



**Fundamentals of Hematology
And Bone Marrow Failure Syndromes**



Aplastic Anemia & MDS International Foundation, Inc.
Fighting Bone Marrow Failure Diseases Through Patient Support & Research Since 1983

National Patient and Family Conference, Indianapolis, Indiana, July 2009

David P Steensma MD FACP
 Division of Hematology


Mayo Clinic
 Rochester, Minnesota

What is "Hematology"?



- "The medical specialty concerned with disorders of the blood and blood-forming elements." – American Society of Hematology (ASH)
- This includes:
 - Cellular elements in the circulating blood
 - Bone marrow
 - Lymph nodes and other lymphocyte sites
 - Spleen
 - Clotting factors

Who Is Your Hematologist?



- *Typical training (US) – 13+ years post-H.S.:*
 - 4 or 5 years college/university
 - 4 years medical school, leading to MD degree
 - 3 years internal medicine internship/residency
 - 3-4 years hematology/medical oncology fellowship
 - Specialty board certification by American Board of Internal Medicine (ABIM)
- Optional: additional research training, other degrees (e.g. PhD)
- Outside US, university/medical school are combined into a single 6-7 year program

Peripheral Blood Examination

Plasma
White blood cells
Platelets
Red blood cells

} Cellular elements

Human Blood and Bone Marrow

Marrow cells that normally don't circulate in large numbers

- Plasma cells
- Mast cells
- Macrophages
- Undifferentiated blasts
- White cell precursors (promyelocytes, metamyelocytes, others)
- Red cell precursors (erythroblasts, proerythroblasts, reticulocytes, others)
- Stem cells

Normal Mayo Clinic Laboratory Ranges

Hemoglobin:
 ♀ 12.0 - 15.5 g/dL
 ♂ 13.5 - 17.5 g/dL

Hematocrit:
 ♀ 34.9 - 44.5%
 ♂ 38.8 - 50.0%

Lymphocytes (lymphs)
 0.9 - 2.9 x 10⁹/L or 16 - 52% of WBCs

Monocytes (mono)
 0.3 - 0.9 x 10⁹/L
 1 - 11% of WBCs

Neutrophils (granulocytes, gran, segs, poly, others)
 1.7 - 7.0 x 10⁹/L (ANC > 1700)
 42 - 75% of WBCs

Eosinophils (eoso)
 0.3 - 0.5 x 10⁹/L
 0 - 4% of WBCs

Platelets (thrombocytes)
 0.05 - 0.50 x 10⁹/L
 0 - 7% of WBCs

Circulating cells:

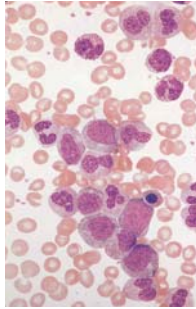
- Carry oxygen to the body → Red blood cells (RBCs, erythrocytes)
- Fight infections → White blood cells (leukocytes)
- Promote clotting and stop bleeding → Platelets (thrombocytes)

Bone Marrow Examination

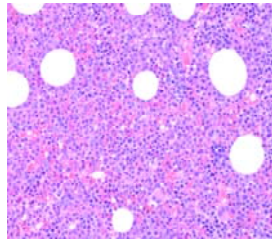
- Local anesthetic vs. sedation
- Use of aspirate vs. biopsy
- Why the hip?

Biopsy illustrations from NIH (US Gov rights-free)

Marrow Aspirate vs. Biopsy: Complementary Assays



Liquid Aspirate



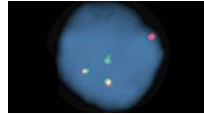
Fixed, cut core biopsy

Courtesy Dr Rebecca McClure,
Mayo Clinic Hematopathology

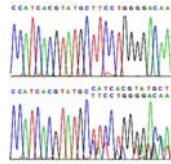
Cytogenetic and Molecular Tests



Karyotype – whole chromosomes



FISH probes – large DNA segments
or individual genes



DNA sequencing – base pair changes

What Is Meant By “Bone Marrow Failure”?



- Due to an intrinsic defect of the marrow cells or external suppression, the bone marrow fails to keep up with the body's needs for production of healthy blood cells
- Conditions included in this category:
 - Inherited conditions (most are very rare)
 - Fanconi anemia, Diamond Blackfan anemia, Congenital Dyserythropoietic Anemia, etc.
 - Acquired conditions
 - Aplastic anemia
 - Paroxysmal nocturnal hemoglobinuria
 - Myelodysplastic syndromes

Therapies Employed

- Blood cell growth factors
- Transfusions
- Immune suppressing/modulating therapy
- Chemotherapy/cytotoxic treatments
 - Systemic (vein), intrathecal (spinal fluid)
- “Biological therapy” (Aren’t they all?)
- Stem cell transplantation
 - Autologous vs allogeneic
 - Related vs unrelated (incl. cord blood)
 - Full conditioning vs reduced intensity
- Radiation therapy



Types of Clinical Trials

- Industry-sponsored
- Co-operative group
- Phase I, II, III




Collaborators




- **Nurses**
- **Caregivers/family**
- Physicians assistants and nurse practitioners
- Pharmacists
- Surgical teams
- Pathologists
- Radiotherapists
- Social workers
- Physical/occupational therapists
- Respiratory therapists
- Specialists in other disorders
- Radiologists
- Clinical trial specialists
- Industry liaisons
- Office staff
- Billing/insurance specialists
- Chaplains
- Hospice workers

Hope is dynamic, not static.



Crying Giant
Sculptor: Tom Otterness
Scheveningen, NL



Hope, Arizona
city limits