Chronic Leukaemias

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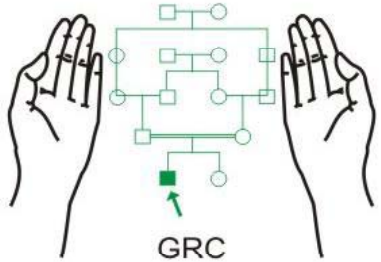
Genetics Resource Centre (GRC)



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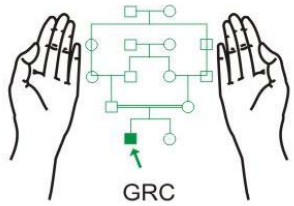
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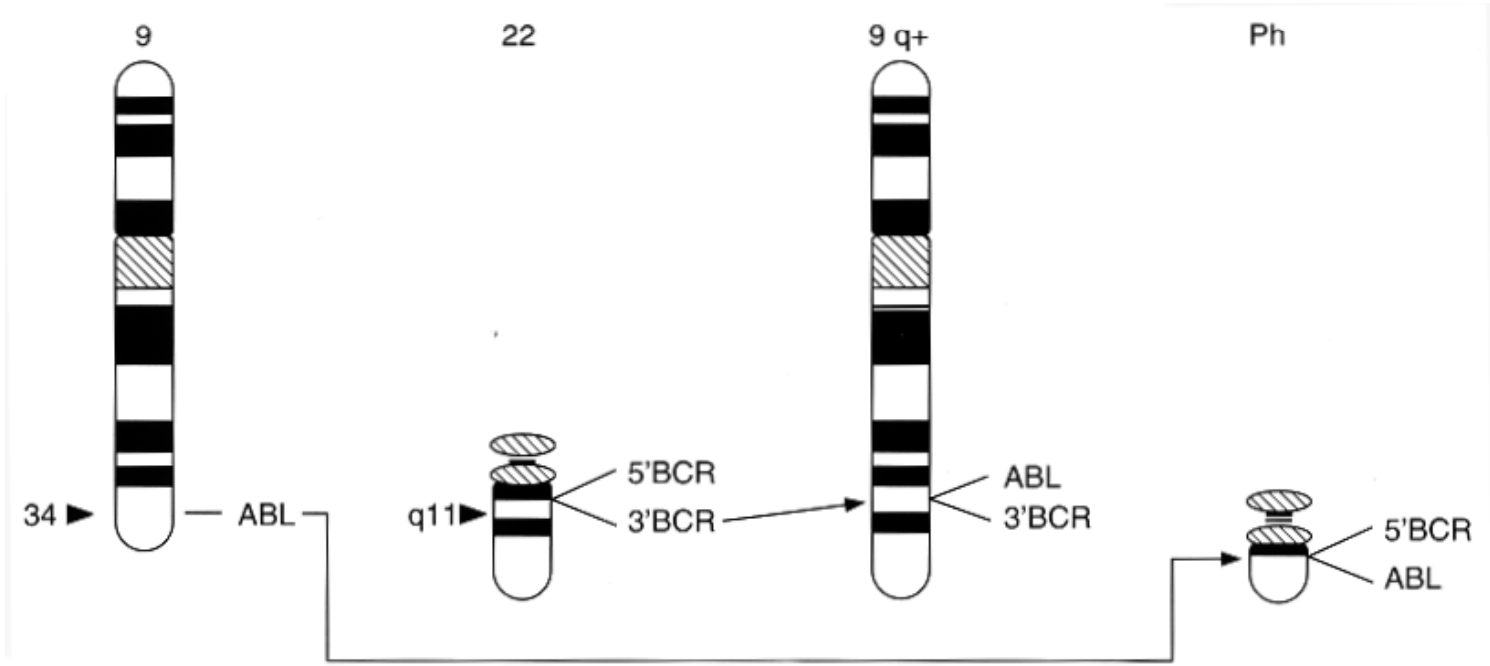
