunophenotypic subtypes. The genes located at the breakpoints of recurring chromosomal rearrangements have received considerable attention because of their potential role in neoplasia. Such altered genes may either transform progenitor cells directly or play a role in the multistep process leading to malignant transformation. Consistent chromosomal translocations also provide a genetic classification schema that can be used to estimate prognosis.

About 30 nonrandom structural abnormalities in acute lymphoblastic leukemia (ALL) were recognized at the Ninth Human Gene Mapping (HGM9) Conference; additional nonrandom changes were described at a subsequent meeting (HGM10). The chromosomal abnormalities most closely associated with childhood ALL include the \((8;14)(q24;q32)\) in B-cell cases, \(14q11\) and \(7q35\) translocation breakpoints in T-cell cases, \((t119)(q23p13)\) in pre-B-cell cases, \((t4;11)(q21q23)\) and \(12p\) abnormalities in all types of B-lineage ALL, and \((t9;22)(q34;q11)\) and 9p abnormalities in either T- or B-lineage ALL. Despite numerous reports of chromosomal findings in childhood ALL, the addition of new cytogenetic subgroups to this list has been limited. Here we describe seven new recurring chromosomal rearrangements and discuss their unique clinical and biologic features.

**Materials and Methods**

From December 1979 to September 1988, 802 consecutive children with newly diagnosed ALL were admitted to St Jude Children’s Research Hospital. The diagnosis of ALL was based on morphologic criteria of the French-American-British Cooperative Group (FAB) and negative myeloperoxidase and esterase staining. Four hundred eighty-three cases had bone marrow (BM) leukemic cell metaphases adequate for cytogenetic evaluation; of these, 242 (= 50%) had a chromosomal translocation. A translocation was identified if the karyotype contained a reciprocal rearrangement or an identifiable derivative chromosome resulting from a translocation. The B-cell ALL cases with \((8;14)\) (n = 18) were not included in this analysis. Descriptions of the karyotypes of some of these cases have been included in previous publications.

With three exceptions, each patient was enrolled in Total Therapy Study X or XI, which evaluated different approaches to intensive, multiagent chemotherapy. One child (No. 21) was pretreated with steroids before arriving at the hospital and was excluded from the Total Therapy trials. Another child (No. 17) was treated for ALL elsewhere and was evaluated at this institution only at the time of first relapse. The remaining child (No. 13) was treated on a less intensive protocol because the parents refused permission for blood products on religious grounds. Written informed consent was obtained from the patients or their parents, and the investigations were approved by the institution’s clinical trials review committee.

**Cytogenetic Analysis**

BM samples were prepared by a direct method, with or without short-term (24-hour) culture; a modified trypsin-Giemsa technique was used for chromosome banding. From 20 to 25 metaphases were completely analyzed in each case. Chromosomes were identified and classified according to the International System for Human Cytogenetic Nomenclature.

**Blast Cell Phenotyping**

Leukemic blasts were isolated from BM specimens (each containing ≥ 85% blasts) by density gradient centrifugation. Cell surface antigens were detected by standard indirect immunofluorescence...
assays relying on monoclonal antibodies (MoAbs) to lymphoid-associated antigens. Samples were analyzed with a flow cytometer (EPICS-C; Coulter Diagnostics) or fluorescence microscopy. Blast cells were also tested for surface (sIg) and cytoplasmic (cIg) Ig. Cells were classified as T (CD7+, CD5+, CD2+), B (sIg+), pre-B (cIg+), or early pre-B (cIg−, sIg−, HLA-DR+, CD19+, CALLA±) according to their reactivity with the MoAb panel.

