WHO CLASSIFICATION OF HAEMATOLYMPHOID TUMOURS 5TH EDITION

BILL SEWELL

St Vincent's Hospital Sydney

Garvan Institute

University of NSW

IARC - LYON, FRANCE

WHO-IARC BLUE BOOKS ON TUMOURS

- **Head and Neck**
- **Endocrine**
- **Urinary and Male Genital**
- **Paediatric**
- **Central Nervous System**
- **Thoracic**
- **Female Genital Organs**
- **Soft Tissue and Bone**
- **Breast**
- **Digestive**
- **Skin**
- **Eye**
- **Haematolymphoid**

- Volumes will be available on-line as well as in hard copy.
- Current plan is for a new edition of each book every 5 years.
- There is potential for on-line versions to be updated more frequently

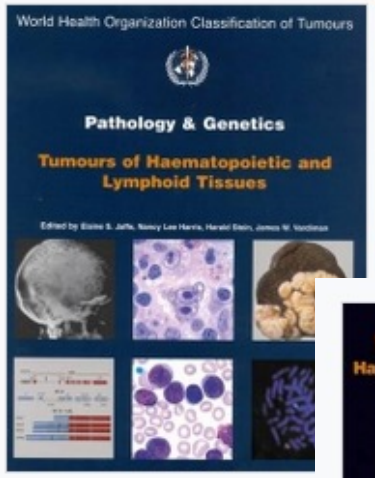
- Haematolymphoid 5th edition:
  - Available on line to IARC subscribers
  - Final publication by end 2023
  - The largest blue book

Blue Books
Membership of authorship and editorial teams

Covers:

- Anatomical pathology
  - Including:
    - Cytology
    - Immunophenotyping: IHC, and flow cytometry for haematolymphoid
- Genetics / molecular biology / ISH & karyotyping
- Clinical experts
- Imaging experts
- Epidemiologists

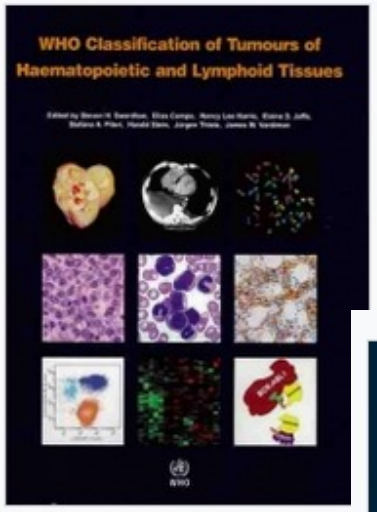
- Haematolymphoid 5th edition : > 60 editors, > 400 authors



Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues

WHO Classification of Tumours, 3rd Edition, Volume 3

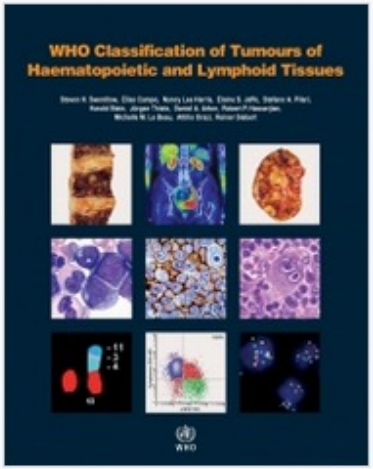
Edited by Jaffe ES, Harris NL, Stein H, Vardiman JW
2001
Formats: Buy Book



WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues

WHO Classification of Tumours, 4th Edition, Volume 2

Edited by Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, Vardiman JW
2008
Formats: Buy Book



WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues

WHO Classification of Tumours, Revised 4th Edition, Volume 2

Edited by Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J
2017
Formats: Buy Book, Web Access

DETAILS

REVIEW ARTICLE OPEN

Check for updates

The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/ Dendritic Neoplasms

Joseph D. Khoury[1✉], Eric Solary[2✉], Oussama Abla[3], Yassmine Akkari[4], Rita Alaggio[5], Jane F. Apperley[6], Rafael Bejar[7], Emilio Berti[8], Lambert Busque[9], John K. C. Chan[10], Weina Chen[11], Xueyan Chen[12], Wee-Joo Chng[13], John K. Choi[14], Isabel Colmenero[15], Sarah E. Coupland[16], Nicholas C. P. Cross[17], Daphne De Jong[18], M. Tarek Elghetany[19], Emiko Takahashi[20], Jean-Francois Emile[21], Judith Ferry[22], Linda Fogelstrand[23], Michaela Fontenay[24], Ulrich Germing[25], Sumeet Gujral[26], Torsten Haferlach[27], Claire Harrison[28], Jennelle C. Hodge[29], Shimin Hu[1], Joop H. Jansen[30], Rashmi Kanagal-Shamanna[1], Hagop M. Kantarjian[31], Christian P. Kratz[32], Xiao-Qiu Li[33], Megan S. Lim[34], Keith Loeb[35], Sanam Loghavi[1], Andrea Marcogliese[19], Soheil Meshinchi[36], Phillip Michaels[37], Kikkeri N. Naresh[35], Ya
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LYMPHOMA

