Approach to Anemia

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Notes are done by Kowthar

Definition of Anemia

- Hemoglobin concentration is at least 2 standard deviations below mean for age, gender, and race
- A term child will have a hb of 16, so if you have an infant with a hb of 12, you need to investigate

Age-Specific Blood Cell Indexes

Age	*Hemoglobin, g/dL (g/L)*	*Hematocrit (%)*	*MCV, μm³ (fL)*	*MCHC, g/dL (g/L)*	*Reticulocytes*
26 to 30 weeks' gestation*	13.4 (134)	41.5 (0.42)	118.2 (118.2)	37.9 (379)	—
28 weeks' gestation	14.5 (145)	45 (0.45)	120 (120)	31.0 (310)	(5 to 10)
32 weeks' gestation	15.0 (150)	47 (0.47)	118 (118)	32.0 (320)	(3 to 10)
Term† (cord)	16.5 (165)	51 (0.51)	108 (108)	33.0 (330)	(3 to 7)
1 to 3 days	18.5 (185)	56 (0.56)	108 (108)	33.0 (330)	(1.8 to 4.6)
2 weeks	16.6 (166)	53 (0.53)	105 (105)	31.4 (314)	
1 month	13.9 (139)	44 (0.44)	101 (101)	31.8 (318)	(0.1 to 1.7)
2 months	11.2 (112)	35 (0.35)	95 (95)	31.8 (318)	
6 months	12.6 (126)	36 (0.36)	76 (76)	35.0 (350)	(0.7 to 2.3)
6 months to 2 years	12.0 (120)	36 (0.36)	78 (78)	33.0 (330)	
2 to 6 years	12.5 (125)	37 (0.37)	81 (81)	34.0 (340)	(0.5 to 1.0)
6 to 12 years	13.5 (135)	40 (0.40)	86 (86)	34.0 (340)	(0.5 to 1.0)
12 to 18 years					
Male	14.5 (145)	43 (0.43)	88 (88)	34.0 (340)	(0.5 to 1.0)
Female	14.0 (140)	41 (0.41)	90 (90)	34.0 (340)	(0.5 to 1.0)
Adult					
Male	15.5 (155)	47 (0.47)	90 (90)	34.0 (340)	(0.8 to 2.5)
Female	14.0 (140)	41 (0.41)	90 (90)	34.0 (340)	(0.8 to 4.1)

Approach to Anemia

- History (two imp: diet and family hx)
- Physical examination (lymph nodes, jaundice, cafe au late spots..)
- CBC, differential
- Reticulocytes (to see the activity of bone marrow)
- Peripheral blood smear
- Other labs as indicated (depending on your initial)

Classification of Anemias

- Physiological classification:
  - ↓ Production of RBCs:
    - Absolute failure of erythropoiesis e.g.
      - Inherited or acquired aplastic anemia
      - Pure red cell aplasia
      - Impaired erythropoietin production (e.g. chronic renal failure)
    - Erythrocyte maturation disorders (ineffective erythropoiesis)
      e.g. Thalassemia, Vit B12 or folate deficiency.
  - ↑ Destruction of RBCs:
    - Defects in hemoglobin (e.g. thalassemia)
    - Defects in RBC membrane
    - Defects in RBC metabolism (G6PD)
    - Immune mediated/drug induced
    - others

Classification of Anemias

- Morphological classification (based on MCV):
  - Microcytic:
    - Iron deficiency anemia (anemia of chronic can be normal or micro)
    - Lead poisoning
    - Thalassemia syndromes
    - Sideroblastic anemia
    - Chronic inflammation
  - Macrocytic:
    - Vitamin B12 or folic acid deficiency
    - Orotic aciduria
    - Inherited or acquired aplastic anemia
    - Hypothyroidism
    - Liver disease
  - Normocytic: (hemolytic or acute anemia)
    - Congenital or acquired hemolytic anemias
    - Acute blood loss
    - Chronic inflammation

History

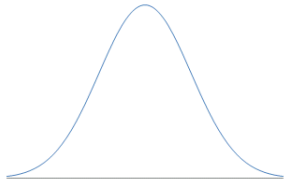
- Age
- Gender
- Race/Ethnicity
- Diet (very imp)
- Diarrhea (malabsorption?) (if chronic diarrhea think of celiac disease)
- Drugs (chemo)
- Infections (parvovirus)
- Family history

Physical Examination

- Skin:
  - hyperpigmentation (Fanconi)
  - Petechiae/purpura (thrombocytopenia)
  - Cavernous hemangioma (MAHA) =microangiopathic hemolytic anemia
- Face:
  - Frontal bossing (B-thalassemia major) (extramedullary hematobiosis)
- Mouth:
  - Glossitis (Vit B12 or iron def)
- Hands:
  - Abnormal thumbs (Fanconi)
  - Spoon nails (iron def) (rare)
- Spleen/Liver/lymph nodes

Initial Workup

- CBC:First: WBC, Hb, Platelets, differential
  - Second: Reticulocytes
    MCV/MCHC
    RDW



	Normal RDW	**High RDW**
Low MCV	Thalassemia trait (all rbcs are small)	Iron Deficiency
Normal MCV	Normal	Sickle Cell
High MCV	Aplastic anemia	Vitamin B12 or folate deficiency

- Peripheral blood smear

Case 1

- 18 months old boy with DDH who was admitted for routine surgery. Preoperative CBC: Hb 7.5 (microcytic and hypochromic), RDW high. Normal WBC and platelets.

Case 1

What will you do next?

- Reassure family and tell the surgeon that it is ok to proceed with surgery.
- Obtain a detailed history with specific focus on nutritional history.
- Perform a bone marrow study.
- Urgent PRBC transfusion because he was already booked for surgery.

