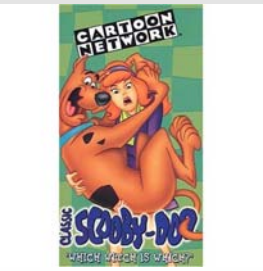
Who's Who in WHO ??

J. Douglas Rizzo, MD MS

CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

a.k.a WHICH WITCH IS WHICH?



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WHO's UP TO WHAT?

- New Standard classification of hematologic neoplasms
- Large consensus effort > 50 pathologists worldwide, 1995-1999
- Define disease entities recognizable to pathologists and with clinical relevance

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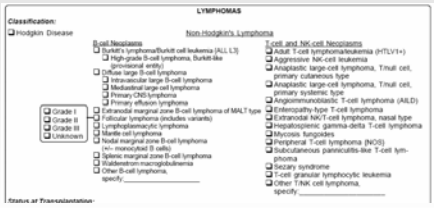
WHO CLASSIFICATION

- Hematologic Neoplasms
  - Myeloid
  - Lymphoid
- Recognize / Define specific entities with prognostic significance

LYMPHOID NEOPLASMS

- Adapted from the REAL classification system
- Divided into
  - B- and T-cell neoplasms
  - Precursor and Mature
  - Hodgkin's Lymphoma

LYMPHOMA – NOT MUCH CHANGE!


LYMPHOMAS

Classification:

☐ Hodgkin Disease

Non-Hodgkin's Lymphoma

B-cell Neoplasms

☐ Burkitt's lymphoma/Burkitt cell leukemia (ALL L3)
☐ High-grade B-cell lymphoma, Burkitt-like (provisional entity)
☐ Diffuse large B-cell lymphoma
☐ Intravascular large B-cell lymphoma
☐ Mediastinal large cell lymphoma
☐ Primary CNS lymphoma
☐ Primary effusion lymphoma
☐ Extranodal marginal zone B-cell lymphoma of MALT type
☐ Follicular lymphoma (includes variants)
☐ Lymphoplasmacytic lymphoma
☐ Mantle cell lymphoma
☐ Nodal marginal zone B-cell lymphoma (+/- monocytoid B cells)
☐ Splenic marginal zone B-cell lymphoma
☐ Waldenstrom macroglobulinemia
☐ Other B-cell lymphoma, specify: _____

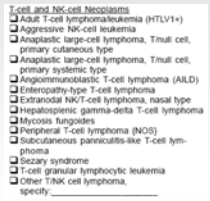
☐ Grade I
☐ Grade II
☐ Grade III
☐ Unknown

T-cell and NK-cell Neoplasms

☐ Adult T-cell lymphoma/leukemia (HTLV1+)
☐ Aggressive NK-cell leukemia
☐ Anaplastic large-cell lymphoma, T/null cell, primary cutaneous type
☐ Anaplastic large-cell lymphoma, T/null cell, primary systemic type
☐ Angioimmunoblastic T-cell lymphoma (AILD)
☐ Enteropathy-type T-cell lymphoma
☐ Extranodal NK/T-cell lymphoma, nasal type
☐ Hepatosplenic gamma-delta T-cell lymphoma
☐ Mycosis fungoides
☐ Peripheral T-cell lymphoma (NOS)
☐ Subcutaneous panniculitis-like T-cell lymphoma
☐ Sezary syndrome
☐ T-cell granular lymphocytic leukemia
☐ Other T/NK cell lymphoma, specify: _____

Status at Transplantation:

T and NK Neoplasms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- Clinical syndromes important to definition
- No clear cytogenetic or T cell receptor types to sub-classify

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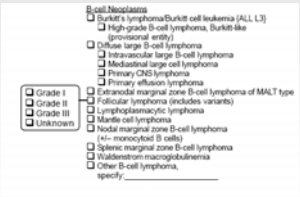
Mature B Cell Neoplasms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- ❑ Waldenstrom macroglobulinemia
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Mature B cell Neoplasms

- Largely preserves REAL
- Follicular:
  - Grade # large cells, report diffuse areas
- CLL: B-cell CLL, SLL same
- Burkitt Lymphoma:
  - Same as FAB L3, call Burkitt
  - Includes Burkitt-like

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Mature B cell Neoplasms

- Distinct subtypes of DLBCL should be listed
  - Primary mediastinal
  - Primary effusion
  - Intravascular lymphoma

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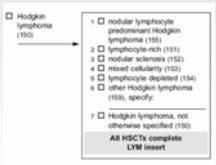
Hodgkin's Lymphoma



- Lymphocyte rich classical HD specific entity
  - Distinct from Nodular lymphocyte-predominant

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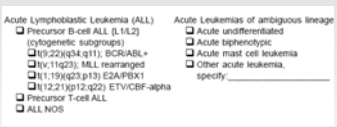
Pre-Cursor T or B Neoplasms



- FAB not relevant {L1, L2} to predict clinical behavior
- Leukemia vs. lymphoma – same entity-most present as leukemia
- Include relevant cytogenetics

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MYELOID NEOPLASMS

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Myeloid Neoplasms

- Major changes to accommodate significant impact on outcomes from:
  - Genetic features (cytogenetic and molecular genetics)
  - Prior therapy and history of MDS

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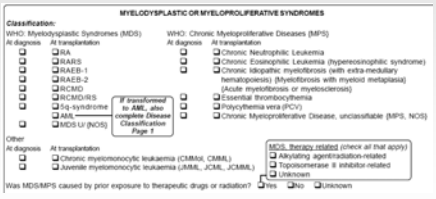
MDS/MPD


