Abnormal CBC

Tom DeLoughery, MD MACP FAWM

Oregon Health and Sciences University

GENERAL HEMATOLOGY

Abnormal CBC

- What I look at in a CBC
- Approach to specific abnormalities

What I look at in a CBC

- Hct
- MCV
- MCHC
- Plts
- WBC
- Diff - # not %!

MCV

- < 70 fl
  - Either thalassemia or iron deficiency
- > 100 fl but not anemic
  - Alcohol
  - Smoking
  - Dysproteinemia
  - Normal variant

Microcytosis

- Iron Deficiency
- Thalassemia
- Anemia of chronic disease
  - Rarely < 70fl
- Sideroblastic
  - Rare

Meltzer Index

- MCV/RBC
- > 13 – Iron deficiency
- < 13 – Thalasemmia

MCHC

- Mean Corpuscular Hemoglobin
  - Moves with MCV
- > 36 can be a sign of hereditary spherocytosis

Differential

- Absolute counts not percent that matters.

Anemia

- My approach

Work-Up: I

- Reticulocyte Count
- Smear Review
- Nutritional
  - Ferritin
  - Methylmalonic acid
  - Homocystine
  - Copper
    - Neutropenia
    - Sensory deficits/ataxia

Ferritin: Bottom Line

- Ignore lab reference ranges!
  - < 15 ng/ml 100% specific
  - > 100 ng/ml rules-out
- In older patients ferritins < 100ng/ml consider GI work-up
- Iron supplementation to women with ferritins < 50ng/ml improves fatigue

Work-Up II

- ACD/Renal
  - Erythropoietin Level
  - CMP
- Hemolysis
  - Reticulocyte count
  - LDH
  - Bilirubin – total and direct
  - Direct antibody test
  - Haptoglobin

Work-Up III

- SPEP/Serum Free Light Chains
  - Older patient
  - Back pain
  - New onset renal disease
  - Severe anemia

When to Do a Bone Marrow?

- Circulating immature cells
- Severe pancytopenia
- Very low reticulocyte count (<0.01%)
- Nucleated red cells
- Evidence of marrow infiltration
- Staging of malignancies
- Unexplained anemias

Erythrocytosis

- Hemoglobin > Men: 18.5 (16.5) or Women 16.5 (16)
- High hematocrit and other blood counts up
- Big question – Polycythemia vera vs other causes

Differential Diagnosis

- Polycythemia vera
- Hypoxia
  - Lung disease
  - High altitude
  - Sleep apnea (nocturnal desaturation)
- Impaired oxygen delivery
  - Smoking
    - > 1 PPD -> Hbg by 1

Testosterone

- Increased sensitivty to EPO
- Onset months
  - Can take several months to resolved
- Phlebotomy with hct >54%
- Space out injections
- Transdermal

Other Important Causes

- Renal
  - Cancer
  - Big renal cysts
  - Renal artery stenosis
- Hepatic
  - Hepatomas
  - Hepatitis
- Endocrine Tumors

Genetic Causes

- Abnormal Hemoglobins
  - Impaired oxygen delivery
  - Most common
- EPO-R mutations
- HIF pathways

Work-up I

- Suspicion for PRV increases if
  - Other counts elevated
  - Splenomegaly
  - Aquagenic pruritus
- JAK2 mutation assay
  - Abnormal in 99% of PRV
  - Diagnostic test