RESULTS

Of the 242 ALL cases with one or more chromosomal translocations, a third comprised well-recognized recurring abnormalities: t(1;19)(q23;p13) or der(19)t(1;19) (n = 32), t(9;22)(q34;q11) (n = 19), t(4;11)(q21;q23) (n = 8), t(11;14)(p13;q11) (n = 5), t(11;14)(p15;q11) (n = 1), dic(9;12)(p11;p12) (n = 5), t(10;14)(q24;q11) (n = 4), t(11;19)(q23;p13) (n = 4), and t(8;14)(q24;q11) (n = 3). Most translocations in the remaining cases had unique chromosomal breakpoints, but only seven were frequent enough to warrant consideration as cytogenetic subgroups.

Details of the seven previously unreported rearrangements are shown in Table 1. One of these changes was identified in five cases, two in four cases, and the remaining in one or two cases each. Seventeen cases (67%) had only one translocation, and in six (29%) the translocation was the only structural abnormality. In four subgroups, the translocations were reciprocal and balanced, while in three they were unbalanced with the formation of a dicentric chromosome. Overall, 71% of these 21 cases had other structural abnormalities; 33% had additional translocation(s), none of which was a well-recognized nonrandom abnormality [eg, t(4;11), t(9;22)]. Structural abnormalities other than translocations involved different chromosomes, except for a del(6q) that was observed in three cases (Nos. 9, 14, and 18). The modal chromosome numbers in the stemlines of these 21 cases were 45 (n = 11, 52%), 46 (n = 8, 38%), and 47 (n = 2, 9%). None of the cases had a hyperdiploid karyotype with greater than 50 chromosomes. Eight of the cases with a dicentric chromosome had a modal number of 45; the remaining three (Nos. 10, 12, and 21) had extra chromosomes 21, 20, and 10. All dicentrics were formed from the q arms of chromosomes 7, 9, 12, and 17, with partial loss of their respective p arms. The chromosomal regions most often affected by these rearrangements were 12p and 9p, as in other chromosomal rearrangements and deletions in ALL.18,25

Table 2 summarizes the presenting features of patients with any one of the seven new chromosomal translocations. Blast cell surface antigens were characteristic of B-lymphoid differentiation (n = 16) or T-lymphoid derivation (n = 4), or unclassifiable (n = 1). Within the B-cell lineage, nine cases were subclassified as early pre-B (cIg−) and seven as pre-B (cIg+). Two of the four T-cell cases (Nos. 11 and 18) and one of the early pre-B cases (No. 21) also expressed a myeloid-associated antigen (CD33).

Description of Subgroups

t(17;19)(q22;p13). Four cases had identical 17;19 translocations with breakpoints in the q arm of chromosome 17 at q22 and in the p arm of chromosome 19 at p13 (Fig 1A). The t(17;19) was the sole chromosomal abnormality in two of these cases (Nos. 1 and 2) but was associated with additional abnormalities in the remaining two. In case 3 the rearrangements were highly complex. Case 4 showed a derivative (19)t(17;19) with loss of one chromosome 17 and no evidence of a der(17); an independent line containing a t(13;14)(q32;q11) as the only abnormality was also present. This case was unclassifiable by immunophenotyping; it expressed CD7 and CD10 but not TdT, cIg, sIg, CD2, CD5, CD13, CD22, or CD33. Patients 1 and 2 had remarkably similar immunophenotypic (CD19+, CD10+, CD21+, cIg−) and one case (No. 2) expressed Mo-1. Both patients presented with disseminated intravascular coagulation that improved during antileukemic therapy.