MYELODYSPLASTIC OR MYELOPROLIFERATIVE SYNDROMES

Classification:

WHO: Myelodysplastic Syndromes (MDS)

At diagnosis / At transplantation

- RA
- RARS
- RAEB-1
- RAEB-2
- RCMD
- RCMD/RS
- 5q- syndrome
- AML
- MDS U/ (NOS)

If transformed to AML, also complete Disease Classification Page 1

WHO: Chronic Myeloproliferative Diseases (MPS)

At diagnosis / At transplantation

- Chronic Neutrophilic Leukemia
- Chronic Eosinophilic Leukemia (hypereosinophilic syndrome)
- Chronic Idiopathic myelofibrosis (with extra-medullary hematopoiesis) (Myelofibrosis with myeloid metaplasia) (Acute myelofibrosis or myelosclerosis)
- Essential thrombocythemia
- Polycythemia vera (PCV)
- Chronic Myeloproliferative Disease, unclassifiable (MPS, NOS)

Other

At diagnosis / At transplantation

- Chronic myelomonocytic leukaemia (CMMoL; CMML)
- Juvenile myelomonocytic leukaemia (JMML, JCML, JCMML)

MDS, therapy related (check all that apply)

- Alkylating agent/radiation-related
- Topoisomerase II inhibitor-related
- Unknown

Was MDS/MPS caused by prior exposure to therapeutic drugs or radiation? Yes No Unknown

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MDS

- AML now blasts >= 20%
- New distinct entity for refractory cytopenia with multilineage dysplasia
  - Dysplasia 2 or more cell lines
- RA includes erythroid line only
- Distinct 5q- syndrome [del(5q)]

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MDS

- RAEB-1
  - 5-9% blasts BM
  - <5% blasts blood
- RAEB-2
  - 10-19% blasts BM
- Major prognostic significance of MDS occurring in relation to prior radiation/chemotherapy

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MPD

- Should always check bcr/abl
- JMML considered a separate category
  - Distinct from CML, CMML
- Atypical CML (Ph1 neg, bcr/abl neg)
  - Distinct from Ph1 + CML (worse)
  - Needs new name

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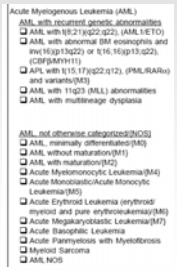
AML


Acute Myelogenous Leukemia (AML)

AML with recurrent genetic abnormalities
- ❑ AML with t(8;21)(q22;q22), (AML1/ETO)
- ❑ AML with abnormal BM eosinophils and inv(16)(p13q22) or t(16;16)(p13;q22), (CBFβ/MYH11)
- ❑ APL with t(15;17)(q22;q12), (PML/RARα) and variants/(M3)
- ❑ AML with 11q23 (MLL) abnormalities
- ❑ AML with multilineage dysplasia

AML, not otherwise categorized/(NOS)
- ❑ AML, minimally differentiated/(M0)
- ❑ AML without maturation/(M1)
- ❑ AML with maturation/(M2)
- ❑ Acute Myelomonocytic Leukemia/(M4)
- ❑ Acute Monoblastic/Acute Monocytic Leukemia/(M5)
- ❑ Acute Erythroid Leukemia (erythroid/myeloid and pure erythroleukemia)/(M6)
- ❑ Acute Megakaryoblastic Leukemia/(M7)
- ❑ Acute Basophilic Leukemia
- ❑ Acute Panmyelosis with Myelofibrosis
- ❑ Myeloid Sarcoma
- ❑ AML NOS

- **New recognition of specific cytogenetic and molecular categories as distinct diseases**
- **These do not correlate with FAB, except M3**

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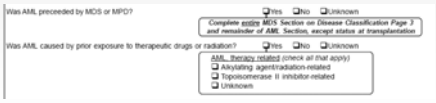
AML

- **Must account for adverse prognosis of AML preceded by**
  - **MDS**
  - **Prior exposure to radiation or chemotherapy**


Was AML preceded by MDS or MPD? ❑Yes ❑No ❑Unknown

Complete entire MDS Section on Disease Classification Page 3 and remainder of AML Section, except status at transplantation

Was AML caused by prior exposure to therapeutic drugs or radiation? ❑Yes ❑No ❑Unknown

AML therapy related *(check all that apply)*
- ❑ Alkylating agent/radiation-related
- ❑ Topoisomerase II inhibitor-related
- ❑ Unknown

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Myeloid Neoplasms

- **Report cytogenetic abnormalities whenever they exist on the appropriate disease insert, even if they are not "defining" of a specific entity**
  - **Often of prognostic significance**

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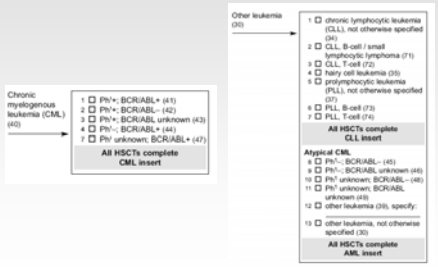
CML



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CML

- DEFINED by
  - Ph1 + or
  - Bcr/abl positive

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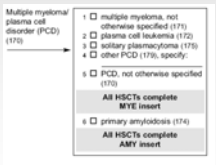
A CHERISHED FAVORITE !



- **Report Waldenstrom's in Lymphoma as per WHO**

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MORE INFORMATION

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