

**Historical backgrounds of
classification of lymphoma
and
Updated Kiel classification of
canine lymphoma**

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Conceptual changes in the nomenclature of lymphomas

- Traditionally, various tumors have been classified according to their histogenesis and the degree of differentiation.
- The rapid progress in immunology and molecular biology were reflected in conceptual change in the nomenclature and classification of lymphomas.
- Although the microscopic appearance of lymphocytes is deceiving, T- and B-cells can be identified by newly developed methods.

Today's menu

- **Historical backgrounds of human Non-Hodgkin's lymphoma (NHL) classification**
- Updated Kiel classification of canine lymphomas
- Comparison of canine NHL and human NHL

Historical changes of classification of lymphoma

1832	Hodgkin	A report of seven lymphoma cases
1940	Gall & Mallory	Classification of malignant lymphoma
1966	Rappaport	Rappaport classification
1974	Lukes & Collins	Lukes and Collins classification
1978	Lennert	Kiel classification
1982	NCI	Working Formulation of NHL
1988	Stansfeld, et al.	Updated Kiel classification
1994	Harris, et al.	REAL classification
2001~		New WHO classification

Rappaport classification of human NHLs (1966)

Nodular

VS

Diffuse

Lymphocytic, well-differentiated

Lymphocytic, poorly differentiated

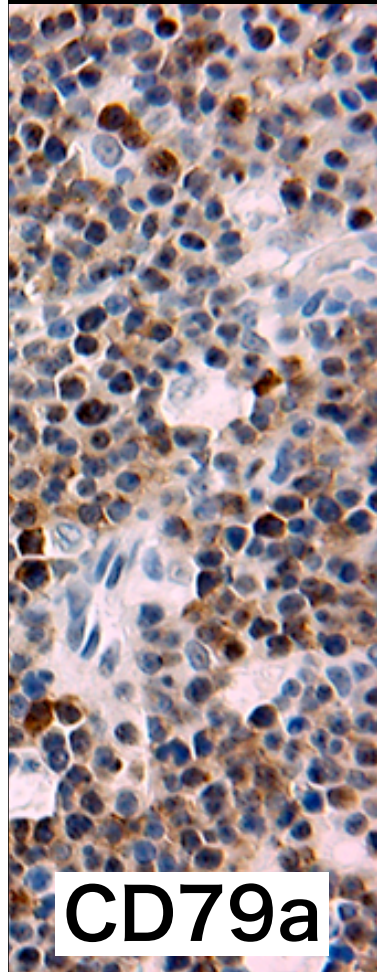
Lymphoblastic

Mixed (lymphocytic and histiocytic)

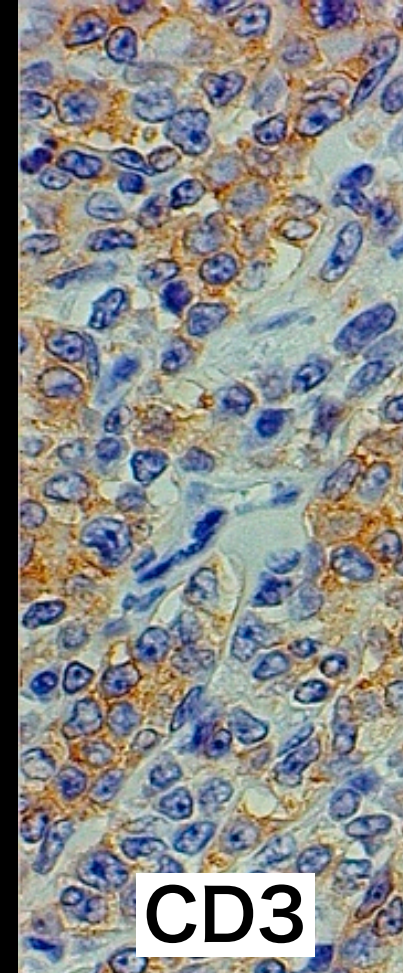
Histiocytic

Others, Undifferentiated

Lukes and Collins classification of human NHLs (1974)



- **T-cell type**
 - small lymphocytic
 - sezary-mycosis fungoides
 - convoluted lymphocytic
 - immunoblastic sarcoma (T-cell)
- **B-cell type**
 - small lymphocytic
 - plasmacytoid lymphocytic
 - follicular center cell
 - immunoblastic sarcoma (B-cell)
 - histiocytic
- Undefined cell type



