

MORPHOLOGY IN ACTION

Mini-case studies using morphology



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Description

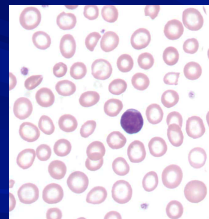
- Mini-case studies will be used to integrate patient presentation and laboratory test results to construct a working diagnosis. Emphasis will be on peripheral blood and bone marrow morphology. ***Interactive participation is expected.***



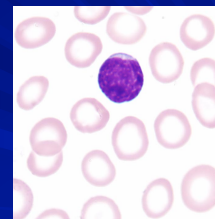
OBJECTIVES

- Correlate hemogram results with peripheral blood morphology.
- Correlate peripheral blood findings with expected bone marrow morphology.
- **Using mini-cases, determine a working diagnosis and additional testing needed.**

MINI-CASE ONE



PB x 500



PB x 1000

Differential Diagnosis

- Iron deficiency anemia
- Thalassemia minor
- Lead poisoning
- Anemia of chronic inflammation

Laboratory Results

- Hb - 6.1 g/dL (9.6 - 15.6)
- Hct - 22.4 vol% (34-48)
- **MCV - 49 fL (76-92)**
- MCHC - 27.2 g/dL (%)
- Retic - 4.5% (0.5-1.5%)
- Platelets - 676 x 10⁹/L (150-450)
- **RDW - 18.0% (11-14)**

Tests to be ordered

- Ferritin
- Serum Iron
- TIBC
- Reticulocyte count

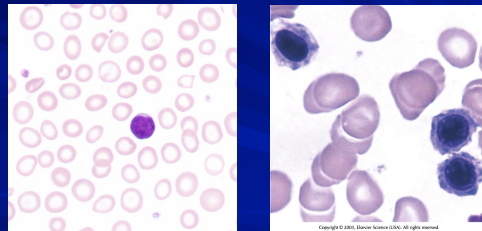
Additional Lab Results

- Total protein - 5.9 g/dL (6.0 - 7.6)
- Albumin - 3.5 g/dL (3.5 -4.7)
- **Serum iron - 3 µg/dL (50-160)**
- TIBC - 373 µg/dL (250-400)
- % Saturation - 1%
- **Ferritin - <1ng/mL (10-106)**

Patient history

- 18 month old who drank 64-80 oz of whole milk daily
- No vitamin supplements
- Mostly rice, bread, cereal, potatoes, very little meat

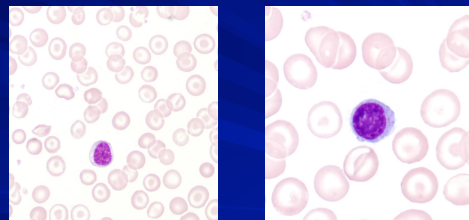
IRON DEFICIENCY ANEMIA



BM x1000



MINI-CASE 2



PB x 500

PB x 1000

Differential Diagnosis

- Iron deficiency anemia
- Thalassemia minor
- Hemoglobinopathy
- (Liver disease)

Laboratory Results

- WBC - $8.0 \times 10^9/L$
- RBC - $5.74 \times 10^{12}/L$
- Hb - 10.2 g/dL
- Hct - 35.5%
- RDW – 12.0%
- MCV – 62 fL
- MCHC – 28.7 g/dL

Tests to be ordered

- Iron studies
 - Ferritin
 - Serum iron
 - TIBC
- Hemoglobin electrophoresis

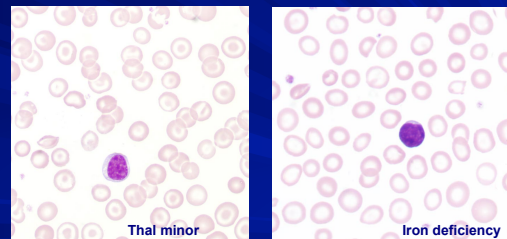
Additional Lab Results

- Ferritin – Within Reference Interval (WRI)
- Serum iron – WRI
- TIBC – WRI
- Hb electrophoresis – Hb A₂ increased
 - 5.0 % by column chromatography

