Myeloid Neoplasms

2011 Reporting Requirements and CSv02.01.02
Standard Treatment Guidelines

FCDS 2011 Educational Webcast Series
November 2, 2011
Steven Peace, CTR

Presentation Outline

- Overview – Incidence/Mortality, Signs and Symptoms, Risk Factors
- WHO 2008 Classification of Myeloid Neoplasm – 6 Groups
- Characteristics of Major Classification Groups
- Characteristics of Specific Myeloid Neoplasm
- Standard Treatment Guidelines for Specific Conditions
- Hematopoietic Multiple Primary and Histology Coding Rules Refresher
- Collaborative Stage Data Collection System (CSv02.01.02)
- 2011 FCDS Required C.S. Site Specific Factors
- Text Documentation

Overview of the Myeloid Neoplasms

Incidence and Mortality
Signs and Symptoms
Risk Factors
Myeloid Neoplasm Characteristics

- 2011 estimates in the United States
  - 44,600 new leukemia cases – All types
  - 12,930 new AML cases
  - 5,130 new CML cases
  - 6,200 other leukemia Cases
  - 9,050 AML deaths and 270 CML deaths

- No published data for myeloproliferative disorders – new cases/deaths
- No published data for myelodysplastic syndrome – new cases/deaths

- 2011 estimates in the State of Florida
  - 2079 new leukemia cases – All types
  - 705 new AML cases
  - 244 new CML cases
  - 1131 other leukemia Cases
  - 634 AML deaths and 63 CML deaths

Source: American Cancer Society Cancer Facts and Figures, Florida Cancer Data System

Risk Factors

- Exposure to ionizing radiation including medical radiation
- Exposure to cytotoxic chemotherapeutic agents
- Family history
- Cigarette smoking
- Benzene exposure – industrial chemicals, gasoline, cigarettes

Proliferation and Differentiation

- Regulation of proliferation
- Regulation of differentiation
- Both affect development along cell
- Turn on/Turn off
  - Growth factors
  - Genes (including mutations)
  - Proteins
- Ongogenesis – becoming malignant
Signs and Symptoms

- Fatigue
- Paleness
- Weight loss
- Repeated infections
- Fever
- Easy bruising
- Nosebleeds and other hemorrhage

[Link to symptoms of acute myeloid leukemia]
[Link to symptoms in adults]

Signs and Symptoms

- AML usually has sudden onset of symptoms
- CML usually progresses slowly with 4-5 years lapsing prior to transformation to acute phase
- Other myeloid neoplasms have varying courses of disease
  - Some have more predictable disease progression
  - Others may remain in chronic phase for many years
  - A few rapidly advance to AML

Work Up and Confirmation Testing

- CBC
- Peripheral Blood Smear
- Bone Marrow Aspirate
- Bone Marrow Biopsy
- Histology/Morphology
- Cytochemistry
- Flow Cytometry (Immunophenotype)
- Molecular Genetic Studies
Myeloid Neoplasm Disease Course

- Initial Diagnosis is based on abnormal CBC and symptoms
- Many are chronic and relatively asymptomatic
- Diagnosis of Inclusion and Exclusion
- Specific types tend to stay in chronic phase
- Some types predictably progress to acute (blastic) phase

Reclassification Myeloid Conditions

- Before 2000 myelodysplastic and myeloproliferative conditions were felt to be pre-leukemia blood disorders – not malignant
- Scientific evidence confirmed single cell line affected – met criteria
- ICD-O-3 “behavior” changed from /1 to /3
- WHO in 2008 reclassified again into six new categories
- Diagnosis and treatment occur outside hospital in office only
- Florida and ALL other states are underreporting these cases

Myeloid Neoplasm Research

- National Institutes of Health
- National Heart, Lung and Blood Institute
- National Cancer Institute
- Pharmaceutical company studies
- Device company funded studies
- Public/Private collaborations
Myeloid Neoplasm Research

Myeloid Neoplasm Research

Office of the Director

National Heart, Lung and Blood Institute

Myeloid Neoplasm Research

NHLBI - Division of Blood Diseases and Resources

The Division of Blood Diseases and Resources (DBDR) is part of the National Heart, Lung, and Blood Institute (NHLBI), one of 27 institutes and centers at the National Institutes of Health (NIH). DBDR supports research on the causes, prevention, and treatment of nonmalignant blood diseases, including anemias, sickle cell disease, and thalassemia; premalignant processes such as myelodysplasia and myeloproliferative disorders, leukemias, and other abnormalities of hematopoiesis and thrombosis; and immune dysfunction. Funding encompasses a broad spectrum of research ranging from basic biology to medical management of blood diseases.

