

## Nonrandom Chromosome Abnormalities in Lymphoma<sup>1</sup>

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### ABSTRACT

G-banded chromosomes were studied from involved lymph nodes or other tumor masses in 94 patients with malignant lymphoma. Clonal chromosome abnormalities were identified in 91 patients including all 81 B-lymphomas but only 6 of 9 T-lymphomas. Many recurring chromosome abnormalities were found. Most common numerical alterations involved gains of chromosomes 12 (19% of patients), 18 (13%), 7 (12%), and 21 (10%). Structural abnormalities, which were more frequent than numerical alterations, most commonly involved chromosome regions 14q (71% of patients), 18q (36%), 6q (31%), 1p (24%), and 8q (19%). Seven recurring translocations were identified, and all except one involved 14q32. The most frequent were t(14;18)(q32;q21) in 22 patients, t(8;14)(q24;q32) in 9 patients, and t(1;14)(q42;q32) in 3 patients. Deletions most frequently involved the long arm of chromosome 6 at band q21 (11 patients) or q23 (7 patients). The common recurring chromosome abnormalities were correlated with histology (International Working Formulation for Clinical Usage) and immunological phenotype. Four abnormalities were significantly associated with specific histologies. Eighteen (82%) patients with t(14;18)(q32;q21) were follicular. Similarly, 82% of patients with del(6)(q21) were large cell lymphomas. Lymphomas with trisomy 7 were either diffuse large cell or follicular, while patients with t(8;14)(q24;q32) were either diffuse large cell or small noncleaved cell. A significant association with immunological phenotype was seen for t(14;18) only. All patients were either B- or complement lymphomas, and the heavy chain(s) was more commonly  $\gamma$  and less frequently  $\delta\mu$  than among the total B-lymphoma population. We conclude that essentially all lymphomas have cytogenetic abnormalities; further study is required to determine their significance. Particularly, it will be of interest to see if oncogenes are found in the regions of these chromosome abnormalities.

### INTRODUCTION

Limited data are available regarding chromosomal abnormalities in non-Hodgkin's malignant lymphoma other than Burkitt's (26, 31, 33, 34). The few reported studies of banded chromosomes have generally been small, composed of less than 50 patients, and have often included many incomplete karyotypes. Bone marrow, blood, or effusions have frequently been studied rather than lymph nodes or other primary tumor masses. Moreover, for a given lymph node, no large series has correlated chromosome findings with histology and immunological phenotype.

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Since July 1978, we have prospectively studied chromosomal abnormalities in tumor masses from patients with lymphoma and correlated them with histology and immunological phenotype as defined using a large panel of immunological assays (2, 5, 22). Our data indicate that there are many recurring chromosome abnormalities. In this manuscript, we present a detailed discussion of these nonrandom chromosome abnormalities including their associations with specific histologies or immunological phenotypes. Subsequent papers will focus on specific subgroups of lymphoma (histological or immunological) and their karyotype findings.

### MATERIALS AND METHODS

**Tumor Procurement and Histological Classification.** Chromosomes from involved lymph nodes or other tumor masses from 94 patients (ages 8 to 85 years; median, 54) with non-Hodgkin's malignant lymphoma biopsied at the University of Minnesota Hospitals between July 1978 and April 1982 were studied. In 59 patients, neoplastic tissue was analyzed at diagnosis prior to any treatment; in 35 patients, tissue was first studied at relapse. In all instances, the tumor was simultaneously studied for histology, immunological markers, and G-banded chromosomes. The portion of the tumor studied for histology was fixed in B5. Histological classification was done using the International Working Formulation for Clinical Usage (27).

Histologically, the MLs<sup>3</sup> in this series included 16 patients of Group A ML, small lymphocytic; 21 cases of Group B ML, follicular, predominantly small cleaved cell; 4 cases of Group C ML, follicular, mixed, small cleaved and large cell; 8 cases of Group D ML, follicular, predominantly large cell; one case of Group E ML, diffuse, small cleaved cell; 13 cases of Group F ML, diffuse, mixed, small and large cell; 19 cases of Group G ML, diffuse, large cell; 3 cases of Group H ML, large cell, immunoblastic; 2 cases of Group I ML, lymphoblastic; 4 cases of Group J ML, small noncleaved cell; and 3 cases of ML, unclassifiable. Seven of the patients had a peripheral blood picture compatible with CLL; 5 of these had lymph nodes classified as Group A, one was unclassifiable, and one was classified as Group F. In 5 patients, the diagnosis on the lymph node studied at relapse differed from that of the initial biopsy. In 2 patients who were classified initially as Group B, the subsequent biopsy was Group C (Table 1, Patient 41) or Group D (Patient 49). Other changes were from Histological Groups A to F (Table 1, Patient 58), A to G (Patient 75), and C to G (Patient 82).

**Immunological Phenotyping.** Immunological phenotyping in all patients was based on study of both single-cell suspensions and tissue frozen sections. All patients were studied for SIg and CIg and receptors for complement, Fc $\gamma$ , and unsensitized sheep erythrocytes. Fifty-six patients were also studied for terminal deoxynucleotidyl transferase and with a panel of monoclonal antibodies (13).

Our techniques for immunological analysis have been described in detail (3, 13). In brief, suspensions of viable neoplastic cells were studied for the presence of SIg by immunofluorescence with monospecific antisera against heavy and light chains, for receptors for unsensitized sheep

<sup>3</sup> The abbreviations used are ML, malignant lymphoma; CLL, chronic lymphocytic leukemia; SIg, surface immunoglobulin; CIg, cytoplasmic immunoglobulin.



Table 1  
Clinical data, histology, immunological phenotype, and cytogenetic findings in 94 patients with lymphoma