Case 1

After you obtained a detailed history, his mother mentioned that his diet is mainly cow milk and he hardly eat any thing else. No family history of anemia. Your exam was unremarkable except for a pale child.

Case 1

What is the most likely diagnosis and how will you further investigate and treat this patient?

- G6PD deficiency, will check G6PD level and transfuse PRBC.
- Thalassemia, will check Hb electrophoresis and transfuse PRBC.
- Iron deficiency anemia, will reschedule the surgery, obtain iron studies, and start patient on iron.
- Not sure and want more information.

Etiology of Iron deficiency

- Inadequate iron stores at birth (if the child had bleeding in utero or later)
- Insufficient iron in diet
- Blood loss (e.g. hookworm infestation)
- Malabsorption of iron (e.g. celiac disease, crohn disease, chronic giardiasis)

Why too much cow milk causes iron deficiency?

- Contains minimal iron (<1 mg/L)
- Iron poorly absorbed (5-10%) compared to breast milk (50% absorption)
- Leads to reduced intake of other foods.
- May cause GI bleeding
- (its good to check on the rbcs after one year of age to make sure nothings wrong, because moms don't change their children's diet)

Diagnosis of Iron deficiency

- History (diet, bleeding, irritability, pica)
- Physical examination
  - Non-specific findings of anemia
  - “Specific” findings (koilonychia, chlorosis, etc.) rarely seen in children
- Laboratory tests

Sever iron def anemia, they start to eat paintings (rare)

Fig. 6-5. Daily diet of pebbles taken for 3 years by a boy 7½ years of age with pica and iron-deficiency anemia. (From Lanzkowsky, P.: Arch. Dis. Child. **34:**140, 1959.)

a Little Golden Book

Disney's

THE LION KING

Walt Disney's

Disney's Wonderful World of Reading

PETER PAN and WENDY

Very imp slide!
You have to give iron for at least 3 months when the hb level is back to normal to make sure that the stores are full!
it's wrong to stop the treatment when you see it normal, you need to think of the diet and other factors (level of iron stored).