BLOOD DISEASES BRANCH

The Blood Diseases Branch supports research and training programs focusing on a wide variety of blood diseases that include sickle cell disease (SCD), thalassemia, Fanconi anemia, Diamond-Blackfan anemia and other aplastic anemias as well as outcomes-related research.

THROMBOSIS AND HEMOSTASIS BRANCH

This Branch supports research and training programs on basic research, clinical studies, and technology development in hemostasis, thrombosis, and endothelial cell biology. The main focus is to understand the pathogenesis of both arterial and venous thrombosis in order to improve diagnosis, prevention, and treatment of thrombosis in heart attack, stroke, and peripheral vascular disease. A major goal is to find additional platelet inhibitors, anticoagulants, and fibrinolytic agents that will improve specificity and reduce side effects used in treating thrombotic and thromboembolic disorders. Specialized Centers of Clinical Research (SCCRs) support collaborative studies on hemostatic and thrombotic disorders.

Finding effective treatments for bleeding disorders is another priority. The Branch supports research on hemophilia and von Willebrand Disease as well as autoimmune disorders such as idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, and medical disorders. Emerging areas of interest are gene transfer, clinical proteomics, inflammation and thrombosis, stroke, coagulation activation, autoimmune disease, and thrombotic complications of obesity, diabetes, and cancer.
Myeloid Neoplasm Research

- NHLBI - Division of Blood Diseases and Resources
- TRANSFUSION MEDICINE AND CELLULAR THERAPIES BRANCH

This Branch supports research and research training in transfusion medicine, stem cell biology and disease, clinical cellular medicine, and blood supply adequacy and safety. Research focuses on the use, safety, and availability of blood and blood components for transfusion and cellular therapies. Research areas include transmission of disease, non-infectious complications of transfusions, immunobiology, stem biology and disease, novel cell-based therapies, hematopoietic stem cell transplantation, and overall product availability. The Branch develops programs for basic and clinical research related to normal and abnormal cellular biology and pathology. It also collaborates with governmental, private sector, and international organizations to improve the safety and availability of the global supply of blood and blood components.

- The Branch also supports two clinical research networks to promote efficient comparisons of innovative treatment strategies. The Bone Marrow Transplant Clinical Trials Network (BMTCTN) supports trials for patients undergoing blood or marrow transplantation. The Transfusion Medicine/Hemostasis Clinical Trials Network (TMHCTN) supports trials for patients with hemostatic disorders, such as idiopathic thrombocytopenia and thrombotic thrombocytopenic purpura. Specialized Centers of Clinically Oriented Research support collaborative studies on transfusion biology and medicine.

Myeloid Neoplasm Research

- WHO no longer classifies Myeloproliferative Disorders
- All are now Myeloproliferative Neoplasms
- Initial Reclassification 2000
- Updated Reclassification 2008
- New Registry Rules 2010

World Health Organization 2008 Classification of Myeloid Neoplasms
2008 - WHO Classification of Tumors


WHO Classification of Myeloid Neoplasms

Incorporates:
- Morphology
- Stage of differentiation
- Immunophenotype
- Genotypic features
- Clinical features

Myeloid – 6 Classification Groups

- Myeloproliferative Neoplasms
- Myeloid and Lymphoid Neoplasms with Eosinophilia and Abnormalities of PDGFRα, PDGFRB or FGFR1
- Myelodysplastic/Myeloproliferative Neoplasms
- Myelodysplastic Syndromes
- Acute Myeloid Leukemia and Related Precursor Neoplasms
- Acute Leukemias of Ambiguous Lineage
Myeloproliferative Neoplasms