The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms

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The International Consensus Classifications (ICC) of the Clinical Advisory Committee

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The International Consensus Classification of Mature Lymphoid Neoplasms: A Report from the Clinical Advisory Committee

Tracking no: BLD-2022-015851-CR2

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International Consensus Classification of Myeloid Neoplasms and Acute Leukemia: Integrating Morphological, Clinical, and Genomic Data

Tracking no: BLD-2022-015850-CR1

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Campo E et al Blood. 2022 Jun 2

Arber DA et al. Blood. 2022 Jun 29

WHO-IARC and ICC controversy

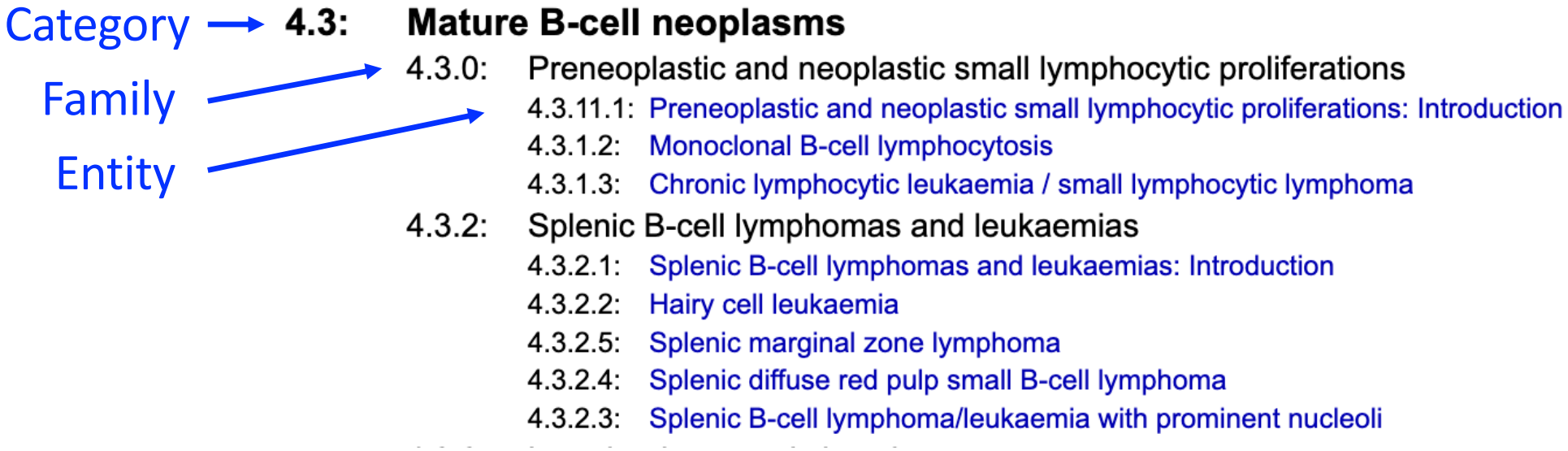
- The Clinical Advisory Committee (CAC) was formed by the Society for Hematopathology (SH) and the European Association for Haematopathology (EAHP).
- The CAC has edited the previous editions of the Haematolymphoid blue books.
- WHO-IARC does not allow a Society-appointed editorial board such as the CAC to control a blue book.
- The impasse was not resolved and most CAC members declined to join the WHO 5th ed blue book.
- Instead, the CAC prepared and published its own International Consensus Classification (ICC), which is not identical to the WHO 5th edition.
- Fortunately, most classifications are consistent, and some of the inconsistent entities lack a good evidence base and need further research.

Grouping of disorders by lineage

- Design of Table of Contents was led by Joseph Khoury.
- Lineage defined by immunophenotype – flow and/or IHC
- Hodgkin lymphoma is now a category in B cell disorders
- Plasmacytoid dendritic cell neoplasm moved to dendritic cell category
- However T and NK cell disorders remain in the same category:
  - Some entities appear to be on a spectrum of T through to NK lineage:
    - e. g. extranodal NK/T cell lymphoma

Joseph Khoury
MD Anderson

Example of Table of Contents



Subtypes, if any, are listed within the entities. For example, the subtypes of monoclonal B-cell lymphocytosis are:

- MBL, low count or clonal B-cell expansion (CLL/SLL type)
- MBL, CLL/SLL type
- MBL, non-CLL/SLL type

HIERARCHY

- Classification of Entities is based on defining genetic abnormalities where possible
- “Variants” fall below the “Subtypes”. Features of variants are included in the descriptions in the relevant subheadings.
- No “provisional entities” – emerging entities are described as having “other defined genetic alterations”
- Within each family, entities are ordered from indolent to aggressive where possible, for example -

5.3.1: Mature T-cell and NK-cell leukaemias

- 5.3.1.1: Mature T-cell and NK-cell leukaemias: Introduction
- 5.3.1.2: T-prolymphocytic leukaemia
- 5.3.1.3: T-cell large granular lymphocytic leukaemia
- 6.0.0.2: NK-cell large granular lymphocytic leukaemia
- 5.3.1.4: Adult T-cell leukaemia/lymphoma
- 5.3.1.5: Sezary syndrome
- 6.0.0.4: Aggressive NK-cell leukaemia

Example of an entity to illustrate subheadings - 1

6.0.0.2: NK-cell large granular lymphocytic leukaemia

"Definitions" are shorter; IARC wants definitions used as widely as possible.