Work-Up II

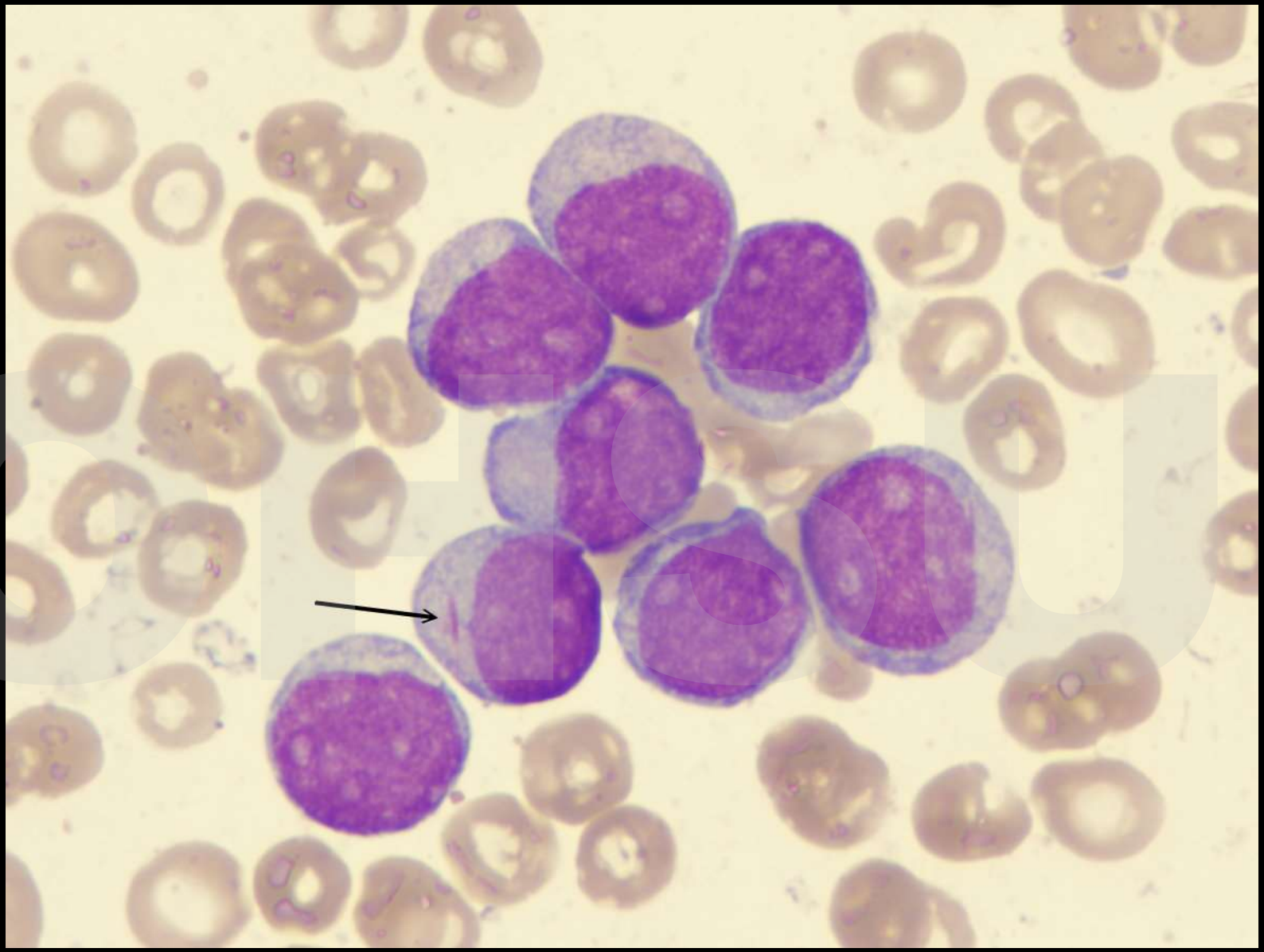
- Erythropoietin levels
  - PRV if below normal
- Oxygen saturation
- Sleep Studies
- Carboxyhemoglobin
- Renal/Liver imaging
- Hemoglobin electrophoresis
- P_{50} studies (Mayo Clinic)

Therapy

- PRV
  - Phlebotomy
  - Hydroxyurea
  - Ruxolitinib
- Secondary
  - Congenital cardiac – NO!
  - Lung disease hct > 57
  - Oxygen, CPAP, …

Neutrophilia

- Neutrophils > 10,000/ul
- Red Flags
  - Immature forms (blasts)
  - > 20,000/ul