Table B1: Myeloproliferative Neoplasms

<table>
<thead>
<tr>
<th>WHO Preferred Term</th>
<th>ICD-O-3</th>
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<tbody>
<tr>
<td>Chronic eosinophilic leukemia, NOS (CEL)</td>
<td>9964/3</td>
</tr>
<tr>
<td>Chronic myelogenous leukemia (CML; BCR-ABL1+ (Ph+)</td>
<td>9875/3</td>
</tr>
<tr>
<td>Chronic neutrophilic leukemia (CNL)</td>
<td>9965/3</td>
</tr>
<tr>
<td>Cutaneous mastocytosis (SM)</td>
<td>9740/3</td>
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<tr>
<td>Essential thrombocythemia (ET)</td>
<td>9962/3</td>
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<tr>
<td>Mast cell leukemia (SM)</td>
<td>9742/3</td>
</tr>
<tr>
<td>Mast cell sarcoma (SM)</td>
<td>9740/3</td>
</tr>
<tr>
<td>Myeloproliferative neoplasm, unclassifiable (MPN-U)</td>
<td>9975/3</td>
</tr>
<tr>
<td>Polycythemia vera (PV)</td>
<td>9966/3</td>
</tr>
<tr>
<td>Primary myelofibrosis (PMF)</td>
<td>9964/3</td>
</tr>
<tr>
<td>Systemic mastocytosis (SM)</td>
<td>9741/3</td>
</tr>
</tbody>
</table>

Interrelationship of MPNs

[Diagram showing the interrelationship among the chronic myeloproliferative disorders leading to acute leukemia (~10%).]
Framework for MPNs

MPN

Classic

Non-classic

BCR-ABL+  BCR-ABL-
CML (Ph+)
PV ET PMF

CEL CNL SM MPN-U

Philadelphia Chromosome

BCR ABL Fusion Gene
Molecular Defects in MPNs

### Table: The Chronic Myeloproliferative Disorders

<table>
<thead>
<tr>
<th>Disease</th>
<th>Molecular Defect*</th>
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<tbody>
<tr>
<td>Chronic myelogenous leukemia</td>
<td>BCR-ABL</td>
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<tr>
<td>Chronic eosinophilic leukemia and the</td>
<td></td>
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<tr>
<td>hypereosinophilic syndrome</td>
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<tr>
<td>Chronic mastocytosis</td>
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</tr>
<tr>
<td>Systemic mastocytosis</td>
<td></td>
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<tr>
<td>Polycythemia vera</td>
<td></td>
</tr>
<tr>
<td>Essential thrombocytosis</td>
<td></td>
</tr>
<tr>
<td>Primary myelofibrosis</td>
<td></td>
</tr>
</tbody>
</table>


CML as Our Primary Example

Chronic Myelogenous Leukemia
- Today known as Chronic Myelogenous Leukemia BCR-ABL1 +
- Previously known as Chronic Granulocytic Leukemia
- Diagnostic work up should include bone marrow aspirate cytogenetics, fluorescent in situ hybridization (FISH) and quantitative polymerase chain reaction (QPCR).
  - Most patients with CML are found to be Philadelphia chromosome positive (Ph+) or BCR-ABL positive.
  - BCR-ABL is a chromosomal abnormality that can be detected by QPCR.
Chronic Myelogenous Leukemia

**Initial Indicators:**
- The white blood cell count can range from ~25,000/L to >300,000/L.
- Mild anemia is common.
- Thrombocytosis is present in ~30 to 50% of patients, and the platelet count can exceed 1,000,000/L.

**Peripheral Blood Smear:**
- The blood smear in CML is very characteristic.
- There is a marked granulocytosis including all stages of granulocytic maturation, from blasts to segmented neutrophils.
- There is a predominance of more mature forms, from myelocytes to segmented neutrophils.
- Myeloblasts are typically only 1 to 2% of WBCs and are always <10% in the chronic phase.
- **Basophils are always increased in number and usually in the percentage of WBC.**

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**Figure 14-1 Chronic myelogenous leukemia blood smear. All stages of granulocyte maturation are present, with a predominance of mature forms; several basophils are present.**

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**Table 14-1 Characteristics of Chronic Myelogenous Leukemia (Chronic Phase)**

<table>
<thead>
<tr>
<th>Characteristic</th>
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<tbody>
<tr>
<td>Blast</td>
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<tr>
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<tr>
<td>Granulocyte precursors</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Predominance of myelocytes and segmented neutrophils</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Metabolic basophilia (~2% always &lt;10%)</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Hypergranulocyte</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Thrombocytosis</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Basophils</td>
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<tr>
<td>Increased</td>
</tr>
<tr>
<td>Hypercellularity</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Hypergranulocyte</td>
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<tr>
<td>Increased</td>
</tr>
<tr>
<td>Increased megakaryocytes</td>
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<tr>
<td>Normal</td>
</tr>
<tr>
<td>Increased Megakaryocytes</td>
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<tr>
<td>Normal</td>
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<tr>
<td>Mk in one-third of patients</td>
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<tr>
<td>Normal</td>
</tr>
<tr>
<td>Increased Mk size</td>
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<tr>
<td>Normal</td>
</tr>
<tr>
<td>Decreased LMR score</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Phospholipid phosphatase (PLP)</td>
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<tr>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Elevated serum bilirubin (B)</td>
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<tr>
<td>Normal</td>
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<tr>
<td>Elevated serum bilirubin (B)</td>
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<tr>
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<tr>
<td>Normal</td>
</tr>
<tr>
<td>Unusual</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Unusual</td>
</tr>
</tbody>
</table>