dic(7;9)(p13;p11). In four cases, the leukemic blast cells

<table>
<thead>
<tr>
<th>Subgroup of Translocations</th>
<th>Patient No.</th>
<th>Karyotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(17;19)</td>
<td>1</td>
<td>45.XY,t(17;19)(q22;p13)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>46.XY,t(17;19)(q22;p13)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>46.XY, t(17;19)(q22;p13), t(8;14)(q24;q11)</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>46.XY, t(17;19)(q22;p13), t(8;14)(q24;q11)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>45.XY, dic(7;9)(p13;p11), dup(l)(p373→p38)/45.XY, same, del(8)(p22)/46.XY, dup(l)(p373→p38)</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>45.XX, dic(7;9)(p13;p11), t(17;19)(q22;p13), t(8;14)(q24;q11)</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>45.XY, dic(7;9)(p13;p11)</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>45.XX, dic(7;9)(p13;p11)</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>45.XY, dic(7;12)(p11;p12), del(6)(q14q23)/46.XY, dic(7;12)(p11;p12), del(6)(q14q23), t(17;19)(q22;p13), t(8;14)(q24;q11)</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>46.XY, +21, dic(7;12)(p11;p12), del(1)(q32)</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>45.XY, dic(7;12)(p11;p12), 46.XY, +t(17;19)(q22;p13), t(8;14)(q24;q11)</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>47.XX, +20, dic(7;12)(p11;p12), dic(7;12), t(11;15)(q23;q15=q21)</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>45.XX, dic(7;12)(p11;p12), del(9)(p21)</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>45.X-, X, del(6)(q13q21), t(11;3)p34p21</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>46.XY, t(1;13)p34p21/46.XY, +t(13)t(13)(q36q37), t(1;13)p34p21</td>
</tr>
<tr>
<td></td>
<td>16</td>
<td>47.XY, +8, X, del(1)(q14), t(17;9)</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>45.X-, Y, -20, del(1)(q12), del(3)(q34), t(13)(q14), t(17;9)</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>46.XY, -6, +der(11)t(11;11)(q22), t(17;9), t(13)(q14), t(17;9), t(13)(q14), t(17;9)</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>46.XY, -6, +der(19)t(19;19)(q13;7), t(12;13)p13p13, t(12;13)p13p13</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>45.XX, dic(12;17)(p11;p11), inv(5)</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>46.XX, t(17;19)(q22;p13), del(5)(q22)</td>
</tr>
</tbody>
</table>

Table 1. Karyotypes of the Seven Translocation Subgroups in Childhood ALL
had a dicentric chromosome, dic(7;9), that contained the long arms of chromosomes 7 and 9, with partial loss of 7p and 9p (Fig 1B). In each case, the modal chromosome number was 45; in two cases, the dicentric chromosome was the only abnormality. Consistent presenting characteristics of these patients were an L1 FAB subtype, age less than 6 years, and organomegaly. In three cases, the pre-B leukemic blasts expressed cIg+, while in the other, the phenotype and morphology, although the karyotype retained the t(7;9) (Fig 1E).

t(12;13)(p13;q14). The breakpoint on chromosome 12 in these cases was clearly defined as p13; the breakpoint at 13q was more difficult to assign (Fig 1F). One of these karyotypes (in case 18) had multiple chromosomal abnormalities. Both translocations occurred in boys less than 6 years old with low leukocyte counts who are currently in remission after completing all chemotherapy.

dic(12;17)(p11;p11p12). These two cases had leukemic blasts with a dicentric chromosome containing the long arms of chromosomes 12 and 17 (Fig 1G). Thus, the malignant cells were deficient for both p arms. This was the sole translocation in both cases.

**DISCUSSION**

The diversity of chromosomal translocations in childhood ALL is impressive, with the majority involving unique breakpoints that affect the arms of virtually every chromosome. We have identified seven new nonrandom translocations in 21 cases of ALL. Most of these abnormalities had at least one breakpoint in regions commonly affected by cytogenetic changes in this disease (9p11-p24 [n = 6], 12p11-p13 [n = 9], 19p13 [n = 4]); the others occurred within less frequently involved regions (1p34 [n = 2], 3p21 [n = 2], 7p11-p15 [n = 11], 13q14 [n = 2], 17p11-p12 [n = 2], and 17q22 [n = 4]).