Patient	Age	Sex	Lymphocyte surface markers <sup>a</sup>	Prior treatment	No. of cells studied			Karyotype
					Total	Normal	Abnormal	
Group A ML, small lymphocytic								
1	69	M	δμκ		17	3	11	43,XY,-4,-7,-9,-11,-13,-17,t(1;14)(p32;q32),t(6;12)(q21;p13),+der(7)t(7;?)p(22;?),+der(13)t(13;?)q(34;?),+der(17)t(17;?)p(13;?)
							3	44,XY,-4,-7,-9,-11,-13,-17,+20,t(1;14)(p32;q32),t(6;12)(q21;p13),+der(7)t(7;?)p(22;?),+der(13)t(13;?)q(34;?),+der(17)t(17;?)p(13;?)
2 <sup>b</sup>	58	M	δμκ		15	2	13	46,XY,?t(14;19)(q32;q13)
3 <sup>b</sup>	58	M	δμκ		5	3	2	46,XY,-714,+?der(14)t(14;?)q(32;?)
4	13	M	T		10	1	9	46,XY,-12,+del(6)(q15),t(12;13)(p13;q22)
5	52	M	μλ		12	2	10	46,XY,del(11)(q21)
6	84	F	μκ		8	3	5	46,XX,dup(11)(q13→q25)
7 <sup>b</sup>	79	M	δμλ		5	1	4	47,XY,+12
8	64	M	μκ		10	0	10	47,XY,+12
9	68	M	T		14	7	7	48,XY,+3,-6,-8,+14,+del(1)(p13),dup(1)(q22→qter),inv(2)(p11;q21),t(11;14)(p11;q32),+der(6)t(6;?)q(27;?)
							5	49,XY,+10,+12,+21
10	65	M	δμκ		5	0	5	45,XX,-7,-12,-14,ins(1)(q11),del(6)(q23),t(13q15q),+der(7)t(7;?)q(36;?)
11 <sup>b</sup>	75	F	μκ	+	12	4	8	?,+der(12)t(12;?)p(13;?),+der(14)t(14;?)q(32;?)
							14	46,XX,-2,del(15)(q26),t(7;14)(p22;q22),+der(3)t(3;?)p(27;?)
12	74	F	δμλ	+	15	1	14	46,XY,?del(14)(q22)
13	71	M	δμλ	+	4	0	4	46,X,?t(X;8)(q22;q24)
14	72	F	μλ	+	17	12	5	47,XY,+15,t(11;14)(q22;q32)
15 <sup>b</sup>	50	M	δμλ	+	11	0	11	47,XY,-8,+18,del(1)(p31→p35),t(11;14)(q13;q32),+der(8)t(8;?)q(24;?)
16	59	M	δμκ	+	15	1	14	
Group B ML, follicular, predominantly small cleaved cell								
17	71	M	μλ		6	1	5	43,X,-Y,-7,-9,del(11)(q23),t(1;8)(p31;q22),?t(3;14)(p21;q32),?t(6;17)(q15;p13)
18	70	F	αδλ		4	1	3	45,XX,-10,-14,+der(14)t(14;?)q(32;?)
19	69	F	μκ		5	3	2	46,XX,del(16)(q22)
20	49	M	δμλ		14	4	10	46,XY,-5,t(8;14)(q22;q32),+der(5)t(5;?)p(15;?)
21	59	M	μκ		4	0	4	46,XY,?t(14;18)(q32;q21)
22	63	F	κ		22	2	20	46,XX,del(1)(p36),del(16)(p13),t(1;14)(q42;q32),t(2;3)(q21;q27),t(6;18)(q21;q23)
23	64	F	μκ		7	1	6	46,XX,t(14;18)(q32;q21)
24	61	F	γλ		6	2	4	47,X,-X,+9,-11,+18,del(4)(p14),?inv(11)(p11;q13),+del(18)(q21),t(14;18)(q32;q21)
25	50	M	μκ		10	2	8	47,XY,+3,-4,del(5)(q14),del(6)(q23),del(7)(q32),t(1;14)(q23;q32),+mar
26	44	M	μκ		15	10	5	48,XY,+13,-14,+del(6)(q23),+der(14)t(14;?)q(32;?)
27	46	F	μκ		14	3	11	48,XX,+10,+18,t(14;18)(q32;q21)
28	49	M	δμκ		11	3	8	48,XY,+X,+2,?t(7;14)(q34;q32)
29	48	F	γλ		15	8	7	49,XX,-1,+3,+8,+12,del(6)(q21),t(14;18)(q32;q21),+der(1)t(1;?)p(36;?)
30	39	M	μλ	+	5	0	5	47,XY,-10,del(7)(q22),t(3;6)(p22;p21),t(14;18)(q32;q21),+der(10)t(10;?)p(15;?)
							3	?,+mar
31	29	F	μλ	+	3	0	3	47,XX,-1,?del(8)(q22),del(13)(q31),+t(17q),t(14;18)(q32;q21),+der(1)t(1;?)p(36;?)
32	24	M	γλ	+	6	2	4	47,XY,+7,t(14;18)(q32;q21)
33	27	M	γλ	+	15	3	12	47,XY,-4,-9,+20,del(2)(p12),del(18)(q12),dir dup(12)(q13→q21),t(5;14)(q23;q32),+der(4)t(4;?)q(35;?),+der(18)t(18;?)q(23;?)
34	56	M	μκ	+	10	0	10	47,XY,-2,+12,ins(3)(q11),del(6)(q15),t(17q),t(14;18)(q32;q21),+der(2)t(2;?)p(25;?)
35	73	F	μκ	+	13	1	12	48,XX,del(6)(q23),dir dup(12)(q13→q21),?t(14;18)(q32;q21),+2mar
36	53	F	μκ	+	12	3	9	48,XX,-14,+15,?t(4;18)(p15;q21),+der(12)t(12;?)q(24;?),+der(14)t(14;?)q(32;?)
37	35	M	γλ	+	12	3	9	(Hypertetraploid)98,XXYY,+1,+21,t(6;21)(p21;q22),t(14;18)(q32;q21),der(20)t(20;?)q(13;?),+mar
Group C ML, follicular, mixed small cleaved and large cell								
38	37	M	κ		14	2	6	46,XY,+12,-17,?t(1;14)(q42;q32)
							6	(Tetraploid)92,XXYY,+12,-17,?t(1;14)(q42;q32)
39	47	F	Unknown		19	4	15	47,XX,-1,+7,-13,-14,+der(1)t(1;?)p(36;?),+der(13)t(13;?)p(13;?),+der(14)t(14;?)q(32;?)
40	45	M	μκ		15	0	15	50,XY,+X,+3,+8,+?,-11,-16,-20,?del(2)(q14),t(17q),t(1;8)(q32;q22),t(5;13)(q15;p13),t(14;18)(q32;q21),+der(1)t(1;?)p(15;?),+der(20)t(20;?)q(13;?),+ring
41 <sup>d</sup>	39	F	γλ	+	10	0	10	48,XX,+8,+del(18)(q21),?del(22)(q12),t(14;18)(q32;q21)
Group D ML, follicular, predominantly large cell								
42	54	F	μκ		10	1	4	46,XX,?t(14;17)(q32;q21)
							5	(Tetraploid)92,XXXX(cannot karyotype)
43	43	M	γλ		10	7	3	46,XY,del(3)(p25)
44	80	M	Complement +		17	3	14	47,XY,+7,dup(17)(q22→24),t(14;18)(q32;q21)
45	51	M	μκ		14	5	9	51,XY,-3,+10,+14,+21,+del(2)(q23),t(1;17)(q25;q24),t(2;14)(q23;q32),+der(3)t(3;?)q(29;?),+ring
46	48	M	δμκ		15	1	14	55,XY,+1,+5,-13,+18,+19,del(2)(q32),+del(3)(p22),t(6;12)(p21;q24),t(1;14)(q42;q32),+2der(7)t(1;7)(q23;q12),+der(12)t(6;12)(p21;q24),+der(13)t(13;?)q(34;?)
							16	?,+mar
47	82	M	γκλ		16	0	16	(Hypertetraploid)98,XXYY,+9,+10,+12,?t(14;18)(q32;q21)
48	51	F	δμλ		12	5	7	(Hypertetraploid)94,XXXX,-3,+12,del(2)(q23),del(6)(q21),t(17q),t(14;18)(q32;q21),+der(3)t(3;?)q(29;?)
49 <sup>d</sup>	59	M	γλ	+	14	1	13	49,XY,+7,+14,-17,del(6)(q21),t(14;18)(q32;q21),+der(17)t(17;?)q(25;?)
							?	?,+der(19)t(19;?)p(13;?)
Group E ML, diffuse, small cleaved cell								
50	53	M	δμκ	+	14	5	9	47,XY,+19,t(1;19)(p16;q13)
Group F ML, diffuse, mixed small and large cell								
51	48	F	δμλ		4	1	3	46,XX,del(14)(q24)
52	53	M	T		5	1	4	46,XY,?t(1;14)(q23;q32)
53	78	M	T		11	11	0	46,XY
54	52	F	T		7	3	4	47,XX,-1,+12,del(17)(q23),t(7q),t(10;14)(q22;q32),+der(1)t(1;?)p(36;?)