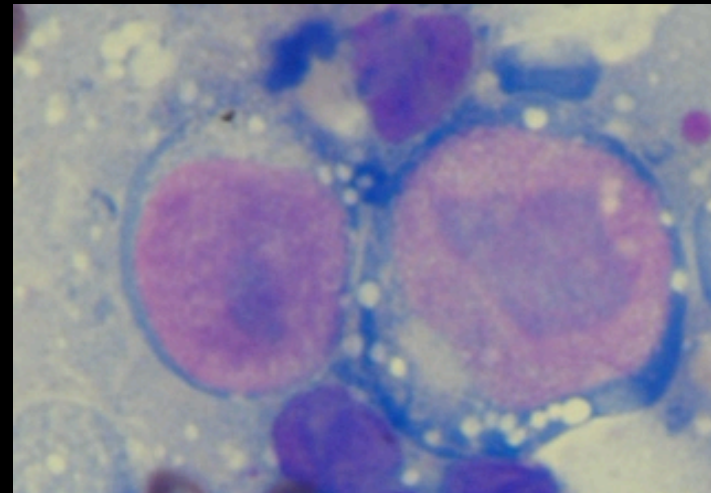
Kiel classification of human NHLs (1978)

- **Low grade malignancy**

- lymphocytic
- lymphoplasmacytoid
- centrocytic
- centroblastic - centrocytic

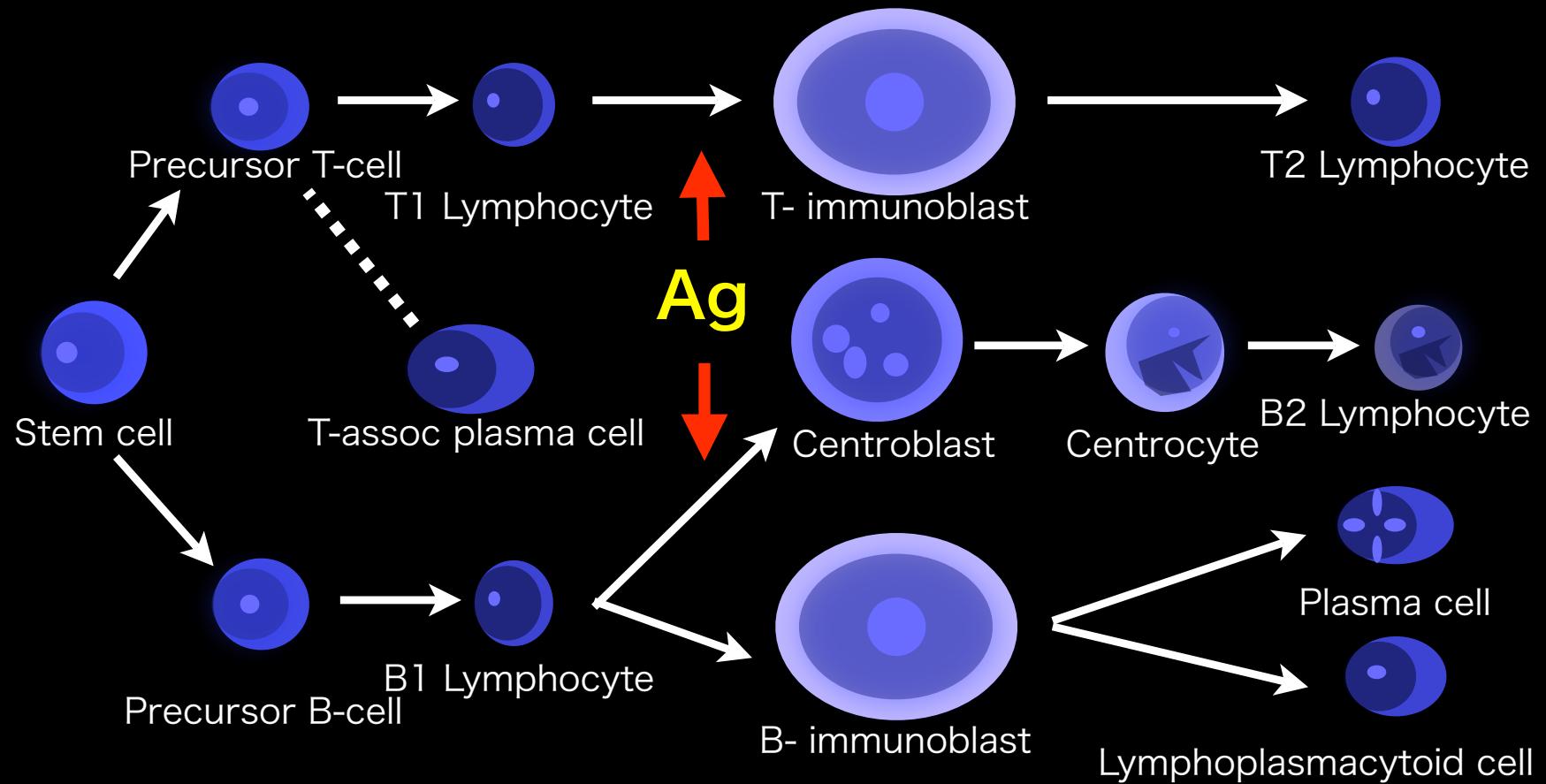
- **High grade malignancy**

- centroblastic
 - lymphoblastic
 - follicular center cell
 - immunoblastic
- Unclassified