Definition
NK-cell large granular lymphocytic leukaemia (NK-LGLL) is a neoplasm characterized by a persistent increase in peripheral blood

ICD-O coding
9831/3 NK-cell large granular lymphocytic leukaemia

ICD-11 coding
2A90.2 Chronic lymphopr

Synonyms changed to "Related terminology"
Terms are either "acceptable" or "not recommended".

Related terminology
Acceptable: chronic lymphoproliferative disorder of NK cells; chronic NK-large granular lymphocyte lymphoproliferative disorder
Not recommended: chronic NK-cell lymphocytosis; indolent leukaemia of NK-cells

Subtype(s)
None

"Subtypes" is a new subheading.

Localization
NK-LGLL typically involves the peripheral blood and bone marrow. Splenomegaly is uncommon, and hepatomegaly, lymphaden

Clinical features
Most patients are asymptomatic. Some may present with neutropenia and/or anemia or these may develop over the course of the haematologic neoplasms, and neuropathy {33819354}. However, these associations may not be as frequent as seen in T-large gra

Epidemiology
NK-LGLL is predominantly a disease of adults with a median age of 60 years, without gender predilection. Unlike aggressive NK

Etiology
Unknown. Stimulation of innate immunity, possibly due to viral infection, is postulated to play a role in the development of NK-LG disease.

Pathogenesis
Activating mutations of *STAT3* affecting the SH2 domain {22859607} are present in approximately one-third of NK-LGLL. 25% to 3 32321919}. Mutations of the gene *CCL22* encoding Chemokine (C-C Motif) Ligand 22 are found in 21.5% of cases of NK-LGLL, be may define a distinct subgroup of NK-LGLL. Mutations in *TNFAIP3* and PI-3 kinase pathway genes are also found in a minority of c by the NK-cells and their ability to recognize self-MHC-I may also be a contributing factor to leukaemogenesis {24616720}.

"Pathogenesis" is new, separate from "Etiology", typically includes extensive information on genetics. Earlier subheading "Postulated normal counterpart" has been removed; this information is included in "Pathogenesis."

Macroscopic appearance
Not relevant

"Macroscopic Appearance" is a new separate subheading.
Conforms to other Blue Books

Example of an entity to illustrate subheadings - 2

Flow cytometry does not have its own subheading, but is included in immunophenotype. The 5th edition often (but not always) makes it clear which testing is done by flow versus IHC.

Histopathology
The abnormal cells in the blood are usually intermediate to large in size, with abundant pale-staining cytoplasm and variably abundant azuroph
nuclei are typically small and round with condensed chromatin and minimally irregular nuclear contours {8324214}. NK-LGLL cannot be distingu

Lymphocytes may be increased in bone marrow aspirate smears, but the lymphocyte cytoplasm is often difficult to visualize in these preparatio
marrow involvement is common, usually displaying an intrasinusoidal pattern although interstitial infiltrates may also be seen {12648073}. The
the spleen, intrasinusoidal infiltration of the red pulp may also be seen {8324214}.

Immunophenotyping:
Flow cytometry shows that NK-LGLL are CD16 positive and surface CD3 negative; cytoplasmic CD3-epsilon expression may be present. CD56
{26234181;28431200}. A diminished expression of CD2 and CD7 may also be present. Expression of CD8 is varyingly reported {36870881; 29
15368309; 17509985}. All cases have abnormal killer-cell immunoglobulin-like receptor (KIR) expression, either complete lack of detectable KI
abnormalities of NK-cell receptors are uniform, bright CD94/NKG2A heterodimer expression and weak or absent expression of CD161.
Expression of cytotoxic granule proteins (TIA-1, Granzyme B, Granzyme M) is detectable by flow cytometric immunophenotyping and immunoh
bone marrow and spleen, which can be difficult to detect by histologic examination {12648073}. NK-LGLL and T-LGLL are indistinguishable by

Differential diagnosis:
The differential diagnosis of NK-LGLL includes mature T-cell neoplasms with leukaemic presentation, in particular T-LGLL, a disorder with cons
leukaemia n … and lack of nuclear EBV-positivity.

"Cytology" is a new separate subheading.

Cytology
See Histopathology for blood results

"Genetic Profile" has been changed to "Diagnostic molecular pathology". Genetic information not used in diagnosis is now in "Pathogenesis".