*Source: National Cancer Institute - PDQ Hematology*
**Chronic Myelogenous Leukemia**

- Directly associated with translocation of specific area of the Philadelphia chromosome (Ph) resulting in juxtaposition of abl (Abelson leukemia virus) gene on chromosome 9 fusing with the bcr (breakpoint cluster region) on chromosome 22 [aka: t(9;22)]

- This is referred to as the *bcr/abl* fusion gene found in nearly 100% of all CML patients

**Chronic Myelogenous Leukemia**

- Philadelphia chromosome [t(9;22)(q34;q11)] present in ~85 to 95% of cases standard cytogenetic analysis (QPCR)

- Variant cytogenetic abnormality present in ~5 to 10% of cases.

- Occasionally, no Philadelphia chromosome or other detectable abnormality is noted by RT PCR, but a t(9;22) is detected by fluorescence in situ hybridization (FISH)

- Other *bcr/abl* rearrangement is detected by molecular test

**Chronic Myelogenous Leukemia**

If there is no Philadelphia chromosome or variant by standard cytogenetics (standard cytogenic analysis or RT PCR), and no evidence of a *bcr/abl* rearrangement is identified by FISH or other molecular tests, then the diagnosis is not CML!
Chronic Myelogenous Leukemia
Treatment Recommendations

- Treatment by Phase
- Chronic Phase: 3 month, 6 month, 12 month F/U
- Accelerated and Blast Phase

Treatment by Phase
- Based on the percent of blasts in the peripheral blood, patients are diagnosed as:
  - Chronic Phase (<10% blasts)
  - Accelerated phase (10-19% blasts)
  - Blast phase (>20% blasts)
- Some patients progress directly from chronic phase to blast crisis, without an intermediate accelerated phase.
- Some patients never progress to more advanced phase.

Chronic Phase CML: Recommendations
- Ph+ chronic phase CML is typically treated with a tyrosine kinase inhibitor (TKI).
  - TKIs include imatinib, nilotinib or dasatinib.
- All TKIs are given orally so there will be no "administration" documentation rather the patient will be given prescriptions
- Other treatment options include clinical trial or Hematopoietic Stem Cell Transplant [HSCT].
Tyrosine Kinase Inhibitor (TKI).
- Imatinib (Gleevec®) 400 mg po daily (with a meal and large glass of water)
- Nilotinib (Tasigna®) 300 mg po twice daily (no food 2 hours before or 1 hour after dose)
- Dasatinib (Sprycel®) 100mg po daily (with or without a meal)
- Patients are typically asked during follow up appointments if they are taking meds as prescribed or to bring back their pill bottles so the pills can be counted to determine compliance.

Chronic Phase CML – Follow-up
- Patients are evaluated for a cytogenetic response
- Treatment is based on response
  - Complete Response – no Ph⁺ positive metaphases
  - Partial Response – 1 % - 35% Ph⁺ positive metaphases
  - Major Response – 0 % - 35% Ph⁺ positive metaphases
    * Complete + Partial
  - Minor – > 35% Ph⁺ positive metaphases

Chronic Phase CML – 3 Month F/U
- Patients achieving a complete hematologic response are continued on their current medication at the same dose.
- Patients who fail to achieve a complete hematologic response are evaluated for compliance, drug-drug interaction and possibly mutational status but generally are switched to an alternate TKI as second line treatment.
- Other treatment options include evaluation and discussion of HSCT and clinical trial.
Chronic Phase CML – 6 Month F/U

- Patients achieving a complete hematologic response are continued on their current medication at the same dose.

- Patients who fail to achieve a complete hematologic response are evaluated for compliance, drug-drug interaction and possibly mutational status but generally are switched to an alternate TKI as second line treatment.

- Other treatment options include evaluation and discussion of HSCT and clinical trial.

Chronic Phase CML – 12 Month F/U

- Patients are again evaluated for a cytogenetic response

- Treatment is based on response
  - Complete – continue same med, same dose
  - Partial - continue same med at same dose. If taking imatinib, increase daily dose to 800mg po as tolerated.
  - Minor or no - evaluated for compliance, drug-drug interaction and possibly mutational status but generally are switched to an alternate TKI as second line treatment.