http://www.mog-eg.com/apps/photos/photo?photoid=38256199

Neutrophilia - DDX

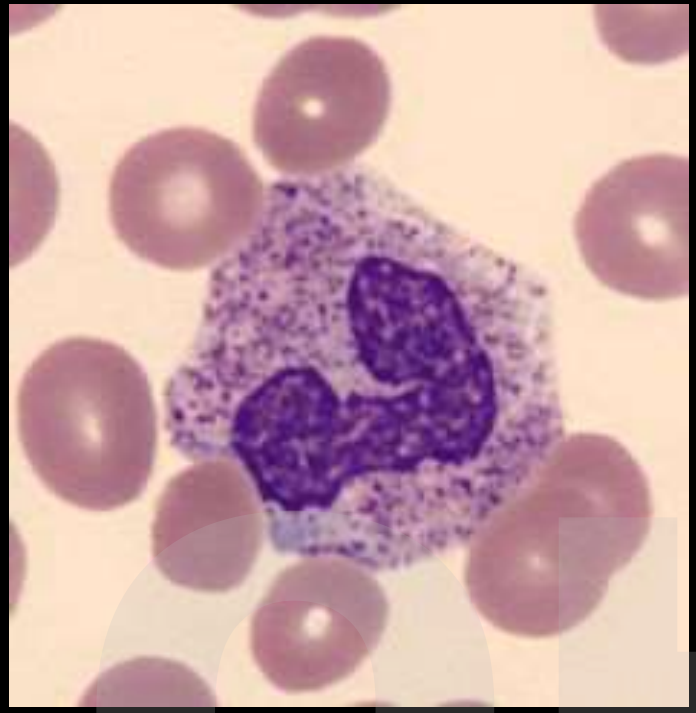
- Neoplastic
  - Acute myelogenous leukemia
    - Blasts
  - Chronic myelogenous leukemia
    - Immature cells
  - Chronic neutrophilic leukemia
    - High neutrophils counts

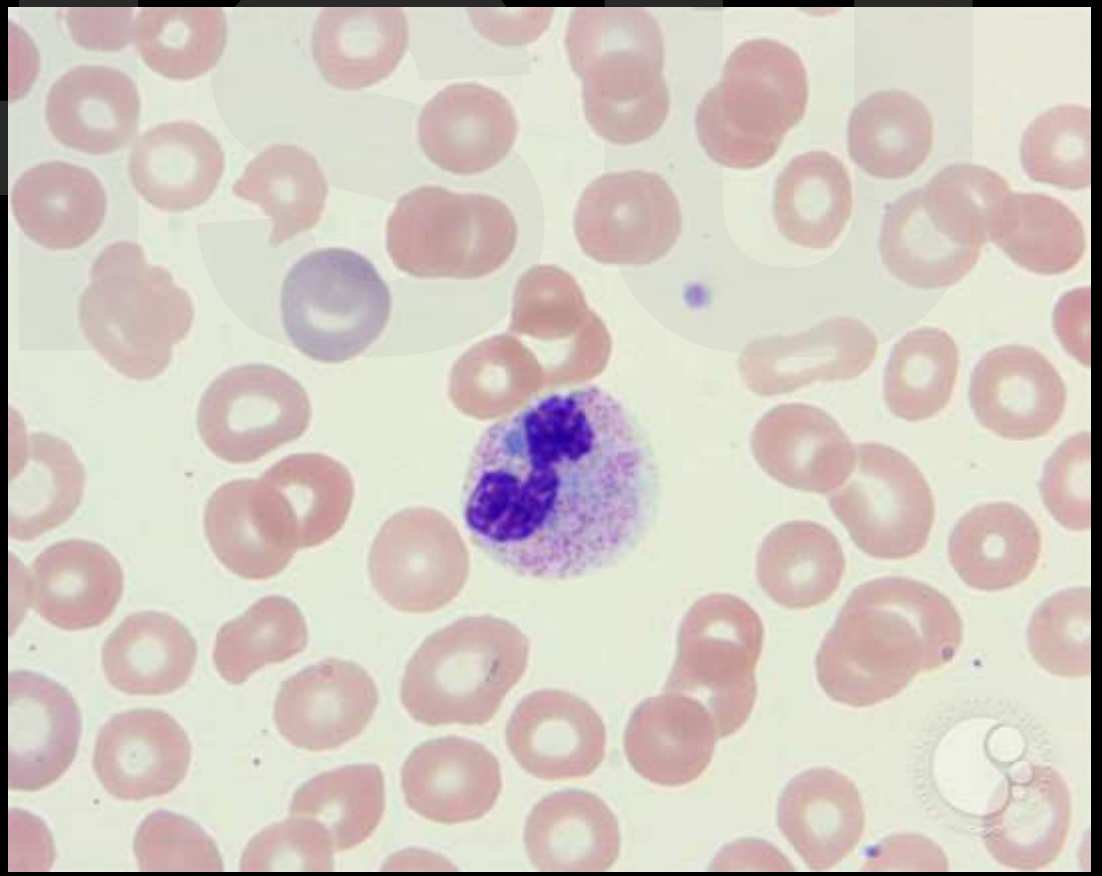
Neutrophilia - DDX

- Infections
- Rheumatic conditions
- Obesity
  - Adipose cells make growth factors
- Smoking
  - Doubles WBC
- Pregnancy
- Steroids
  - Cushings