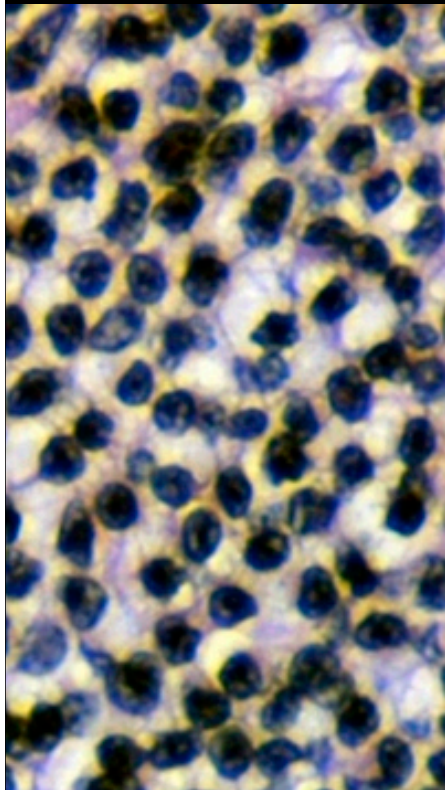
Kiel classification of human NHLs (1978)

Conceptual figure for Kiel classification

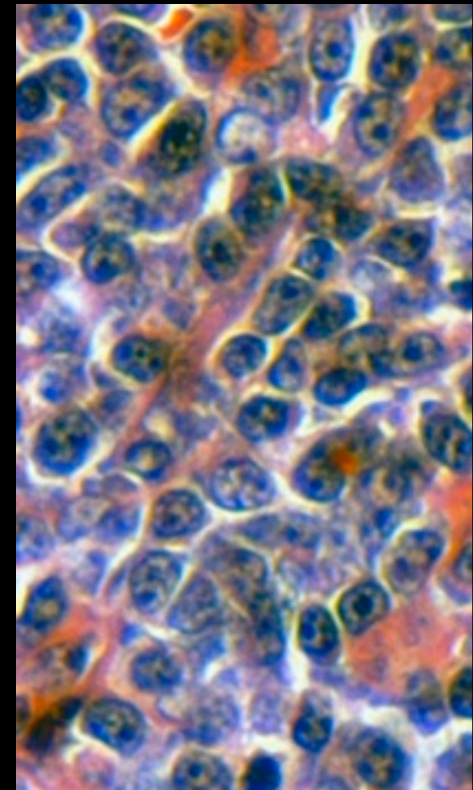


A Working Formulation of human NHLs for clinical usage (1982)

As a means for translation of terminology among six different NHL classifications. 1175 NHL cases, 12 pathologists.



- **Low grade**
- **Intermediate grade**
- **High grade**
- **Miscellaneous**



A Working Formulation of human NHLs for clinical usage (1982)

- **Architecture : Follicular, Diffuse**
- **Cell size : compare to RBC size**
 - small 1.5-2 X RBC
 - medium 2-3 X RBC
 - large >3 X RBC
- **Mitotic index**

A Working Formulation of human NHLs for clinical usage (1982)

- **Low grade**

- Small lymphocytic (CLL type, plasmacytoid)
- Follicular, predominantly small cleaved cell
- Follicular, mixed small cleaved and large cell

A Working Formulation of human NHLs for clinical usage (1982)

- **Intermediate grade**

- Follicular, predominantly large cell
- Diffuse, small cleaved cell
- Diffuse, mixed small and large cell
- Diffuse, large cell

A Working Formulation of human NHLs for clinical usage (1982)

- **High grade**

- Large cell immunoblastic
- Lymphoblastic
- Small non-cleaved cell
(Burkitt's or non-Burkitt's)

A Working Formulation of human NHLs for clinical usage (1982)

● **Miscellaneous**

- Composite
- Mycosis fungoides
- Histiocytic
- Extramedullary plasmacytoma
- Unclassifiable
- Other

Merits and drawbacks of the NCI-Working Formulation

● Merits

- Easy to use (diagnostic histopathology)
- Based purely on morphologic assessment (predominantly architecture and cell size)

● Drawbacks

- Most of the categories are heterogeneous
- Does not take lineage into consideration
- Prognostic groups was based on survival data from patients treated in the 1960s and 70s
- Many new entities have been recognized since the introduction of WF

Updated Kiel classification of human NHLs (1988)

B-cell low-grade

T-cell low-grade

B-cell high-grade

T-cell high-grade

Updated Kiel classification of human NHLs (1988)

● **B-cell low grade**

- Lymphocytic, CLL-type
- Lymphoplasmacytic/-cytoid (PL immunocytoma)
- Plasmacytic
- Centrocytic/Centroblastic
- Monocytoid B-cell, including marginal zone cell

Updated Kiel classification of human NHLs (1988)

- **B-cell high grade**
 - Centroblastic
 - Immunoblastic
 - Large cell anaplastic Ki-1 lymphoma
 - Burkitt's lymphoma
 - Lymphoblastic

Updated Kiel classification of human NHLs (1988)