Diagnostic molecular pathology
Mutations of *STAT3* (30%) {22859607} and

Essential and desirable diagnostic criter
Essential:
1) Increase in circulating NK-cells, typically > $2x10^9$/L, persisting for longer than 6 months
2) Flow cytometric evidence of peripheral blood or bone marrow involvement by a uniform population of surface CD3 negative, CD16 positive N
3) KIRs restricted pattern of expression, demonstrated by flow cytometry analysis (either a dominant expression of a relevant KIR or lack of KIF
If both 2 and 3 are present, a diagnosis of NK-LGLL can be made in the absence of documented persistence of an absolute peripheral blood N

Desirable:
Bone marrow involved by intra-sinusoidal NK-cells
Demonstration of *STAT3* and/or *TET2* mutations with NK-c

"Essential and desirable diagnostic criteria" is an excellent new subheading. The "desirable" criteria include testing that may not be universally available.

Staging
Not relevant

"Staging" is a new subheading.

Prognosis and prediction
In over one-half of NK-LGLL cases, the clinical course is indolent and no therapy is required; some cases may even show spontaneous reg
usually determined by the presence of absence of associated cytopenias. Cytopenias and recurrent infections may be harbingers of a worse

Individual Disorders

Acute leukaemias and myeloid disorders

To date, acute leukaemia is the only neoplastic condition for which the WHO Essential Diagnostics List recommends flow cytometry.

AML Table of Contents

2.3: Acute myeloid leukaemia

2.3.1.1: Acute myeloid leukaemia: Introduction

Defined by genetics

2.3.1: Acute myeloid leukaemia with defining genetic abnormalities
- 2.3.1.2: Acute promyelocytic leukaemia with PML::RARA fusion
- 2.3.1.3: Acute myeloid leukaemia with RUNX1::RUNX1T1 fusion
- 2.3.1.4: Acute myeloid leukaemia with CBFB::MYH11 fusion
- 2.3.1.6: Acute myeloid leukaemia with DEK::NUP214 fusion
- 2.3.1.7: Acute myeloid leukaemia with RBM15::MRTFA fusion
- 2.3.1.8: Acute myeloid leukaemia with BCR::ABL1 fusion
- 2.3.1.5: Acute myeloid leukaemia with KMT2A rearrangement
- 2.2.4.2: Acute myeloid leukaemia with MECOM rearrangement
- 2.3.1.9: Acute myeloid leukaemia with NUP98 rearrangement
- 2.2.4.1: Acute myeloid leukaemia with NPM1 mutation
- 2.3.1.12: Acute myeloid leukaemia with CEBPA mutation
- 2.3.1.11: Acute myeloid leukaemia, myelodysplasia-related
- 2.3.1.10: Acute myeloid leukaemia with other defined genetic alterations

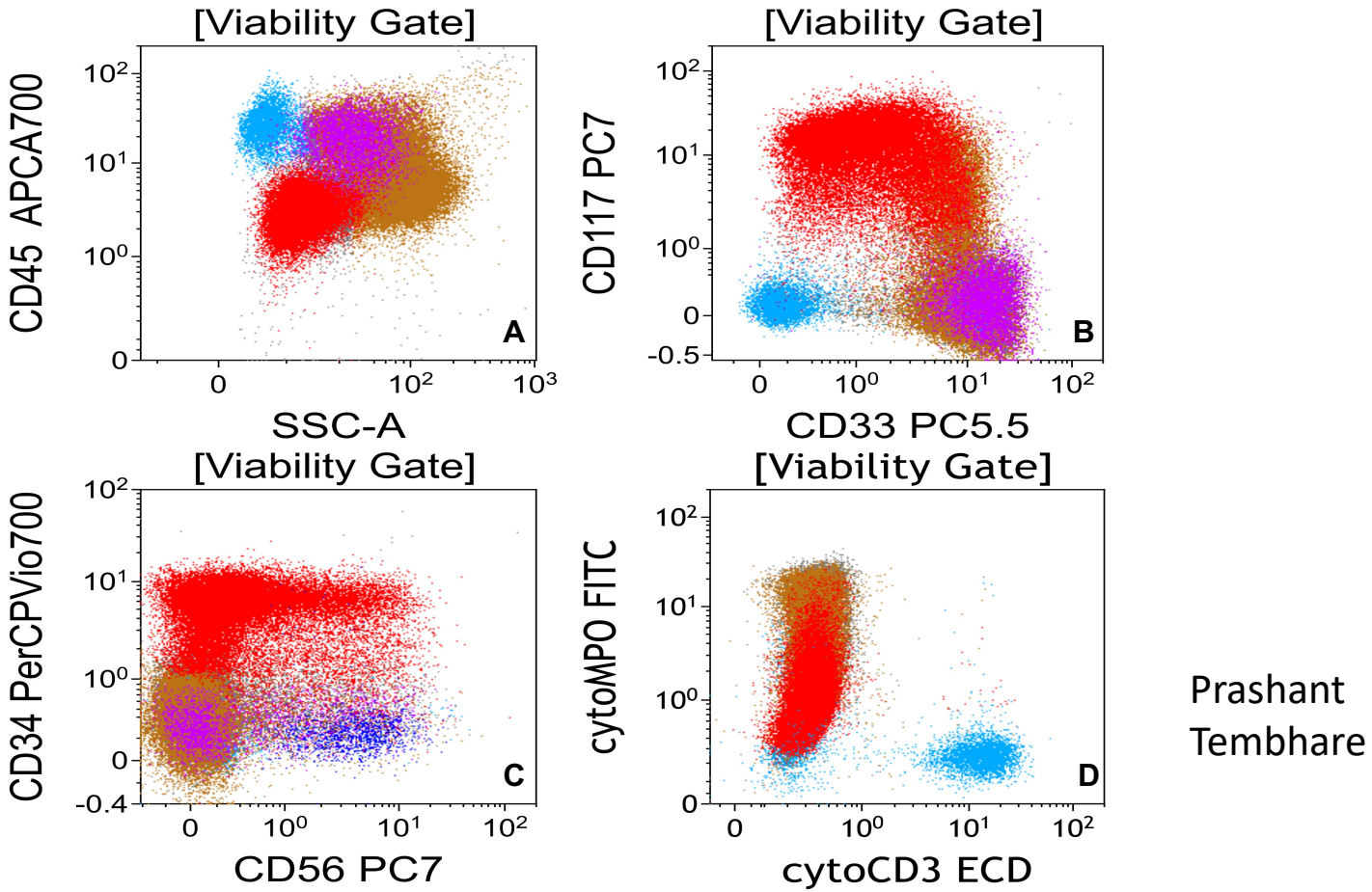
Defined by morphology and immunophenotype