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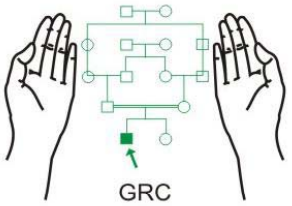
22
9 q+
Ph
34
ABL
q11
5'BCR
3'BCR
ABL
3'BCR
5'BCR
ABL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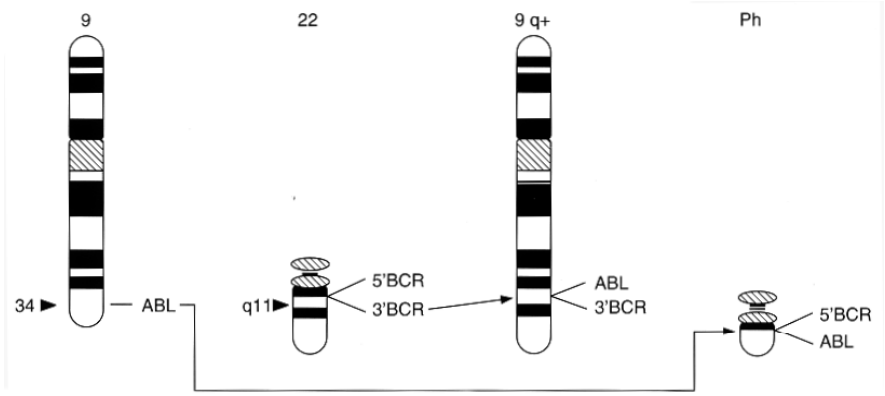
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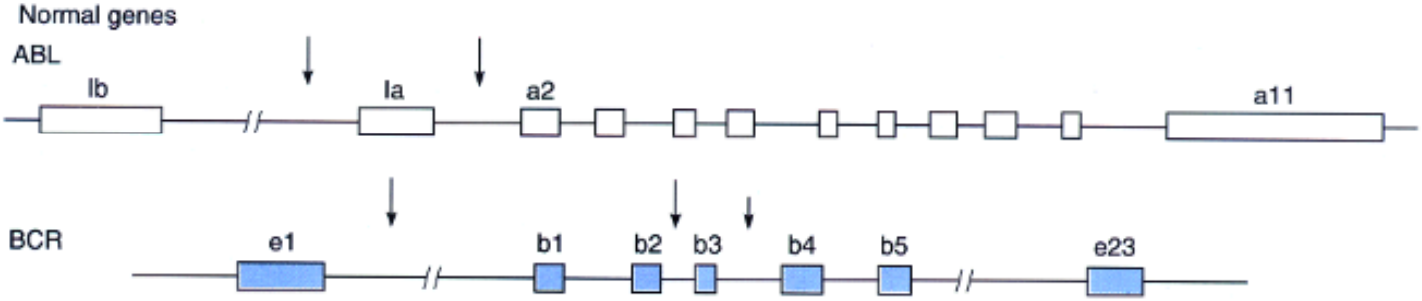
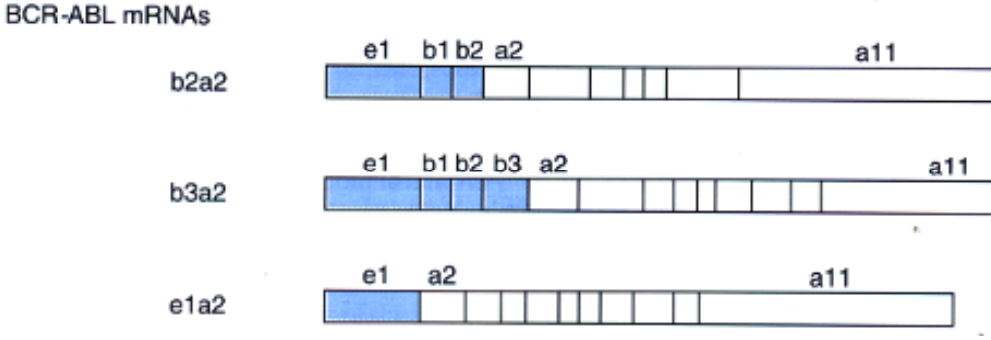
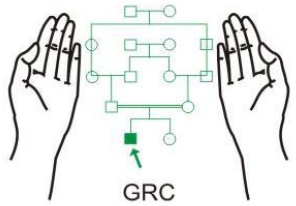