● T-cell low grade

- Lymphocytic, CLL-type
- Small cerebriform cell (mycosis fungoides, Sézary syndrome)
- Lymphoepithelioid (Lennert's) lymphoma
- Angioimmunoblastic T-cell lymphoma
- T-zone lymphoma
- Pleomorphic T-cell lymphoma, small cell

Updated Kiel classification of human NHLs (1988)

- **T-cell high grade**
 - Pleomorphic T-cell lymphoma, medium and large cells
 - Immunoblastic
 - Large cell anaplastic Ki-1 lymphoma
 - Lymphoblastic

Merits and drawbacks of the updated Kiel classification

● Merits

- Easy to use (diagnostic cytology)
- Characterizes many biologically relevant entities
- Take lineage into consideration (There is good evidence that T-cell lymphomas generally are much aggressive than B-cell lymphomas)

● Drawbacks

- The classification is mainly for nodal lymphomas
- Some categories are not reproducible
- Adult T-cell lymphoma/leukemia is not recognized as a distinct entity
- NK-cell neoplasms are not recognized

Revised European-American Lymphoma (REAL) classification of lymphoid neoplasms(1994)

- The REAL classification is **not** based on the histogenesis of lymphoma cells. The classification is “**a list**” of well defined clinicopathological entities.

Precursor B-cell
neoplasm

Precursor T-cell
neoplasm

Peripheral (mature)
B-cell neoplasm

Peripheral T-cell
and NK-cell
neoplasm

Merits and drawbacks of the REAL/WHO classification

● Merits

- Simply a list of disease entities, thus the classification can easily updated
- Emphasizes distinct biologic entities defined by a combination of clinical, morphologic, immunophenotypic, and genotypic feature
- High reproducibility

● Drawbacks

- Often mandates immunohistochemical and/or genetic studies
- Difficult to apply the classification if clinical information is incomplete or not available
- Just a list, difficult to learn the classification

Today's menu

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- **Updated Kiel classification of canine lymphomas**
- **Comparison of canine NHL and human NHL**

Updated Kiel classification of human NHLs (1988)

B-cell low-grade

T-cell low-grade

B-cell high-grade

T-cell high-grade

Updated Kiel classification of canine lymphomas, Fournel-Fleury et al. (1997)

B-cell low-grade

Small cell
Lymphocytic
Lymphoplasmacytic
Prolymphocytic
Centrocytic
Centroblastic/centrocytic
Macronucleolated medium-sized cell

T-cell low-grade

Small cell
Clear cell
Prolymphocytic
Pleomorphic small cell
Mycosis fungoides

B-cell high-grade

Centroblastic
Monomorphic
Polymorphic
Immunoblastic
Small cell, unclassifiable
Burkitt-type
Plasmacytoid
Lymphoblastic

T-cell high-grade

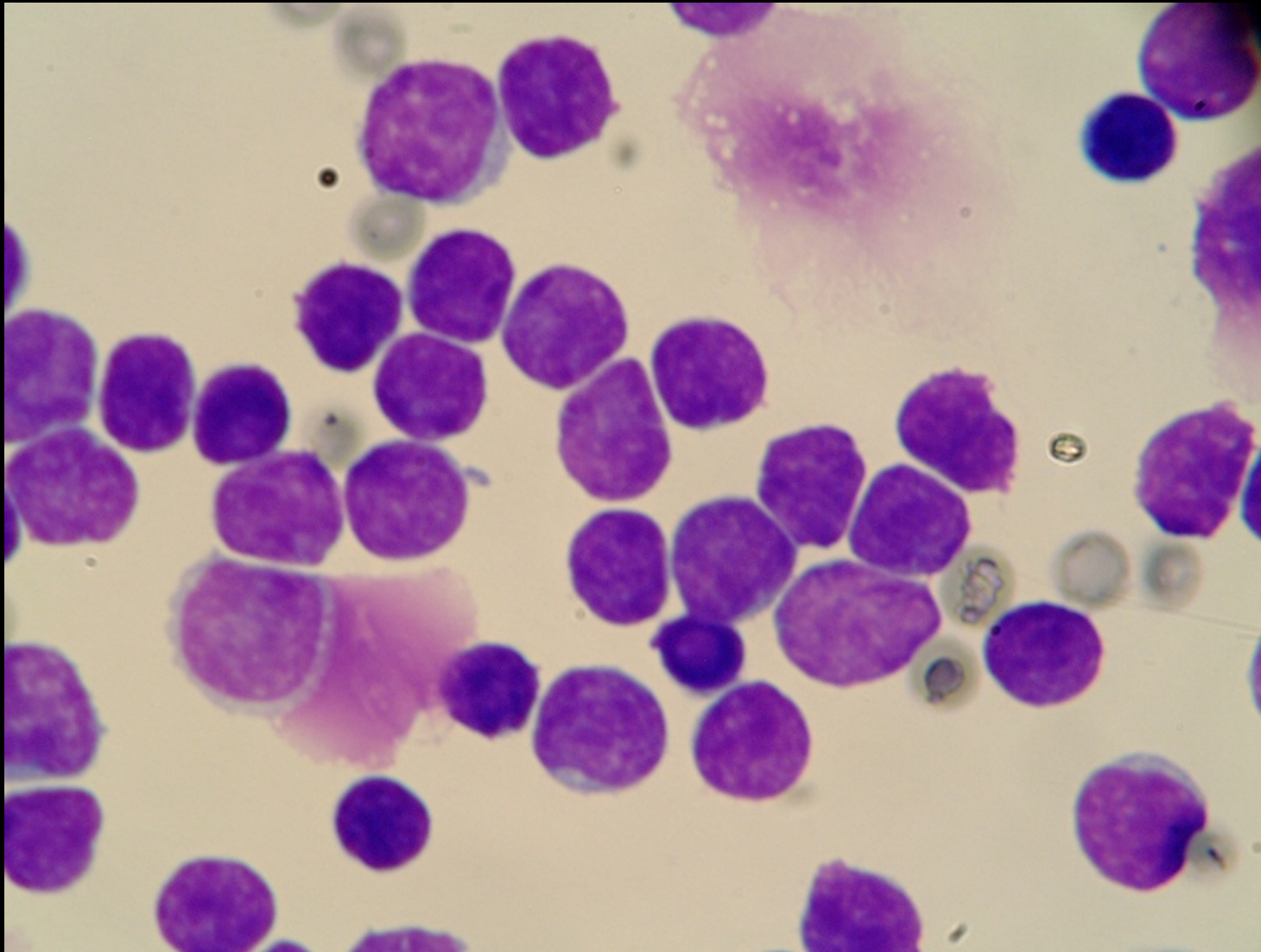
Pleomorphic, mixed, small and large cell
Pleomorphic large cell
Immunoblastic
Small cell, unclassifiable, plasmacytoid
Lymphoblastic

