MDS: Who gets it and how is it diagnosed?

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Myelodysplastic Syndrome: Let’s build a definition

- Myelo – bone marrow

What is bone marrow?
Dysplastic
- Dysplasia – abnormal appearance of cells when viewed under the microscope
- Difference shapes, sizes, granules (particles within cells)
- Can be caused by many medical conditions, not only MDS

Syndrome
- Collection of signs and symptoms associated together
Myelodysplastic Syndrome

- Heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, progressive pancytopenia, morphologic abnormalities and propensity to transform to AML.
- Dysplastic hematopoiesis
  - Impaired differentiation
  - Accumulation of blasts
- Hypercellular bone marrow in ~90%
- Peripheral cytopenias
- Risk of progression to AML in 25-35%
- Abnormal bone marrow cytogenetics in ~50%

Risk Factors

- Cause is unknown in >80% of patients
- Prior exposure to chemotherapy and/or radiation
- Advancing age
- Congenital diseases (Fanconi anemia, congenital neutropenia, rare familial MDS)
- ? Environmental toxins

<table>
<thead>
<tr>
<th>MDS Risk Factors</th>
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<tbody>
<tr>
<td>Factor</td>
</tr>
<tr>
<td>Increasing Age</td>
</tr>
<tr>
<td>Male Gender</td>
</tr>
<tr>
<td>Chemotherapy Agents/XRT</td>
</tr>
<tr>
<td>Benzene/Solvents</td>
</tr>
<tr>
<td>Smoking</td>
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<tr>
<td>Pesticides/Herbicides/Fertilizers</td>
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<tr>
<td>Ionizing Radiation</td>
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<tr>
<td>Hair Dye</td>
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</tbody>
</table>

Slide Courtesy of S. Strom
Bone Marrow Failure: Signs and Symptoms

**Anemia**
- Fatigue, pallor
- Shortness of breath, decreased exercise tolerance
- Exacerbation of heart failure, angina

**Neutropenia**
- Active infection (bronchitis, sinusitis, pneumonia, etc.)
- Risk of infections

**Thrombocytopenia**
- Petechiae, bruising, bleeding
- Risk of bleeding

Performing a bone marrow aspiration

Other diseases of bone marrow failure
- Hematologic conditions: congenital (hereditary sideroblastic anemia, congenital dyserythropoietic anemia, Fanconi anemia, etc.)
- Nutritional: deficiencies of vitamin B12, folate, iron
- Aplastic anemia (AA)
- Pure red cell aplasia
- Paroxysmal nocturnal hemoglobinuria (PNH)
- Systemic mastocytosis
- Hairy cell leukemia (HCL)
- Large granular lymphocye disease (LGL)
- Myeloproliferative syndromes (idiopathic myelofibrosis, advanced polycythemia vera or essential thrombocythemia)
- Toxins (alcohol, medications, etc.)
- Chronic diseases, viral infections, malignancies
**Diseases of bone marrow failure**

- Aplastic Anemia
- AML
- MDS
- Paroxysmal Nocturnal Hemoglobinuria

**Required Initial Evaluation**

NCCN (2008) Guidelines

- H&P
- CBC with diff, platelet count, & retic
- Examination of peripheral blood smear
- BM aspirate with iron stain and cytogenetics
- BM biopsy
- Baseline serum EPO level prior to RBC transfusion
- RBC folate and serum B12
- Serum iron/TIBC/ferritin
- Documentation of transfusion history

**MDS: US Epidemiology**

- Risk increases with age
  - Median age at diagnosis = 76 years
  - 88% of cases diagnosed in individuals ≥60 years
- Incidence rate higher in men vs women
  - 4.5 per 100,000 per year in men
  - 2.7 per 100,000 per year in women
- Incidence rate greater in whites
  - White > black > American Indian/Alaska native
- Asian/Pacific Islander
- 10,300 cases diagnosed in US in 2003
- Overall 3-yr survival rate 35%
- Median survival by FAB subtype
  - RA 26 mo; RAEB 11 mo; RARS >36 mo