Table 1—Continued

Patient	Age	Sex	Lymphocyte surface markers <sup>a</sup>	Prior treatment	No. of cells studied			Karyotype
					Total	Normal	Abnormal	
55	69	M	$\delta\mu\kappa$		17	1	16	48,X,-Y,-9,+18,del(6)(q21),+i(3q),t(17q),t(6;11)(p22;p15),+der(9)t(3;9)(p21;p13),+der(18)t(1;18)(q25;q23)
56	55	F	Unknown		15	2	13	48,XX,t(7;9)(q34;q22),+t(7;9)(q34;q22)
57 <sup>b</sup>	33	F	$\delta\mu\lambda$	+	10	1	7	46,XX,t(4;20)(q35;q12),t(14;19)(q32;q13)
							2	47,XX,+1,t(1;10)(q42;q22),t(4;20)(q35;q12),t(14;19)(q32;q13)
58 <sup>d</sup>	74	M	$\mu\kappa$	+	16	3	13	46,XY,-8,del(11)(q23),+der(8)t(8;?)p23;?)
59	63	M	T	+	4	3	1	46,XY,-3,-14,-17,del(1)(q32),+der(3)t(3;?)q29;?),+der(14)t(14;?)q32;?)
							4	47,XY,-1,+12,t(5;6)(q35;q21),?t(14;18)(q32;q12),+der(1)t(1;?)p36;?)
60	31	M	C1g $\mu\kappa$	+	8	3	1	48,XY,-1,+12,t(5;6)(q35;q21),?t(14;18)(q32;q12),t(7;11)(p22;q13),+der(1)t(1;?)p36;?),+ring
							4	48,XY,-1,+12,t(5;6)(q35;q21),?t(14;18)(q32;q12),t(7;11)(p22;q13),+der(1)t(1;?)p36;?),+ring
61	75	M	$\gamma\kappa$	+	15	0	15	48,XY,+12,-13,-14,+18,+2mar
62	49	F	$\mu\lambda$	+	2	0	2	50,XX,+1,-14,+18,del(2)(p12),+del(2)(p12),del(7)(q32),+der(11)t(11;?)q25;?)
							2	50,XX,+1,-14,+18,del(2)(p12),+del(2)(p12),del(7)(q32),+der(11)t(11;?)q25;?)
63	67	M	$\gamma\kappa$	+	18	6	12	(Hypertetraploid)106,XXYY,+del(6)(q23),t(1;16)(p22;q24),+t(1;2)(p11;q11),t(3;11)(q21;p13),+der(6)t(6;?)q27;?),+der(20)t(20;?)p13;?),+2mar
Group G ML, diffuse, large cell <sup>e</sup>								
64	18	F	$\gamma\kappa$		2	0	2	46,XX,t(8;14)(q24;q32)
65	66	F	Complement +		17	2	15	47,XX,-2,-13,+21,t(14;18)(q32;q21),+der(2)t(2;?)p25;?),+der(13)t(13;?)q34;?)
66	85	F	$\mu\kappa$		10	0	10	48,XX,-9,+18,-19,+der(9)t(3;9)(p21;q34),+der(19)t(3;19)(q12;q13),+ring
67	52	M	$\gamma\lambda$		14	1	13	49,XY,-3,-14,-19,+21,del(1)(p36),+del(9)(q22),+der(3)t(1;3)(q23;p26),+der(14)t(1;14)(q23;q32)
68	52	M	$\mu\kappa$		15	0	15	49,XY,+10,del(2)(p16),+del(3)(p11),dup(1)(q13→qter),t(5;13)(q31;q32),+der(18)t(18;?)q23;?)
69	8	F	$\gamma\kappa$		15	0	12	49,XX,+2,+7,+10,del(6)(p21),t(3;22)(q21;q11),t(8;14)(q24;q32)
							3	49,X,+2,+7,+10,i(Xq),del(6)(q21),t(3;22)(q21;q11),t(8;14)(q24;q32)
70	64	M	$\mu\kappa$		13	2	11	49,XY,+9,+11,+14,del(1)(p22→p32),del(6)(q23),t(3;14)(p21;q32)
71	19	M	$\gamma\kappa$		20	0	20	51,XY,-1,+12,-14,+20,+21,del(2)(p23),del(5)(p13),+i(10q),+der(1)t(1;?)p36;?)
							1	51,XY,-1,+12,-14,+20,+21,del(2)(p23),del(5)(p13),+i(10q),+der(1)t(1;?)p36;?)
72	44	M	$\delta\mu\lambda$		13	0	1	53,XY,+X,-11,+12,-16,+18,+del(6)(q15),+?del(18)(q12),+der(11)t(11;?)q25;?)
							12	53,XY,+X,-11,+12,-16,+18,+del(6)(q15),+?del(18)(q12),+der(11)t(11;?)q25;?)
							16	(Hypertetraploid)106,XXYY,+X,-11,+12,-16,+18,+del(6)(q15),+?del(18)(q12),+der(11)t(11;?)q25;?),+der(14)t(14;?)q32;?),+2mar
73	65	F	$\delta\mu\lambda$		20	4	16	(Hypertetraploid)82,XXX,+7,+13,+15,+20,+21,+del(1)(p22),+?del(2)(q32),+del(6)(q21),del(12)(p11),t(2;4)(q32;q35),t(3;6)(p25;q21),t(5;6)(q15;q27),?t(8;15)(q24;q24),t(14;18)(q32;q21),+t(14;18)(q32;q21),+3mar
74	24	M	$\mu\kappa$	+	5	1	4	43,XY,-4,-16,-17,?t(14;18)(q32;q21)
75 <sup>d</sup>	43	M	T	+	7	1	6	49,XY,-4,-7,del(1)(p31),+del(4)(q21),del(6)(q21),+i(17q),t(2;3)(q21;q27),?t(4;19)(q21;q13),+der(7)t(7;?)p22;?)
76	78	M	$\mu\kappa$	+	15	0	15	49,XY,-4,-7,-13,-17,dup(1)(q22→q44),del(6)(q21),i(18q),+i(18q),t(8;14)(q24;q32),+der(4)t(4;?)q35;?),+der(13)t(13;?)p13;?),+der(17)t(17;?)q25;?),+ring
77	40	M	$\mu\lambda$	+	15	0	15	49,Y,+3,+7,+18,del(6)(q21),dir dup(12)(q13→q21),del(17)(q23),t(8;14)(q24;q32),?t(X;18)(p22;q12)
78	85	M	$\mu\lambda$	+	6	0	6	49,XY,+?10,+19,del(1)(p36),+del(18)(q12),i(17q),?t(3;6)(q29;q21),?t(8;14)(q24;q32)
79	67	F	$\mu\kappa$	+	15	0	15	50,X,-1,+2,-8,-10,+18,+18,+20,del(X)(p11),del(5)(q22),del(9)(q22),t(2;18)(q14;q23),?t(15;20)(q21;q13),+der(1)t(1;?)p36→q44;?),+der(3)t(3;?)q29;?),+der(8)t(8;?)q24;?)
80	38	F	$\delta\mu\kappa$	+	23	1	6	54,XX,+2,+3,+3,+6,+7,+12,-17,-19,+21,-22,del(4)(p14),?del(8)(p12),+?del(11)(p11),t(1;3)(q32;q27),+t(1;3)(q32;q27),t(2;6)(q37;q21),+mar
							16	(Hypertetraploid)108,XXXX,+2,+3,+3,+6,+7,+12,-17,-19,+21,-22,del(4)(p14),?del(8)(p12),+?del(11)(p11),t(1;3)(q32;q27),+t(1;3)(q32;q27),t(2;6)(q37;q21),+mar
81	67	F	$\mu\kappa$	+	13	0	13	54,XX,+3,+3,+7,+12,+13,-14,-17,+18,+19,?t(1;2)(p35;q31),+der(14)t(14;?)q32;?),+der(14)t(14;?)q32;?),+der(17)t(17;?)p13;?)
82 <sup>d</sup>	62	F	$\gamma\kappa$	+	11	0	11	(Hypertetraploid)96,XXXX,-2,+7,+12,del(6)(q21),?t(8p),t(14;18)(q32;q21),+der(2)t(2;?)p25;?)
Group H ML, large cell, immunoblastic								
83	67	M	$\mu\kappa$		12	2	10	47,XY,+12,del(5)(q14),t(6;11)(q21;p14),?t(4;19)(p14;p13)
84	54	M	$\mu\kappa$		15	1	14	48,XY,-1,-4,+20,del(6)(q21),+der(1)t(1;?)p36;?),+der(4)t(4;?)q35;?),+mar
85	69	M	$\mu\kappa$	+	15	1	14	(Hypertetraploid)96,XXYY,-3,+del(1)(p13),del(6)(q21),t(8;13)(q22;q32),+der(3)t(3;?)q29;?),+der(12)t(12;?)p13;?)
Group I ML, lymphoblastic								
86	13	M	T		10	0	10	45,Y,-X,-1,+21,i(17q),t(11;14)(p15;q23),t(14q15q),+der(1)t(1;?)p36;?)
87	20	F	T		15	15	0	46,XX
Group J ML, small noncleaved cell								
88	18	M	$\mu\kappa$		15	0	15	46,XY,t(8;14)(q24;q32)
89	8	F	$\mu\kappa$		11	1	10	46,XX,t(8;14)(q24;q32)
90	13	M	$\mu\lambda$		15	0	15	46,XY,dir dup(1)(q22→qter),del(4)(q26),t(8;14)(q24;q32)
91	71	F	$\mu\kappa$		15	0	15	46,XX,t(8;14)(q24;q32)
ML, unclassifiable								
92	49	F	$\mu\lambda$		20	0	20	47,XX,+12,t(14;18)(q32;q21)
93	64	M	$\gamma\lambda$		15	1	14	50,XY,-2,-9,+11,-14,+22,del(3)(q26),del(6)(q23),+del(18)(q12),+der(2)t(2;?)q37;?),+der(9)t(9;?)q34;?),+der(12)ins(12)(q21),+der(14)t(14;?)q32;?)
94 <sup>b</sup>	61	F	$\mu\lambda$	+	10	0	10	45,XX,-7