Normal genes
ABL
Ib
Ia
a2
a11
BCR
e1
b1
b2
b3
b4
b5
e23


BCR-ABL mRNAs
b2a2
e1 b1 b2 a2
a11
b3a2
e1 b1 b2 b3 a2
a11
e1a2
e1 a2
a11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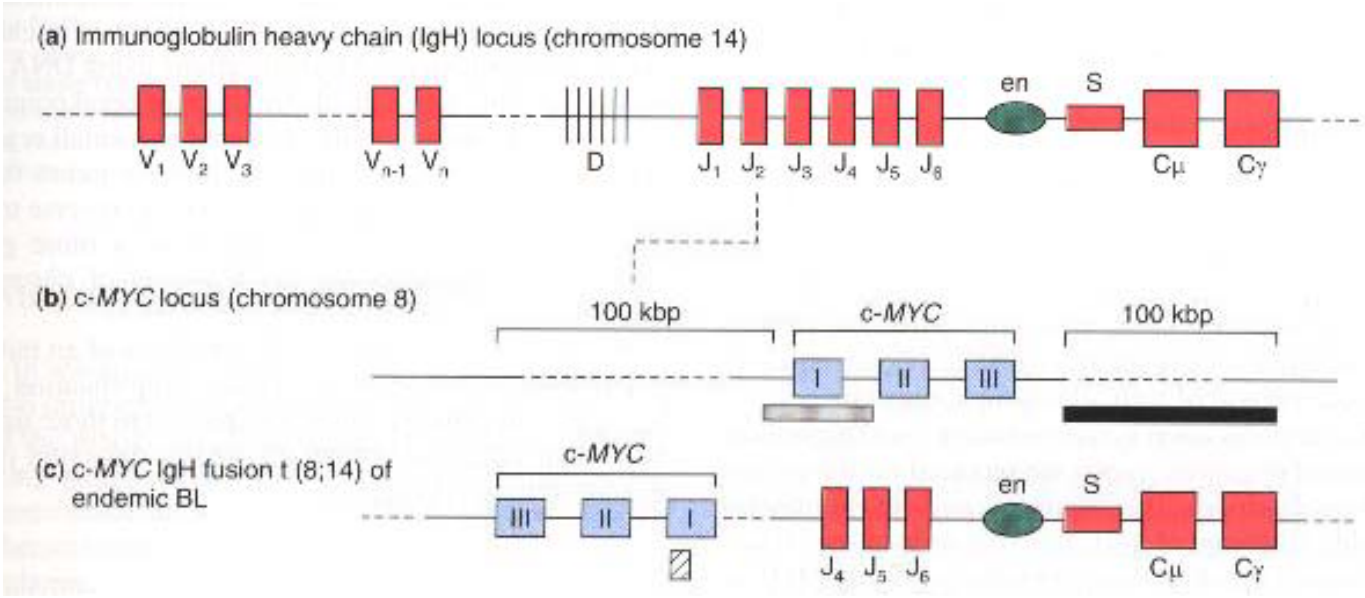
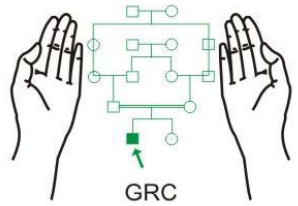
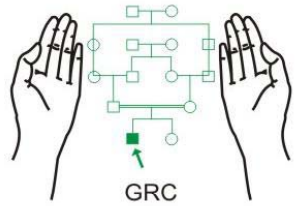

(a) Immunoglobulin heavy chain (IgH) locus (chromosome 14)
V1 V2 V3
Vn-1 Vn
D
J1 J2 J3 J4 J5 J6
en
S
Cμ
Cγ
(b) c-MYC locus (chromosome 8)
100 kbp
c-MYC
100 kbp
I
II
III
(c) c-MYC IgH fusion t (8;14) of endemic BL
c-MYC
III
II
I
J4 J5 J6
en
S
Cμ
Cγ



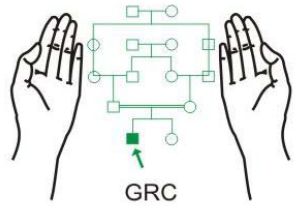
Classification of Leukaemia

- Clinical
- Morphological
- Immunological
- Cytogenetic and Molecular Genetic
- Integrated



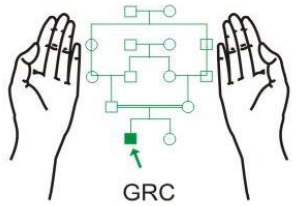
Clinical Classification

- Acute Leukaemia
- Chronic Leukaemia



Pathophysiology

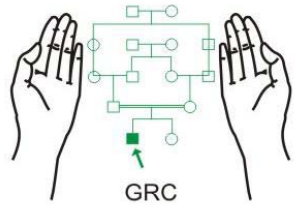
- Cell Transformation
- Clonal Expansion
- Suppression of Normal Haematopoietic Tissues
- Cytopaenias
- Clinical Presentation



Diagnosis

- Clinical Presentation
- Blood Counts
- Cell Morphology
- Bone-marrow Examination

CML



Chronic phase

Ability to reduce spleen size and restore and maintain a 'normal' blood count with appropriate therapy

Accelerated phase

(defined by one or more of the following features)

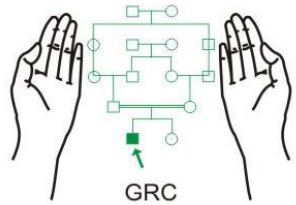
- Blasts 10–19% of white blood cells in peripheral blood and/or of nucleated bone marrow cells
- Peripheral blood basophils ≥ 20%
- Persistent thrombocytopenia ($< 100 \times 10^9$/L) unrelated to therapy, or persistent thrombocytosis ($> 1000 \times 10^9$/L) unresponsive to therapy
- Increasing spleen size and increasing white blood cell count unresponsive to therapy
- Megakaryocyte proliferation in sheets or clusters in association with marked reticulin or collagen fibrosis