- Other treatment options include evaluation and discussion of HSCT depending on response to secondary therapy or clinical trial.

CML Tx in Accelerated or Blast Phase

- About 85% of patients are diagnosed in the chronic phase

- The accelerated phase of CML is characterized by 10% - 19% blasts in the WBC of peripheral blood (WHO)

- Note: There are alternative ways to define the accelerated phase proposed by Sokal et al., the International Bone Marrow Transplant Registry, and MD Anderson.

- The blast phase, also referred to as blast crisis, is most often defined as >20% blasts WBC of peripheral blood.
Treatment for Accelerated or Blast Phase

- NCCN recommendations for patients who present with de novo accelerated or blast phase CML include
  - Treatment with combination chemotherapy and TKI or a clinical trial.
  - For patients with a CML of the lymphoid lineage, ALL-type induction chemotherapy should be used in combination with a TKI. (Listing/description of ALL regimens to be provided as a handout.)
  - For patients with a CML of the myeloid lineage, AML-type induction chemotherapy should be used in combination with a TKI. (Listing/description of AML regimens to be provided as a handout.)

FDA Approved CML Anti-Neoplastic Agents

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Brand Name</th>
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<tbody>
<tr>
<td>Clafen (Cyclophosphamide)</td>
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<tr>
<td>Cytarabine</td>
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<td>Cytosar-U (Cytarabine)</td>
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<tr>
<td>Cytoxan (Cyclophosphamide)</td>
<td></td>
</tr>
<tr>
<td>Dasatinib</td>
<td></td>
</tr>
<tr>
<td>Gleevec (Imatinib Mesylate)</td>
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<tr>
<td>Imatinib Mesylate</td>
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</tr>
<tr>
<td>Neosar (Cyclophosphamide)</td>
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<tr>
<td>Nilotinib</td>
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</tr>
<tr>
<td>Sprycel (Dasatinib)</td>
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</tr>
<tr>
<td>Tarabine PFS (Cytarabine)</td>
<td></td>
</tr>
<tr>
<td>Tasigna (Nilotinib)</td>
<td></td>
</tr>
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</table>

CML Treatment Support Care Drugs

- Growth Factors
  - filgrastim (Neupogen®)
  - pegfilgrastim (Neulasta®)
- Diuretics (aldactone, hydrochlorothiazide [HCTZ]), steroids (prednisone 20mg/day x 3 for effusions)
- Topical steroids (hydrocortisone cream)
- Antidiarrheal agents (loperamide [Imodium®])
- Analgesics (acetaminophen, ibuprofen)
### Primary Myelofibrosis

Diagnosis requires meeting 3 major criteria and 2 minor criteria.

**Major criteria:**
1. Presence of megakaryocyte proliferation and dysplasia usually accompanied by extramedullary hematopoiesis.
2. In the absence of significant vascular thrombosis, the megakaryocytic changes must be accompanied by an increased bone marrow cellularity characterized by granulocytic proliferation and other decreased erythropoiesis, or prominent extramedullary hematopoiesis.
3. Not meeting WHO criteria for polycythemia vera (BCR-ABL, a positive familial myelodysplasia syndrome, or a myeloproliferative disorder).
4. Presence of JAK2 V617F in an essential marker (e.g., MPN-ASV617K).
5. Presence of a history of JAK2 V617F in another clonal marker (e.g., MPN-ASV617K).
6. Presence of the above clinical criteria, no evidence that bone marrow fibrosis is secondary to infection, arthromenons disorder, or other chronic inflammatory condition, hairy cell leukemia, or other myeloproliferative neoplasms.

**Minor criteria:**
1. Presence of a history of JAK2 V617F in an essential marker.
2. Elevated erythropoietin levels associated with anemia.
3. A bone marrow biopsy showing typical myeloid metaplasia.
5. Presence of a history of JAK2 V617F in an essential marker.

*Vardiman JW et al. Blood, 2009; 114:937*

### Polycythemia Vera

Diagnosis requires the presence of both major criteria and one minor criterion or the presence of the first major criterion together with two minor criteria.

**Major criteria:**
1. Hypertension: > 15.0 g/dL in men, > 15.5 g/dL in women or evidence of increased vascular resistance.
2. Presence of JAK2 V617F or another functional JAK2 mutation such as JAK2 V617F.