<sup>a</sup> Immunological phenotype.<sup>b</sup> At presentation, the diagnosis of the peripheral blood was CLL.<sup>c</sup> +, prior treatment at the time of biopsy of the tumor.<sup>d</sup> Lymph node histology at diagnosis differed from that at relapse (see text).<sup>e</sup> Patients 64 to 70, 72, and 73 had predominantly noncleaved cells. Patient 71 had predominantly large cleaved cells.



erythrocytes by rosette formation with unsensitized sheep erythrocytes, for complement by the erythrocyte-antibody-complement (specific for IgM) rosette assay, and for Fc $\gamma$  by immunofluorescence with fluoresceinated aggregated human IgG. When 2 or more heavy or light chains were found on the surface of lymphoid cells, the cells were treated with polyvalent antiserum, and/or incubated at 37° for 24 hr, or subjected to both procedures and then studied for the presence of reconstituted SIg. In the rosette assays, cytocentrifuge preparations were stained with Wright's Giemsa, and the proportion of malignant cells forming rosettes was determined.

Cryostat sections of the tumor masses were prepared from a portion of the same neoplastic tissue from which suspensions were made. Serial cryostat sections were studied for histological features by staining with hematoxylin and eosin and for the presence of immunoglobulin (SIg and CIg), complement, and Fc $\gamma$  using the methods described above for cell suspensions.

This series included 9 cases of T-cell lymphoma (as defined by the presence of receptors for unsensitized sheep erythrocytes and positivity with anti-unsensitized sheep erythrocyte monoclonal antibodies (OKT11/9.6) (13). It included 81 cases of B-cell lymphoma as defined by the presence of surface and/or cytoplasmic monotypic immunoglobulin and the absence of unsensitized sheep erythrocyte receptors. Thirty-eight patients demonstrated only SIg; 22 had SIg and CIg; 20 had SIg, but the presence of CIg was not determined; and one had CIg only. In addition, 2 patients lacked SIg, CIg, and unsensitized sheep erythrocyte receptors but demonstrated complement receptors (complement lymphoma). In 2 cases, immunological studies were inadequate to define the immunological phenotype.

**Cytogenetic Techniques.** For cytogenetic studies, a portion of the same tumor mass biopsied for histology and immunological phenotyping was obtained directly from the surgical pathology laboratory and processed within 1 hr of biopsy. Surgical blades were used to mince the tissue finely into an even cell suspension. Metaphase chromosomes were then harvested from direct preparations and unstimulated or methotrexate-synchronized short-term (24- and 48-hr) cultures using methods described previously (14, 37). G-banding was done using the Wright's technique of Sanchez et al. (32). Photographs of metaphases were taken on high-contrast S0115 film, and multiple photokaryotypes were constructed in each case.

Chromosomes have been designated according to the ISCN (1978), and the karyotypes are expressed as recommended under this system (15). Chromosome abnormalities were designated as clonal if 2 or more metaphase cells had identical structural anomalies or extra chromosomes or if 3 or more metaphase cells had identical missing chromosomes.

In each case, we attempted to analyze 10 to 20 metaphase cells. This was possible in 70 of the 94 cases in which analyzable metaphases were obtained. During the time period of this study, specimens from an additional 44 patients with lymphoma were processed that yielded either no mitoses ( $n = 37$ ) or metaphases that could not be completely karyotyped ( $n = 7$ ). Early in the study (July 1978 to December 1980), analyzable metaphases were obtained from 62% (45 of 73) of the patients; more recently, analyzable metaphases have been obtained from 75% (49 of 65).