Blastic phase

(defined by one or more of the following features)

- Blasts > 20% of peripheral blood leucocytes or of nucleated bone marrow cells
- Extramedullary blast proliferation
- Large foci or clusters of blasts in the bone marrow biopsy

Note: In this classification, unlike some other classifications, the acquisition of new cytogenetic abnormalities in addition to the Ph chromosome is not by itself a criterion for 'promoting' a chronic phase patient to accelerated phase.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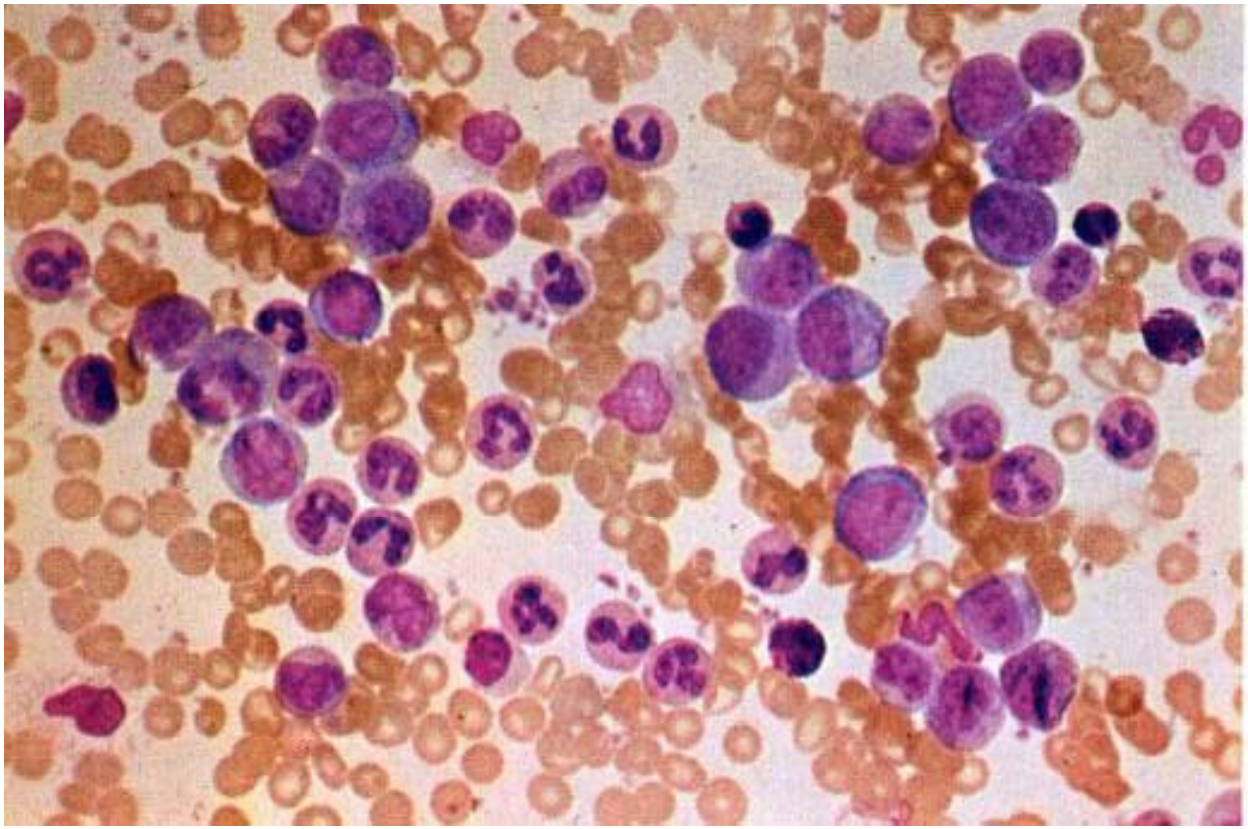