Updated Kiel classification of canine lymphomas

- **B-cell low-grade malignancy (15/92)**
 - Small cell
 - Lymphocytic 0
 - Lymphoplasmacytic 2
 - Prolymphocytic 2
 - Centrocytic 1
 - Centroblastic/Centrocytic 1
 - Macronucleolated medium-sized cell 9

Fournel-Fleury et al. (1997)

Lymphocytic lymphoma (B-cell)



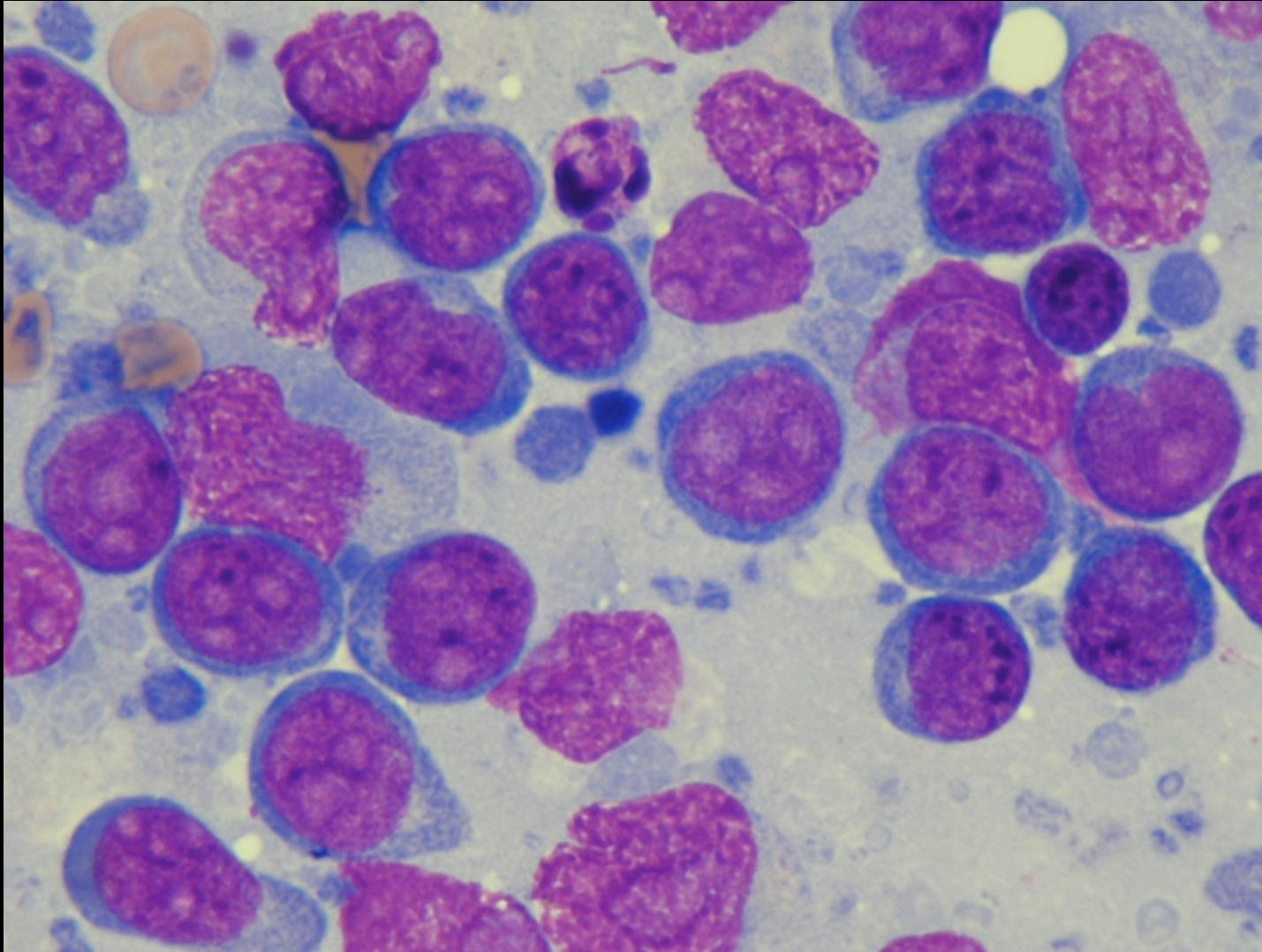
Updated Kiel classification of canine lymphomas

