We report a series of 20 non-Hodgkin’s lymphomas (NHL) in which cytogenetic analysis showed a translocation involving band 3q27 and the site of one of the three Ig genes [14q32, 2q12, 22q11] in the neoplastic cells. These cases were found in a series of 319 patients with clonal chromosomal abnormalities studied over a 7-year period. Fourteen patients had diffuse lymphoma, mainly of large cell type and the remaining six were follicular lymphomas. All cases studied were of B-cell phenotype. A t(3;14)(q27;q32) was commonest, found in 15 patients (47%), with the two variant translocations, t(3;22)(q27;q11) and t(2;3)(p12;q27), being found in three and two patients, respectively. Additional chromosomal defects were present in most patients, but two patients had this type of translocation as the sole abnormality. These results indicate that translocations involving band 3q27 and Ig genes are not uncommon, and suggest that a novel oncogene, located at band 3q27, may be implicated in B-cell NHL.

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RESULTS

Good quality metaphases were obtained in 347 of the 383 patients (91%), and 319 of them demonstrated clonal chromosomal abnormalities. Ninety-two of these 319 patients had a follicular lymphoma, in 64 of whom (70%) a typical t(14;18)(q32;q21) was present. Fifty patients with diffuse lymphoma exhibited a previously reported cytogenetic abnormality, namely, t(14;18)(q32;q21) in 18 cases, t(8;14)(q24;q32) in 17 cases, t(2;8)(p12;q24) in three cases, t(8;22)(q24;q11) in two cases, t(11;14)(q13;q32) in seven cases, t(2;5)(p23;q35) in 13 cases, and a del(14)(q22) in four other patients.

Twenty patients had a translocation involving band 3q27 and the site of one of the three Ig genes (Fig 1). Their main

PATIENTS AND METHODS

Patient population. Biopsy specimens were obtained from 383 consecutive adult patients admitted to the Centre Henri Becquerel (Rouen, France) between September 1984 and October 1991 for the diagnosis and treatment of NHL.

Tissue samples. Fresh lymph nodes were divided into three portions for morphologic, immunologic, and cytogenetic studies. Fragments of each sample and also suspended cells were kept frozen. All histologic material was reviewed by the same pathologist, without knowledge of cytogenetic data, and classified according to the Working Formulation for Clinical Usage.7 Cell surface phenotype was studied in cell suspensions using a panel of specific antibodies as previously described.8 From 1988, immunoperoxidase studies were also performed on paraffin-embedded sections using reagents.9

Cytogenetic analysis. Biopsy specimens were minced with surgical blades, and cells were dissociated and suspended at a concentration of about 2 × 10⁶ cells/mL in RPMI 1640 medium supplemented with 10% fetal calf serum (FCS). Cells were cultured overnight in the presence of Colchicine (0.02 μg/mL). Preparations were incubated for 25 minutes at 37°C in 0.075 mol/L potassium chloride, fixed in methanol-acetic acid (3:1), and spread on clean, dry slides. R-banding was performed according to Schesters.9 Karyotypes are described according to the International System for Human Cytogenetic Nomenclature.10

RESULTS

Good quality metaphases were obtained in 347 of the 383 patients (91%), and 319 of them demonstrated clonal chromosomal abnormalities. Ninety-two of these 319 patients had a follicular lymphoma, in 64 of whom (70%) a typical t(14;18)(q32;q21) was present. Fifty patients with diffuse lymphoma exhibited a previously reported cytogenetic abnormality, namely, t(14;18)(q32;q21) in 18 cases, t(8;14)(q24;q32) in 17 cases, t(2;8)(p12;q24) in three cases, t(8;22)(q24;q11) in two cases, t(11;14)(q13;q32) in seven cases, t(2;5)(p23;q35) in 13 cases, and a del(14)(q22) in four other patients.

Twenty patients had a translocation involving band 3q27 and the site of one of the three Ig genes (Fig 1). Their main
chromosome 1 or whole 1q was gained in 10 patients either as a duplication, an isochromosome, or a derivative chromosome. Abnormalities of the 7p at different bands were found in six cases, all of which exhibited a diffuse growth pattern. Other recurrent defects were present in at least three patients: +X, +7, +5, +21, del(6q), and dup(12q).

Case 29, a follicular lymphoma, which was analyzed at relapse after more than 5 years of an indolent course, had a t(14;18) in addition to a t(2;3).