Leukemoid Reactions

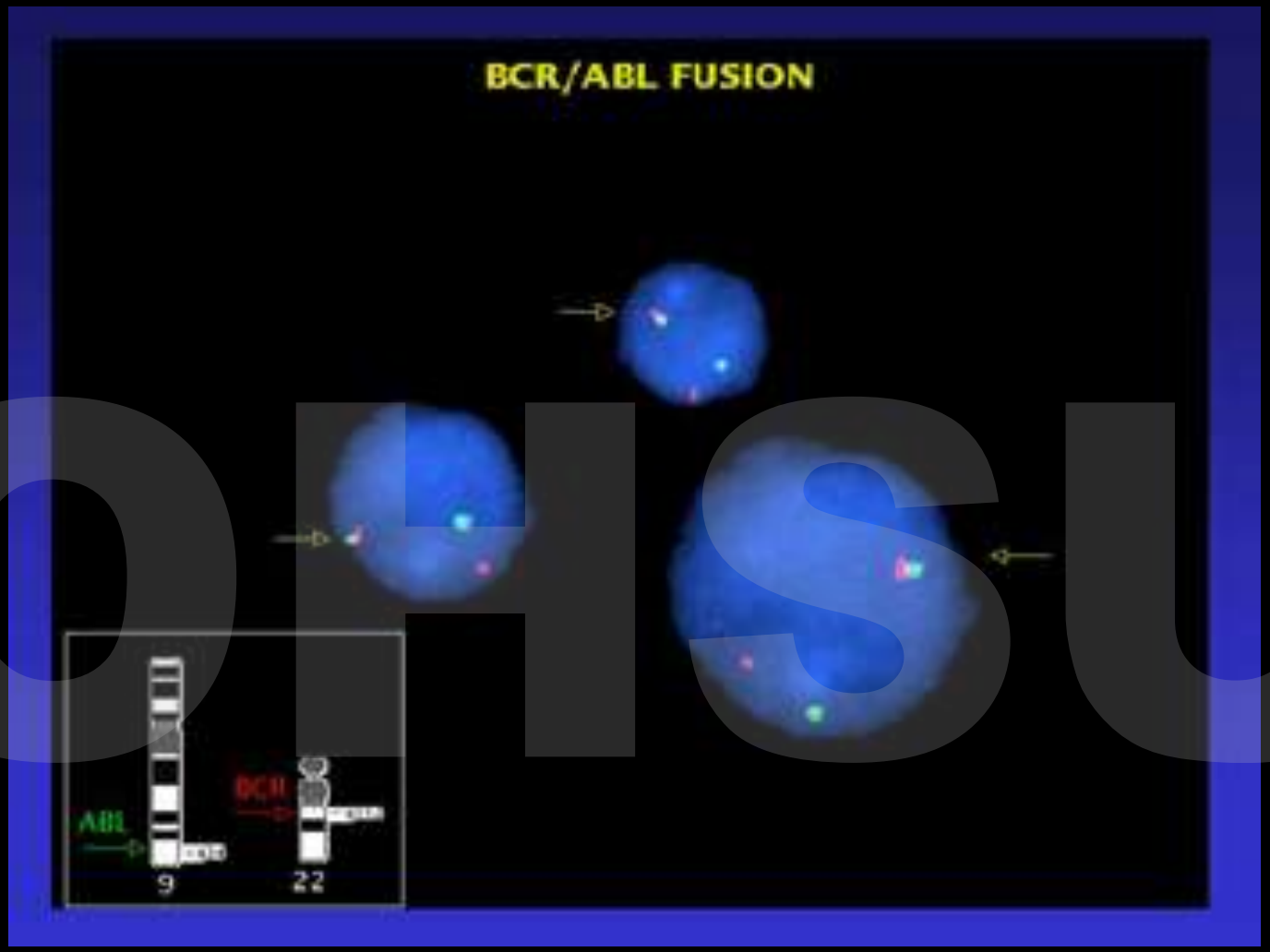
- Very high blood counts (up to 100,000)
  - Predominantly neutrophil
- Chronic infections
- Bad C diff
- Solid tumors