● **B-cell high-grade malignancy (53/92)**

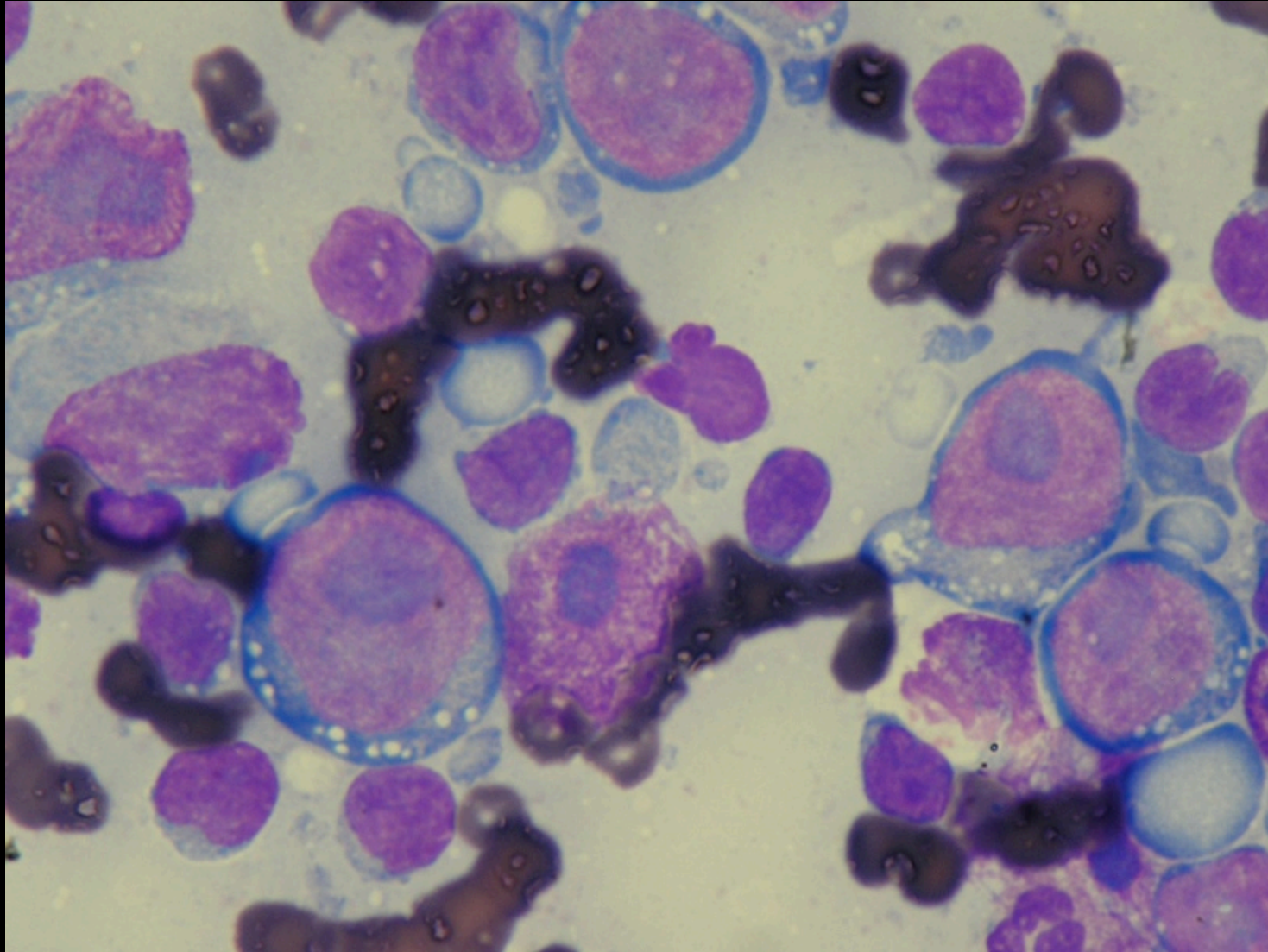
- Centroblastic
 - Monomorphic 1
 - Polymorphic 37
- Immunoblastic 13
- Small cell, unclassifiable
 - Burkitt-type 1
 - Plasmacytoid 1
- Lymphoblastic 0