Direct preparations were set up in all 138 cases. Sufficient cells were available to prepare also 24-hr unstimulated cultures in 115 cases and methotrexate-synchronized cultures in 57 cases. The 3 methods were compared with regard to their utility in obtaining satisfactory mitoses for analysis. A study was defined as successful when at least 2 metaphase cells with the same abnormal karyotype or at least 5 banded metaphase cells without abnormalities were found. Using these criteria, the direct preparation was successful in 30% of cases; the 24-hr unstimulated culture was successful in 43%; and the methotrexate-synchronized culture was successful in 42%. When the direct method was successful, the 24-hr unstimulated culture was successful in 49%, and the methotrexate-synchronized culture was successful in 35%. When the direct method failed, the 24-hr unstimulated culture was successful in 40%,

and the methotrexate-synchronized culture was successful in 45%. Among the 47 patients where all 3 techniques were used, the methotrexate synchronization was the only successful approach in 21%; the direct preparation only was successful in 15%; and the 24-hr unstimulated culture in 6%. All 3 techniques failed in 32% of patients; the methotrexate-synchronized culture failed in 55% of patients; the direct method failed in 72%; and the 24-hr unstimulated culture failed in 70%. These data suggest that, if sufficient cells are available for only one method of processing, methotrexate synchronization should be used. When sufficient cells for 2 methods are available, a direct preparation should be set up also. However, ideally all 3 techniques should be used since they are complementary. Although the frequency of success of a given technique varied among histological and immunological groups, no one technique was clearly better for one group than for another.<sup>4</sup>

## RESULTS

**Chromosome Abnormalities.** All but 3 of the 94 patients had clonal chromosome abnormalities (Table 1, Patients 53, 59, and 87). In one of these patients, one of 4 cells was abnormal; this cell had chromosome abnormalities similar to those found in other lymphoma patients. Three patients had 2 different, but in each instance related, abnormal clones (Table 1, Patients 1, 57, and 69). Most clones had multiple chromosome abnormalities (Fig. 1). Normal metaphases were also identified in 63 patients (67%). Twenty-seven % of the patients studied at diagnosis had no normal metaphase cells compared to 43% at relapse ( $p = 0.01$ ).

Modal chromosome number of the primary abnormal clone was most frequently 46 (i.e., pseudodiploid); this occurred in 25 (27%) of the 91 patients with clonal chromosome abnormalities (Chart 1). The abnormal karyotypes were hypodiploid in 7 patients (8%) and hyperdiploid in the remaining 56 patients. The modal number was 46, 47, 48, or 49 in 77% of the patients. A tetraploid or hypertetraploid clone was identified in 10 patients (Patients 37, 38, 42, 47, 48, 63, 72, 80, 82, and 85). In 4 patients, this clone was identified in conjunction with the corresponding diploid or hyperdiploid abnormal clone.

The karyotypic abnormalities were defined completely in 47 patients although, in patients with very complex karyotypes, the precise assignment of breakpoints and rearrangements was occasionally subjective. In 41 patients, the origin of material added to a derived chromosome could not be determined with certainty. In 15 patients, unidentified marker chromosomes ( $n = 11$ ) or rings ( $n = 4$ ) were found.

The abnormal karyotype included gains of one or more whole chromosomes (without apparent structural abnormalities) in 57 patients and losses of one or more whole chromosomes in 18. As indicated in Chart 2, most frequently gained were chromosomes 12 (19% of patients), 18 (13%), 7 (12%), and 21 (10%). Most frequently lost were chromosomes 4, 9, 16, and 17 in 3 (3%) patients each. Structural abnormalities were much more frequent than numerical alterations occurring in 87 patients. All chromosomes were affected but with striking variations in frequency (Chart 3). Most commonly involved were the long arms of chromosomes 14 (71% of patients), 18 (36%), 6 (31%), and 8 (19%) and the short arm of chromosome 1 (24%). The type of structural abnormality in which a given chromosome arm was likely to be involved also varied (Chart 3).

<sup>4</sup> D. C. Arthur, L. L. Lindquist, and C. D. Bloomfield, manuscript in preparation.



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Fig. 1. G-banded karyotype from Patient 40: XY, +X, +3, +8, +? 8, -11, -16, -20, ? del(2)(q14), i(17q), t(1;8)(q32;q22), t(5;13)(q15;p13), t(14;18)(q32;q21), +der(11)t(11;?)(p15;?), +der(20)t(20;?)(q13;?), +ring. This case demonstrates 3 of the common recurring chromosome abnormalities, t(14;18)(q32;q21), i(17q), and +3.

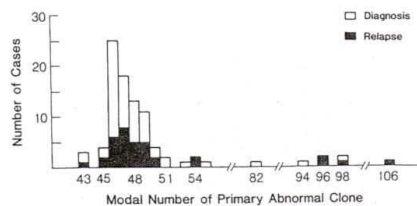


Chart 1. Histogram of modal number of the primary abnormal clone in 91 cases of lymphoma. Numbers of patients studied at diagnosis and relapse are indicated separately.

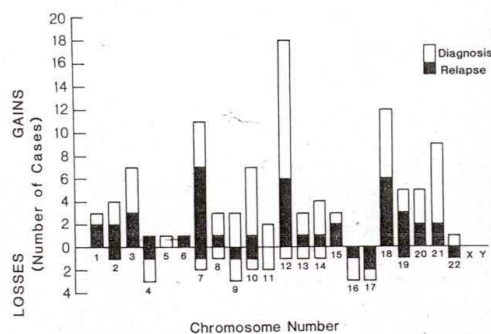


Chart 2. Histogram of gains and losses of whole chromosomes in 91 cases of lymphoma. A given patient may have more than one chromosome gained or lost.

Structural abnormalities most frequently were translocations. Fifty-eight different translocations were identified 93 times in 67 patients (Chart 4). Seven recurring translocations were identified, all except for one involving the end of the long arm of one chromosome 14 at band q32: t(14;18)(q32;q21) in 22 patients; t(8;14)(q24;q32) in 9 patients; t(1;14)(q42;q32) in 3 patients; and, in 2 patients each, t(2;3)(q21;q27), t(3;14)(p21;q32), t(11;14)(q23;q32), and t(14;19)(q32;q13). The second most common type of structural abnormality involved deletions. Forty-six deletions were identified 81 times in 52 patients. Deletions most frequently involved the long arm of chromosome 6 at band q21 (in 11 patients) or band q23 (in 7 patients). In the case of deletions, the missing material could not be found, but it is possible in some cases that it was incorporated as part of an unidentified marker chromosome. The third most common structural abnormality involved derived chromosomes. Derived chromosomes were found 76 times in 44 patients. For most of the derived chromosomes ( $n = 68$ ), the source of the added material was unknown. Other common structural abnormalities seen included isochromosomes in 12 patients [the only recurring one was i(17q) which was found in 8 patients<sup>5</sup>] and duplications in 9 patients (most commonly involving the long arm of chromosomes 1 and 12).