**Minor criteria:**
1. Bone marrow biopsy showing hyperplasia of any age with proliferation of megakaryocytes, myeloid metaplasia, and megakaryocytic fibrosis.
2. Increased erythropoietin levels in plasma.
3. Anemia requiring erythropoietin therapy.

*Vardiman JW et al. Blood, 2009; 114:937*

### Essential Thrombocythemia

Diagnosis requires meeting all 6 criteria.

1. Sustained platelet count > 450 x 10^9/L.
2. Bone marrow biopsy specimen showing proliferation of the megakaryocytic lineage with increased numbers of megakaryocytes, no significant increase or lefthand shift of neutrophils, granulocytes, or erythrocytes.
3. Not meeting WHO criteria for polycythemia vera, primary myelofibrosis, or myelodysplastic syndrome or another myeloproliferative disorder.
4. JAK2 V617F or another essential marker, or in the absence of JAK2 V617F, no evidence of reactive thrombocythemia.

*Vardiman JW et al. Blood, 2009; 114:937*
FDA Approved - Myeloproliferative Anti-Neoplastic Agents

<table>
<thead>
<tr>
<th>Name</th>
<th>ICD-O-3</th>
</tr>
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<tbody>
<tr>
<td>ADE</td>
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<tr>
<td>Adriamycin PFS (Doxorubicin Hydrochloride)</td>
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<td>Adriamycin RDF (Doxorubicin Hydrochloride)</td>
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<td>Rubidomycin (Daunorubicin Hydrochloride)</td>
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<td>Vincristine Sulfate</td>
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Myeloid and Lymphoid Neoplasms with Eosinophilia and Abnormalities of PDGFRA, PDGFRB or FGFR1

Table B2: Myeloid and Lymphoid Neoplasms with Eosinophilia and Abnormalities of PDGFRA, PDGFRB or FGFR1

<table>
<thead>
<tr>
<th>WHO Preferred Term</th>
<th>ICD-O-3</th>
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<tbody>
<tr>
<td>Myeloid and lymphoid neoplasm with FGFR1 abnormalities</td>
<td>9967/3</td>
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<tr>
<td>Myeloid and lymphoid neoplasm with PDGFRA rearrangement</td>
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<tr>
<td>Myeloid neoplasm with PDGFRB rearrangement</td>
<td>9966/3</td>
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Myelodysplastic /Myeloproliferative Neoplasm

Table B3: Myelodysplastic /Myeloproliferative Neoplasms

<table>
<thead>
<tr>
<th>WHO Preferred Term</th>
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<tr>
<td>Myelodysplastic/myeloproliferative neoplasm, myelodysplastic</td>
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</tr>
<tr>
<td>Myelodysplastic/myeloproliferative neoplasm, unclassifiable</td>
<td>9982/3</td>
</tr>
<tr>
<td>Myelodysplastic/myeloproliferative neoplasm, unspecified</td>
<td>9982/3</td>
</tr>
<tr>
<td>Refractory anemia with ring sideroblasts</td>
<td>9982/3</td>
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Chronic Myeloid Neoplasms

MDS

MDS/MPN

MPN

Myelodysplastic Syndromes

Table B4: Myelodysplastic Syndromes

<table>
<thead>
<tr>
<th>WHO Preferred Term</th>
<th>ICD-O-3</th>
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<tbody>
<tr>
<td>Myelodysplastic syndrome associated with isolated del(5q)</td>
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<tr>
<td>Myelodysplastic syndrome, unclassifiable</td>
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<tr>
<td>Refractory anemia</td>
<td>9990/3</td>
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<td>Refractory anemia with excess blasts</td>
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<td>Refractory anemia with ring sideroblasts</td>
<td>9997/3</td>
</tr>
<tr>
<td>Refractory cytopenia of childhood</td>
<td>9998/3</td>
</tr>
<tr>
<td>Refractory neutropenia</td>
<td>9999/3</td>
</tr>
<tr>
<td>Refractory thrombocytopenia</td>
<td>9992/3</td>
</tr>
</tbody>
</table>

National Cancer Institute

Myelodysplastic Syndromes Treatment (PDQ®)