Patient 370, an 18-year-old woman, received a kidney transplant 18 months before developing a huge mesenteric mass that was diagnosed as a large cell lymphoma. After transplantation, she had received immunosuppressive therapy with steroids, cyclosporine, and azathioprine. Five months after the procedure, an episode of graft rejection occurred that was successfully treated with an anti-CD3 monoclonal antibody. Nine months after transplantation, she developed serologic evidence of Epstein-Barr virus infection. Lymphoma cells, in this patient, did not express surface Ig; nevertheless, clonality could be ascertained by the presence of the chromosomal abnormality and of molecular monoclonal rearrangements of both JH and Ck genes.

**Fig 1.** Partial karyotypes of patients 370 (A), 340 (B), and 51 (C) showing, respectively, t(2;3)(p12;q27), t(3;14)(q27;q32), and t(3;22)(q27;q11). The normal chromosome of each pair is on the left; the derivative chromosome on the right.

characteristics and karyotypes are listed in Table 1. Sixteen analyses were performed at the time of primary diagnosis and four at relapse (patients 19, 184, 224, and 340). Fourteen patients had a diffuse lymphoma, mainly of large cell type, and six patients had a follicular lymphoma. Immunologic data were obtained in 15 cases, all of which demonstrated a B-cell phenotype. Cell-surface Ig chains were identified in eight samples, and all expressed κ light chains.

Fifteen patients had a t(3;14)(q27;q32), three had a t(3;22)(q27;q11), and two had a t(2;3)(p12;q27). In two cases, a t(3;14) or a t(2;3) was found as the sole anomaly. Additional chromosomal defects present in other patients appeared to be nonrandom. Part of the long arm of chromosome 1 or whole 1q was gained in 10 patients either as a duplication, an isochromosome, or a derivative chromosome. Abnormalities of the 7p at different bands were found in six cases, all of which exhibited a diffuse growth pattern. Other recurrent defects were present in at least three patients: +X, +7, +5, +21, del(6q), and dup(12q).

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**DISCUSSION**

Two major models of oncogenesis in NHL, both involving deregulated expression of the normal cellular oncogenes after their translocation to the vicinity of Ig genes, have been described.

In Burkitt’s lymphoma, the MYC oncogene is frequently translocated, as a result of t(8;14)(q24;q32), into the vicinity of the heavy chain Ig gene. Less frequently, the same gene is translocated in this type of lymphoma into the vicinity of a light chain gene, accompanied by the neoplastic cell expression of the appropriate light chain, ie, κ chain in t(2;8)(p12;q24) and λ chain in t(8;22)(q24;q11).

In follicular lymphoma, the BCL2 oncogene is commonly translocated to the J region of the heavy Ig chain gene, as the result of t(14;18)(q32;q21). Much less frequently, the same gene can translocate to the vicinity of the Ig κ light chain gene, in t(2;18)(p12;q21), and to the vicinity of the λ gene in t(18;22)(q21;q11), as described in chronic lymphocytic leukemia.

We report here 20 cases of NHL in each of which chromosomal translocation juxtaposed the site of one of the Ig genes with a region (q27) on chromosome 3. These cases were detected in a series of 319 cases of NHL with clonal chromosomal abnormalities, representing a frequency of 6.3%. The t(3;14)(q27;q32) was present in 15 cases and was thus the third most common recurring translocation (4.7%), after t(14;18) and t(8;14). The cytogenetic appearance of this telomeric reciprocal translocation makes it difficult to recognize, and in some patients it was initially misinterpreted as a 3q27 deletion associated with a 14q+ chromosome of unknown origin.

The 20 patients shared some common morphologic, immunologic, and cytogenetic features. Except for patient 229, who exhibited an isolated t(3;14)(q27;q32), all of these tumors had a large cell component. All tumors tested were
Table 1. Principal Characteristics and Cytogenetic Features of the 20 Patients