Recurring chromosome abnormalities were surprisingly frequent in this series. Three identical abnormal karyotypes were seen: 46,t(8;14)(q24;q32) in 4 patients; and, in 2 patients each, 47,XY,+12 and 46,t(14;18)(q32;q21). When specific chromosome abnormalities (identical gains or losses of whole chromo-

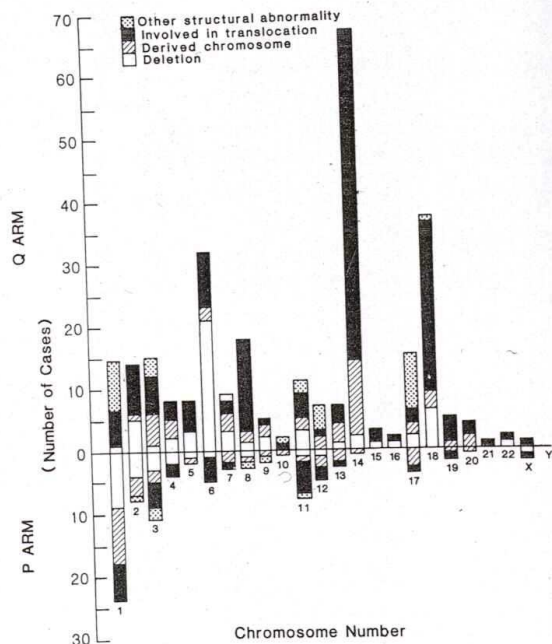


Chart 3. Histogram of structural abnormalities involving each chromosome in 91 cases of lymphoma. Arm involved and type of abnormality (e.g., deletion or translocation) are indicated. A given chromosome arm in a single patient may be involved in more than one type of structural anomaly and is thus listed more than once.

somes, translocations, deletions, or isochromosomes) were considered, 48 occurred more than once. The 11 most frequent of these specific recurring chromosome abnormalities are listed in Table 2. Certain chromosome abnormalities seemed to be associated. Those of the 11 most common chromosome abnormalities that had an additional anomaly that occurred in at least one-third of cases are shown in Table 3.

**Recurring Chromosome Abnormalities and Histology.** The distributions of the various histological subtypes of lymphoma for the 11 most common recurring chromosome abnormalities are shown in Table 2. In 4 instances, the chromosome abnormalities demonstrated a significant association ( $p \leq 0.01$ ) with specific histologies. Thus, 82% of patients with lymphoma with  $t(14;18)(q32;q21)$  were follicular; all remaining patients were Group G ML, diffuse, large cell. One of the 4 patients with diffuse large-cell lymphoma had evolved from a follicular lymphoma at diagnosis. Similarly, all patients with +7 were of these 2 histologies but, in this instance, 64% were Group G ML, diffuse, large cell. All patients with  $t(8;14)(q24;q32)$  were of either diffuse, large cell, or small noncleaved cell type. It is of interest that the patient with  $t(8;14)$  with a different breakpoint on 8 (q22) was of follicular, predominantly small cleaved cell type. Finally, 82% with  $del(6)(q21)$  were large cell lymphomas (2 Group D ML, follicular, predominantly large cell; 5 Group G ML, diffuse, large cell; and 2 Group H ML, large cell, immunoblastic).

Most patients with identical abnormal karyotypes were of the same histology. Thus, in 3 of 4 cases with  $46,t(8;14)(q24;q32)$  were Group J ML, small noncleaved cell; both patients with  $47,+12$  were Group A ML, small lymphocytic cell type; and both patients with  $46,t(14;18)(q32;q21)$  were Group B ML, follicular, predominantly small cleaved cell.

Chart 4. Pictorial display of chromosome regions involved in specific translocations in 91 cases of lymphoma. Small numbers in boxes, number of translocations involving a given pair of chromosomes. Lower numbered (first) chromosome involved in the translocation, X axis; higher numbered (second) chromosome, Y axis. For each possible chromosome pair, the 4 possible arm combinations (pp, pq, qp, qq) are designated by quadrants, i.e., in 2 cases, translocations involved the p arm of chromosome 11 and the q arm of chromosome 14 (2, left lower quadrant of the box for chromosome pair 11 and 14).

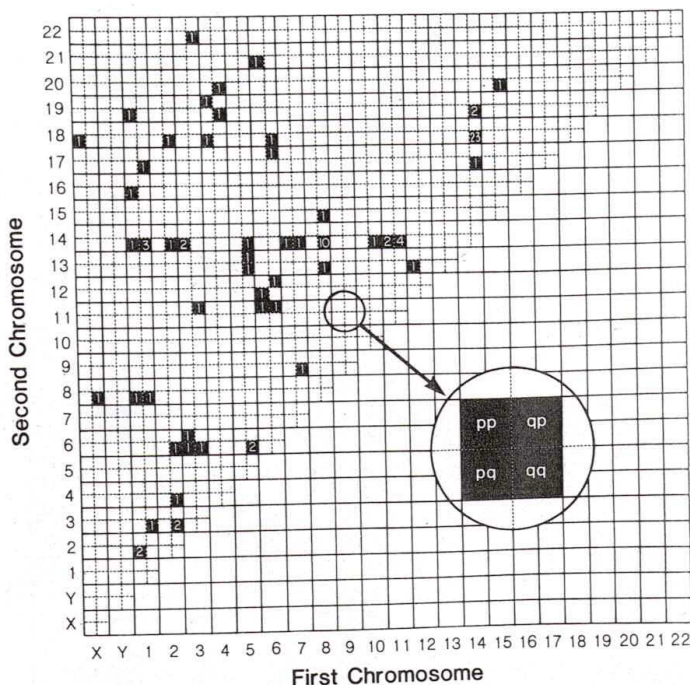




Table 2  
Histology among the common recurring chromosome abnormality groups

Histology Group	% of patients with a given chromosome abnormality showing a given histology <sup>a</sup>									
	t(14;18)(q32;q21) (n = 22)	+12 (n = 18)	+18 (n = 12)	del(6)(q21) (n = 11)	+7 (n = 11)	+21 (n = 9)	t(8;14)(q24;q32) (n = 9)	i(17q) (n = 8)	del(6)(q23) (n = 7)	+3 (n = 7)
A, small lymphocytic (17%) <sup>b</sup>	0 <sup>c</sup>	17	8	0 <sup>c</sup>	0 <sup>c</sup>	11	0 <sup>c</sup>	0	14	14
B-D, follicular (36%)	82	33	25	27	36	22	0	50	43	43
F, diffuse mixed (14%)	0	17	25	9	0	0	0	13	14	0
G, diffuse large cell (20%)	18	28	42	45	64	56	56	25	14	43
H, immunoblastic (3%)	0	6	0	18	0	0	0	0	0	0
J, small noncleaved (4%)	0	0	0	0	0	0	44	0	0	0

<sup>a</sup> Percentages do not always add to 100% because all histologies are not listed.

<sup>b</sup> Numbers in parentheses, frequency of this histology among the 94 lymphomas studied. This is indicated here to allow comparison with the percentage of a given histology among each of the specific chromosome abnormalities.

<sup>c</sup> Histological distribution for this chromosome abnormality differed significantly from histological distribution of total population studied ( $p < 0.01$ ).

Table 3  
Associations among the more common recurring chromosome abnormalities

Chromosome abnormality	No. of patients	Associated anomaly (% of patients)	
del(6)(q21)	11	+7(45)	t(14;18)(36)
+7	11	del(6)(q21)(45)	t(14;18)(36)
+21	9	+12(33)	t(14;18)(33)
t(8;14)(q24;q32)	9	+7(33)	
i(17q)	8	t(14;18)(50)	del(6)(q21)(38)
+3	7	+7(43)	+12(43)

Among the less common (and thus not listed in Table 2) recurring chromosome abnormalities, only 2 translocations and 3 deletions were associated with the same histologies. All 3 patients with t(1;14)(q42;q32) were follicular, and both patients with t(14;19)(q32;q13) were initially diagnosed as CLL. Both patients with del(2)(q23) were follicular; both with del(9)(q22) were Group G ML, diffuse, large cell; and both with del(18)(q21) were follicular. Since there were so few patients with each of these chromosome abnormalities, it is hard to know if the similarities in histology were simply fortuitous.