Patient history

- 24 year old male medical student
- Sicilian ancestry
- Several siblings died from thalassemia major

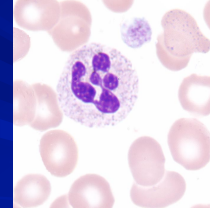
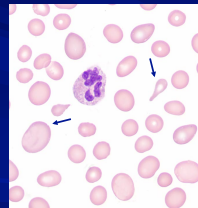
THALASSEMIA MINOR



QUESTIONS?



MINI-CASE 3



Differential Diagnosis

- Vitamin B₁₂ deficiency
- Folate deficiency
- Myelodysplastic syndrome
- Liver disease

Laboratory Results

- Hb - 1.8 g/dL (12.0 -15.0)
- Hct - 5.5%
- RBC - $0.45 \times 10^{12}/L$
- MCV = 120 fL
- MCHC = 32.7 g/dL
- Plat - $8.0 \times 10^9/L$ (150-450)
- WBC - $1.6 \times 10^9/L$
- "blast-like" cells seen on diff

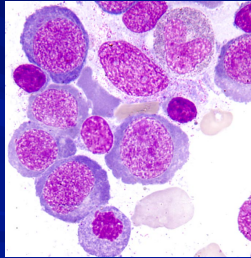
What is the term for a reduction
in all cell lines?

- *Pancytopenia*

Tests to be ordered

- Vitamin B₁₂
- Folate
- Liver function tests
- Bone marrow

Bone Marrow



BM x1000

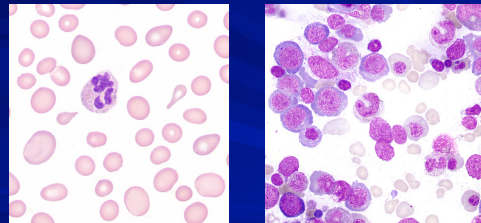
Additional Lab Results

- Vitamin B₁₂ – 23 pg/mL ↓ (200-850)
- Folic acid – decreased
- Bone marrow
 - F:C 0:100
 - Marked megaloblastic changes
- LD ->12,000U/L ↑ (370-840)
- Protime-36.5 sec ↑ (10.1-13.7)
- APTT – 82.5 sec ↑ (25.8-39.8)
- Glucose – 17 mg/dL ↓ (65-200)

Patient history

- 9 year old biracial female
- Weight – 45 pounds
- Palpable liver and spleen; enlarged heart
- Born at home; no medical care
- Breast fed until 4 years old
- Strict vegan

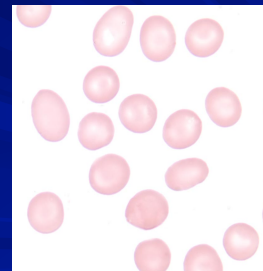
MEGALOBLASTIC ANEMIA



Questions



MINI-CASE 4



Differential Diagnosis

- Aplastic anemia
- Fanconi anemia
- Megaloblastic anemia
- Myelodysplastic syndrome
- Paroxysmal nocturnal hemoglobinuria (PNH)
- Hemolytic anemia
- Leukemia

Laboratory results

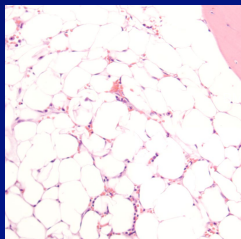
- Hb - 10.0 g/dL ↓ (14.0-18.0)
- Hct - 30 % ↓ (40-54)
- RBC - $2.77 \times 10^{12}/L$ ↓ (4.6-6.0)
- MCV - 108 fL ↑ (80-94)
- MCHC - 33.3 g/dL (32-36)
- WBC - $2.2 \times 10^9/L$ ↓ (4.5 – 11.5)
- PLT - $26.0 \times 10^9/L$ ↓ (150-450)