2.3.2: Acute myeloid leukaemia defined by differentiation
- 2.3.2.2: Acute myeloid leukaemia with minimal differentiation
- 2.3.2.3: Acute myeloid leukaemia without maturation
- 2.3.2.4: Acute myeloid leukaemia with maturation
- 2.3.2.5: Acute basophilic leukaemia
- 2.3.2.6: Acute myelomonocytic leukaemia
- 2.3.2.7: Acute monocytic leukaemia
- 2.3.2.9: Acute erythroid leukaemia
- 2.3.2.10: Acute megakaryoblastic leukaemia

There is no AML, NOS category.

Comments on AML

- AML with defining genetic abnormalities
  - 95% of AML cases, in Huber et al (2023).
    - Most types can be now defined with < 20% blasts
      - WHO requires “increased” blasts; ICC requires > 10% blasts.
- AML defined by differentiation
  - The proportion of AML cases that fall into this group is now small, because of the march of genetics
  - May be useful in flow labs pending genetics results
  - Useful for final diagnosis in resource-limited settings
  - 5th ed supported by fantastic flow figures from Prashant Tembhare



Prashant Tembhare

Fig. 2.03… Acute myeloid leukaemia with maturation: flow cytometry histograms. Blasts are red.

B-ALL

- “B-ALL is diagnosed by morphology and immunophenotyping, while further classification is largely by defined cytogenetic and/or molecular abnormalities.”
- NOS (not otherwise specified) is for cases that have been extensively analysed for genetic abnormalities
- NFC (not further classified) should be used when comprehensive testing for genetic abnormalities has not been done.

B-ALL/LBL Table of Contents

4.2: Precursor B-cell neoplasms

4.2.1: B-lymphoblastic leukaemias/lymphomas

4.2.1.1: B-lymphoblastic leukaemias/lymphomas: Introduction

4.2.1.0: B-lymphoblastic leukaemia/lymphoma

Defined by genetics

- 4.2.1.7: B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy
- 4.2.1.8: B-lymphoblastic leukaemia/lymphoma with hypodiploidy
- 4.2.1.14: B-lymphoblastic leukaemia/lymphoma with iAMP21
- 4.2.1.2: B-lymphoblastic leukaemia/lymphoma with BCR::ABL1 fusion
- 4.2.1.5: B-lymphoblastic leukaemia/lymphoma with BCR::ABL1-like features
- 4.2.1.3: B-lymphoblastic leukaemia/lymphoma with KMT2A rearrangement
- 4.2.1.4: B-lymphoblastic leukaemia/lymphoma with ETV6::RUNX1 fusion
- 4.2.1.15: B-lymphoblastic leukaemia/lymphoma with ETV6::RUNX1-like features
- 4.2.1.16: B-lymphoblastic leukaemia/lymphoma with TCF3::PBX1 fusion
- 4.2.1.17: B-lymphoblastic leukaemia/lymphoma with IGH::IL3 fusion
- 4.2.1.21: B-lymphoblastic leukaemia/lymphoma with TCF3::HLF fusion
- 4.2.1.6: B-lymphoblastic leukaemia/lymphoma with other defined genetic alterations

Genetic studies do not provide a classification.