Neutrophilia - Evaluation

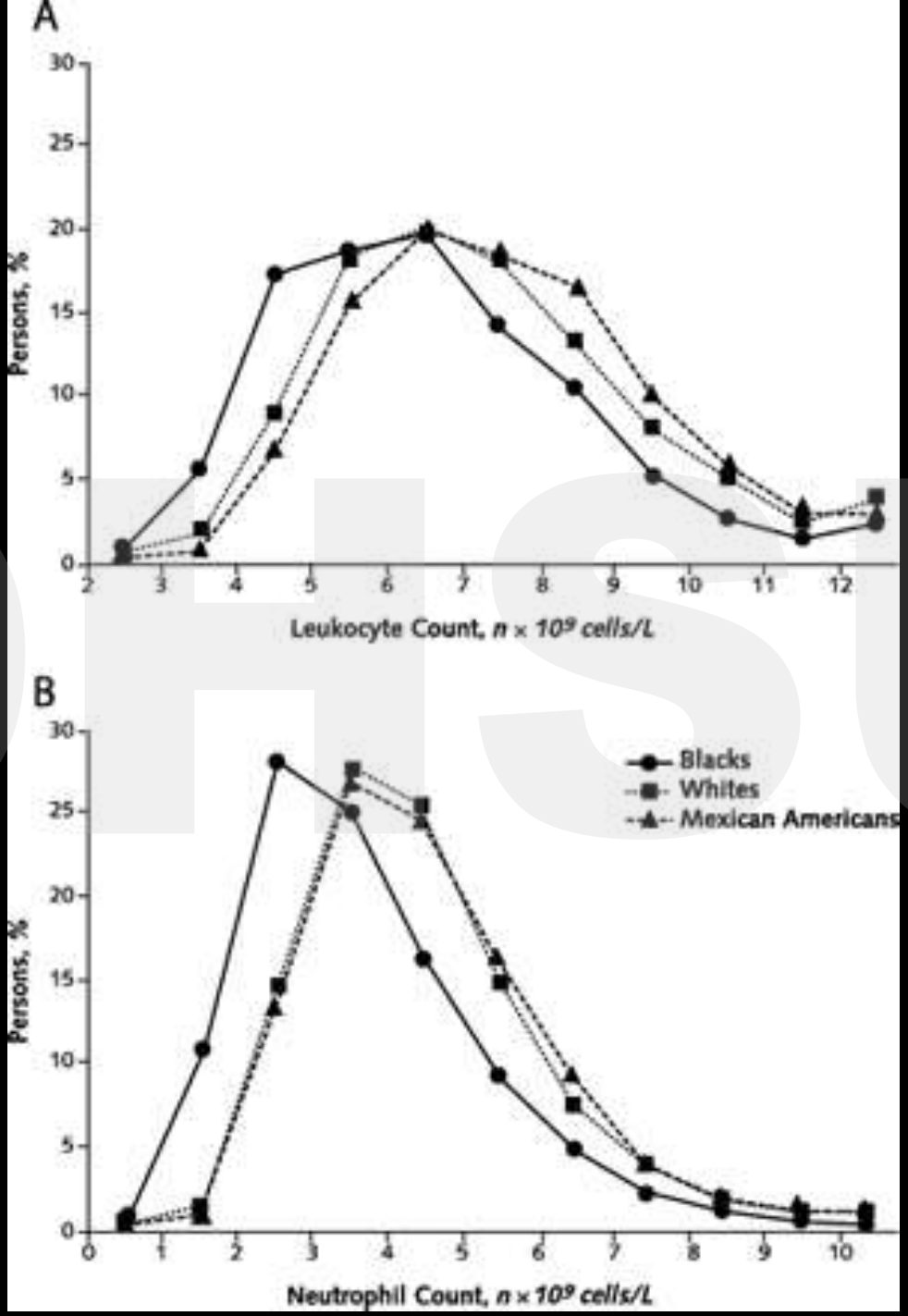
- History/physical
  - Smoking/obestiy
- Testing – rule out neoplasm
- CML – obtain FISH for BCR-ABL
- Other counts up – JAK2
- Bone Marrow if > 20,000/ul



http://www.bwhct.nhs.uk/genetics-index/reglab_oncology.htm

Neutropenia

- Mild Neutropenia is very common!
- Concern
  - ANC < 1000
- Really concerned
  - ANC < 500



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Neutropenia

- Ethnic
  - 800-1000
  - Lack of Duffy blood group
- SSRI
  - Mild neutropenia
- Copper deficiency
  - Usually anemic
  - Sensory neurologic defects

Drugs

- Antiseizure medications
  - Dilantin
- Nonsteroidal Anti-inflammatory
- Vancomycin
- Penicillins
- TMP-SMZ
- Anti-Thyroid