PANCYTOPENIA

Tests to be ordered

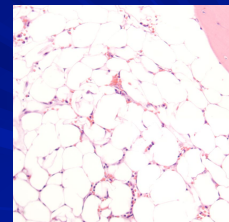
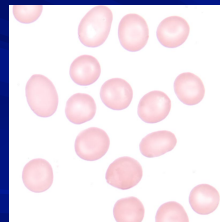
- Vitamin B₁₂
- Folate
- DAT
- Acidified serum
- Hb F
- Diepoxybutane induced breakage (for Fanconi)
- Chromosome analysis
- Bone marrow

Bone Marrow



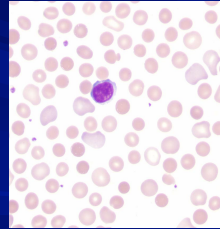
- Marked hypocellularity
- F:C 90:10
- 3% blasts with no evidence of leukemia

APLASTIC ANEMIA

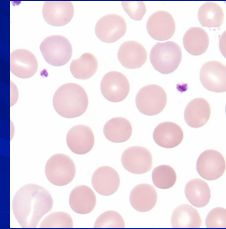




MINI-CASE 5



PB x 500



PB x 1000

Differential Diagnosis

- Hemolytic anemia
 - Inherited
 - Acquired

Laboratory Results

- Hb - 6.7 g/dL (10.4-15.6)
- Hct - 18.2 % (35-51)
- MCV - 76 fL (78-102)
- MCHC – 36.8 g/dL (32-36)
- Retic - 16.3% (0.5-1.5)
- Platelet – 575 x 10⁹/L (150-450)

Tests to be ordered

- Direct Antiglobulin Test (DAT)
- Osmotic fragility

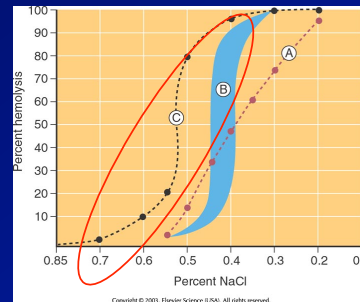
Additional Lab Results

- DAT - negative
- Osmotic fragility - increased

Osmotic Fragility

| % NaCl | % hemolysis | Ref range |
|--------|-------------|-----------|
| 0.65 | 81 | 0-10 |
| 0.60 | 87 | 0-40 |
| 0.55 | 89 | 15-70 |
| 0.50 | 92 | 40-85 |
| 0.45 | 94 | 55-95 |

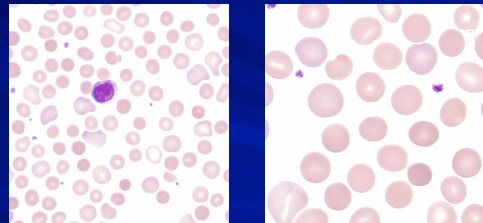
Osmotic Fragility



Patient History

- Father had splenectomy for Hereditary Spherocytosis
- Patient received transfusions from directed donors until age 3½
- Splenectomy for huge spleen and 4 accessory spleens.

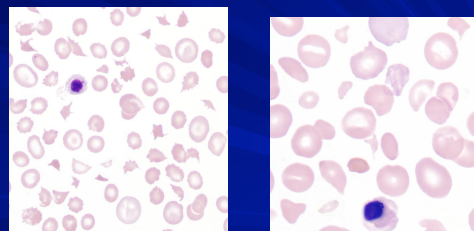
HEREDITARY SPHEROCYTOSIS



QUESTIONS?