- 4.2.1.13: B-lymphoblastic leukaemia/lymphoma NOS

T-ALL/LBL Table of Contents

5.2: Precursor T-cell neoplasms

5.2.1: T-lymphoblastic leukaemia/lymphoma

5.2.1.1: T-lymphoblastic leukaemia/lymphoma NOS

5.2.1.2: Early T-precursor lymphoblastic leukaemia/lymphoma

Classification is based entirely on morphology and immunophenotype.

Immunophenotype of ETP-ALL/LBL

ETP-ALL/LBL: Must meet all 5 criteria of antigen expression
1. CD3 (cytoplasmic +/surface-[a])
2. Absent myeloperoxidase (<10% by flow cytometry, <3% by cytochemistry)
3. Absent CD1a and CD8
4. ≥25% of blasts with ≥1 of stem cell or myeloid markers: CD34, CD117, CD13, CD33, CD65, CD11b, HLA-DR
5. Dim to negative CD5 (<75% of blasts positive)[b]
Near ETP-ALL: Criteria 1-4 met, however ≥75% blasts are CD5 positive

a. Expression of surface CD3 is rare.
b. Dim CD5 can also be defined as MFI at least 1 log less than that of normal T cells.

Acute leukaemias of mixed or ambiguous lineage
Table of Contents

Diagnosis of this category depends on immunophenotype, largely flow. Entities are then classified as below.

2.6: Acute leukaemias of mixed or ambiguous lineage

2.5.2.1: Acute leukaemias of mixed or ambiguous lineage: Introduction

Defined by genetics	2.6.1:	Acute leukaemia of ambiguous lineage with defining genetic abnormalities
	2.5.2.2:	Mixed-phenotype acute leukaemia with BCR::ABL1 fusion
	2.5.2.3:	Mixed-phenotype acute leukaemia with KMT2A rearrangement
	2.5.2.7:	Acute leukaemia of ambiguous lineage with other defined genetic alterations
Defined by immunophenotype	2.5.3:	Acute leukaemia of ambiguous lineage defined immunophenotypically
	2.5.2.4:	Mixed-phenotype acute leukaemia, B/myeloid
	2.5.2.5:	Mixed-phenotype acute leukaemia, T/myeloid
	2.5.2.8:	Mixed-phenotype acute leukaemia, rare types
	2.5.2.6:	Acute leukaemia of ambiguous lineage NOS
	2.5.2.9:	Acute undifferentiated leukaemia

Lineage Assignment Criteria for MPAL – Brent Wood

	Criterion
B lineage	
CD19 strong [1] OR CD19 weak [2]	1 or more also strongly expressed: CD10, CD22, or CD79a[3] 2 or more also strongly expressed: CD10, CD22, or CD79a[3]
T lineage	
CD3 (cytoplasmic or surface) [4]	Intensity in part exceeds 50% of mature T cells by flow cytometry OR Immunocytochemistry positive with non-zeta chain reagent
Myeloid lineage	
Myeloperoxidase (MPO) OR Monocytic differentiation	Intensity in part exceeds 50% of mature neutrophil level 2 or more expressed: Non-specific esterase, CD11c, CD14, CD64 or lysozyme

1 CD19 intensity > 50% of normal B cell progenitors by flow
2 CD19 intensity < 50% of normal B cell progenitors by flow
3 Cannot use CD79a if T lineage under consideration
4 CD3ε chain antibody

Mature lymphoid disorders

Diagnostic Criteria for CLL/SLL

*The majority of cases with CLL/SLL present with a leukaemic phase and diagnosis can be established on peripheral blood.

	Positive	**Negative/weak**
ESSENTIAL DIAGNOSTIC CRITERIA		
Peripheral blood	Classic morphology of CLL cells; Absolute monoclonal B-cell count $\geq 5\times10^9$/L	
Immunophenotyping	CD19, CD5, CD20, CD23 (variable) & light chain (weak)	
Tissue samples	Lymphadenopathy/organomegaly or altered architecture on microscopy; classic morphology of SLL*	
Immunohistochemistry	CD20 (positive/weak), CD5 (positive/weak), CD23 (variable)	cyclin D1 (weak positivity in subset of cells in proliferation centers is allowed) {27247372}.
DESIRABLE DIAGNOSTIC CRITERIA		
Immunophenotyping	CD200, ROR1, CD43	FMC7, CD79b (weak/negative), CD10, CD81
Immunohistochemistry	CD23, LEF1, CD43, MUM1 (proliferation centers)	CD10, SOX11

Monoclonal B-cell lymphocytosis subtypes

- MBL now divided into:
  - CLL/SLL-type (0.5 - 5 x 10^9/L) *
  - Low count MBL (< 0.5 x 10^9/L) *
  - Non-CLL/SLL type