Neutropenia

- "Benign"
  - ANC < 500
  - Responds to infections
- NK/T-Suppresser cell leukemia
- Hairy cell Leukemia
- Felty's syndrome

Neutropenia - Evaluation

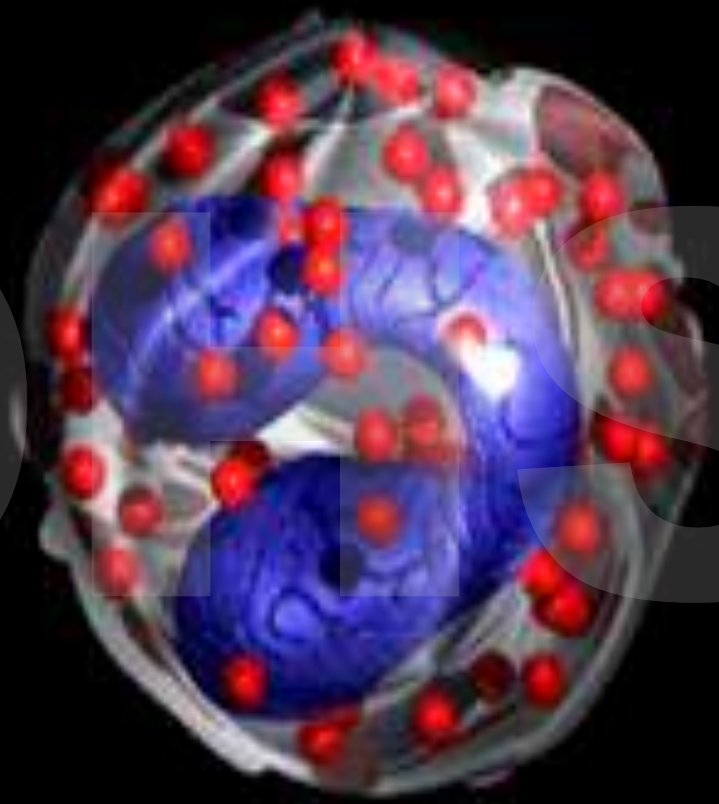
- Sudden and sick
  - Admit
  - Stop new medications
  - Prophylactic antibiotics
  - Growth factors

Neutropenia - Evaluation

- History
- < 1000/ul
  - Flow cytometry for abnormal lymphocytes
  - Anti-granulocyte antibodies
- Copper levels
- Evaluation for other rheumatoid disorders
- Duffy blood group

Therapy

- Immune
  - Immunosuppression
- Hairy cell
  - Chemotherapy
- Benign - nothing



Eosinophilia

- Very common issue
- Almost always secondary to other process
- Hypereosinophilia syndrome rare but interesting disease

Causes of Hypereosinophilia

- Neoplastic
- Allergic/Asthma
- Addison
- Collagen Vascular
- Parasites

Neoplastic

- Hodgkin disease classic
- Solid tumors (lung, pancreas, colon, GYN)
- Lymphoma
- Hyper Eosinophilic Syndrome (HES)

What is HES?

- Eosinophil count > 1500/uL
  - 6 months*
- End organ damage
  - Heart
  - Neurological
  - Skin
  - GI
- No other obvious cause

Allergic

- Seasonal allergies
- Asthma
- Drug allergies

Addison

- Lack of endogenous steroids

Collagen Vascular

- Churg-Strauss
  - Pulmonary involvement
- Any Vasculitis

Parasites

- Any tissue invasive parasite
- Toxocara – dog and cat poop
- Strongyloides – can reoccur after many years
- Trichinella – why we need to cook our pork!

DDX of Eosinophilia by Eos Counts

500-1,000/uL

- Endocrine disorders
- Allergies
- Dermatologic disorders
- Solid tumors

1,000-5,000/uL

- Asthma
- Aspirin allergies
- Parasites
- Vasculitis
- HES

5,000-50,000/uL

- Churg-Strauss
- Hypereosinophilic syndrome
- Visceral larva migrans
- Tropical pulmonary eosinophilia

Eosinophilia: Evaluation

- Detailed history
- Guided by counts
- May need stool samples, biopsies, etc..