MINI-CASE 6



PB x 500

PB x 1000

Differential Diagnosis

- Microangiopathic Hemolytic Anemia (MAHA)
 - HUS
 - TTP
 - DIC
- Severe burns

Laboratory Results

- WBC - $23.0 \times 10^9/L$ (5.5-17.5)
- Hb - 6.2 g/dL (9.6-15.6)
- Hct - 18.3% (34-48)
- Plat - $32 \times 10^9/L$ (150-450)

Tests to be ordered

- DAT
- Prothrombin Time
- APTT
- D-dimer
- Cultures

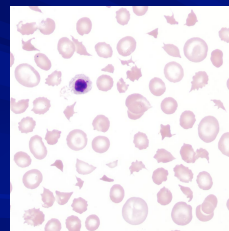
Additional Lab results

- DAT - negative
- PT - 12.8 sec (10.0-12.9)
- APTT - 32.5 sec (26-36)
- D-dimer - negative
- Creatinine - 4.6 mg/dL (0.8-1.8)

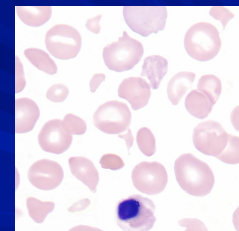
Patient History

- 13 mo male - previously healthy
- GI prodrome
- Petechiae on chest/legs
- Edema in extremities
- Lethargic
- Anuric

MICROANGIOPATHIC HEMOLYTIC ANEMIA (HUS)



PB x 500

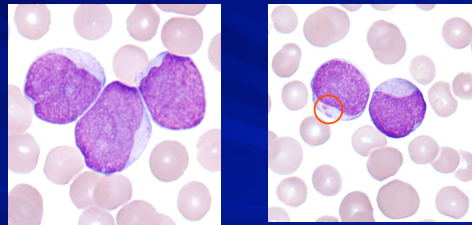


PB x 1000

QUESTIONS??



MINI-CASE 7



Differential Diagnosis

- Acute leukemia
 - Lymphoid
 - Myeloid

Laboratory Results

- WBC – $43.3 \times 10^9/L$
- Hb – 8.3 g/dL
- Hct – 24 %
- Platelets – $44.0 \times 10^9/L$
- Blasts – 37% - Auer rods noted

Tests to be ordered

- Bone marrow
- Cytochemistry
- Cytogenetics and molecular genetics
- Flow cytometry

Bone Marrow

- Markedly hypercellular
- Blasts >90% of non-erythroid cells

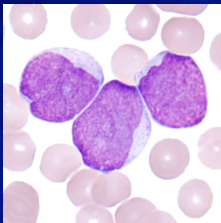
Additional Lab Results

- Cytochemistry
 - MPO - positive
 - NSE – negative
 - PAS – diffuse positivity
- Immunophenotype
 - CD 11+
 - CD 13+
 - CD 33+
- Cytogenetics and molecular genetics
 - No abnormalities found

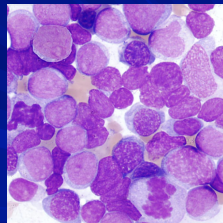
Patient History

- 32 year old female
- Three week history of fatigue, weakness, exertional dyspnea, palpitations, occasional chills and fever

ACUTE MYELOID LEUKEMIA- without maturation

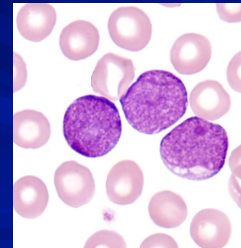


PB x 1000



BM x 500

MINI-CASE 8



Differential Diagnosis

- Acute Leukemia
 - Lymphoid
 - Myeloid

Laboratory Results

- WBC - $3.2 \times 10^9/L$
- Hb - 8.0 g/dL
- Hct - 24 vol%
- Platelets - $44.0 \times 10^9/L$

Tests to be ordered

- Cytochemistry panel
- Immunophenotyping
- Bone Marrow
- Cytogenetics

Cytochemistry

- Myeloperoxidase -
- Nonspecific esterase ±
- Periodic Acid Schiff +

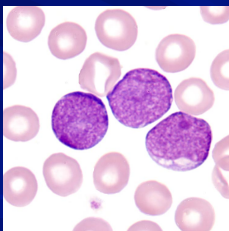
Immunophenotype positive markers

- CD 10
- CD 19
- CD 20
- CD 23
- CD 24
- CD 38
- CD 73

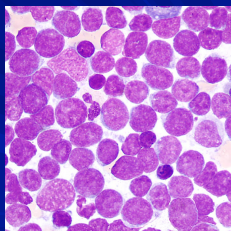
Clinical History

- Six year old male
- Migrating bone pain
- Mild leukopenia
- Few reactive lymphocytes
- (no molecular studies available)

