APPENDIX – MALIGNANT HEMATOLOGY

REAL/WHO CLASSIFICATION

INDOLENT LYMPHOMA (40%)

- B-cell CLL/Prolymphocytic leukemia/Small lymphocytic lymphoma (7%)
- Lymphoplasmacytoid lymphoma/Waldenstroms macroglobulinemia (<1%)
- Follicular (follicle center) lymphoma (25%)
- Extra nodal marginal zone B-cell lymphoma (Mucosal-Associated Lymphoid Tissue)(7%)
- Nodal marginal zone B-cell lymphoma (<1%)
- Splenic marginal zone B-cell lymphoma (<1%)

AGGRESSIVE NHL (55%)       HIGHLY AGGRESSIVE NHL (5%)

- Diffuse large B cell lymphoma (31%)
- Peripheral T cell lymphoma (15%)
- Mantle cell lymphoma (7%)
- Anaplastic large cell lymphoma (2%)
- Burkitt’s lymphoma (<2%)
- Adult T-cell lymphoma/leukemia (<2%)
- Precursor T-cell lymphoblastic lymphoma (<2%)
- Precursor B-cell lymphoma (<2%)

SUMMARY OF MORE COMMON NHLs

DIFFUSE LARGE B CELL LYMPHOMA (DLBCL)

- Present with enlarging mass in a nodal or extralymphatic site, often symptomatic
- Median survival 4 years; >50% cure
- Prognostic features:
  - > 60 years of age
  - Increased LDH
  - PS >1
  - Stage III/IV
  - Extranodal involvement > 1 site in pts >60

Risk Group | Number of Factors | Survival |
- Low | 0,1 | 73% |
- Low-Intermediate | 2 | 51% |
- High-Intermediate | 3 | 43% |
- High | 4,5 | 26% |

FOLLICULAR LYMPHOMA

- Typically asymptomatic at presentation
- Treatment indications: cytopenias secondary to bone marrow infiltration, threatened end-organ infiltration, symptoms attributable to disease, bulky adenopathy, steady progression over 6 mos., histologic transformation, massive splenomegaly
- Follicular Lymphoma International Prognostic Index (FLIPI)
  - 60 years of age, Stage III/IV, increased LDH, > 4 involved nodal sites, Hb<12
  - Risk group | Risk factors | 5 year surv |
    - Low | 0-1 | 90% |
    - Intermediate | 2 | 77 |
    - High | 3-5 | 52 |
MARGINAL ZONE LYMPHOMA

- Median age 60
- Female
- Extra nodal marginal zone lymphoma: Mucosal associated lymphoid tissue (MALT) comprise 8% B-cell lymphomas and 50% gastric lymphoma. Gastric MALT results from gastritis secondary to H. pylori, treatment with antibiotics yields durable remissions

MANTLE CELL LYMPHOMA

- Middle age to older men
- Involves lymph nodes, spleen, liver, bone marrow
- Extranodal sites common
- GI tract frequently involved with multiple lymphomatous polyposis
- Prognosis poor: chemoresponsive, but median survival 30 mos, with CHOP-type chemo

BURKITT LYMPHOMA

3 Subtypes often presenting in extra nodal sites, usually associated with EBV infection, and involve c-myc oncogene:

1. Endemic, presents as jaw or facial masses in young boys in equatorial Africa
2. Sporadic, any age, intra abdominal mass
3. Immunodeficiency associated

- Diffuse growth pattern dominated by “starry sky” produced by macrophages
- Bone marrow and leptomeningeal disease are poor prognostic signs
- Adults treated with intensive regimens

T CELL LYMPHOMAS

- 12% of NHL
- Most frequent are peripheral T cell (PTL) and anaplastic large cell (ALCL)