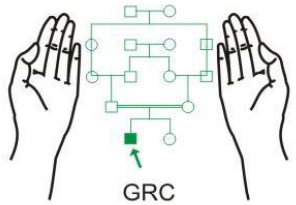
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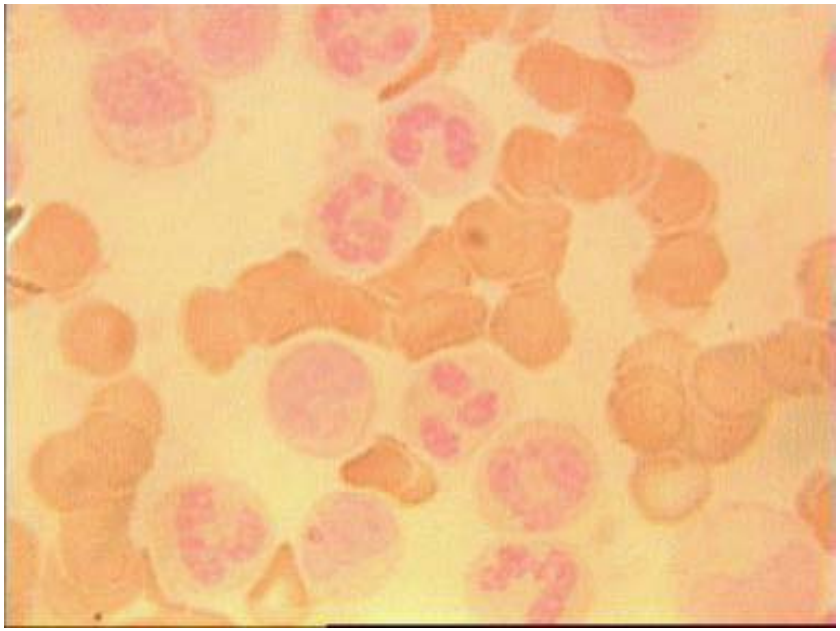

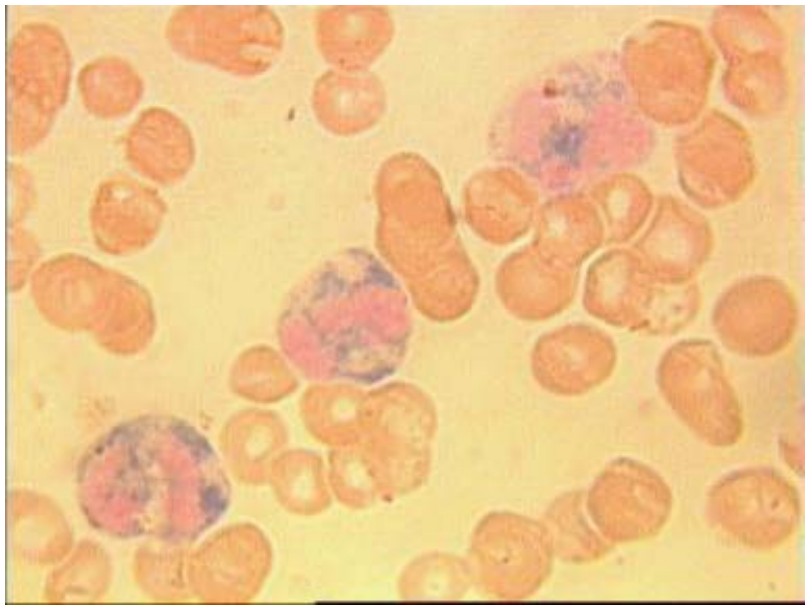

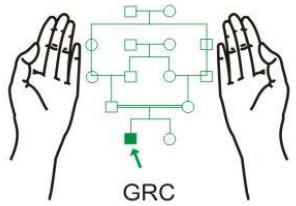
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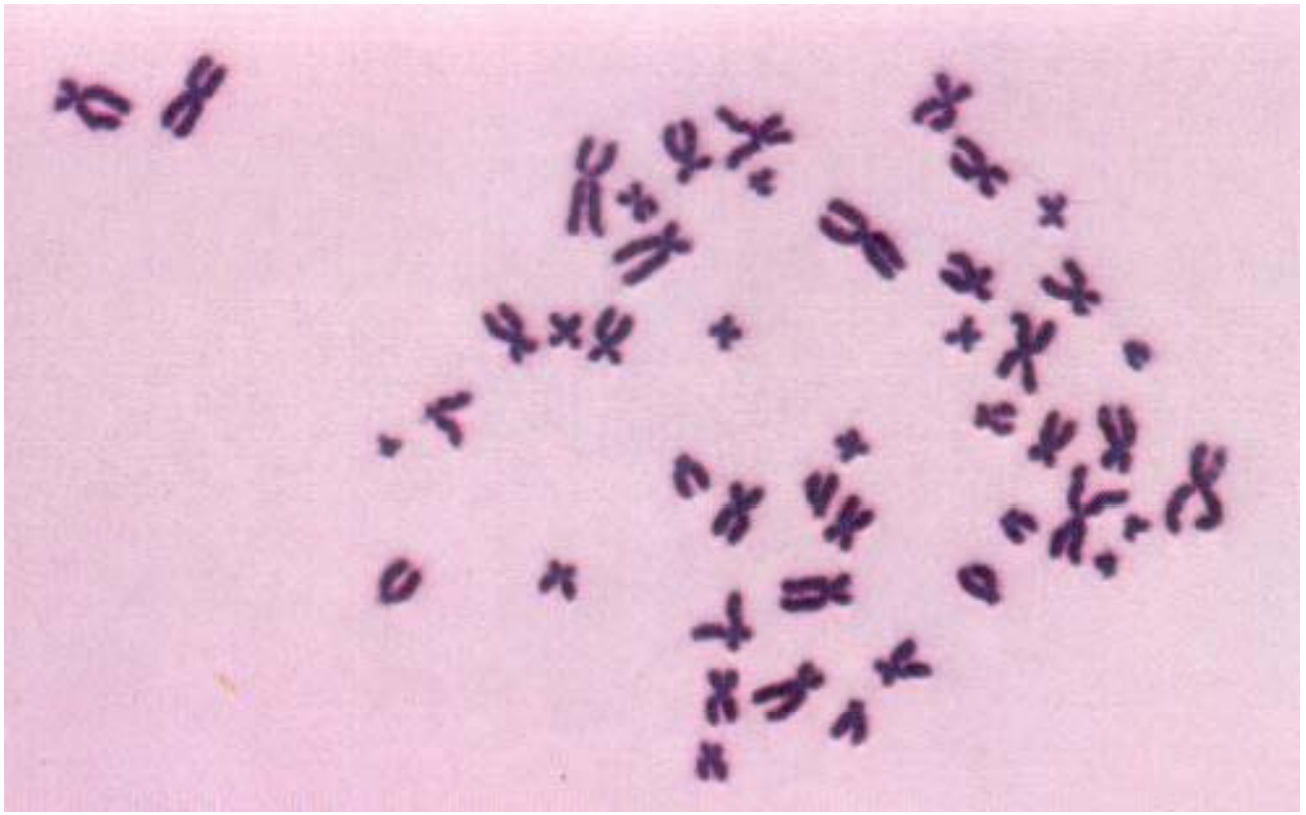


