Myeloproliferative disease and look-a-likes

PLEASE NOTE: These notes are meant as a reference guide and are not meant to be an outline of the presentation. However, the presentation will expand upon the points included herein.

HELPFUL DEFINITIONS
Leukemia: The presence of neoplastic hematopoietic cells in the blood and/or bone marrow. With no modifiers, leukemia is a general term which includes leukemias of any hematopoietic lineage (i.e. lymphoid or myeloid (erythrocyte, monocyte, granulocyte, megakaryocyte)).

Acute leukemia: A definition which includes neoplasia (often originating in the marrow) due to either immature myeloid or immature lymphoid cells. In these cases, morphologic features may not allow conclusive identification of cell lineage (i.e. one cannot distinguish between myeloid or lymphoid origin).

Chronic leukemia: Chronic designates a neoplastic proliferation of differentiated cell types (i.e. mature lymphocytes). Of the chronic leukemias, chronic lymphoid leukemia is the most common.

INTRODUCTION TO MYELOID NEOPLASMS
Hematopoietic cells are derived from a pluripotent stem cell which gives rise to the lymphoid lineage and the myeloid lineage. Fully differentiated myeloid cells include RBC, granulocytes (comprised of neutrophils, eosinophils and basophils), monocytes and platelets. Each of these lineages is derived from immature precursors (full maturation not shown). Myeloid neoplasms are comprised either of immature precursors (e.g. earlier RBC precursors like rubriblasts) or mature myeloid cells (e.g. mature red cells). Neoplasms of immature myeloid cells are termed acute myeloid leukemia (AML) and those of mature cells are termed myeloproliferative neoplasms (MPN). MPN are exceedingly rare and are a diagnosis of exclusion; it is best to know the non-neoplastic causes of increased numbers of mature myeloid cells (see below).
NON-NEOPLASTIC CAUSES WHICH COULD MIMIC MYELOPROLIFERATIVE NEOPLASMS (NEOPLASMS OF MATURE CELLS)

CAUSES OF EYRHTROCYTOSIS
1. Relative: Dehydration, splenic contraction
2. Absolute:
   a. Secondary (stimulated by erythropoietin)
      i. Appropriate (e.g. as a result of hypoxemia)
      ii. Inappropriate (e.g. as a result of tumor producing erythropoietin)

CAUSES (MAJOR) OF LEUKEMOID RESPONSE (NEUTROPHIL NUMBERS {ANY AND ALL TYPES} >50,000/UL)
1. Immune-mediated hemolytic anemia (IMHA) with resulting tissue necrosis/death from severe anemia-induced hypoxemia (e.g. centrilobular hepatic necrosis) and/or thromboembolic disease
2. The ‘Ps’ – Pyometra (& stump pyometra), pyothorax, peritonitis (although this is infrequently a chronic condition), pyelonephritis (look for azotemia), pneumonia (chronic, not acute pneumonia), paraneoplastic (rare)
3. Neoplasia with necrotic portions of the tumor (outgrew its blood supply)
4. *Hepatozoon* infection (southern USA, Texas)

CAUSES (MAJOR) OF MONOCYTOSIS
1. Stress/cortisol-mediated
2. Chronic inflammation
   • With neutrophilia
3. Compensatory response (can occur with neutropenia)
CAUSES (MAJOR) OF EOSINOPHILIA
1. Worms, i.e. Parasites
2. Wheezes, i.e. Hypersensitivity reactions
3. Weird diseases (neoplasia, hypoadrenocorticism)

CAUSES (MAJOR) OF THROMBOCYTOSIS
1. Physiologic/redistribution
   • Epinephrine-mediated splenic contraction & release of platelet
   • Look for concurrent:
     ▪ Mature neutrophilia (mild)
     ▪ Mild lymphocytosis
     ▪ ± Erythrocytosis
2. Reactive (secondary) → common
   • Chronic hemorrhage & Iron deficiency
     o (IL-6, +/- EPO)
   • Inflammation
     o IL-6 + other cytokines?
   • Decreased removal
     o Post-splenectomy
     o Steroids

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<thead>
<tr>
<th>Mature cell type</th>
<th>Non-neoplastic causes for increased numbers</th>
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<tbody>
<tr>
<td>Red blood cells</td>
<td>Relative: hemoconcentration, redistribution, absolute: e.g. ↓FiO2, R→L shunt, Epo producing tumor</td>
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<tr>
<td>Granulocytes</td>
<td>Neutrophils &gt;50K IMHA, pyometra, pyothorax, peritonitis, pyelonephritis, pneumonia, paraneoplastic, necrosis, Hepatozoon</td>
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<tr>
<td>Eosinophils</td>
<td>Worms, wheezes, weird diseases</td>
</tr>
<tr>
<td>Basophils</td>
<td>Usually similar to eosinophilia</td>
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<tr>
<td>Monocyte</td>
<td>Stress/cortisol, chronic inflammation, compensatory</td>
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<tr>
<td>Platelets</td>
<td>Reactive (chronic hemorrhage and iron def, chronic inflammation, decreased removal), splenic contraction</td>
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**MYELOPROLIFERATIVE DISEASE (neoplasia of myeloid lineage)**

1. Neoplastic proliferation of immature (precursors of mature cells) or mature myeloid cells (e.g. erythrocytes, granulocytes, monocytes)
   b. Acute myeloid leukemia
      i. blasts and/or poorly differentiated cells of the myeloid lineage
   a. Myeloproliferative neoplasms (MPN) – mature cells (so can be challenging to differentiate from reactive causes, although if neoplastic, cells can display atypical features)
      i. MPN of RBCs – polycythemia vera, DDX: relative or absolute secondary erythrocytosis
      ii. MPN of neutrophils – Chronic neutrophilic leukemia, DDX: leukemoid response
      iii. Neoplasia of basophils, eosinophils, monocytes may be more obviously neoplastic due to numbers of each of those cell types normally present (i.e. low)
         DDX: eosinophils—worms, wheezes and weird diseases (basophils, similar DDX)
         DDX: monocytes—Chronic inflammation, compensatory, stress
      iv. MPN of platelets – Essential thrombocythemia, DDX: Reactive thrombocytosis

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<thead>
<tr>
<th>Myeloproliferative disease (myeloid neoplasms)</th>
<th>What we see in blood</th>
<th>Ancillary tests</th>
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<tbody>
<tr>
<td>Acute myeloid leukemia (AML)</td>
<td>Blasts and/or poorly differentiated myeloid cells</td>
<td>Flow cytometry (preferred)</td>
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<tr>
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<td>can be difficult to tell which lineage is affected</td>
<td>PARR (May not distinguish myeloid from lymphoid)</td>
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<td>Myeloid blasts can be difficult to distinguish from lymphoid blasts based on morphology alone</td>
<td>Bone marrow (may not differentiate myeloid from lymphoid based on morphology alone)</td>
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<tr>
<td>Myeloproliferative neoplasms (MPN) (e.g. Chronic myeloid leukemia)</td>
<td>Excessive numbers of mature cell line (diagnosis of exclusion)</td>
<td>There are no markers for clonal proliferations of mature cell lines (diagnosis of exclusion)</td>
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<td>Bone marrow NOT useful</td>
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