**Recurring Chromosome Abnormalities and Immunological Phenotype.** Recurring chromosome abnormalities were seen most often in B-cell lymphomas, since 81 cases studied were B-, only 9 were T-, and 2 were complement lymphomas (Table 4). The only common chromosome abnormality associated with a distribution of immunological phenotypes significantly different from that of the total population studied was the t(14;18)(q32;q21) ( $p = 0.01$ ); all 22 cases were either B- or complement lymphomas. The distribution of immunological phenotype among cases with the +7 was similar.

None of the common recurring chromosome abnormalities was associated significantly with expression of a specific light chain (Table 4). However, among patients with identical abnormal karyotypes, all 4 lymphomas with 46,t(8;14)(q24;q32) expressed  $\kappa$  light chain as did both patients with 46,t(14;18)(q32;q21). Of the 7 recurring translocations seen, only one was associated with expression of a single light chain type. All 3 lymphomas with t(1;14)(q42;q32) expressed  $\kappa$  light chain. In 2 of the 3 patients, there was no heavy chain present; none of the other B-cell lymphomas studied had only a light chain.

Among the less common recurring deletions, 3 were associated with the same light chain, in all instances,  $\kappa$ : del(4)(p14); del(5)(q14); and del(18)(q21). Two deletions were more commonly associated with  $\lambda$  than with  $\kappa$  light chain; 2 of 3 cases of del(1)(p36); and 3 of 4 cases of del(18)(q12). More lymphomas with each of these recurring abnormalities must be studied before

the significance of these associations can be assessed.

The frequency of the various surface heavy chains in lymphomas with the common recurring chromosome abnormalities is also shown in Table 4. The only chromosome abnormality that differed significantly in its associated heavy chains from the B-cell lymphoma population as a whole was t(14;18) ( $p = 0.04$ );  $\gamma$  was expressed more frequently and  $\delta$  less frequently in these patients; t(8;14)(q24;q32) was associated with  $\mu$  in 7 of 9 patients; and the remaining patients expressed  $\gamma$  heavy chain ( $p = 0.14$ ).

Among patients with identical karyotypes, 3 patients with 46,t(8;14)(q24;q32) expressed  $\mu$  surface heavy chain as did both lymphomas with 46,t(14;18)(q32;q21). Among lymphomas with the less common recurring translocations, the same heavy chain was seen in 2 instances. Both patients with t(3;14)(p21;q32) expressed  $\mu$  heavy chain, and both patients with t(14;19)(q32;q13) expressed  $\delta\mu$ .

## DISCUSSION

We have studied karyotypes from neoplastic lymph nodes or other primary tumors in 94 patients with lymphoma. Clonal chromosome abnormalities were identified in 91 patients (97%). Others, in smaller series, have also found that most lymphomas have chromosome abnormalities (9, 16). We have found chromosome abnormalities in all cases of B-lymphoma. The 3 lymphomas in which a clonal chromosome abnormality was not found were all T-cell. The reason for this difficulty in identifying an abnormal clone in T-lymphomas is unknown, but similar difficulties have been reported in T-acute lymphoblastic leukemia (4, 36).

Cells of the abnormal clone most frequently had a modal number of 46 chromosomes. This was especially true of patients studied at diagnosis, 35% of which were pseudodiploid as compared to 15% at relapse ( $p = 0.06$ ). In over one-half of the patients, the modal number of the cells in the abnormal clone deviated from a normal number of 46 by only one chromosome. These results help to explain the low frequency of aneuploidy often identified by DNA flow cytometry (1, 21).

Certain chromosomes were involved preferentially in the clonal abnormalities. Numerical alterations most frequently involved chromosomes 12, 18, 7, and 21. Most common was a gain of chromosome 12 which was seen in 19%. Trisomy 12 has been reported in as many as 50% of cases of CLL (12, 29). In our series, trisomy 12 occurred with almost all histologies and was not unusually frequent in ML, small lymphocytic type. However,



Table 4  
Immunological phenotype among the common recurring chromosome abnormality groups

	% of cases with a given recurring chromosome abnormality having a specific phenotype <sup>a</sup>										
	t(14;18)(q32;q21) (n = 22)	+12 (n = 18)	+18 (n = 12)	del(6)(q21) (n = 11)	+7 (n = 10)	+21 (n = 9)	t(8;14)(q24;q32) (n = 9)	i(17q) (n = 8)	del(6)(q23) (n = 7)	+3 (n = 7)	+10 (n = 7)
Immunological class											
B (n = 81), 88% <sup>b</sup>	91	94	100	91	90	78	100	75	100	86	100
T (n = 9), 10%	0	6	0	9	0	11	0	25	0	14	0
Complement (n = 2), 2%	9 <sup>c</sup>	0	0	0	10	11	0	0	0	0	0
Light chain											
κ (n = 51), 65% <sup>d</sup>	58	67	75	60	67	57	67	50	86	67	83
λ (n = 28), 35%	42	33	25	40	33	43	33	50	14	33	17
Heavy chain											
δμ (n = 20), 26% <sup>d</sup>	10	33	33	30	22	43	0	33	0	17	14
μ (n = 40), 52%	50	33	50	40	33	14	78	67	71	67	57
γ (n = 17), 22%	40 <sup>c</sup>	33	17	30	44	43	22	0	29	17	29

<sup>a</sup> e.g., 91% of patients with t(14;18) were B-cell.

<sup>b</sup> Frequency among the 92 lymphomas with adequate immunological studies.

<sup>c</sup> Immunological feature distribution for this chromosome abnormality differed significantly from its distribution among total population studied.

<sup>d</sup> Frequency among the B-lymphomas.

both patients with +12 as their only abnormality were of small lymphocytic type. The only numerical abnormality significantly correlated with a specific histological or immunological type was trisomy 7 which was found only among follicular lymphomas and lymphomas of diffuse large cell type. Seven of 11 patients with +7 were of the latter histology; a frequent association with the corresponding Rappaport histology (diffuse histiocytic lymphoma) has been reported (11, 31).

Structural aberrations were much more frequent than were numerical alterations and also preferentially involved specific chromosomes, most commonly, in descending order of frequency, 14, 6, 1, and 18. With the exception of chromosome 18, these chromosomes are different from those involved in numerical changes. Certain chromosome regions tended to be affected. Most commonly involved, in 71% of patients, was the long arm of chromosome 14; The other regions frequently involved were 18q, 6q, 1p, and 8q. Review of 128 cases of banded chromosomes in non-Burkitt's lymphoma revealed a similar preponderance of structural anomalies of chromosomes 14, 1, and 6 and a similar frequency of involvement of 14q and 1p (34). While our results do not differ qualitatively from those reported previously, we do find an increased frequency of many of the structural abnormalities. Most striking is the increase of involvement of 18q. The increased frequency of specific abnormalities probably reflects the lower frequency of unidentified marker chromosomes in our series and the relatively large number of follicular lymphomas.