Chromosome 12p12 is the region most often involved in nonrandom abnormalities in childhood ALL (10% of all cases). In our original report of 23 cases with 12p12 abnormalities, 18 were classified as "common," three as

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**Table 2. Clinical and Laboratory Features of Patients With Specific Translocations**

<table>
<thead>
<tr>
<th>Translocation Subgroup</th>
<th>Patient No.</th>
<th>Age (y)</th>
<th>Race/ Sex</th>
<th>Leukocyte Count (x 10^9/L)</th>
<th>Hemoglobin Level (g/dL)</th>
<th>Platelet Count (x 10^9/L)</th>
<th>Liver/ Spleen (cm)*</th>
<th>FAB Subtype</th>
<th>Immunophenotype</th>
<th>Clinical Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(1;3)(p34;p21)</td>
<td>1</td>
<td>16.9</td>
<td>W/M</td>
<td>11.8</td>
<td>9.4</td>
<td>24</td>
<td>2/5</td>
<td>L1</td>
<td>Early-B</td>
<td>Died in CCR</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>15.5</td>
<td>W/F</td>
<td>4.3</td>
<td>6.4</td>
<td>48</td>
<td>4/7</td>
<td>L2</td>
<td>Early-B</td>
<td>CCR on therapy</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>2.2</td>
<td>W/M</td>
<td>16.7</td>
<td>6.7</td>
<td>15</td>
<td>0/2</td>
<td>L1</td>
<td>Early-B</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td>dic(7;9)</td>
<td>4</td>
<td>11.1</td>
<td>W/M</td>
<td>71.9</td>
<td>9.3</td>
<td>29</td>
<td>5/11</td>
<td>L1</td>
<td>Unclassified</td>
<td>Failed induction</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>5.5</td>
<td>W/M</td>
<td>11.1</td>
<td>9.6</td>
<td>192</td>
<td>3/0</td>
<td>L1</td>
<td>Pre-B</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>2.5</td>
<td>W/F</td>
<td>64.0</td>
<td>8.4</td>
<td>34</td>
<td>6/8</td>
<td>L1</td>
<td>Pre-B</td>
<td>CCR on therapy</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>1.0</td>
<td>W/M</td>
<td>88.6</td>
<td>11.4</td>
<td>56</td>
<td>5/3</td>
<td>L1</td>
<td>Pre-B</td>
<td>CCR on therapy</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>6.0</td>
<td>W/F</td>
<td>6.0</td>
<td>4.3</td>
<td>362</td>
<td>1/1</td>
<td>L1</td>
<td>Pre-B</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td>dic(7;12)</td>
<td>9</td>
<td>2.3</td>
<td>W/M</td>
<td>30.0</td>
<td>12.6</td>
<td>23</td>
<td>7/10</td>
<td>L1</td>
<td>Early-B</td>
<td>Died</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>2.5</td>
<td>W/M</td>
<td>107.2</td>
<td>7.8</td>
<td>9</td>
<td>4/4</td>
<td>L1</td>
<td>Pre-B</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>10.8</td>
<td>B/M</td>
<td>66.5</td>
<td>13.6</td>
<td>80</td>
<td>4/5</td>
<td>L2</td>
<td>T-cell</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>8.7</td>
<td>W/F</td>
<td>4.0</td>
<td>7.0</td>
<td>380</td>
<td>0/0</td>
<td>L2</td>
<td>Pre-B</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>2.3</td>
<td>W/F</td>
<td>65.2</td>
<td>9.8</td>
<td>42</td>
<td>5/3</td>
<td>L1</td>
<td>Pre-B</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td>t(1;3)</td>
<td>14</td>
<td>11.1</td>
<td>W/F</td>
<td>3.0</td>
<td>11.7</td>
<td>371</td>
<td>0/0</td>
<td>L1</td>
<td>Early-B</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>16.1</td>
<td>W/M</td>
<td>163.0</td>
<td>16.1</td>
<td>131</td>
<td>8/9</td>
<td>L1</td>
<td>T-cell</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>16.0</td>
<td>W/M</td>
<td>2.0</td>
<td>5.7</td>
<td>320</td>
<td>—</td>
<td>L1</td>
<td>Pre-B—AML</td>
<td>Died</td>
</tr>
<tr>
<td>t(12;13)</td>
<td>18</td>
<td>5.9</td>
<td>W/M</td>
<td>7.8</td>
<td>9.5</td>
<td>103</td>
<td>1/1</td>
<td>L2</td>
<td>T-cell</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>4.8</td>
<td>W/F</td>
<td>7.9</td>
<td>4.5</td>
<td>70</td>
<td>0/1</td>
<td>L1</td>
<td>Early-B</td>
<td>CCR off therapy</td>
</tr>
<tr>
<td>dic(12;17)</td>
<td>20</td>
<td>14.7</td>
<td>W/F</td>
<td>85.7</td>
<td>12.1</td>
<td>310</td>
<td>0/0</td>
<td>L2</td>
<td>T-cell</td>
<td>Died</td>
</tr>
<tr>
<td></td>
<td>21</td>
<td>3.0</td>
<td>B/F</td>
<td>53.4</td>
<td>4.3</td>
<td>23</td>
<td>0/0</td>
<td>L1</td>
<td>Early-B</td>
<td>CCR off therapy</td>
</tr>
</tbody>
</table>