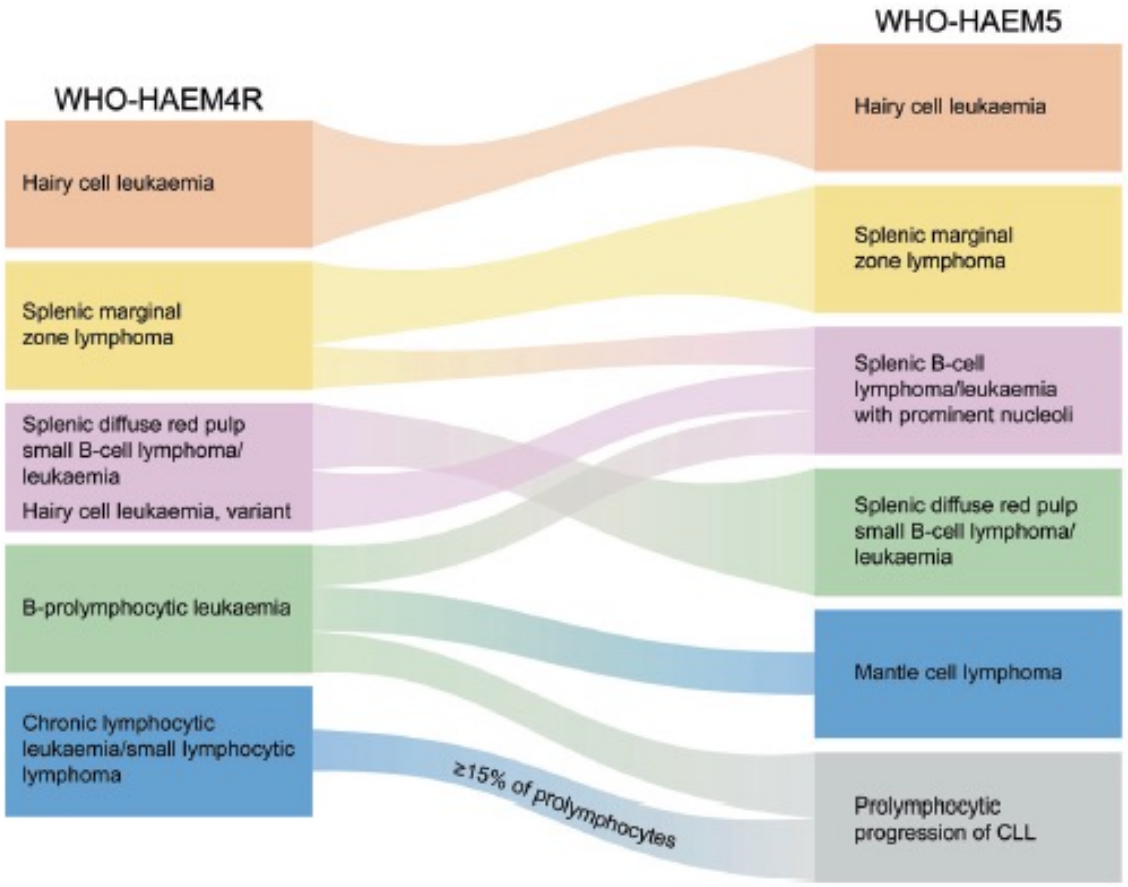
- Atypical CLL-type is no longer recognized

* The numbers are inconsistently based on either monoclonal B-cell count or total B-cell count.