ACUTE LYMPHOID LEUKEMIA

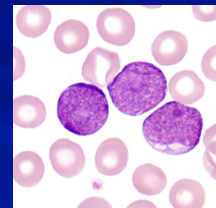
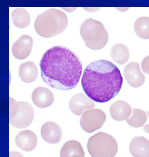
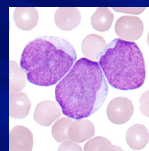


PB x 1000



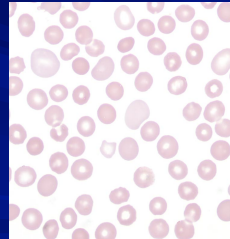
BM x 500

Compare last 2 cases

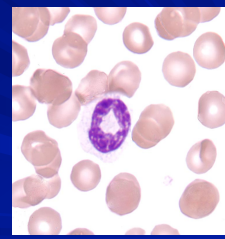




MINI-CASE 9 part one

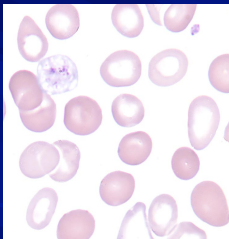


PB x 500

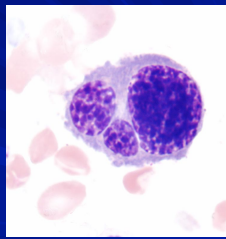


PB x1000

MINI-CASE 9 part 2



PB x 1000



BM x 1000

Differential Diagnosis

- Acute Myeloid Leukemia (M6), erythroid leukemia
- Myelodysplastic syndrome

Laboratory Results

- WBC – $2.9 \times 10^9/L$
- Hb – 6.1 g/dL
- MCV – 132 fL
- Platelets – $51.0 \times 10^9/L$
- RDW – 20%
- No blasts

Tests to be ordered

- Vitamin B₁₂
- Folate
- Bone marrow
- Cytogenetics

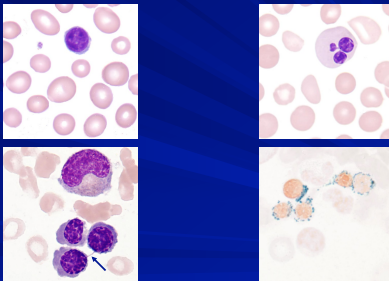
Additional Lab Results

- Vitamin B₁₂ – 377 pg/mL (200-850)
- Folate – within reference range
- Bone marrow
 - Erythroid hyperplasia with marked dyspoiesis
 - Decreased granulopoiesis and megakaryopoiesis, with dysplastic maturation
 - Blasts – 3%
 - Hemosiderin – 3+ with 50-60% ringed sideroblasts
- Cytogenetics – duplication of 1q

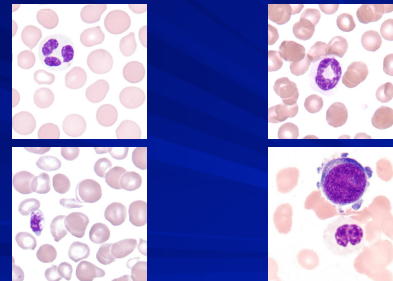
Myelodysplastic Syndrome

- Refractory Anemia with Ringed Sideroblasts (RARS)