Fournel-Fleury et al. (1997)

Polymorphic lymphoma with a centroblastic component,
Predominantly small-cell type (PSC)



Immunoblastic lymphoma



Updated Kiel classification of canine lymphomas

• T-cell low-grade malignancy (15/92)

- Small cell
 - Clear cell 4
 - Polymphocytic 2
 - Pleomorphic small cell 2
- mycosis fungoides 7

Fournel-Fleury et al. (1997)

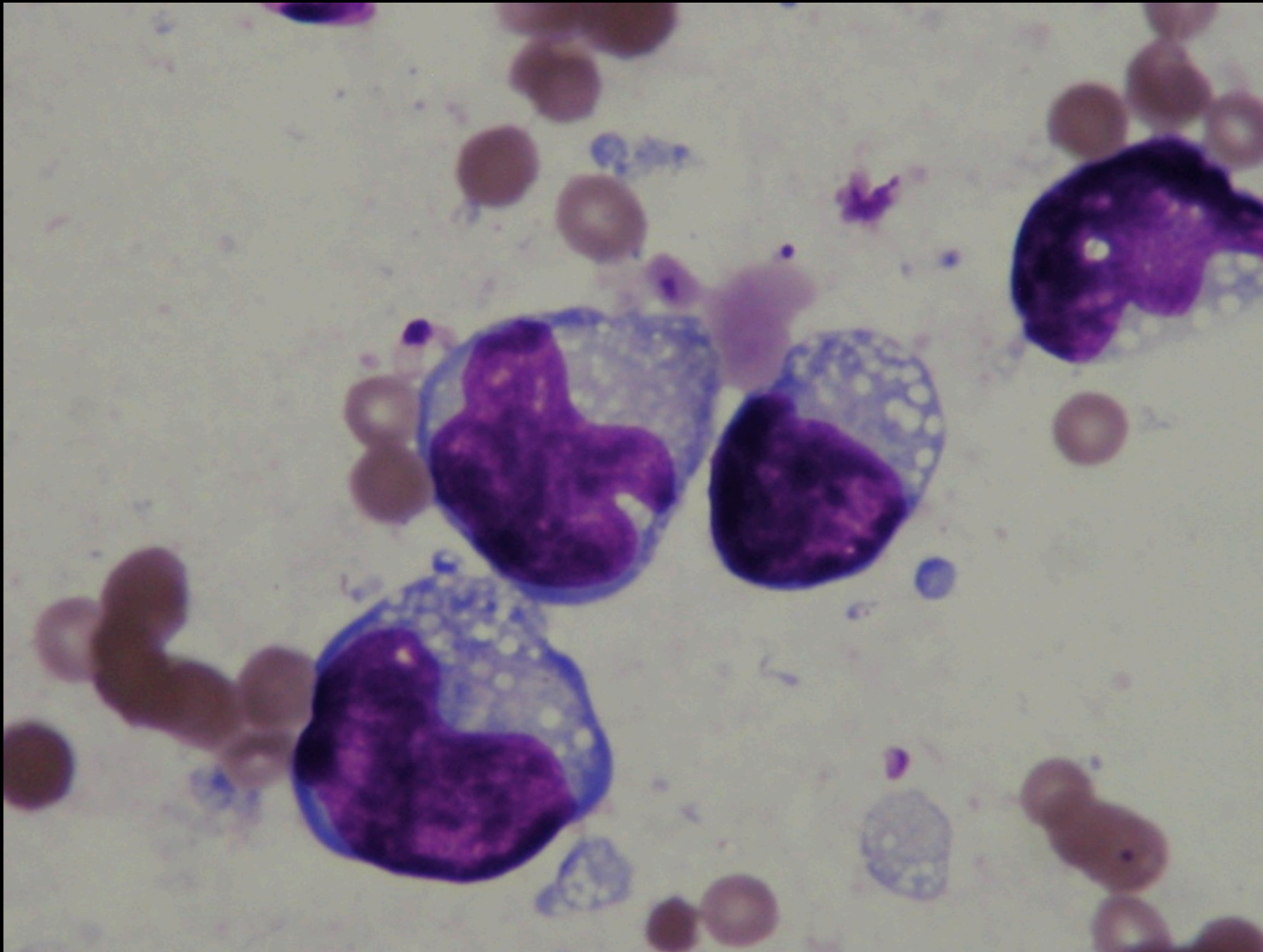
Updated Kiel classification of canine lymphomas

● T-cell high-grade malignancy (9/92)