Changes to B cell entries

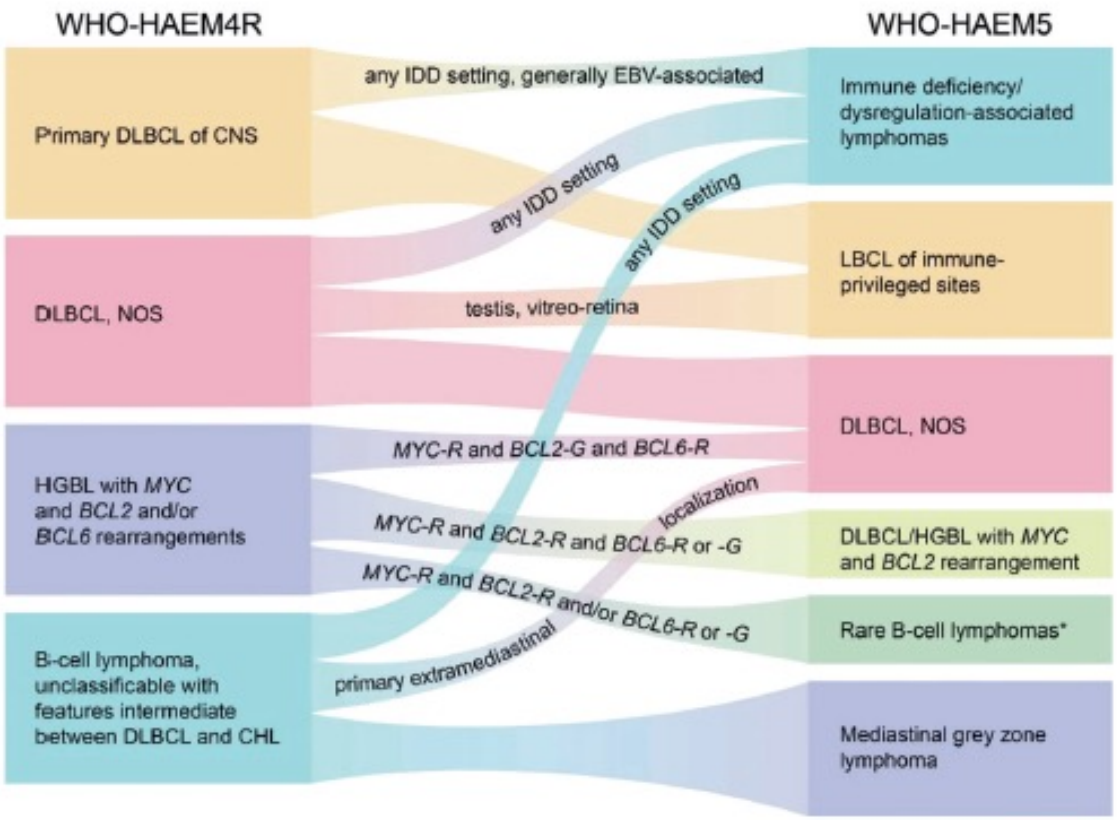
- B-cell prolymphocytic leukemia (B-PLL) no longer an entity.
  - The previous entity of B-PLL was morphologically defined. Under the new classification it could be:
    - “Splenic B-cell leukaemia/lymphoma with prominent nucleoli”
    - A variant of mantle cell lymphoma
    - Prolymphocytic progression of CLL/SLL (> 15% prolymphocytes)
- The new category “Splenic B-cell lymphoma/leukaemia with prominent nucleoli” (SBLPN) encompasses:
  - HCL-variant (genetically distinct from HCL)
  - CD5-negative prolymphocytic leukemia

Changes to B cell classifications



Alaggio R, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022 Jul;36(7):1720-1748. Epub 2022 Jun 22.

Changes to Large B-cell Lymphomas



Alaggio R, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022 Jul;36(7):1720-1748. Epub 2022 Jun 22.

Revised system of classification of immune deficiency/dysregulation-associated disorders

Table 5. Three-part nomenclature for lymphoid proliferations and lymphomas arising in the setting of immune deficiency/dysregulation.

Histological diagnosis	Viral association	Immune deficiency/dysregulation setting
◦ Hyperplasia (specify type) ◦ Polymorphic lymphoproliferative disorder ◦ Mucocutaneous ulcer ◦ Lymphoma (classify as for immunocompetent patients)	◦ EBV +/− ◦ KSHV/HHV8 +/−	◦ Inborn error of immunity (specify type) ◦ HIV infection ◦ Posttransplant (specify: solid organ/bone marrow) ◦ Autoimmune disease ◦ Iatrogenic/therapy-related (specify) ◦ Immune senescence

Major changes to plasma cell disorders and other conditions with paraproteins

- Additions where underlying clonal B-cells or plasma cells do not satisfy criteria for malignancy:
  - Cold agglutinin disease
  - Monoclonal gammopathy of renal significance

- PC neoplasms with paraneoplastic syndromes
  - Now 3 full subtypes:
    - POEMS (already in 4R)
    - TEMPI (provisional in 4R; telangiectasias, elevated EPO, monoclonal gammopathy, perinephric fluid, intrapulmonary shunting)
    - AESOP (not in 4R; adenopathy and extensive skin patch overlying a plasmacytoma)

Major points in T lineage lymphomas

- Grouping and re-naming of nodular T follicular helper (TFH) cell lymphomas:
  - Nodular TFH cell lymphoma, angioimmunoblastic type (formerly AITL)
  - Nodular TFH cell lymphoma, follicular type
  - Nodular TFH cell lymphoma, NOS
    - These all express TFH markers such as CD10 and PD-1
- Peripheral T cell lymphoma (PTCL), NOS
  - PTCL-TBX21 and PTCL-GATA3 are recognized as variants, with Th1 and Th2 features, respectively, but are not sufficiently well characterized to be subtypes.

Genetic Predisposition Syndromes

- Most importantly:
  - Ataxia Telangiectasia (ATM mutations)
  - Nijmegen-Breakage Syndrome (NBN mutations)
- Relevant to treatment toxicity, carrier and genetic counselling
- Lymphomas and leukaemias are classified according to standard criteria but should be labelled AT-related or NBS-related.

Table 15. Immunophenotypic diagnostic criteria of blastic plasmacytoid dendritic cell neoplasm.

Expected positive expression:
CD123*
TCF4*
TCL1*
CD303 *
CD304*
CD4
CD56
Expected negative markers:
CD3
CD14
CD19
CD34
Lysozyme
Myeloperoxidase
Immunophenotypic diagnostic criteria:
-Expression of CD123 and one other pDC marker(*) in addition to CD4 and/or CD56.
or,
-Expression of any three pDC markers and absent expression of all expected negative markers.

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