Therapy

- Remove primary cause!
- HES:
  - Imatinib
  - Steroids
  - Hydroxyurea
  - IL-5 antibodies

Monocytosis

- The Poor Man's Sed Rate
  - Any inflammation
- > 1000 or abnormal monocytes
  - Chronic myelomonocytic leukemia
  - Can be subtle
  - Worry about if other counts are low

Elevated Immature Granulocytes

- The curse of every hematologist existence
- Essentially meaningless
  - Validity for a few conditions
  - Often up in inflammation
- Lab will call out blasts, etc..
- I ignore

Lymphocytosis

- Lymphocytes > 5000/uL
- Very common!!!
  - Up to 4-5% of the population will have clonal lymphocytes
  - Monoclonal B-lymphocytosis (MBL)

Lymphocytosis - DDX

- Clonal
  - CLL
  - MBL
- Reactive
- Post-splenectomy

CLL vs MBL

- Old criteria for CLL was lymphocytes > 15,000/ul
- With new lab techniques lowered to 5,000/ul
- MBL – clonal lymphocytes but less than 5000/ul

CLL vs MBL

- Risk of progression higher with counts > 10,000/uL
- BUT – can progress at any count (~ 1-2%/yr)

Rarer Causes of Lymphocytosis

- T-cell CLL
- Hairy cell leukemia
- Lymphoma

Work-Up

- Work-up if > 5,000/uL
- Flow Cytometry
  - Detects cell surface proteins
  - Looks for clonal populations
- Lymph node exam

Prognosis: MBL and Stage O CLL

- Overall good but moving target
- Unclear if more elaborate testing will help

Thrombocytosis

- > 450,000/uL
- Primary
  - Myeloproliferative
- Secondary
- Idiopathic?

Thrombocytosis

- Myeloproliferative
  - Essential thrombocytosis
  - Polycythemia rubra vera
  - Chronic myelogenous leukemia

Secondary

- Can be > 1,000,000/ul
- Inflammation
- Iron deficiency
- Post-splenectomy
- “Rebound”

Clues to ET

- Splenomegaly
- Erythromelalgia
- Thrombosis
  - Visceral vein thrombosis
- Bleeding

Work-up

- Myeloproliferative
  - JAK2/CALR/MPL
  - BCR-ABL
  - Splenic ultrasound
- Secondary
  - Ferritin
  - CRP

“Idiopathic”

- Patients with mild increases in platelets and no positive tests
  - Essential thrombocytosis
  - Congenital
  - ?
- Avoid labeling
- Treat with aspirin
- Follow closely

The Paradox of Essential Thrombocytosis

- The higher the platelet count, the greater the risk of bleeding!

Essential Thrombocytosis

- Very prolonged natural history
- Therapy
  - Aspirin if not bleeding
  - Cytoreduction if
    - > age 60
    - Vascular risk factors
    - Previous thrombosis

Thrombocytopenia

- Classic definition
  - < 150,000
- DBM definition
  - < 100,000

Thrombocytopenia

- Production defects
- Sequestration
- Destruction
  - Immune destruction
  - Non-immune destruction

Thrombocytopenia

1. Production defects
   - Rare cause of isolated thrombocytopenia
2. Sequestration
   - “Hypersplenism”
3. Immune destruction
   - Immune thrombocytopenia
4. Non-immune destruction
   - Thrombotic thrombocytopenia purpura

< 10,000/ul Platelets

- Immune thrombocytopenia
- Drug induced thrombocytopenia

Thrombocytopenia

- 10-50,000/uL
  - DIC
  - TTP
  - ITP
  - Congenital
- 50,-100,000/uL
  - Liver disease
  - ITP
  - TTP
  - Myelodysplasia
  - Congenital

Basic Question #1

- Is the patient sick?
  - Yes: TTP, HIT, DIC, Sepsis, etc…
  - Pregnant and sick: TTP, HELLP, fatty liver

Basic Question #2

- Other cell lines affected?
  - Yes – myelodysplasia, bone marrow issues, liver disease
  - No – ITP or congenital thrombocytopenia

Liver Disease

- Leukopenia common
  - ~ 1,000/ul
- Thrombocytopenia
  - ~ 50,-90,000/uL
- Hypersplenism
- Lack of platelet growth factor