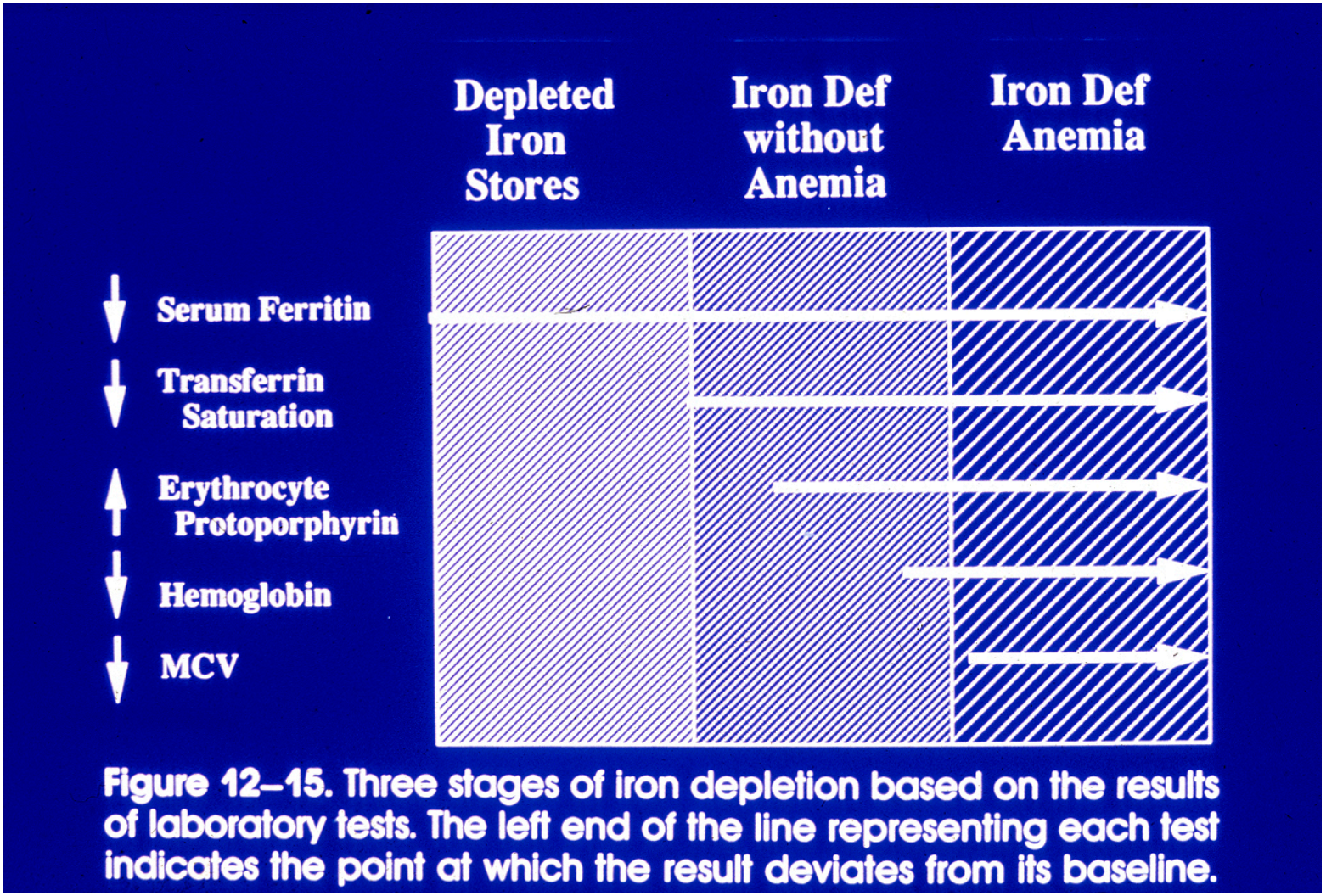
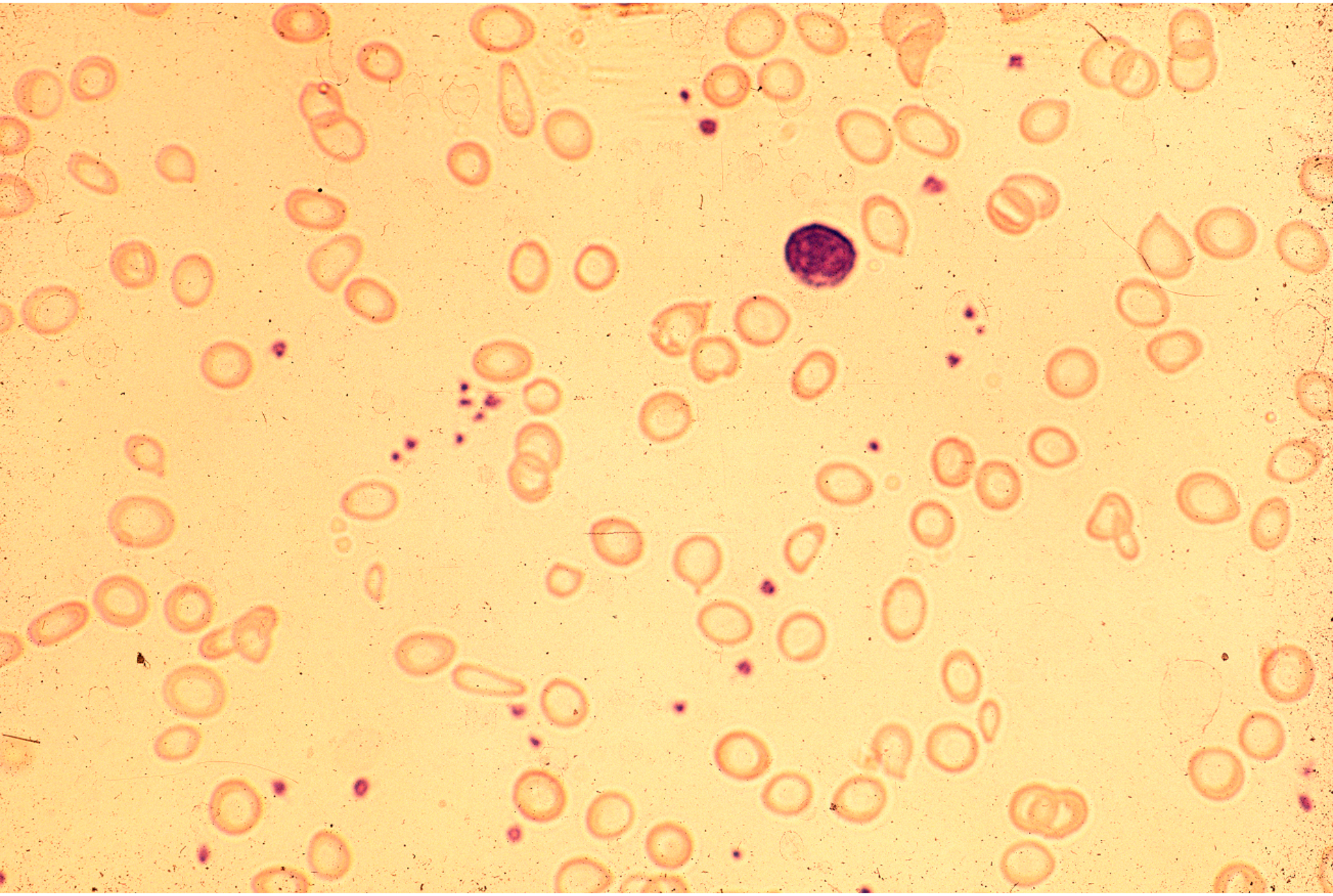


Figure 12–15. Three stages of iron depletion based on the results of laboratory tests. The left end of the line representing each test indicates the point at which the result deviates from its baseline.

From Dallman et al, Nathan & Oski, 4th Edition 1993



Diagnostic test

Complete response to a iron therapy

Treatment of Iron deficiency

- Identify and eliminate cause of iron deficiency
- Oral iron therapy:
  - 3 mg/kg/d elemental iron in single daily dose for mild iron deficiency anemia
  - 5-6 mg/kg/d elemental iron in two divided doses for moderate to severe iron deficiency anemia
- Packed RBC transfusion in severe cases (Hgb < 4 gm/dl) (rare)

Reasons for lack of response to iron therapy

• Parents not administering iron according to instructions, child hates the taste of it	Extremely common
• Diagnosis is incorrect; child doesn't have iron deficiency	Common
• Dose of iron is incorrect	Occasionally
• Child is malabsorbing iron	Rare

Prevention of iron deficiency

- Exclusive Breast feeding limited to the first 4-6 months of life then introduce solid food.
- Iron fortified formula
- Iron fortified infant cereals
- Medicinal iron for “high risk” infants
- Avoid cow milk before 12 months of age
- Limit cow milk intake to 18-24 oz. daily after 12 mo of age

Adverse effects of iron deficiency

- Anemia
- Motor and IQ deficits (not fully reversible even following iron replacement)
- Diminished activity.
- Impaired immunity

In adults they take IV iron one or two times only, but not in pedia, it is reserved for cases that are not responsive.