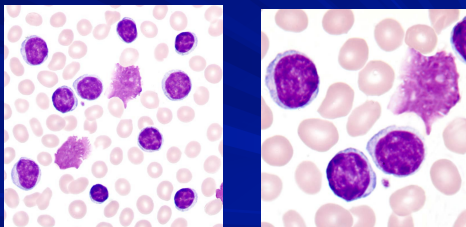
Myelodysplastic Syndrome



MDS



MINI-CASE 10



PB x 500

PB x 1000

Differential Diagnosis

- Reactive lymphocytosis
- Lymphoproliferative disorder
 - Lymphoma
 - Leukemia

Laboratory Results

- WBC – $118.0 \times 10^9/L$
- Hb – 12.9 g/dL (12-15)
- Hct – 39 %
- Platelet – $237 \times 10^9/L$
- Lymphocytes – 96%
- Smudge cells

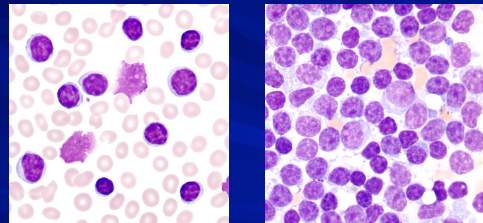
Tests to be ordered

- Immunophenotyping
- Cytogenetics

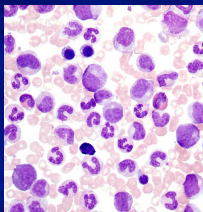
Additional Lab Results

- Immunophenotyping
 - CD 5
 - CD 19
 - CD 20
 - CD 22
 - CD 23
 - HLA-DR
- Genetics
 - Trisomy 12

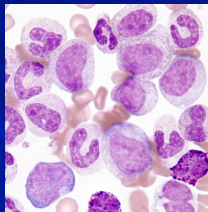
CHRONIC LYMPHOCYTIC LEUKEMIA



MINI-CASE 11



PB x 500



PB x 1000

Differential Diagnosis

- Neutrophilic leukemoid reaction
- Chronic myelogenous leukemia (CML)

Laboratory Results

- WBC – $400.0 \times 10^9/L^*$
 - *(selected diff data)
 - Blasts -2
 - Myelocytes- 22
 - Bands – 22
 - Eos – 7
 - Baso - 6
- Platelets – $600.0 \times 10^9/L$
- Hb 12.0 g/dL (14-18)

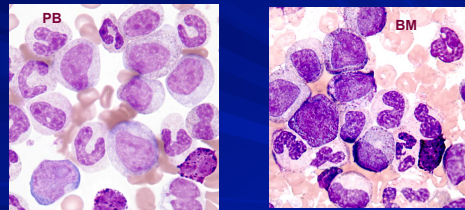
Tests to be ordered

- Leukocyte Alkaline Phosphatase (LAP)
- Bone marrow
- Cytogenetics and molecular genetics

Additional Lab Results

- LAP – score of 3 – markedly reduced
- BM – M:E – 9:1
- Cytogenetics – t(9;22)
- Molecular genetics – BCR/ABL identified

CHRONIC MYELOGENOUS LEUKEMIA

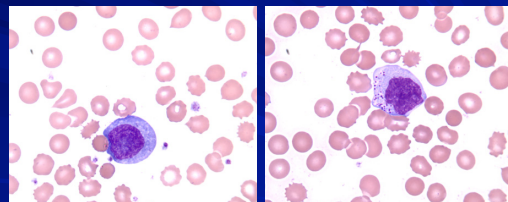


Thanks for your participation!

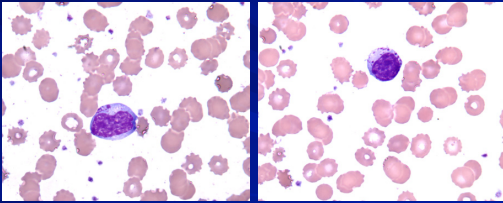


(Tiarnan Butler-Ollry)

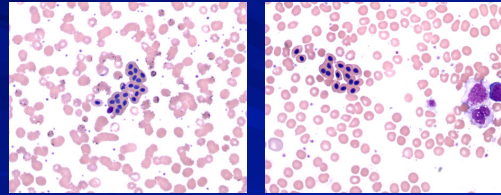
What can these be?