<table>
<thead>
<tr>
<th>No. of Mitoses Analyzed</th>
<th>UPN</th>
<th>Sex/Age</th>
<th>Histology*</th>
<th>Phenotype</th>
<th>Stage</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Karyotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with t(3;14)(q27;q32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>91</td>
<td>F/38</td>
<td>D</td>
<td>IgMD,x</td>
<td>I</td>
<td>12</td>
<td>5</td>
<td></td>
<td>55, XX, +2, +3, +5, +6, +7, +18, +19, +21, der(2)(t;11)(p24; q11), t(3;14)(q27;q32), del(8)(q11q23), del(6)(q15q27), der(16)(t;16)(q21;q24), der(10)(t;10)(q19;p13), +r</td>
</tr>
<tr>
<td>101</td>
<td>M/63</td>
<td>G</td>
<td>IgG,x</td>
<td>IV</td>
<td>0</td>
<td>13</td>
<td></td>
<td>48, XY, der(1)(t;13)(q43;q13), t(3;14)(q27;q32), dup(3)(q21q26), del(6)(t;8)(q12;?), t(7;11)(p13;q23), del(8)(t;8)(p24;?), +mar</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>48, XY, der(1)(t;13)(q43;q13), t(3;14)(q27;q32), del(6)(t;8)(q12;?), t(7;11)(p13;q23), del(9)(t;8)(q34;?), der(16)(t;16)(q31;q22), +mar</td>
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<td>114</td>
<td>F/68</td>
<td>G</td>
<td>IgD,x</td>
<td>III</td>
<td>1</td>
<td>17</td>
<td></td>
<td>45, XX, −12, −16, −19, del(1)(p12p33), dup(2)(p16p24), t(3;14)(q27;q32), der(4)(t;4?)(p16;?), del(15)(t;15;17)(p11;q11), +der(15)(t;15;17)(p11;q11), del(17)(t;17;?) (q26;?), +1mar</td>
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<tr>
<td>169</td>
<td>F/73</td>
<td>ND</td>
<td></td>
<td>IV</td>
<td>0</td>
<td>14</td>
<td></td>
<td>49, XX, +X, +12, +14, t(2;5)(q24;q31), t(3;13)(p13;q33), t(3;14)(q27;q32), inv(5)(p15q12), del(6)(q21q25), t(7;19)(p21;p12), t(8;12)(q11;q23), del(14)(q24)</td>
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<tr>
<td>184</td>
<td>F/65</td>
<td>ND</td>
<td></td>
<td>III</td>
<td>0</td>
<td>18</td>
<td></td>
<td>62, XX, +X, +2, +5, +6, +7, +7, +9, +11, +13, +17, +20, +21, +22, (X; 18)(q25;q21), +del(1)(X;X;?) (q25;?), t(4;9)(q11p; q32), del(6)(q15), inv(7)(q21q31), inv(7)(p1p22), del(1)(t;11)(q11p12), del(16)(q22), +del(16)(q22), del(22)(t;11;22)(q14;q11), del(22)(t;11;22)(q12;?), +1mar</td>
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<tr>
<td>188</td>
<td>M/53</td>
<td>G</td>
<td>B-cell</td>
<td>IV</td>
<td>2</td>
<td>16</td>
<td></td>
<td>95, XY, −Y, +X, +X, +X, +1, +2, +2, +2, +3, +3, +4, +4, +5, +5, +6, +7, +8, +8, +9, +9, +10, +10, +11, +12, +13, +13, +14, +14, +15, +15, +16, +16, +17, +18, +18, +19, +19, +20, +20, +21, +21, +22, t(3;14)(q27;q32), del(6)(h611)(q11;?), +del(6)(h611)(q11;?), del(10)(t;11)q23, del(10)(t;11)q23, dup(12)(q11q15), +dup(12)(q11q15), +del(13)(t;13;?) (q33;?), +del(13)(t;13;?) (q33;?), (+i?7a)</td>
</tr>
<tr>
<td>217</td>
<td>M/49</td>
<td>G</td>
<td>IgM,x</td>
<td>IV</td>
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<td>18</td>
<td></td>
<td>48, XY, +18, +21, t(3;14)(q27;q32)</td>
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<tr>
<td>224</td>
<td>M/42</td>
<td>C</td>
<td>IgMD,x</td>
<td>II</td>
<td>0</td>
<td>19</td>
<td></td>
<td>46, XY, t(3;14)(q27;q32), der(22)(h12;22)(q12;p11)</td>
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<td>229</td>
<td>M/67</td>
<td>E</td>
<td>IgM,x</td>
<td>III</td>
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<td>9</td>
<td></td>
<td>46, XY, t(3;14)(q27;q32)</td>
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<tr>
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<td>F/34</td>
<td>D</td>
<td>IgG,x</td>
<td>IV</td>
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<td>7</td>
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<td>47, XX, +7, dup(1)(q21q31), t(3;14)(q27;q32), t(14;15)(q32;q23), del(18)(t;18;?) (q23;?)</td>
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<tr>
<td>248</td>
<td>M/84</td>
<td>O</td>
<td>B-cell</td>
<td>IV</td>
<td>1</td>
<td>17</td>
<td></td>
<td>49, t(X;10)(p22;p11), Y, +Y, +9, +9, +11, +16, −22, der(1)(t;1)(q32;?), t(2;16)(p16;p13), t(3;14)(q27;q32), del(5)(q13q31), del(9)(t;12q34), del(9)(t;9q22)(p24;q11)</td>
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<tr>
<td>250</td>
<td>M/77</td>
<td>F</td>
<td>ND</td>
<td>III</td>
<td>4</td>
<td>13</td>
<td></td>
<td>48, XY, +X, +7, der(1)(t;1)(p38;p11), dup(1)(q21q31), del(5)(q13q31), dup(2)(p15p21), t(3;14)(q27;q32), del(13)(t;12;13)(p12;?)</td>
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<tr>
<td>335</td>
<td>F/71</td>
<td>C</td>
<td>B-cell</td>
<td>I</td>
<td>1</td>
<td>17</td>
<td></td>
<td>49, XX, +X, +1, +5, −6, (t1q), t(3;14)(q27;q32), i(5p), der(10)(t;10)(q13q25), del(12)(q13q23), del(13)(q13q23), +mar</td>
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<tr>
<td>340</td>
<td>F/78</td>
<td>C</td>
<td>B-cell</td>
<td>IV</td>
<td>1</td>
<td>17</td>
<td></td>
<td>46, XY, t(3;14)(q27;q32), del(4)(q23), del(7)(q25)</td>
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<tr>
<td>43</td>
<td>M/35</td>
<td>F</td>
<td>ND</td>
<td>III</td>
<td>3</td>
<td>15</td>
<td></td>
<td>57, XY, +X, +8, +9, −10, +11, +12, +15, −17, +18, +19, +20, +20, (t1q), t(3;22)(q27;q11), del(8)(t;8)(q35;?), t(7)(t;7)(p22;?), +del(7)(t;7)(p22;?), +del(7)(t;7)(p22;?), +del(12)(t;12)(q13q24), der(13)(t;13;?) (p11;?), +del(14)(t;14;?) (p11;?), der(15)(t;15;?) (q25;?), +mar, +variations</td>
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<tr>
<td>51</td>
<td>M/73</td>
<td>O</td>
<td>ND</td>
<td>II</td>
<td>1</td>
<td>17</td>
<td></td>
<td>52, XY, +X, +4, +5, +7, +9, +21, t(3;22)(q27;q11), del(4)(p14p16), (i6p), del(7)(t;7)(p15;?), del(9)(q13q32)</td>
</tr>
</tbody>
</table>