	Fe deficiency	Anemia of chronic disease
Serum Fe	↓ to NI	↓ to NI
TIBC	High NI to ↑	↓ to low NI
% Iron Saturation	↓ ↓	↓
Serum ferritin	↓ ↓ (absence of concomitant infection, inflammation, malignancy)	NI to ↑ ↑ (ESR and CRP mostly ↑)
MCV	↓ to ↓ ↓	↓ to NI
RDW	↑	NI to ↑
sTfR (investigational)	↑	NI
Hepcidin (investigational)	↓	↑

-Hepcidine is very important in liver disease, if it's high it will not allow iron to be absorbed.
-Diff between ferrite and serum iron: ferrite storage, and serum iron is the indicator of what is the level in blood at the time you checked (not a real indicator)

	Fe deficiency	Thalassemia trait
RBC count	↓	Nl to ↑
Mentzer index (MCV/RBC)	> 13	< 13
RDW	↑	Nl
Serum ferritin	↓	Nl
Hgb A2	↓ to Nl	↑ in B-thal trait

-In thalassemia there is a lot of rbcs but مافيهم بركة, so iron is still low.

-In beta thalassemia major= no hgb A, almost all are hgb F

-How to diagnose alpha thalassemia? normal electrophoresis but rbcs are low.

Case 2

- You are evaluating an 8-month-old infant for anemia. At 6 months of age, iron supplementation was prescribed when a CBC revealed anemia. Follow up CBC shows that the anemia has persisted, although the child's mother insists she has been giving the iron supplements. The infant has been exclusively bottle-fed with fresh goat's milk since age 4 months. Cereal and baby foods have not yet been introduced. Of the following, the most likely cause for this infant's persistent anemia is (very common question in smle)
  - Iron deficiency
  - Vitamin B12 deficiency
  - Vitamin E deficiency
  - Folate deficiency (is deficient in goat milk)
  - Zinc deficiency

Case 3

- You are examining an 12-month-old boy during a routine health supervision visit. He was a full term infant and is exclusively breastfed, and his mother adheres to a strict vegan diet. His CBC shows anemia and peripheral smear reveals macrocytosis and hypersegmented neutrophils.

  Of the following, the most likely cause for anemia is:
  - Iron deficiency
  - Folate deficiency
  - Physiological anemia
  - Vitamin B12 deficiency (vegan!)
  - Vitamin E deficiency

Anemia Due to Folate or Vitamin B_{12} (Cobalamin) Deficiency

- Folate and cobalamin required for DNA synthesis
- Deficiency results in megaloblastic anemia due to impaired DNA replication
- Similar clinical features* in peripheral blood and marrow morphology in folate and cobalamin deficiency

* Exception: Neurologic abnormalities in B_{12} deficiency

Folic acid

- Dietary sources
  - Fresh fruits and vegetables
  - Meat
  - Cow and human milk
  - Cereals and bread (fortified)

- Deficiency (causes):
  - Decreased intake (rare due to supplementation of packaged foods)
    - Severe malnutrition
    - Sick premature infant
    - Unpasteurized goat milk
  - Intestinal malabsorption (celiac disease, inflammatory bowel disease, anticonvulsants)
  - Increased requirements
    - Chronic hemolytic anemia
    - Pregnancy

Vitamin B12

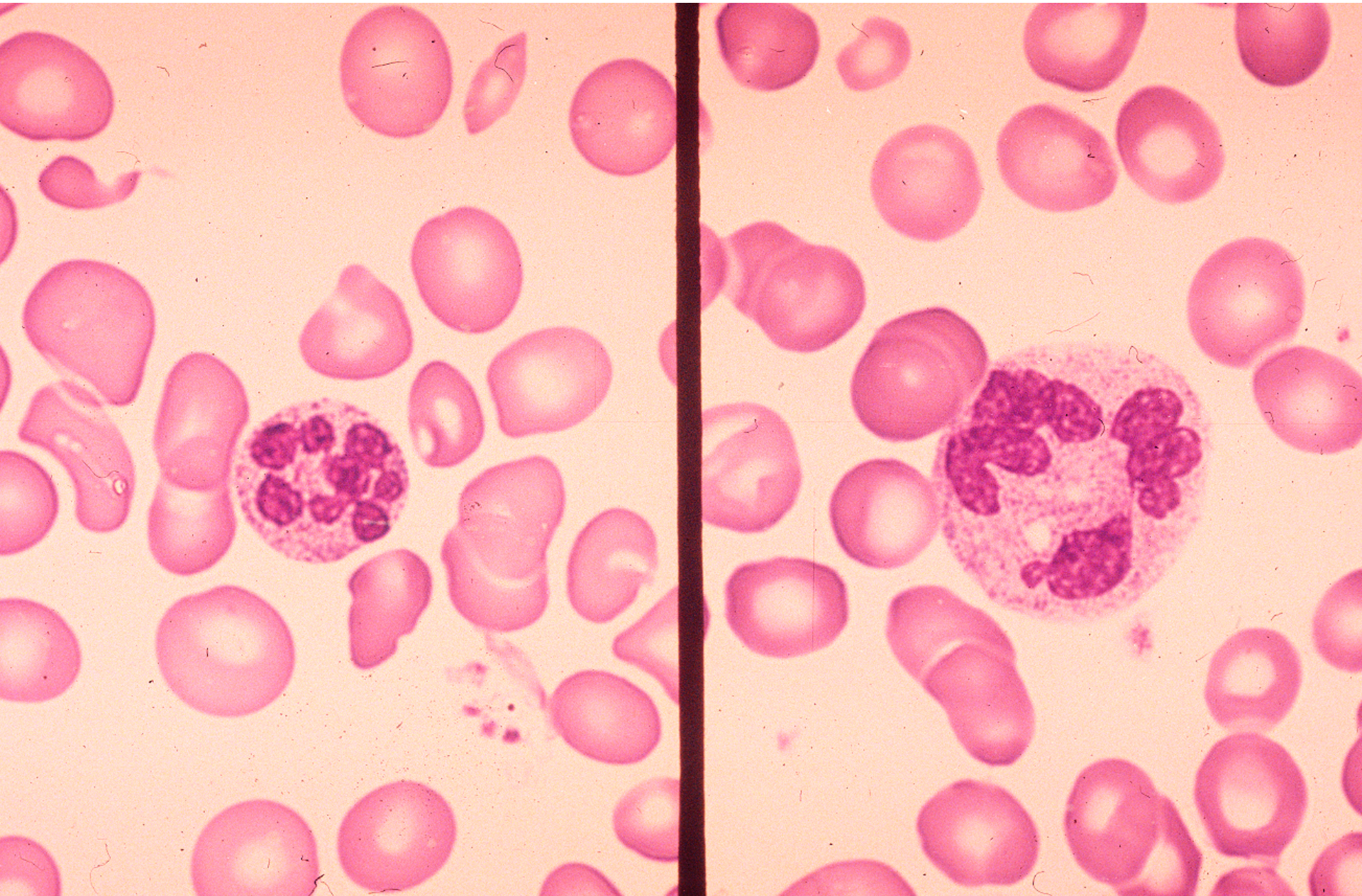
- Sources: Meat and dairy products.

