Screening for Hematologic Malignancies

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Wellness Institute
Cleveland Clinic

2011 Estimated US Cancer Cases*

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>29%</td>
<td></td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Oral cavity</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>All Other Sites</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>All Other Sites</td>
<td>16%</td>
<td></td>
</tr>
</tbody>
</table>

Source: American Cancer Society, 2011

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
2011 Estimated US Cancer Deaths

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>28%</td>
<td>26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>All other sites</td>
<td>22%</td>
<td>23%</td>
</tr>
</tbody>
</table>

Leukemia Stats 2011

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Estimated New Cases</th>
<th>Estimated Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BOTH SIDES</td>
<td>MALE</td>
</tr>
<tr>
<td>Leukemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute lymphocytic leukemia</td>
<td>5,730</td>
<td>3,320</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>14,570</td>
<td>8,520</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>12,950</td>
<td>6,830</td>
</tr>
<tr>
<td>Chronic myeloid leukemia</td>
<td>5,150</td>
<td>3,000</td>
</tr>
<tr>
<td>Other leukemia</td>
<td>6,200</td>
<td>3,650</td>
</tr>
</tbody>
</table>

Source: American Cancer Society, 2011
Incidence Rates by Race

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Male (per 100,000)</th>
<th>Female (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>16.1</td>
<td>9.7</td>
</tr>
<tr>
<td>White</td>
<td>16.8</td>
<td>10.2</td>
</tr>
<tr>
<td>Black</td>
<td>12.9</td>
<td>7.8</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>8.9</td>
<td>6.1</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>9.1</td>
<td>6.5</td>
</tr>
<tr>
<td>Hispanic</td>
<td>11.7</td>
<td>8.4</td>
</tr>
</tbody>
</table>


Screening Recommendations For Hematologic Malignancies

- **USPSTF**
  - No recommendations

- **American Cancer Society**
  - The American Cancer Society recommends screening tests for certain cancers in people without any symptoms, because they are easier to treat if found early. But at this time, no screening tests are routinely recommended to leukemia or lymphoma.

- **Leukemia and Lymphoma Society**
  - There are no routine screening procedures for leukemia and lymphoma. It is typical for a patient to seek medical treatment when symptoms appear or for disease to be identified as an incidental finding when a blood test is ordered for another reason.
Clinical Features Warranting Further Investigations

- Features suggestive of anemia, jaundice or both
- Features suggestive of sickle cell disease
  - Dactylitis or sudden splenic enlargement and pallor in young child
  - Limb, abdominal or chest pain in older child or adult
- Features suggestive of lymphoma or other lymphoproliferative disorder
  - Lymphadenopathy, splenomegaly, thymus enlargement (mediastinal mass on radiology) or other lymphoid organs
  - Skin lesions suggestive of infiltration
  - Bone pain
  - Systemic symptoms (fever, sweating, itching and weight loss)

Clinical Features Warranting Further Investigations

- Features of myeloproliferative disease
  - Splenomegaly, *plethora*, itching or weight loss
- Suspicion for disseminated intravascular coagulation (DIC)
- Acute or recent-onset renal failure or unexplained renal enlargement (particularly in a child)
- Retinal examination showing hemorrhages, exudates, signs of hyperviscosity or optic atrophy
- Suspicion of a bacterial or parasitic disease
# Clinical Features Warranting Further Investigations

- **Features suggestive of disseminated nonhematopoietic cancer**
  - Weight loss, malaise, bone pain

- **General ill health**
  - Often with malaise and fever, suggesting infectious mononucleosis or other viral infection or inflammatory or malignant disease

<table>
<thead>
<tr>
<th>Peripheral Smear – Helpful In</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hemolytic anemia</strong></td>
</tr>
<tr>
<td>- Review of red cell morphology may identify the cause of erythrocyte destruction (eg, the presence of bite cells points to a Heinz body hemolytic anemia) and the ultimate diagnosis (eg, oxidant damage to the red cell secondary to drugs)</td>
</tr>
<tr>
<td><strong>Thrombocytopenia</strong></td>
</tr>
<tr>
<td>- Distinguishing between increased platelet consumption and reduced platelet production can often be made through review of platelet size</td>
</tr>
<tr>
<td><strong>White cell disorders</strong></td>
</tr>
<tr>
<td>- Precise disease classification may rely upon evaluation of abnormal circulating cells (eg, the presence of Auer rods in a blast form in patients with acute myeloid leukemia)</td>
</tr>
</tbody>
</table>
Blood smear

