Hematology 101

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Hematocrits

Plasma
White cells
Red cells

Normal, Hemorrhage, IDA, Leukemia, Hemolysis, B12, P Vera
Normal Peripheral Blood

- Red blood cells
- Platelets
- White blood cells
Aplastic Anemia Peripheral Blood
Red Cells

- Contain a red pigment, hemoglobin
- Carry oxygen from the lung to other tissues that need it
  - Muscles, liver, kidney, heart, brain
- Normally live 4 months
Reticulocytes

Red cells newly released from bone marrow
Fetal Hemoglobin

Kleihauer-Betke stain
Platelets

• Help blood clot
• Live 7-10 days
• Low numbers can lead to:
  • Bruising
  • Petechiae (tiny red dots)
  • Nosebleeds
  • Internal bleeding
# Types of White Cells (Leukocytes)

<table>
<thead>
<tr>
<th>Type</th>
<th>Life Span</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phagocytes (eaters):</td>
<td></td>
</tr>
<tr>
<td>Neutrophil</td>
<td>hours</td>
</tr>
<tr>
<td>Monocyte</td>
<td>days</td>
</tr>
<tr>
<td>Eosinophil</td>
<td>hours</td>
</tr>
<tr>
<td>Basophil</td>
<td>hours</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>months-years</td>
</tr>
</tbody>
</table>
White Blood Cell Functions

- Neutrophils - eat bacteria and fungus
- Lymphocytes - direct the other cells and make antibodies
- Monocytes - eat particles coated with antibody
- Eosinophils - allergies and fight parasites
- Basophils - allergies
Neutrophils (Phagocytes)

- Polymorphonuclear (PMN), segmented, granulocytes
- Bands, juveniles = early forms
- First line of defense against bacterial infection is intact skin and lining of the mouth, throat and intestines
- Second line of defense is neutrophils, which eat bacteria and kill them
- Low neutrophil number increases susceptibility to bacterial and fungal infections
Lymphocytes

- Regulate other white cells
- Make antibodies
  - Proteins that act as flags to stick to bacteria and viruses
  - Tell other cells to eat things
Monocytes

- Phagocytes
- Become tissue macrophages
  - Cells in the tissues that eat particles tagged with antibodies
CBC Machine

- Draw blood from the tube into an electronic counter
- Result is called the complete blood count (CBC)
<table>
<thead>
<tr>
<th>Blood Counts</th>
<th>WBC</th>
<th>RBC</th>
<th>Hb</th>
<th>Hct</th>
<th>MCV</th>
<th>MCH</th>
<th>MCHC</th>
<th>RDW</th>
<th>Plat</th>
<th>MPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/19/85</td>
<td>6.1</td>
<td>4.48</td>
<td>13.6</td>
<td>41.5</td>
<td>92.7</td>
<td>30.4</td>
<td>32.7</td>
<td>13.3</td>
<td>336.</td>
<td>8.4</td>
</tr>
<tr>
<td>Normal Values</td>
<td>7.8±3</td>
<td>5.4±0.7</td>
<td>16±0.2</td>
<td>47±5</td>
<td>87±7</td>
<td>29±2</td>
<td>35±2</td>
<td>13±1.5</td>
<td>8±9±1.5</td>
<td></td>
</tr>
</tbody>
</table>
Red Cells

- Hemoglobin (Hb, Hgb)
  - 12-15 grams/100 ml (g/dl) [lower for children]
- Hematocrit (Hct)
  - 35 to 45%

Anemia = Low Hb/Hct (H/H)
Platelets

- Platelet count (Plt)
  - 150,000 to 400,000/µl

*Thrombocytopenia* = low platelets
White Blood Cells (Leukocytes)

- **WBC =** white blood cell count
  - 5000–10,000/μl, 5 – 10 thousand/μl
- **WBC differential**
  - % Neutrophils, bands, lymphocytes, monocytes, eosinophils, basophils

*Leukopenia* = low WBC
Absolute Neutrophil Count (ANC)

- **ANC** = WBC x % Neutrophils
  - e.g. WBC = 5000/µl, 30% neutrophils
  - ANC = 5000 x 0.30 = 1500/µl
- Normal: above 1500/µl
- OK: above 500
- Low: 200-500
- Very low: below 200

*Neutropenia* = low neutrophils
CBC Summary

• Quick and easy assessment of numbers of blood cells
• Relatively inexpensive
• No single test tells us more about a blood disorder
• Measures all three cell types (RBC, WBC, platelets)
• Provides other valuable details
Causes of Anemia

- Decreased production
  - Decreased reticulocytes
- Increased destruction
  - Increased reticulocytes
- Blood loss
  - Increased reticulocytes
Definitions

- Aplastic Anemia (AA):
  - Pancytopenia due to decreased production
  - Hypocellular bone marrow

- Leukemia:
  - Malignant proliferation of immature cells

- Myelodysplastic syndrome (MDS):
  - Cytopenia with hypercellular bone marrow
Bone Marrow Equipment