The 14q+ anomaly was the single most common chromosome abnormality in this series, as has been found previously (25, 34). It was seen in all 4 cases of small noncleaved cell lymphoma; the donor chromosome in each instance was 8. The 14q+ was found in 66% of our 90 cases of non-Burkitt's lymphomas; it has been found in 43% of 128 reported cases (34). The donor chromosomes were identified in 48 patients in our series (in descending order of frequency) to be: 18, 8, 11, 1, 3, and 19; and 2, 5, 7, 10, and 17 (Chart 4). Among 31 cases of histiocytic and poorly differentiated lymphocytic lymphomas from the literature, Rowley and Fukahara (31) found the most frequent donor chromosomes (in descending order of frequency) to be: 11, 18, 8, and 14; and 1. Although the 14q+ was found in all of our larger histological groups, it was not present in any of the 3 cases of ML, large cell, immunoblastic (2). Similarly, the 14q+

was not found in 4 patients reported to have immunoblastic lymphoma according to the Kiel classification (28). As has been found by others, the 14q+ is not restricted in immunological type to B-lymphomas (31); it was present in 3 of our 9 T-lymphomas.

Five specific structural abnormalities were seen in at least 5% of our patients: t(14;18)(q32;q21); del(6)(q21); t(8;14)(q24;q32); i(17q); and del(6)(q23). Two of these (the translocations) were also found occasionally as the sole chromosome abnormality. All of these abnormalities have been reported previously, although in smaller numbers (31, 33, 34). Three of these demonstrated significant associations with specific histologies: the t(14;18) with follicular lymphomas; the del(6)(q21) with large cell lymphomas; and the t(8;14) with diffuse large cell or small noncleaved cell lymphomas. The t(14;18) has been noted previously to be associated with poorly differentiated lymphocytic lymphoma of Rappaport (largely a follicular center cell neoplasm), although its association with a follicular pattern has not been so clear (10, 31). Similarly, an association of deletions of 6q with diffuse histiocytic lymphomas has been noted (31). The association of t(8;14)(q24;q32) and small noncleaved cell lymphomas is well recognized; that t(8;14) is equally commonly associated with diffuse large cell lymphomas is not so well appreciated, although it has been reported with many histologies (31, 34). Only the t(14;18) showed a statistically significant association with a specific immunological phenotype. Detailed immunological phenotypes have been reported in too few cases of non-Burkitt's lymphomas to compare our results with those of the literature.

In our large series, the same specific chromosome abnormality was frequently found in 2 or 3 patients. Thus, in addition to the t(14;18)(q32;q21) and the t(8;14)(q24;q32), 5 other translocations were seen in more than one patient. Similarly, in addition to del(6)(q21) and del(6)(q23), 14 other deletions were found in 2 to 4 patients each. There are too few cases of each translocation or deletion to determine if they are associated with specific histologies or immunological phenotype. However, the association of both lymphomas that had a t(14;19)(q32;q13) with a prior diagnosis of CLL and the association of 2 of 3 patients with t(1;14)(q42;q32) with κ light chain in the absence of a heavy chain are of interest.

We have identified many more recurring chromosome abnormalities than have previous studies. This is most probably due to the large size of this series, nearly 3 times that of any other



series (8, 9, 16, 24, 28); the fact that the abnormal karyotype was often totally defined; and because involved tumor masses rather than blood, bone marrow, or effusions were studied in all cases. It is of some interest that 6 of the chromosome abnormalities were associated with at least one other common recurring anomaly in one-third or more of the patients (Table 3). The significance of these associations is unknown.

Although some of the recurring chromosome abnormalities were associated with specific histologies or immunological phenotypes, no abnormality, when studied in a reasonable number of patients, was restricted invariably to a given histology or immunological phenotype. There are a number of possible explanations for this. Some of the abnormalities probably have no relationship to histology or immunological phenotype. Others may have their relationship obscured as a result of the multiple chromosome abnormalities usually present; combinations of abnormalities may change the histological or immunological picture. In this regard, it is interesting that, in those instances where lymphomas had identical abnormal karyotypes involving a single chromosome abnormality, the histology usually was identical.

It is also possible that the chromosome abnormality is a fundamental and histology is a secondary phenomenon. For example, it has been noted previously that follicular lymphomas evolve occasionally to diffuse large cell tumors and that some patients have both histologies simultaneously; this might explain the restriction of both the t(14;18) and the +7 to these 2 histologies. It is also possible that current histological classifications are not precise enough descriptors of histological change and that a better histological classification would more strongly correlate with specific chromosome abnormalities. It may be that chromosome abnormalities will carry more clinical significance or complement the clinical utility of histology or immunological phenotype; prospective long-term study of a large number of newly diagnosed patients is required to test this hypothesis. Whatever else, the lack of one-to-one correlation between recurring chromosome abnormalities and histology or immunological phenotype in our series reemphasizes the need for studying large numbers of patients with a given abnormality before drawing definitive conclusions.

The meaning of karyotypic abnormalities in neoplastic lymphoma tissue remains unclear. In most cases, at least 80% of the metaphases studied were abnormal. It is possible that the cells with the normal karyotypes were nonmalignant lymphocytes which are often present, especially in lymph nodes from follicular lymphomas. The fact that, at relapse, when fewer normal lymphocytes are identified morphologically or immunologically, the number of normal metaphase cells was significantly less also suggests that most of the neoplastic cells contain the chromosome abnormality. Study of the clinical significance of these abnormalities may help to determine if chromosome abnormalities are related to the pathogenesis of the lymphoma.

Recently, studies of Burkitt's lymphoma have suggested correlations between the existence of specific translocations and the expression of specific immunoglobulin light chains. Lymphoma cells with t(2;8) express  $\kappa$  chains, and those with t(8;22) express  $\lambda$  chains (18, 19, 20); the gene loci coding for the variable and constant regions of  $\kappa$  light chain have been assigned to chromosome (2 cen→p12) (23), and those for the  $\lambda$ -light-chain constant region have been assigned to chromosome 22 at q11 (6, 35). The high frequency of the 14q+ abnormality with involvement at band q32 in lymphoma and the assignment of the heavy-

chain gene  $\gamma$ 4 constant region to 14q32 (17) also suggest the likelihood of correlations of specific chromosome abnormalities with immunological phenotype. Thus, the rarity of abnormalities in 2p (only 8 cases) and 22q (2 cases) in our large series is of some interest as is the absence of translocations involving chromosomes 8 and 2 or 22. Moreover, of the 2 cases of del(2)(p12), only one expressed  $\kappa$ , and neither case with del(22)(q12) expressed  $\lambda$  light chain. Furthermore, we found few associations of specific chromosome abnormalities with expression of specific immunoglobulin chains. Although study of more cases may allow identification of specific chromosome regions which are related to expression of specific heavy or light chains, it is quite possible that the chromosome abnormalities seen in lymphomas usually do not involve gene regions associated with immunoglobulin expression. The association of Burkitt's lymphoma and immunoglobulin expression may occur, because the DNA sequence involved in the malignant transformation of these cells may be located on the long arm of chromosome 8 at 8q24 (7, 35). Indeed, one of the most fruitful avenues for evaluation of the significance of chromosome abnormalities in lymphoma could be the study of oncogenes in these cases. To date, viral oncogenes have been mapped to human chromosomes 6, 8, 9, 11, 12, 15, 20, and 22, 30. It will be of interest to determine if abnormalities in these chromosomes seen in lymphomas are in the region of the oncogenes.

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