- Deficiency (causes):
  - Reduced B_{12} intake
    - Vegan (no meat or dairy products)
    - Breast-feeding infant of vegan
  - Decreased intestinal B_{12} absorption
    - Reduced intrinsic factor
      - pernicious anemia
    - Malabsorption despite normal intrinsic factor
      - Ileal resection (bowel malabsobtion)
      - Inflammatory bowel disease
      - Imerslund-Gräsbeck syndrome (bowel malabsobtion)
  - Increased intestinal utilization
    - Blind loop or other intestinal stasis
    - Fish tapeworm infection

Folic acid or Vitamin B12 Deficiency

- Non-specific signs and symptoms of anemia
- Jaundice due to ineffective erythropoiesis
- Macrocytic anemia
- Relatively low reticulocyte count
- Hypersegmentation of neutrophils
- Mild thrombocytopenia and/or neutropenia
- Megaloblastic changes in marrow
- Neurological findings (B_{12} deficiency only): loss of position sense, ataxia, psychomotor retardation, seizures

Hyperhsegmented neutrophils



Diagnosis of folate or Vitamin B12 deficiency

- Serum folate level (reflects current status)
- RBC folate level (reflects tissue levels)
- Serum Vitamin B_{12} (cobalamin) level
- Urinary methylmalonic acid excretion
- Plasma homocysteine level

- Methylmalonic acid depends on B12, so good to check when you are in doubt.

Treatment of folate or Vitamin B12 deficiency

Correct diagnosis extremely important!

- Megaloblastic anemia of B_{12} deficiency responds to folic acid in high doses (≥ 1 mg/d)
- Underlying B_{12} deficiency may be masked
- Neurologic deficits of B_{12} deficiency do not respond to folate

Non-Hematologic Effects of Folate Deficiency

- Neural tube defects
- Thrombosis due to elevated plasma homocysteine levels (controversial)

Case 4

- Faisal is 12 y/o boy from Aljouf who was referred to KKUH because of macrocytic anemia. His CBC also showed neutropenia and mild thrombocytopenia. Retics count is low. History was remarkable for strong family history of similar findings. Exam was remarkable for short stature, hyper pigmentation, and abnormal thumbs.

Case 4

- What is the most likely diagnosis?
  - Leukemia.
  - Vitamin B12 deficiency.
  - Fanconi anemia.(pancytopenia!)
  - Brucellosis.

Case 4

- Bone marrow was performed which showed hypocellular marrow (<10%) and no evidence of leukemia. What test will you request to confirm the diagnosis of Fanconi anemia?
  - Pancreatic enzymes.
  - Chromosomal fragility test with DNA cross-linking agents e.g. DEB or MMC.
  - Adenosine deaminase level.
  - High Hgb F.

  - Role of falconi: for DNA repair mechanisms, so if there is a problem it will not fix cells then cancer can happen.

Diagnosing Fanconi Anemia

- Suspicion of Diagnosis
  - CBC: with pancytopenia, macrocytosis
  - Bone marrow aspirate and biopsy

- Screening and Diagnostic Testing
  - Chromosome breakage (fragility) test
  - Molecular diagnosis