Immune Thrombocytopenia

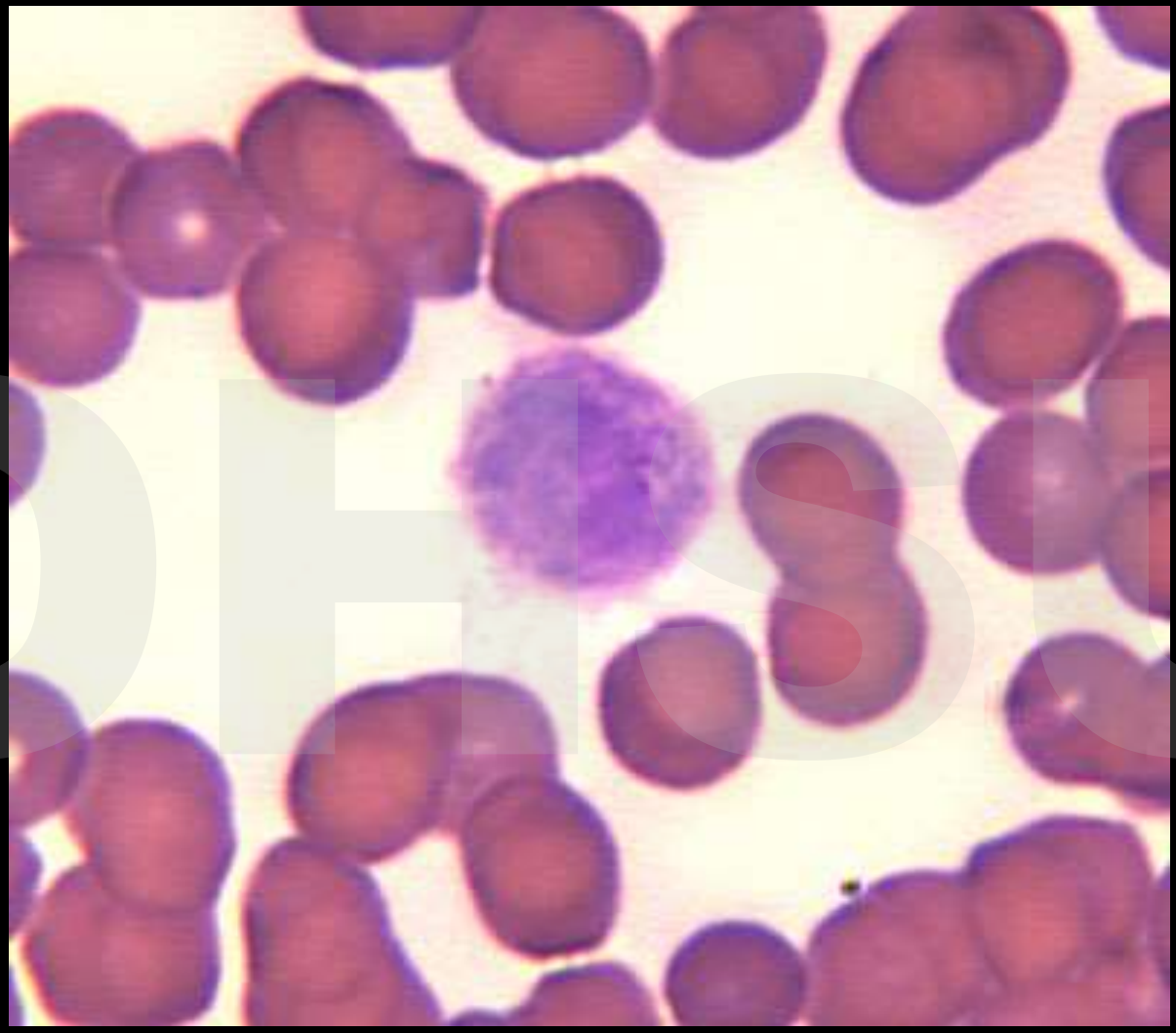
- 1:50,000
- Autoimmune destruction of platelets
- Patients present with very low platelet counts (<1,000/uL)
- Clinical history is diagnostic test
  - No other cause of thrombocytopenia
  - Normal blood smear

Drug Induced Thrombocytopenia

- Most common autoimmune heme complication of medicine
- Implicated drugs:
  - Vancomycin
  - TMP/SMZ
  - NSAID

Congenital Thrombocytopenia

- Counts 10-150,000/uL
- Long history of abnormal counts
- Family history
- “Giant Platelets”
  - Missed by automatic CBC machines



http://www.hscj.ufl.edu/pathology/cases/case1.asp

Work-Up

- Guided by counts
  - Sick -> admit
  - <20,000 -> admit
- Review smear
  - Giant platelets
  - Schistocytes (TTP, HELLP)
- Splenic ultrasound
- Liver panel

The Abnormal CBC

- Find old CBC
- Sudden changes most worrisome
- Is the patient sick?