Abbreviations: CCR, complete clinical remission; AML, acute myeloid leukemia.

*Palpable below the costal margins.
†CD33 positive.
pre-B, and two as T-cell ALL.\textsuperscript{15} None of the 23 cases had the prognostically favorable feature of hyperdiploidy greater than 50 chromosomes, and the median leukocyte count ($30 \times 10^9/L$) was higher than that of cases lacking this abnormality. At that time, we described a $t(7;12)(q11;p12)$; with additional cases and better definition of chromosome morphology, the breakpoint in chromosome 7 has been reassigned to 7p11, and the derivative chromosome has been reclassified as a dicentric. In this study, we also identified two additional nonrandom translocations involving chromosome 12p, a balanced $t(12;13)$ and a dicentric $12;17$. None of these nine patients with 12p abnormalities described in this report had hyperdiploidy greater than 50 chromosomes; six had B-lineage ALL (two pre-B) and three T-cell ALL; five had leukocyte counts greater than $50 \times 10^9/L$; and seven remain in complete clinical remis-

**Fig 1.** Representative G-banded partial karyotypes of rearranged chromosomes and homologues from patients with newly recognized translocations. (A) $t(17;19)(q22;p13)$ from patients 1 and 2; (B) dic(7;9)(p13; p11) from patients 5 and 7; (C) dic(7;12)(p11;p12) from patients 10 and 11; (D) $t(1;3)(p34;p21)$ from patient 15; (E) $t(7;9)(p15; p23-p24)$ from patient 17; (F) $t(12;13)(p13;q14)$ from patients 18 and 19; (G) dic(12;17)(p11;p11-p12) from patient 21.
sion. These findings are similar to those in other 12p12 cases.15

Cases of 12;13 chromosomal translocations similar to those in our report have been described by others.10,26 Descriptions of the t(12;13) published by Keene et al25 correspond to findings in the present study, except that the breakpoints are interpreted differently and their patients had eosinophilic leukemia. The 13q14 band is the site of the RB tumor suppressor gene and is involved, in both retino-blastoma and hematologic malignancies, mostly in deletions.27 17p13.1 is the site of the P53 gene, which has been implicated in many neoplastic diseases.27 It may be of interest that the human cellular homolog of the KRAS-2 gene has been mapped to the region encompassing the 12p12 breakpoint.7