- Anemia
  - Hemolytic anemia
  - Macrocytic anemia
  - Microcytic anemia
  - Hemoglobinopathy and thalassemia

- Thrombocytopenia and thrombocytosis

- Leukemia, lymphoma, or bone marrow failure

Case 1

- 55 yo AA female preparing to visit friends working at the State Department in South Africa

- She begins Primaquine for malaria prophylaxis

- Over the next week, she develops weakness and dark urine

- Two days later, she goes to ER for dyspnea

- She has no h/o of anemia or other blood dyscrasias
**Case 1**

- **PE**
  - T=37.3 C, HR=115, BP=155/100
  - HEENT: slight icterus. No other abnormalities

- **Labs:**
  - Hgb 9.2
  - WBC 10,400
    - 60% neutrophils, 15% bands, 3% metamyelocytes, 15% lymphocytes, 3% eos, 2% nRBC
  - Platelets 325,000
  - Retic count 7.3%
  - Total bili / Indirect bili: 2.0/1.6
  - LD 667 U/l
  - Urine: - for hemoglobin, + hemosiderin
  - SpO₂: 97%

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**Peripheral Smear**

![Peripheral Smear Image](image_url)
Case 1

• Most likely diagnosis is:
  – Sickle cell anemia
  – Microangiopathic hemolytic anemia
  – G6PD deficiency
  – Hereditary spherocytosis
  – Paroxysmal cold hemoglobinuria

Peripheral Smear

Bite size deformities (arrows)  Heinz body prep revealing denatured hemoglobin precipitates
Red-cell Changes In Various Types Of Hemolytic Anemia

- Blister cells in G6PD deficiency
- Spherocytes in hereditary spherocytosis
- Paroxysmal cold hemoglobinuria with erythrophagocytosis

Hemolytic Anemias, Characterized By Different Types Of Poikilocytes

- Hereditary elliptocytosis
- Hereditary pyropoikilocytosis
- Southeast Asian Ovalocytosis
- Microangiopathic hemolytic anemia
Helmet Cells

Peripheral smears from two patients with microangiopathic hemolytic anemia, showing a number of red cell fragments (i.e., schistocytes), some of which take the form of combat (red arrow), bicycle (thick black arrow), or football (blue arrow) “helmets.” Microshperocytes are also seen (thin black arrows), along with a nucleated red cell (green arrow).

Courtesy of Carole von Kapff, SH (ASCP).

Microangiopathic Hemolytic Anemia

• This type of anemia may indicate:
  – Pregnancy-induced hypertension
  – Disseminated cancer
  – Chronic disseminated intravascular coagulation (DIC)
  – Hemolytic-uremic syndrome
  – Thrombotic thrombocytopenic purpura
Case 2

- 74 yo female with h/o diverticulosis, HTN
- C/o progressive fatigue, poor appetite, and generally does not feel well
- She is on Ramipril 5 mg po qd x 5 yrs and ASA 81 mg po qd x 10 years

- Physical exam
  - Afebrile. BP 115/66. HR 100/min
  - No abd tenderness, splenomegaly or lymphadenopathy

- Labs
  - Hgb 7.5   WBC 2,200   PLT 87,000   MCV 105
  - Retic count 0.8%

Case 2 Peripheral Smear
Case 2

• Most likely diagnosis is:
  – Iron deficiency anemia
  – Drug-induced aplastic anemia
  – Myelodysplastic syndrome
  – Vitamin B12 deficiency
  – Myelofibrosis

Myelodysplastic Syndrome

• AKA oligoblastic leukemia, refractory anemia, smoldering acute leukemia, preleukemia

• Collection of heterogeneous hematopoietic disorders derived from proliferative bone marrow, dysplasia of cellular elements and ineffective hematopoiesis

• Can be indolent or aggressive
Myelodysplastic Syndrome

• Important cause of macrocytosis in elderly patients (MCV is commonly elevated)

• Are clonal hematopoietic stem cell disorder that occur predominantly in adults > 50 yo

• Peripheral blood cytopenias and dysplasia of erythroid, granulocytic or megakaryocytic lineages

Red-Cell Changes in Various Types of Macrocytic Anemia

Panel A: Periculous anemia. Macrocytes, oval macrocytes, and hypersegmented neutrophils

Panel B: Myelodysplastic syndrome with blast cell (arrow) and hypogranular or hypolobulated neutrophils.