PERIPHERAL T CELL LYMPHOMA

- Present in advanced stage with nodal, marrow, liver, and spleen involvement, with or without circulating tumor cells and other sites of extralymphatic involvement, particularly the skin.
- Often symptomatic, may have paraneoplastic features including eosinophilia, pruritus or hematophagocytic syndrome
- Prognosis generally poor

CUTANEOUS T CELL LYMPHOMAS

- Mycosis fungoides occurs in older adults, disease limited to skin for many years, history of scaly eruptions, progressing to patches and plaques
- Sezary syndrome is further progression with erythroderma, adenopathy, circulating cerebriform cells. Aggressive
ACUTE LYMPHOCYTIC LEUKEMIA

FAB CLASSIFICATION

<table>
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<tr>
<th>FAB</th>
<th>Incidence %</th>
<th>Morphology</th>
<th>3 yr survival</th>
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<tr>
<td></td>
<td>Adult</td>
<td>Pediatric</td>
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<tr>
<td>L1</td>
<td>30</td>
<td>85</td>
<td>small lymphs, 40-75%</td>
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<td>homogeneous</td>
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<td>L2</td>
<td>60</td>
<td>14</td>
<td>large lymphs 35-50</td>
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<td>heterogeneous</td>
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<td>heterogeneous</td>
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<tr>
<td>L3</td>
<td>10</td>
<td>1</td>
<td>large lymphs 10-20</td>
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<tr>
<td></td>
<td>vacuolated, basophilic</td>
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</table>

WHO CLASSIFICATION

Precursor B cell acute lymphoblastic leukemia, +/-cytogenetics:
t(9;22)(q34;q11)=BCR/ABL

t(v;11q23)=MLL rearrangement
t(1;19)(q23;p13)=E2A/PBX1
t(12;21)(p12;q22)=ETV/CBF-alpha

Precursor T-cell ALL
Burkitt’s cell leukemia

ALL CYTOGENETIC CLASSIFICATION

<table>
<thead>
<tr>
<th>Karyotype</th>
<th>Incidence %</th>
<th>Cure%</th>
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<td>t(9;22)</td>
<td>Adult</td>
<td>20-30</td>
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<td></td>
<td>Pediatric</td>
<td>&lt;5</td>
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<tr>
<td>t(8;14)</td>
<td>Adult</td>
<td>5-10</td>
</tr>
<tr>
<td>t(12;21)</td>
<td>Adult</td>
<td>&lt;5</td>
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<tr>
<td></td>
<td>Pediatric</td>
<td>25-30</td>
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</table>

ANLL: FAB CLASSIFICATION

M0: Acute Undifferentiated Leukemia
uniform, undifferentiated blasts

M1: Acute Myeloid Leukemia (AML)
undifferentiated blasts with azurphlic granules

M2: Acute Myeloid Leukemia (AML)
with differentiation; granulated blasts predominate; +/- Auer rods

M3: Acute Promyelocytic Leukemia (APL)
hypergranular promyelocytes

M4: Acute Myelomonocytic Leukemia (AMMoL)
monoblasts and myeloblasts, inv/del 16

M4E: M4 + eosinophils

M5: Acute Monocytic Leukemia (AMoL)
monoblasts predominate

M6: Acute Erythroleukemia (AEL)
erythroblasts and megaloblasts, no red cell precursors seen

M7: Acute Megakaryocytic Leukemia (AMegL)
undifferentiated blasts, bizarre megakaryocytes

WHO CLASSIFICATION

AML with specific cytogenetic defects
AML with features of inv(16)
AML with features of t(8;21)
Promyelocytic leukemia with t(15;17)
Promyelocytic leukemia with t(v;17)
AML with t(6;9)
AML with trilineage dysplasia (.50% of all cell lineages)

Classify using FAB subgroups (M0-M7)

AML without defining cytogenetic defects of dysplasia

AML M1-M6
Myeloid sarcoma
Acute panmyelosis with myelofibrosis
AML arising is a previously MDS