Congenital Anomalies
Fanconi Anemia

- Microcephaly
- Hypertelorism
- Webbed neck
- Abnormal thumbs
- Dislocated hips

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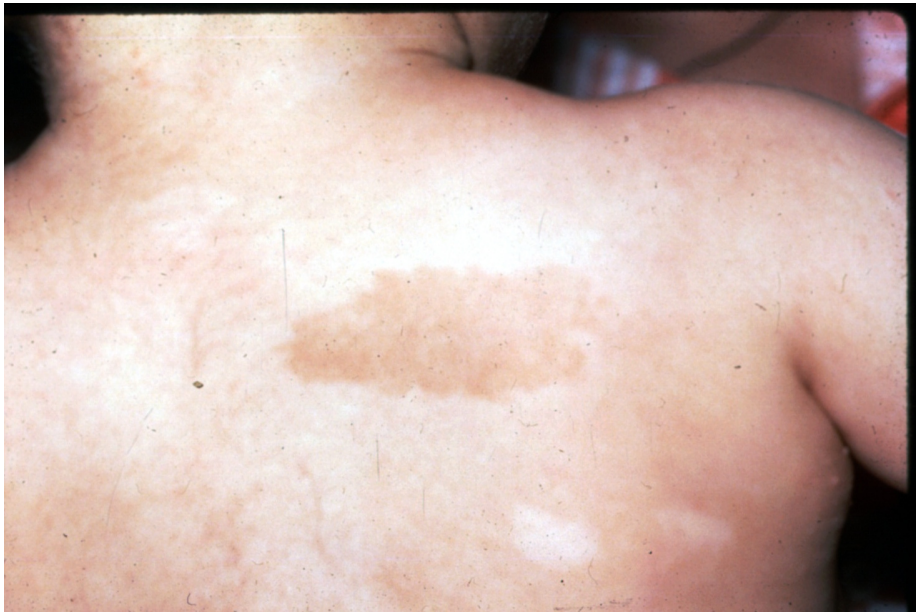
Congenital Anomalies
Fanconi Anemia