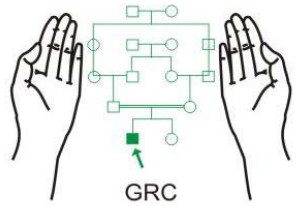


Table 10.11. *Comparison of leukaemoid reactions and leukaemia*

	Leukaemoid reactions	Leukaemia
Clinical features	Clinical features of the causative disorder often obvious	Splenomegaly, lymph node enlargement, and haemorrhage more common than with leukaemoid reactions
Blood examination		
Total white cell count	Increase usually only moderate; seldom exceeds 100×10^9/l	Can exceed 100×10^9/l
Proportion of immature cells	Usually small or moderate. Myelocytes seldom exceed 5–15 per cent, and 'blasts' 5 per cent	Usually numerous
White cell morphology	Toxic changes may be seen in infective cases	Cells often atypical as well as immature. Toxic changes uncommon
Anaemia	May occur, but often slight or absent	Usually present and progressive
Nucleated red cells	Frequent in leuco-erythroblastic anaemia due to marrow infiltration	Less frequent
Platelets	Mainly normal or increased, but reduced in leuco-erythroblastic anaemia and intravascular coagulation	Decreased, except in chronic granulocytic leukaemia
Bone marrow	White cell hyperplasia may be present but seldom to same degree as in leukaemia	Hyperplastic with potentially large proportion of immature cells
Autopsy	Infiltration of organs and tissues absent	Leukaemic infiltration of organs and tissues

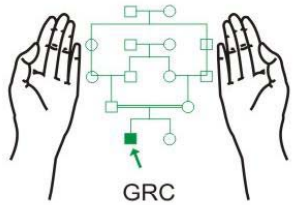
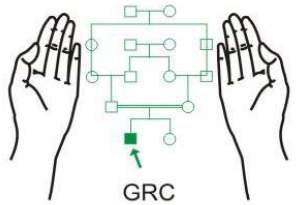


Table 19.2 Classification of B-lymphoproliferative disorders

Leukaemias
Chronic lymphocytic leukaemia
  Common type (CLL)
  With >10% prolymphocytes (CLL/PL)
B-prolymphocytic leukaemia (B-PLL)
  (>55% prolymphocytes)
Hairy cell leukaemia
  Classic form (HCL)
  Variant form (HCL-V)
Plasma cell leukaemia (PCL)