Therapy related AML (Alkylating agent or topoisomerase II inhibitor related)
### COMPARISON OF DIFFERENT TYPES OF LEUKEMIAS

<table>
<thead>
<tr>
<th></th>
<th>AML</th>
<th>ALL</th>
<th>CML</th>
<th>CLL</th>
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<tbody>
<tr>
<td>Median age</td>
<td>60</td>
<td>4</td>
<td>50</td>
<td>60</td>
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<tr>
<td>Initial remission rate</td>
<td>50%</td>
<td>Adult 70%</td>
<td>90%</td>
<td>90%</td>
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<tr>
<td></td>
<td>Child 90%</td>
<td></td>
<td></td>
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<tr>
<td>Median survival with treatment</td>
<td>1 year</td>
<td>Adult 2 years</td>
<td>3 years</td>
<td>5 years</td>
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<tr>
<td>Splenomegaly</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Adenopathy</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Infection risk</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Hemoglobin</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Normal or low</td>
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<tr>
<td>WBC</td>
<td>Variable</td>
<td>Variable</td>
<td>100,000-300,000</td>
<td>&gt;20,000</td>
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<tr>
<td>Platelet count</td>
<td>Low</td>
<td>Low</td>
<td>Normal or low</td>
<td>Normal or low</td>
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</tbody>
</table>

### DURIE-SALMON STAGING SYSTEM FOR MYELOMA

#### Stage I (Myeloma cell mass <0.6-low)
- Hemoglobin ≥ 10 g/dL
- Serum Ca ≤ 12 mg/dL
- Normal skeletal survey or
- Solitary plasmacytoma
- Ig G <5; IgA < 3
- Bence Jones protein < 4 g/24

#### Stage II (cell mass 0.6-1.2-intermediate)
- Not fitting stage I or II

#### Stage III (cell mass >1.2-high)
- Hemoglobin < 8.5
- Serum ca > 12
- Multiple lytic bone lesions
- IgG >7; IgA > 5
- Bence Jones protein > 12 g/24

### MDS International Prognostic Scoring System-Revised

<table>
<thead>
<tr>
<th>Cytogenetic risk</th>
<th>Very good</th>
<th>Good</th>
<th>Intermediate</th>
<th>Poor</th>
<th>Very poor</th>
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<tbody>
<tr>
<td>Group</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Marrow blast</td>
<td>&lt;5%</td>
<td>5-10%</td>
<td>11-20%</td>
<td>21-30%</td>
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</tr>
<tr>
<td>Proportion</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>&gt;10%</td>
<td>&lt;10%</td>
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<tr>
<td>Absolute neutrophil count</td>
<td>&gt;800</td>
<td>&lt;800</td>
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<td></td>
<td></td>
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<tr>
<td>Platelet count</td>
<td>&gt;100K</td>
<td>&lt;100K</td>
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</tr>
</tbody>
</table>

### HYPERVISCOSITY SYNDROME

#### Symptoms
- Neurologic: headache, dizziness, ataxia, paresthesias somnolence, coma
- Visual: diplopia, blurred vision, loss of vision
- Cardiac: congestive heart failure, myocardial ischemia
- Hematologic: spontaneous bleeding–oral, nasal, retinal, GI
- Physical findings: flame shaped retinal hemorrhages, papilledema, “box car” formation of RBCs in retinal vessels
### MDS IPPS-R

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Points</th>
<th>Median survival, years</th>
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<tbody>
<tr>
<td>Very good</td>
<td>0-2</td>
<td>9</td>
</tr>
<tr>
<td>Good</td>
<td>3-5</td>
<td>5.5</td>
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<tr>
<td>Intermediate</td>
<td>6-7</td>
<td>2.9</td>
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<tr>
<td>Poor</td>
<td>8-9</td>
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<tr>
<td>Very poor</td>
<td>10-18</td>
<td>0.7</td>
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### MALIGNANT HEMATOLOGY REFERENCES