Café au lait spot

Hypopigmentation

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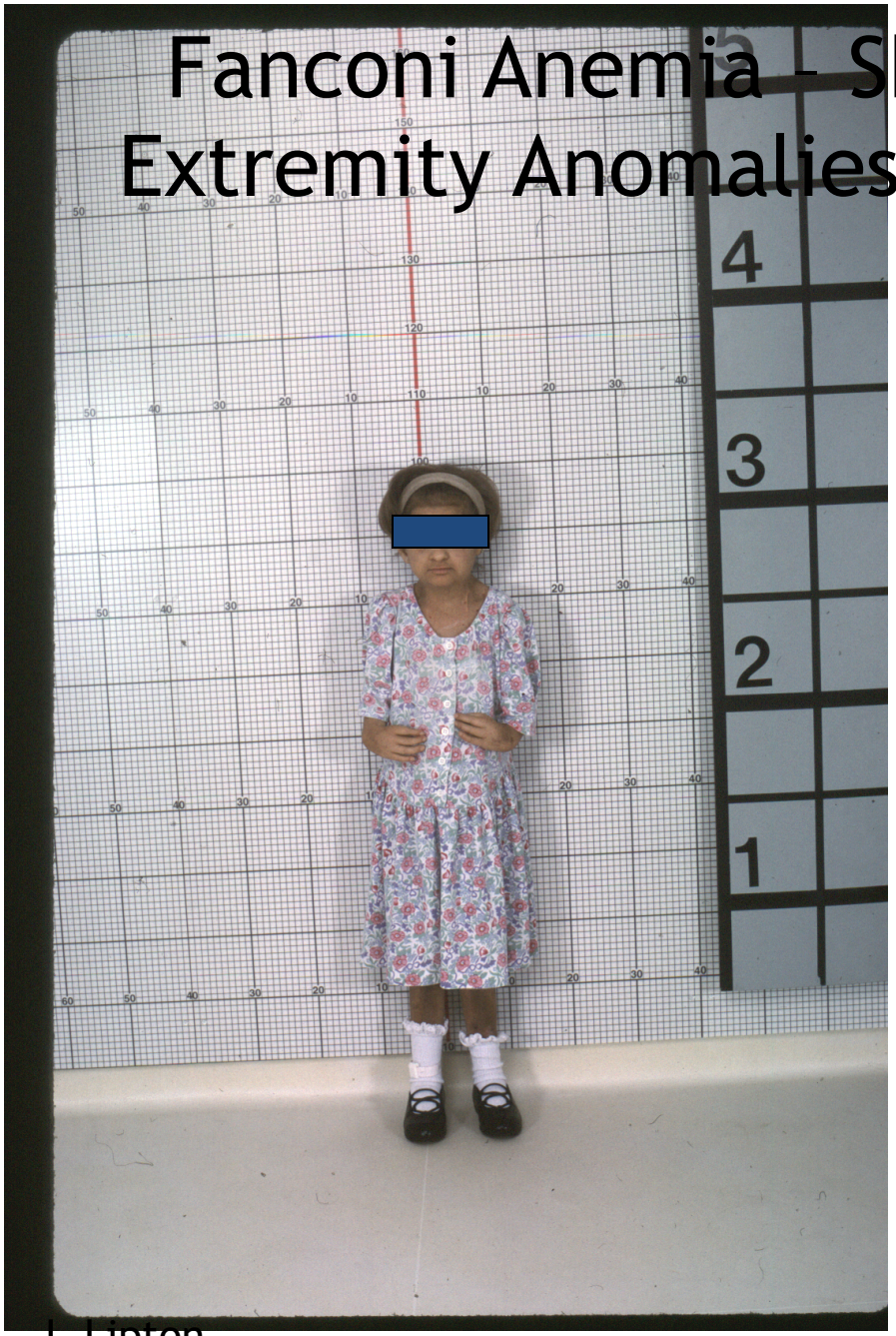
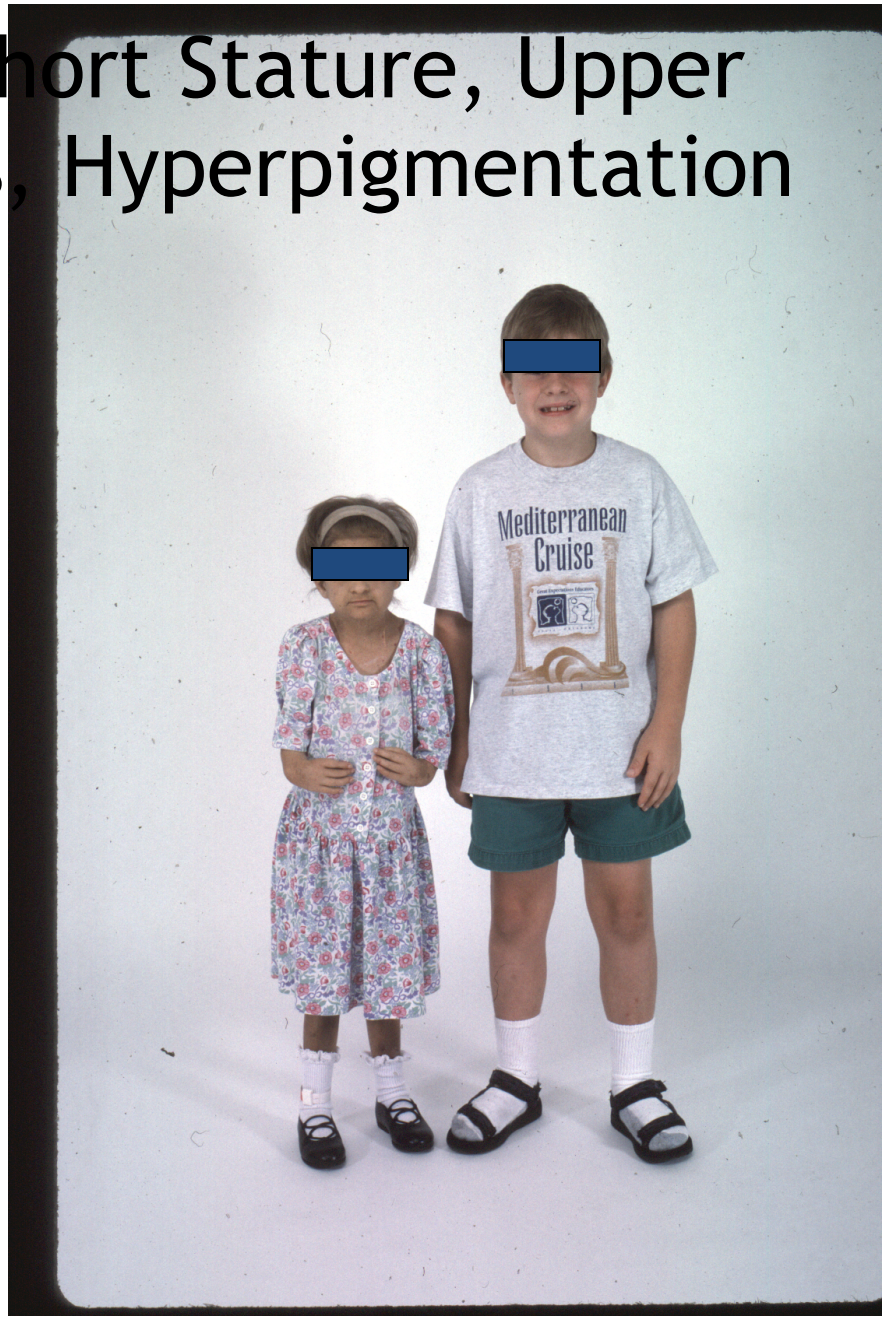
Fanconi Anemia – Short Stature, Upper Extremity Anomalies, Hyperpigmentation