Panel C: Myelodysplastic syndrome with anisocytosis, poikilocytosis, macrocytes, stomatocytes, and an erythrocyte with prominent Pappenheimer bodies (arrow); the smear is also dimorphic, showing well-hemoglobinized macrocytes and hypochromic microcytes.
Types of Leukemia

- Acute Leukemia
  - Acute myeloid leukemia (AML)
  - Acute lymphoblastic leukemia (ALL)

- Myelodysplastic Syndromes

- Chronic Leukemia
  - Chronic myeloid leukemia (CML)
  - Chronic lymphoid leukemia

Acute Leukemia – Clinical Characteristics

- High WBC in younger adults, low WBC in older adults
- Low Platelets and low Hgb in all
- 4 weeks of flu-like symptoms
- May present with active bleeding or infection
- Considered a medical urgency/emergency
Acute Leukemia – Clinical Characteristics

• High WBC Acute Leukemia
  – Leukostasis
  – Tumor lysis syndrome

• Acute Promyelocytic Leukemia (M3): DIC

• A (monocytic) L(M4, M5): Leukemic Infiltration
  – Leukemia cutis
  – Gingival hypertrophy
  – Focal neurologic deficits

Leukemia Cutis
TZIOOTZIOS C, MAKRYGEORGIOU
Cleveland Clinic Journal of Medicine 2011;78:226-227

Gingival hyperplasia
NEJM 2008:359:16
Case 3

• 50 yo male complains of gingival bleeding, epistaxis, and fever x 2 days

• Physical exam
  – Temp 39 C, BP 120/70, HR 120, RR 22
  – General appearance is acutely ill
  – Lungs: Bilateral ronchi

• Labs
  – WBC 12,200 with numerous myeloid blast
  – PLT 15,000 MCV 105

• CXR shows bibasilar pneumonia

Case 3 - Peripheral Smear
Case 3

• Most likely diagnosis is:
  – Acute lymphocytic leukemia (ALL)
  – Acute myelogenous leukemia (AML)
  – Chronic myelogenous leukemia (CML)
  – Leukemoid reaction
  – Myelodysplastic syndrome

Acute Myeloid Leukemia (AML)

• Affects older adults more commonly than children
• Treatment is intensive and supportive care is very important to survival
• Acute Promyelocytic Leukemia (APL) is an important subcategory of AML and treated differently
  – 80% cure rate
• Median age of diagnosis is 67 yo
• In 2011
  – 12,950 diagnosed
  – 9,050 will die
AML – Age at Diagnosis

Is AML a Medical Emergency?

Younger Adults

Older Adults

Acute Lymphoblastic Leukemia (ALL)

- More common in children
- Lymphoblasts, not myeloblasts
- Risk for CNS disease
- Treatment is intensive and supportive care important to survival
- Ph+ ALL is important sub-category of ALL and is treated differently

Chronic Leukemia – Clinical Characteristics

- More common in children
- Lymphoblasts, not myeloblasts
- Risk for CNS disease
- Treatment is intensive and supportive care important to survival
- Ph+ ALL is important sub-category of ALL and is treated differently
Miscellaneous Conditions in Which the Blood Smear Can Be Diagnostically Important

Red-Cell Changes with Lead Poisoning and in Hemoglobinopathies
Table 2. Fortuitous Observations That May Be of Diagnostic Importance.

- Red-cell fragmentation
- Hyposplenism
- Cryoglobulinemia (may indicate hepatitis C virus infection or a plasma-cell neoplasm)
- Red-cell agglutinates (may indicate cold agglutinins, as in mycoplasma infection, infectious mononucleosis, or lymphoproliferative disorder)
- Dysplastic features typical of human immunodeficiency virus infection
- Presence of leukemic blasts or lymphoma or myeloma cells
- Malaria or other parasitic infections (usually malaria but occasionally babesiosis, leishmaniasis, African trypanosomiasis, Chagas’ disease, or filariasis)
- Fungal infection (e.g., candidiasis, histoplasmosis)
- Bacteria (relapsing fever, ehrlichiosis, meningococcal or pneumococcal infection)
Thank you!

Cleveland Clinic

Every life deserves world class care.