Lymphoma/leukaemia syndromes
Follicular lymphoma (FL)
Splenic lymphoma with villous lymphocytes (SLVL)
Mantle cell (MC) lymphoma
Lymphoplasmacytic NHL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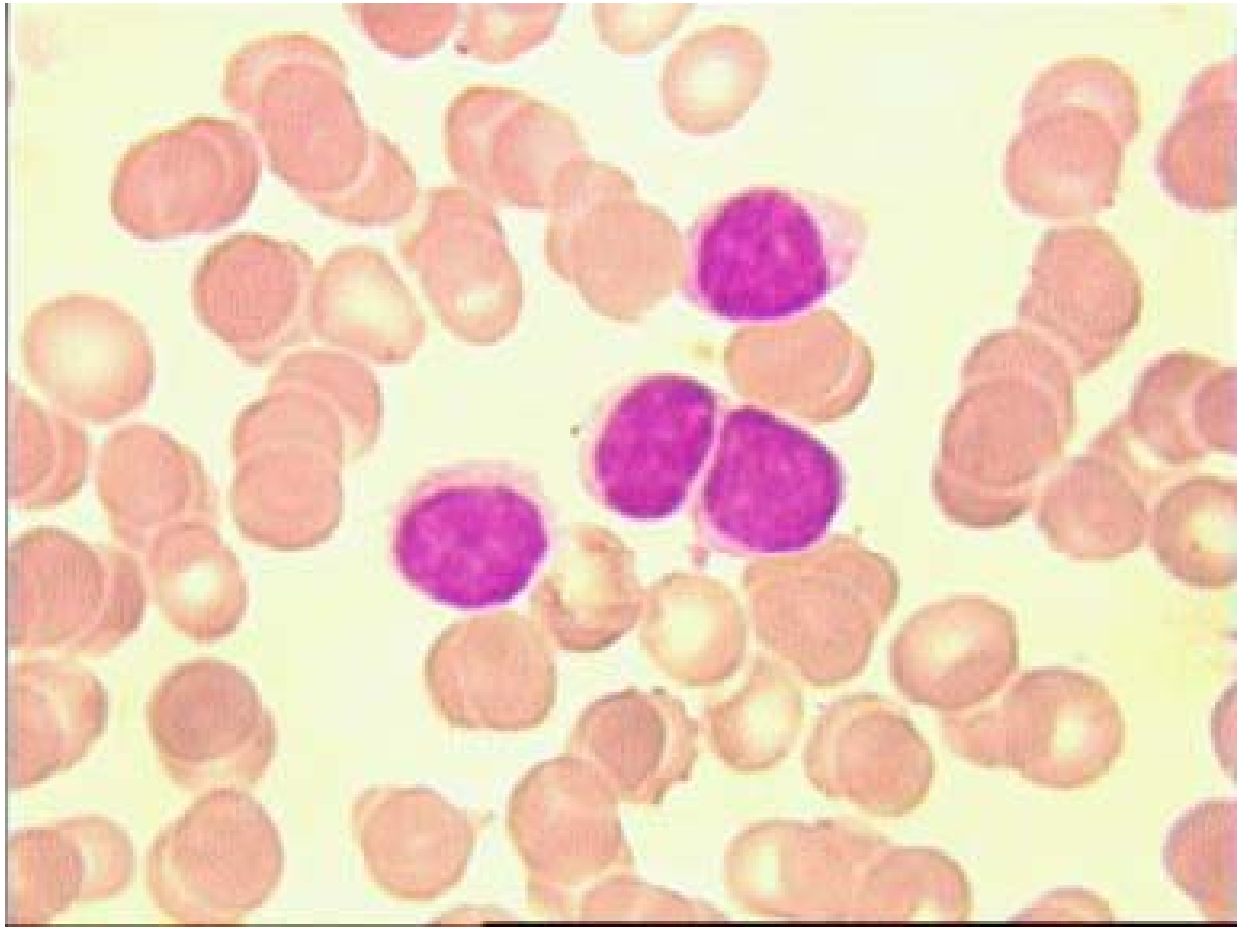