Updated: 06/13/2011

Myelodysplastic Syndromes: Comparison of the FAB and WHO Classifications

<table>
<thead>
<tr>
<th>FAB (FMS)</th>
<th>Myelodysplastic Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractory anemia</td>
<td>Refractory anemia</td>
</tr>
<tr>
<td>Refractory anemia with ring sideroblasts</td>
<td>Refractory anemia with ring sideroblasts</td>
</tr>
<tr>
<td>Refractory anemia with excess blasts</td>
<td>Refractory anemia with excess blasts</td>
</tr>
<tr>
<td>Refractory anemia with excess blasts</td>
<td>Refractory anemia with excess blasts</td>
</tr>
<tr>
<td>Acute myeloblastic leukemia identified as AML with multilineage dysplasia</td>
<td>Acute myeloblastic leukemia identified as AML with multilineage dysplasia</td>
</tr>
</tbody>
</table>

Version: 2.10 June 30, 2010
MDS – 2 Classification Systems

- **De novo myelodysplastic syndrome**
  - Most MDS cases occur de novo with no known cause.
- **Secondary myelodysplastic syndrome**
  - MDS may be increased by exposure to a variety of agents including:
    - Tobacco smoke.
    - Ionizing radiation.
    - Organic chemicals (e.g., benzene, toluene, xylene, and chloramphenicol).
    - Heavy metals.
    - Herbicides.
    - Pesticides.
    - Stone and cereal dusts.
    - Exhaust gases.
    - Nitro-organic explosives.
    - Petroleum and diesel derivatives.
    - Alkylating agents.
    - Marrow-damaging agents used in cancer chemotherapy.
  - Patients with documented exposure to such agents are referred to as having secondary MDS or treatment-related MDS and constitute as many as 30% of all patients with MDS. Secondary MDS typically has a poorer prognosis than does de novo MDS.

Myelodysplastic Syndrome Treatments

- **De Novo and Secondary Myelodysplastic Syndromes**
  - Supportive care with transfusion therapy.
  - High-dose chemotherapy with stem cell transplant using stem cells from a donor.
  - Supportive care with growth factor therapy.
  - Chemotherapy with azacitidine, decitabine, or other anticancer drugs.
  - Supportive care with drug therapy.
  - A clinical trial of a new anticancer drug.
  - A clinical trial of low-dose chemotherapy with stem cell transplant using stem cells from a donor.
  - A clinical trial of a combination of treatments.
  - A clinical trial of growth factor therapy.

Myelodysplastic Syndrome Treatments

- **Previously Treated Myelodysplastic Syndromes**
  - High-dose chemotherapy with stem cell transplant using stem cells from a donor.
  - Chemotherapy with azacitidine or decitabine.
  - Supportive care with transfusion therapy, growth factor therapy, and/or drug therapy.
  - A clinical trial of low-dose chemotherapy with stem cell transplant using stem cells from a donor.
  - A clinical trial of new drug therapy.
  - A clinical trial of a combination of treatments.
  - A clinical trial of growth factor therapy.
Acute Myeloid Leukemia (AML) and Related Precursor Neoplasms

Table B5: Acute Myeloid Leukemia (AML) and Related Precursor Neoplasms

<table>
<thead>
<tr>
<th>WHO Preferred Term</th>
<th>ICD-O-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myeloid leukemias with recurrent genetic abnormalities</td>
<td>9911/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia (megakaryoblastic) with t(1;22)(p13;q13); RBM15-MKL1</td>
<td>9911/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11</td>
<td>9871/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia with inv(3)(q21;q26.2) or t(3;3)(q21;q26.2); RPN1-EVI1</td>
<td>9869/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia with t(8;21)(q22;q22); RUNX1-RUNX1T1</td>
<td>9896/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia with t(9;11)(p22;q23); MLLT3-MLL</td>
<td>9897/3</td>
</tr>
<tr>
<td>Acute promyelocytic leukemia (AML with t(15;17)(q22;q12), PML/RARA)</td>
<td>9866/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia with myelodysplasia-related changes</td>
<td>9895/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia, NOS</td>
<td>9861/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia with minimal differentiation</td>
<td>9872/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia without maturation</td>
<td>9873/3</td>
</tr>
<tr>
<td>Acute myeloid leukemia with maturation</td>
<td>9874/3</td>
</tr>
<tr>
<td>Acute myelomonocytic leukemia</td>
<td>9867/3</td>
</tr>
<tr>
<td>Acute erythroid leukemia</td>
<td>9840/3</td>
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<tr>
<td>Acute megakaryoblastic leukemia</td>
<td>9910/3</td>
</tr>
<tr>
<td>Acute basophilic leukemia</td>
<td>9870/3</td>
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<tr>
<td>Acute panmyelosis with myelofibrosis</td>
<td>9931/3</td>
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<tr>
<td>Myeloid sarcoma</td>
<td>9930/3</td>
</tr>
<tr>
<td>Myeloid proliferations related to Down syndrome</td>
<td>No Code</td>
</tr>
<tr>
<td>Transient abnormal myelopoiesis</td>
<td>9898/1</td>
</tr>
<tr>
<td>Myeloid leukemia associated with Down syndrome</td>
<td>9898/3</td>
</tr>
<tr>
<td>Blastic plasmacytoid dendritic cell neoplasm</td>
<td>9727/3</td>
</tr>
</tbody>
</table>
AML Treatment