NCCN Practice Guidelines in Oncology: Myelodysplastic Syndrome v2.2008
### International Prognostic Scoring System

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<th>Score Index</th>
<th>0.0</th>
<th>0.5</th>
<th>1.0</th>
<th>1.5</th>
<th>2.0</th>
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<tr>
<td>Prognostic variable</td>
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<td>1.0</td>
<td>1.5</td>
<td>2.0</td>
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<tr>
<td>Bone marrow blasts (%)</td>
<td>&lt;5</td>
<td>5-10</td>
<td>11-20</td>
<td>21-30</td>
<td>31-40</td>
</tr>
<tr>
<td>Karyotype*</td>
<td>Good</td>
<td>Intermediate</td>
<td>Poor</td>
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<td></td>
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</table>

*Good=normal, Y;del(5q), del(20q) 
Intermediate=other karyotypic abnormalities 
Poor=complex (>3 abnormalities) or chromosome 7 abnormalities

**Hgb <10 g/dL; ANC <1800/μL; platelet count <100,000/μL

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### Median Survival by IPSS and Age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Median Survival, years</th>
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<tbody>
<tr>
<td>Low</td>
<td>Int-1</td>
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<tr>
<td>All ages</td>
<td>5.7</td>
</tr>
<tr>
<td>&lt;60</td>
<td>11.8</td>
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<tr>
<td>≥60</td>
<td>4.8</td>
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### Newer prognostic models

- Better age stratification (60=90??)
- Duration of diagnosis
- Prior treatments
- Prior transfusions
- Secondary disease
- Performance status
- ?? Molecular diagnostics
The MDS Patient Survey

Objectives:
- To understand what MDS patients know about their disease, their prognosis and their treatment
- To see if their answers differed based on whether they were:
  - Lower-risk or higher-risk
  - Getting supportive care or active treatment

About the MDS Patient Survey

- A self-directed, online survey of MDS patients conducted over a 2-week period in March 2009
- All MDS patients registered with the Aplastic Anemia & MDS International Foundation were invited to participate
- 358 people from 46 states completed the survey
- Results were presented at the American Society of Hematology in December 2009
- Sponsored by the Aplastic Anemia & MDS International Foundation

The Survey Investigators

- Mikkael A. Sekeres, Cleveland Clinic Taussig Cancer Center
- Jaroslaw P. Maciejewski, Cleveland Clinic Taussig Cancer Center
- Alan F. List, H. Lee Moffitt Cancer Center & Research Institute
- David P. Steensma, Dana-Farber Cancer Institute at Harvard University
- Andrew Arte, University of Chicago Hospital
- Arlene S. Swern, Celgene Corporation
- Paul Scribner, Aplastic Anemia & MDS Intl. Foundation
- John Huber, Aplastic Anemia & MDS Intl. Foundation
- Richard M. Stone, Dana Farber Cancer Institute at Harvard University
Who Took the Survey?

- Average age: 65 years old
- Gender: 51% women, 49% men

How Long Did It Take to Get an MDS Diagnosis?

- First abnormal blood test: 3 years
- Diagnosis of MDS

How Doctors First Describe MDS

- Bone marrow disorder
- Anemia
- Blood disorder
- Neutropenia
- Thrombocytopenia
- Syndrome
- Other
- Cancer
- Leukemia
- Hematologic malignancy
Is MDS a Cancer?

- Most experts consider MDS to be a “bone marrow cancer”
- About 1/3 of MDS patients will progress to AML, a form of leukemia

What’s my risk?

Know The Essentials:

Patients often misunderstand essential aspects of their disease and its treatment.

Every patient should:
1. Understand what MDS means
2. Know your risk
3. Know your prognosis
4. Know what to expect from therapy
I’d be happy to see you at Cornell!

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