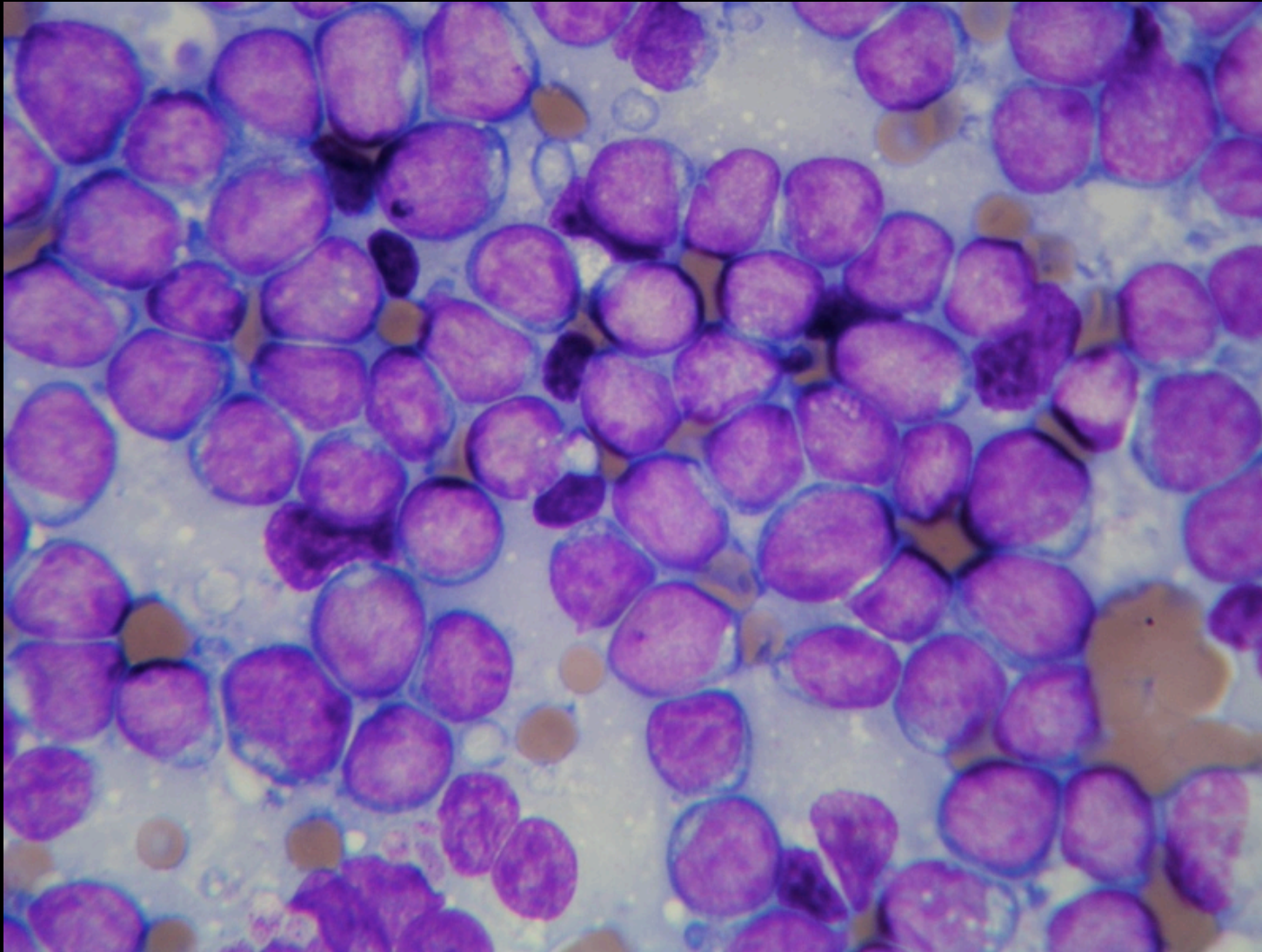
- Pleomorphic, mixed small and large cell 2
- Pleomorphic large cell 4
- Immunoblastic 0
- Small cell, unclassifiable, plasmacytoid 2
- Lymphoblastic 1

Fournel-Fleury et al. (1997)

Pleomorphic lymphoma (T-cell)



Lymphoblastic lymphoma, (T-cell)



Proposed choice of treatment for
canine lymphomas classified by
updated Kiel classification

B-cell high-grade

Combination
chemotherapy protocols

T-cell high-grade

Combination
CCNU ?

B-cell low-grade

Chlorambucil or Melphalan
± Predonisolone

T-cell low-grade

CCNU ?

Consider no treatment unless clinical symptoms exist ?

summary

- A critical feature of any tumor classification is that it be periodically reviewed and updated to incorporate new information.
- In dogs, follicular lymphomas are rare, most major B-cell high grade lymphomas tend to respond better to chemotherapy. Low grade lymphomas show longer survival times without aggressive treatment.
- So use of updated Kiel classification though to be better way to diagnose and treat canine lymphomas for the moment.

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