(Continued on following page)
of B-cell phenotype. It was not possible to ascertain whether the five cases in which the 3q27 region was juxtaposed to the vicinity of light chain genes showed (as in Burkitt's lymphoma) restriction in light chain type expressed, ie, κ chain in t(2;3) and λ chain in t(3;22), because suitable fresh material was only available from one case. It is of interest that in their series of patients with t(3;22), Offit et al demonstrated λ light chain expression in all five patients tested. However, Leroux et al described two patients with the same translocation in which λ chain was present, whereas such an abnormality was present in only 15% of patients in our overall series of NHL. This series did not differ significantly, in terms of the incidence of abnormal chromosome numbers or the incidence of 6q deletion, from our overall series, or from other published series.

In the past few years, two genes involved in neoplastic transformation have been mapped to this region of chromosome 3. One of these is the human homologue of the mouse retroviral integration site FIM3, implicated in Friend murine leukemia virus-induced myeloblastic leukemia,17,18 and the other is EVI1, also expressed in mouse and human myeloblastic leukemia.14,19 This latter gene was studied in patients with diffuse lymphoma. Blood 74:1876, 1989

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Translocations involving band 3q27 and Ig gene regions in non-Hodgkin's lymphoma [see comments]

C Bastard, H Tilly, B Lenormand, C Bigorgne, D Boulet, A Kunlin, M Monconduit and H Piguet

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