Aspirate

Biopsy
Bone Marrow Biopsy

Normal

Aplastic
Normal Bone Marrow Aspirate

Erythroid (red cells)  Myeloid (white cells)
Aplastic Anemia Bone Marrow Aspirate
Bone Marrow Iron
Leukemia Bone Marrow
Hematopoiesis

- Formation and development of blood cells
- Takes place in the bone marrow
- Involves “stem cells”
HEMATopoietic Tree
(With Cytokines)
Hematopoiesis

Early-acting Hematopoietic Growth Factors

IL-3
IL-11
IL-4
IL-1
SF
Flt3 Ligand
GM-CSF

Early-acting Hematopoietic Growth Factors

IL-3
IL-6
IL-11
IL-1
SF
GM-CSF
Flt3 Ligand

Lineage-Specific Hematopoietic Growth Factors

EPO
Thrombopoietin
G-CSF
M-CSF
IL-5

Endothelial cell

IL-1 + TNF

Erythrocyte
Platelet
Basophil
Polymorphonuclear Leukocyte
Monocyte/Macrophage
Eosinophil
B Cell
T Cell

Pre-B Cell
Pre-T Cell
BM Cultures

• CFU-E: colony-forming unit, erythroid
• BFU-E: burst-forming unit, erythroid
• CFU-C: colony-forming unit in culture
• CFU-GM: colony-forming unit, granulocyte-macrophage
CFU-E and BFU-E
Dysplastic Marrow in MDS

- **Erythroid**: megaloblastic, multinucleation, nuclear fragments, increased immature forms, ring sideroblasts
- **Myeloid**: increased immature forms, hypo/hyper-granulation
- **Megakaryocytes**: hypo-/hyper-lobulated, small forms, increased nuclear-cytoplasmic ratio
Bone Marrow in MDS - Erythroid
Bone Marrow in MDS - myeloid and megakaryocytic
FAB CLASSIFICATION

- No MDS
- RA = refractory anemia
- RARS = ring sideroblasts
- RAEB = RA with excess blasts (5-20%)
- CMML = chronic myelomonocytic leukemia, PB monocytes >1000/μL
- RAEBT = RA in transformation
WHO Classification

- RCUD: refractory cytopenia with unilineage dysplasia (≥10% cells in one lineage)
  - RA, RN, RT: anemia, neutropenia, thrombocytopenia
- RARS: ring sideroblasts
- RCMD: multilineage dysplasia (≥2 lineages)
- RAEB-1: 5-9% blasts
- RAEB-2: 10-19% blasts
- MDS-U: unclassified: dysplasia <10% cells, + clone
- MDS del(5q): anemia with isolated del(5q)
Hematopoiesis

A

proliferative potential

self-renewal
mitosis

probability of terminal differentiation

B

generational age (number of mitoses)
terminal differentiation
Blood and Marrow MDS Study

- Aspirate: Morphology
- Biopsy: Cellularity
- Cytochemistry: PAS, MPO, dual esterase, iron
- Flow cytometry: Lymphocytes, granulocytes
- Oncogenes: p53, p21
- Cytogenetics:
  - Classical G banding,
  - FISH (fluorescence in situ hybridization),
  - CGH (comparative genomic hybridization)
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Inherited Bone Marrow Failure Syndromes

Etiologic Investigation of Cancer Susceptibility in Inherited Bone Marrow Failure Syndromes (IBMFS)

Inherited bone marrow failure syndromes (IBMFS) are rare disorders in which there is usually some form of aplastic anemia (failure of the bone marrow to produce blood), associated with a family history of the same disorder. Some of these conditions have typical changes in physical appearance or in laboratory findings which suggest a specific diagnosis. There are several well-described syndromes, which can be recognized by health care experts. There are also patients who are harder to classify, but who appear to belong in this category.

Patients with these syndromes have a very high risk of development of cancer (either leukemia or certain solid tumors). At the moment we cannot predict which specific patient with an IBMFS is going to develop cancer. The NCI IBMFS CoCud Study will enroll North American families in which at least one member has or had an IBMFS. We plan to:

- include individuals known to have an IBMFS as well as their first degree relatives (brothers, sisters, parents, and children);
- collect clinical information from study participants and their physicians;
- perform detailed physical examinations, x-rays and routine laboratory tests on those who are interested in traveling to the NIH to be seen in person by our team;
- attempt (on a research basis) identification of the specific genetic mutation that is associated with each family’s disease;
- screen participants for early changes related to the specific cancer that occurs in each syndrome;
- perform detailed research laboratory tests on blood and tumors collected from study participants, in an effort to understand the process by which cancers develop;
- monitor study participants in an ongoing fashion to determine the rate at which complications develop related to each disease, and to identify those complications more precisely;
- provide suggestions to study participants and their physicians regarding how to best take care of family members who are affected with a particular IBMFS, and
- offer genetic counseling, and an opportunity to learn the results of mutation testing, for those persons who decide that this information will be of use to them.

The Principal Investigator responsible for this study is Blanche P. Alder, MD, MPH. For further information regarding her credentials and experience, please see http://cancer.gov/clinicaltrials/ibmfs.html.

Our overall goal is to reach a better understanding of how cancer develops in persons with IBMFS, so that we may improve the health care which can be offered to persons with these disorders.