The breakpoint of the t(17;19) lies on the short arm of chromosome 19 in the region affected by the 1;19 translocation in pre-B ALL (19p13). This breakpoint has been reported to bisect the E24 transcription factor gene, and produces fusion transcripts containing sequences from PRX, a homeobox-related gene on chromosome 1.28,29 The chimeric gene encodes a new potential transcription factor, in which the E24 DNA binding domain is replaced by the homeodomain of the PRX gene. Conceivably, the 19p13 rearrangement in the four cases we identified also involves the E24 gene. Moreover, the promoter of the BCL3 gene (B-cell leukemia/lymphoma 3) located on chromosome 1q22 causes activation of MYC expression in a t(8;17) found in an aggressive B-cell leukemia,21 and a t(7;19)(q35; p13) results in truncation of the LYL1 gene and its juxtaposition with the T-cell receptor β(TCR-β) gene.22 Whether these genes are involved in the pathogenesis of t(17;19)-positive acute leukemias is unknown at present. It is interesting that two of the children with t(17;19) presented with disseminated intravascular coagulopathy (DIC), which is rare in ALL but common in acute promyelocytic leukemia characterized by a t(15;17)(q22;q21).30 The breakpoints on chromosome 17 in our lymphoblastic cases appear different by light microscopy from those in acute promyelocytic leukemias, suggesting that the mechanisms leading to production of tissue factors responsible for DIC may be different in leukemias carrying these translocations.

Deletion or unbalanced translocation of the short arm of chromosome 9, including bands 9p21 and p22, has been reported in 7% to 14% of cases with ALL.5 Although originally thought to be a nonrandom karyotypic abnormality associated with either a T-cell phenotype or lymphomatous presentation,23,25 this change has since been identified in a broader range of cases.25 We found 9p abnormalities in 40 (10%) of 398 consecutive cases of childhood ALL.25 Compared with patients whose leukemic blasts lacked 9p abnormalities, children with these alterations were significantly older, had higher leukocyte counts, more “lymphomatous” disease, and an increased rate of extramedullary relapse. However, the finding of an abnormal chromosome 9p was not specific for lymphomatous or T-cell lineage, as most cases lacked these features. In this regard, the six cases of 9p translocations described here had B-lineage leukemia; most important, three of the four cases with dic(7;9)(p13;p11) had a pre-A immunophenotype.25 A similar t(7;9)(p15;p22) has been reported in a case of T-cell ALL.26 A cluster of interferon α (IFNa) and IFNB1 genes is located in the 9p22 region.27 Recently, Diaz et al27 found deletions of the IFN genes in 18 (29%) of 62 cases tested, including submicroscopic deletions in eight. Because IFNs can affect cell proliferation and differentiation, the loss of one or more of these genes might alter the proliferation of leukemic cells.

Genes potentially involved in the t(1;3) include a putative T-cell leukemia/lymphoma gene, TCL5 or TAL, and a stem cell leukemia gene (SCL), both located at the 1p32-p34 region.24-26 It may be of interest that one of our cases with the t(1;3) had a T-cell immunophenotype. Also, the human HF:10 finger gene was recently mapped to 3p21-p22,28 a region frequently altered in human cancer.27

In the past, dicentrics were seldom observed in leukemic cells, but as the quality of metaphase preparations has improved, such chromosomes are being identified more often.12,27,28 Dicentrics are known to have a limited life-span because of frequent bridge formation during division. It appears that the dicentrics (7;9)(p13;p11), (7;12)(p13;p12) and (12;17)(p11;p11-p12) may remain stable through multiple cell divisions because the two centromeres are close enough to prevent the formation of anaphase bridges.41 During the process of dicentric formation in our cases, most of the DNA from the p arms of chromosomes 7, 9, 12, and 17 is lost.

With improved karyotyping and optimal sampling techniques, we are now able to identify chromosomal translocations in 50% of cases of ALL. Although a third of the translocations identified in this study were shown to be nonrandom, it is likely that additional studies will reveal more new clusters. The identification of recurring translocations in ALL is important because such changes implicate specific genes whose alteration may contribute to the clinical and biologic properties of the disease. As more is learned about the molecular pathology underlying these rearrangements, it may be possible to devise new therapeutic approaches that are specifically targeted to interfere with aberrant gene products expressed by the leukemic cells.

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