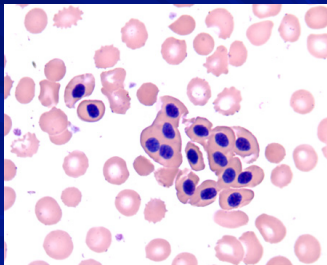
And these?



Scanning...



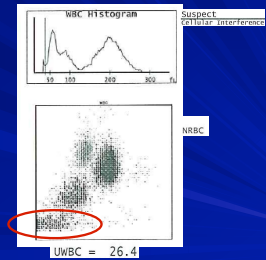
Up close – IDEAS?



In the beginning...

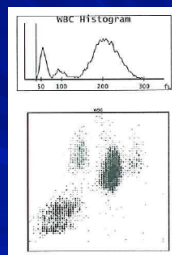
History

- 4 y.o. male brought to ED by mother for treatment of recurrent fever
- 1112 nRBCs/100 WBCs reported in initial manual differential
 - Corrected WBC = 10.2 k
- Patient referred to pediatric hematology clinic for follow-up



And the next day...

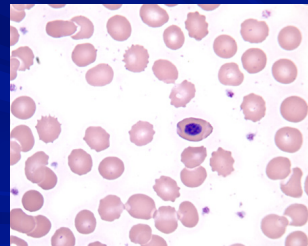
■ NORMAL!



The investigation begins...

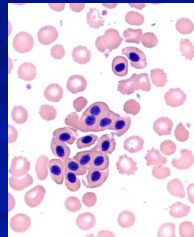
- Sample labeled correctly
- QC okay
- No other samples in batch with similar abnormalities
- Reproduced results on original analyzer
- Made additional slides with new stain – same results
- Alternate staining method – same result
- Reproduced clinic results with analyzer used for ED sample
- All samples run on LH 750s

Microscopic Investigation



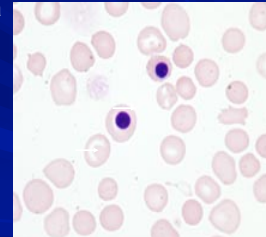
Here's another picture...

- nRBC cytoplasm doesn't appear to be the same color as surrounding cells
- No accompanying polychromatophilia
- nRBC shape is oval or disc-shaped



What you **should** see...

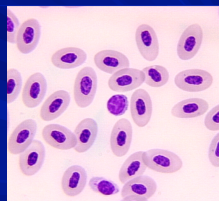
- Polychromatophilia
- Anisocytosis
- Various degrees of maturation



What is it really?

- Total agreement

■ **Avian
nRBCs**



In the end...

- Accidental contamination
 - No source
- Intentional contamination
 - Disgruntled employee
 - Munchausen by Proxy

Münchausen by Proxy Aka Factitious Disorder by Proxy

- Intentional production or feigning of physical or psychological signs or symptoms in another person who is under the individual's care

Characteristics

- Most at risk from 15 mos. to 6 years
- 98% of cases biological mother is responsible
- Symptoms are inappropriate/incongruent
- Child taken to many health care providers
 - Our case study patient was never admitted
- One parent, usually father, is absent during hospitalization
- Symptoms disappear when parent/caretaker is absentParent is overly attached
- Poor tolerance to treatment (vomiting, rash)

Münchausen by Proxy

**THIS IS CHILD
ABUSE**

ACKNOWLEDGEMENT

- Many figures in this presentation were taken from the following publications and used with permission:
Carr JH and Rodak BF: Clinical Hematology Atlas, 3e. Copyright Saunders Elsevier 2009. ISBN 978-1-4160-5039-1

Rodak BF, Fritsma GA, Doig K: Hematology Clinical Principles and Applications, 3e. Copyright Saunders Elsevier 2007. ISBN 978-1-4160-3006-5

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Just following instinct



THE END