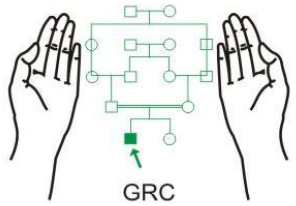
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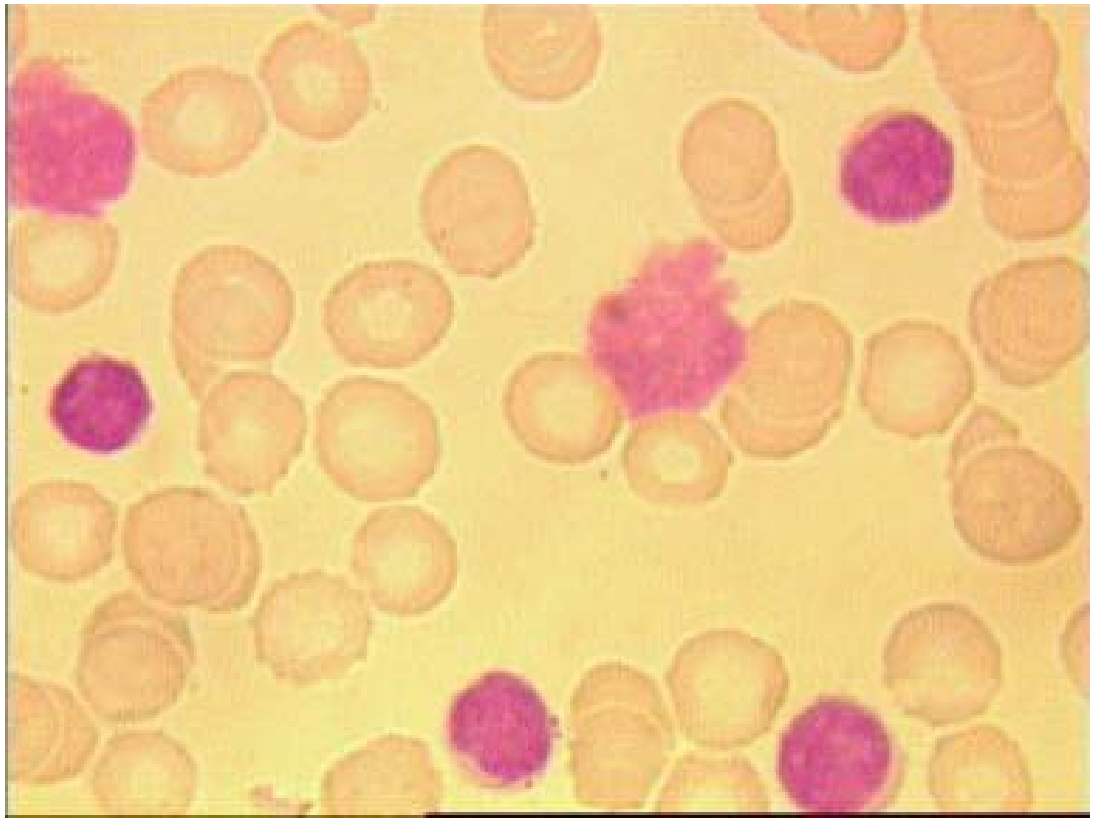


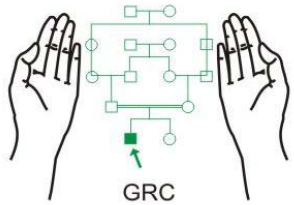


Table 19.3 Membrane markers in chronic B-cell leukaemias and NHL in leukaemic phase

Markers	*CLL*	*B-PLL*	*HCL*	*SLVL/FL/MC*	*PCL*
SmIg*	+/–	++	++	++	–†
CD23	+	–/+	–/+	–/+	–
CD5	+	–/+	–	–	–
FMC7/CD22‡	–/+	++	++	++	–
CD19/20/37 class II	++	++	++	++	–
CD10	–	–/+	–	–/+	–/+
CD11c/25	–/+	–/+	++	–/+	–
HC2/CD103	–	–	++	–	–
CD38	–	–	–	–	++
CD79b*	–	++	–/+	++	ND

+/– weak expression; ++ strong reactivity; –/+ some cases positive.

* The Ig heavy chain classes in CLL, PLL, FL and SLVL are IgM and IgD. In HCL, several heavy chain isotypes are often expressed: IgM, IgD, IgA and IgG; in HCL-V it is almost always IgG only.

† Expression of CyIg only

‡ Membrane immunofluorescence pattern; despite the apparent similar distribution, these two McAb do not detect the same antigen.

* Zomas et al., 1996.

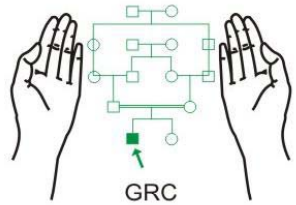


Table 19.4 Diagnostic criteria for CLL based on a scoring system*

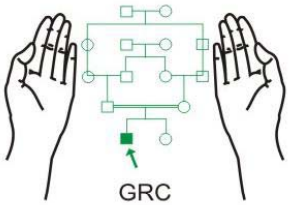
Marker	*CLL (score)*	*Other B-cell leukaemias and NHL (score)*
SmIg	Weak (1)	Moderate/strong (0)
CD5	Positive (1)	Negative (0)
CD23	Positive (1)	Negative (0)
FMC7	Negative (1)	Positive (0)
CD22**	Weak/negative (1)	Moderate/strong (0)
Usual scores	4–5†	0–1‡

* After Matutes et al. 1994b.

** CD22 has been replaced by CD79b (Zomas et al., 1996) in a more recent version of the CLL score (Moreau et al., 1997) which added power for the differential diagnosis with the other B-cell leukaemias.

† In 87% of CLL cases; 10% score 3, 3% score 2 and <1% score 0–1.

‡ In 89% of B-cell leukaemias (PLL, HCL, HCL-V) (10% score 2 and 1% score 3 and none score 0–1); and 72% of B-NHL in leukaemic phase (SLVL, FL, MC and lymphoplasmacytic lymphoma) (23% score 2 and 4% score 3 and <1% score 4–5).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