- Successful treatment of acute myeloid leukemia (AML) requires the control of bone marrow and systemic disease.

- The cornerstone of this strategy includes systemically administered combination chemotherapy.

- Treatment is divided into two phases:
  - remission induction (to attain remission)
  - postremission (to maintain remission).

FD奥巴 Approved AML Anti-Neoplastic Agents

<table>
<thead>
<tr>
<th>ADE</th>
<th>Name</th>
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</thead>
<tbody>
<tr>
<td>Ade</td>
<td>Cytoxan (Cyclophosphamide)</td>
</tr>
<tr>
<td>Adriamycin PFS (Doxorubicin Hydrochloride)</td>
<td>Daunorubicin Hydrochloride</td>
</tr>
<tr>
<td>Adriamycin RDF (Doxorubicin Hydrochloride)</td>
<td>Doxorubicin Hydrochloride</td>
</tr>
<tr>
<td>Arsenic Trioxide</td>
<td>Neosar (Cyclophosphamide)</td>
</tr>
<tr>
<td>Cerubidine (Daunorubicin Hydrochloride)</td>
<td>Rubidomycin (Daunorubicin Hydrochloride)</td>
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<tr>
<td>Clafen (Cyclophosphamide)</td>
<td>Tarabine PFS (Cytarabine)</td>
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<tr>
<td>Cyclophosphamide</td>
<td>Trienox (Arsenic Trioxide)</td>
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<tr>
<td>Cytarabine</td>
<td>Vincasar PFS (Vincristine Sulfate)</td>
</tr>
<tr>
<td>Cytozor-II (Cytarabine)</td>
<td>Vincristine Sulfate</td>
</tr>
</tbody>
</table>
How to Use and Follow the Rules

Rule Basics

1. Is the condition reportable?
2. How many cases do I abstract?
3. How do I code the primary site?
4. How do I code the histology?
5. How do I code the grade?
Case Reportability and MP Rules

Case Reportability Instructions

- 10 Case Reportability Instructions
- Follow the instructions
- Not hierarchical
- Not “rules”
- Text

Multiple Primary – M Rules

- 3 formats
  - Text
  - Matrix
  - Flowchart
- Use Multiple Primary Rules and Database
  - First Apply the Rules
  - If necessary – Apply Multiple Primary Calculator
- DO NOT GO DIRECTLY to the Database
FCDS Required

Site-Specific Factors

<table>
<thead>
<tr>
<th>Schema Name</th>
<th>FCDS Required</th>
<th>CER Required</th>
<th>Cox Additional Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>HemeRetic</td>
<td>SSF1</td>
<td>Non-Standard</td>
<td>SSF1</td>
</tr>
<tr>
<td>CMML</td>
<td>Non-Standard</td>
<td>MDR-ABL</td>
<td>na</td>
</tr>
</tbody>
</table>
REMINDER

2010 Text Documentation Requirements
2011 FCDS DAM / Appendix K, Oct 2011

Text documentation should always include the following components:

- Date(s) – include date(s) references – so the reviewer can determine event chronology
- Location – include facility/physician/other location where the event occurred (test/study/treatment/other)
- Description – include description of the event (test/study/treatment/other) – include positive/negative results
- Details – include as much detail as possible – document treatment plan even if treatment is not given as planned

References & More Information

- **Classification, Characteristics, and Behavior of Myeloid Neoplasms**, G.M. Doros, NCI, 2010
- **North Carolina Central Cancer Registry CER Mini-Guidebook, 2011**
- **Louisiana Tumor Registry Presentation (CML Treatment Guidelines), 2011; Colleen Lemoine, APRN, MN, AOCN, RN-BC**
- **NCCN Treatment Guidelines for CML, 2011**
- **The Chronic Myeloproliferative Disorders and the Myelodysplastic/Myeloproliferative Disorders, Chapter 14**
- **The Myelodysplastic Syndromes, Chapter 15**