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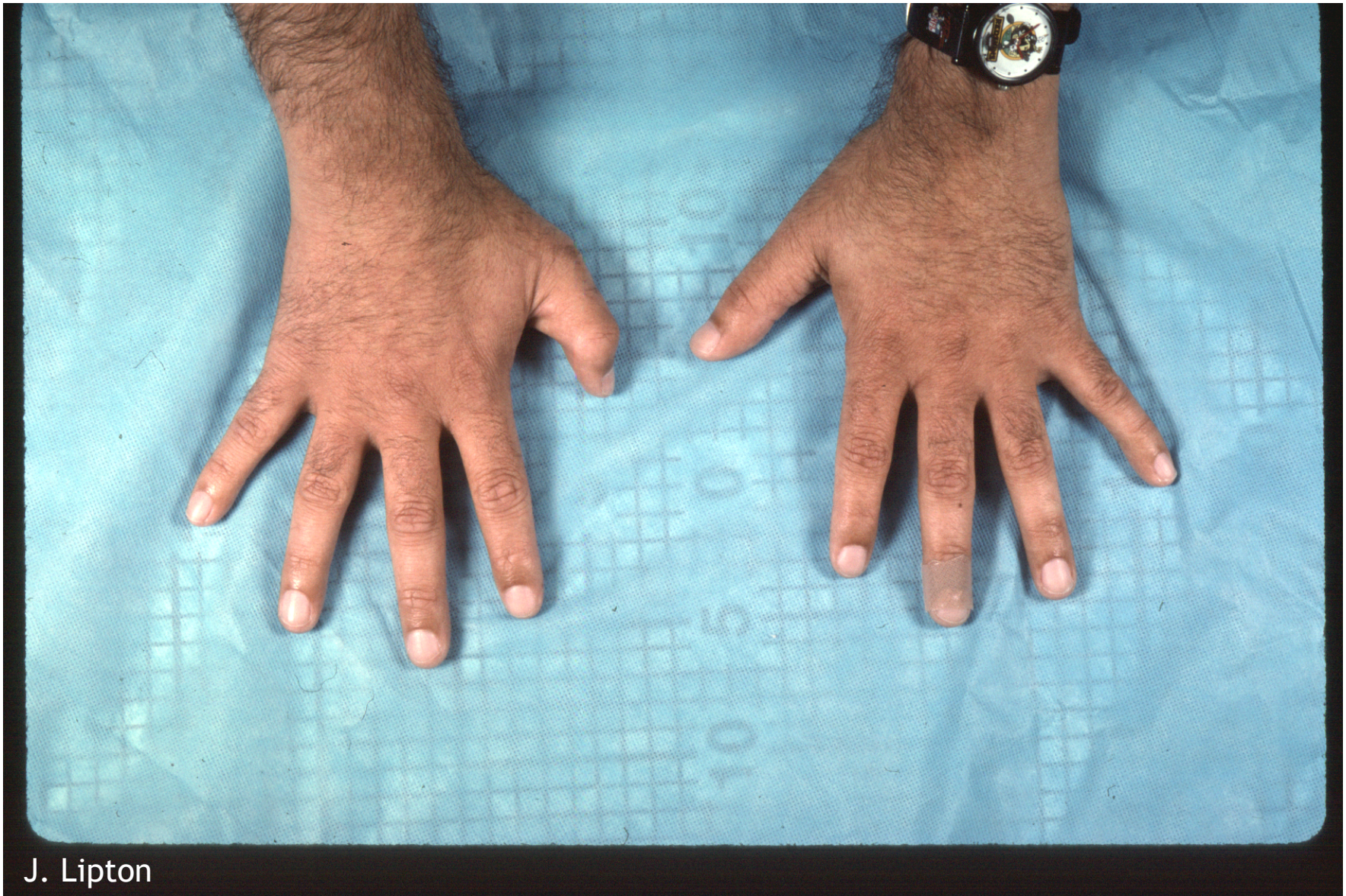
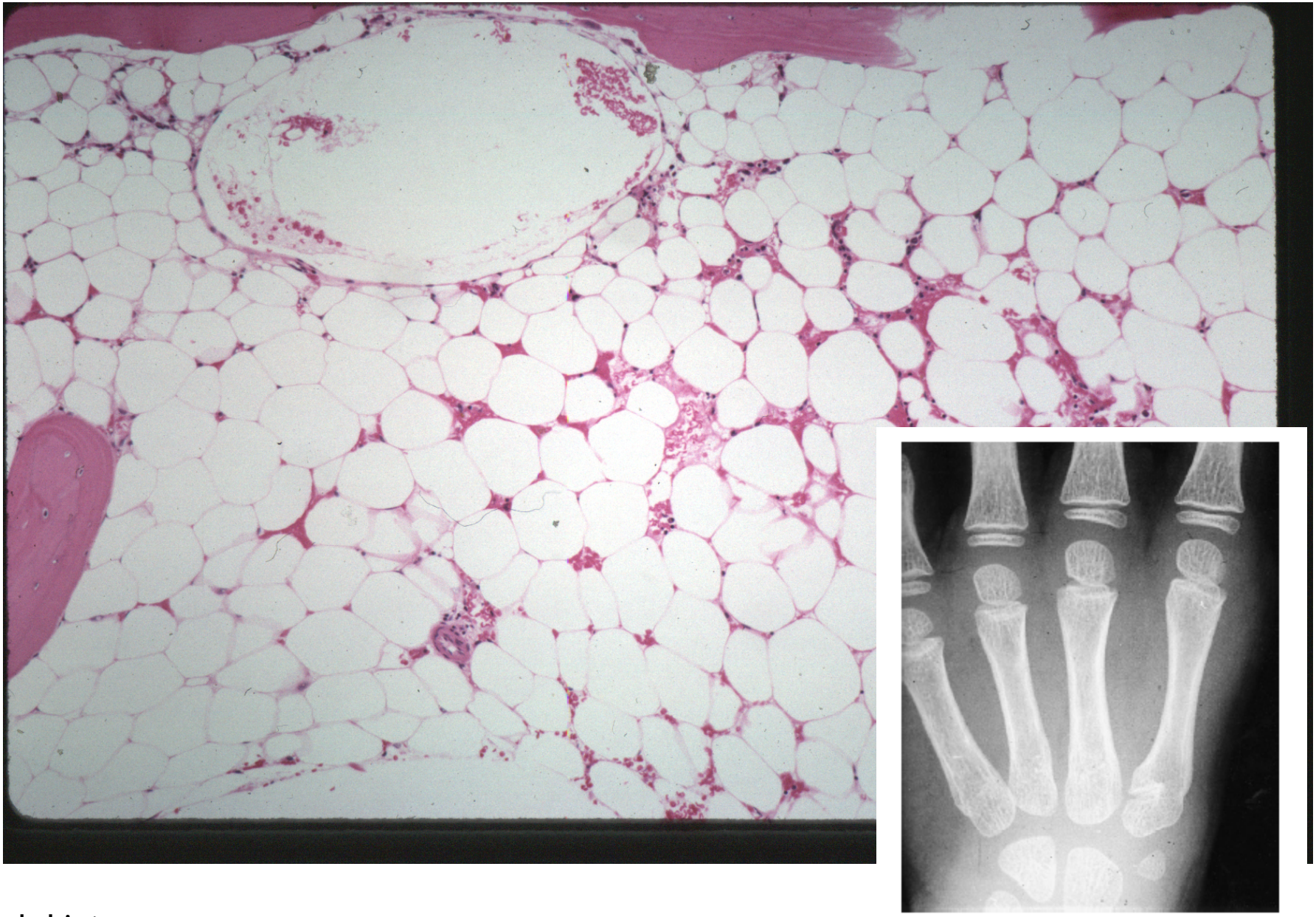
Fanconi Anemia
Subtle Anomalies





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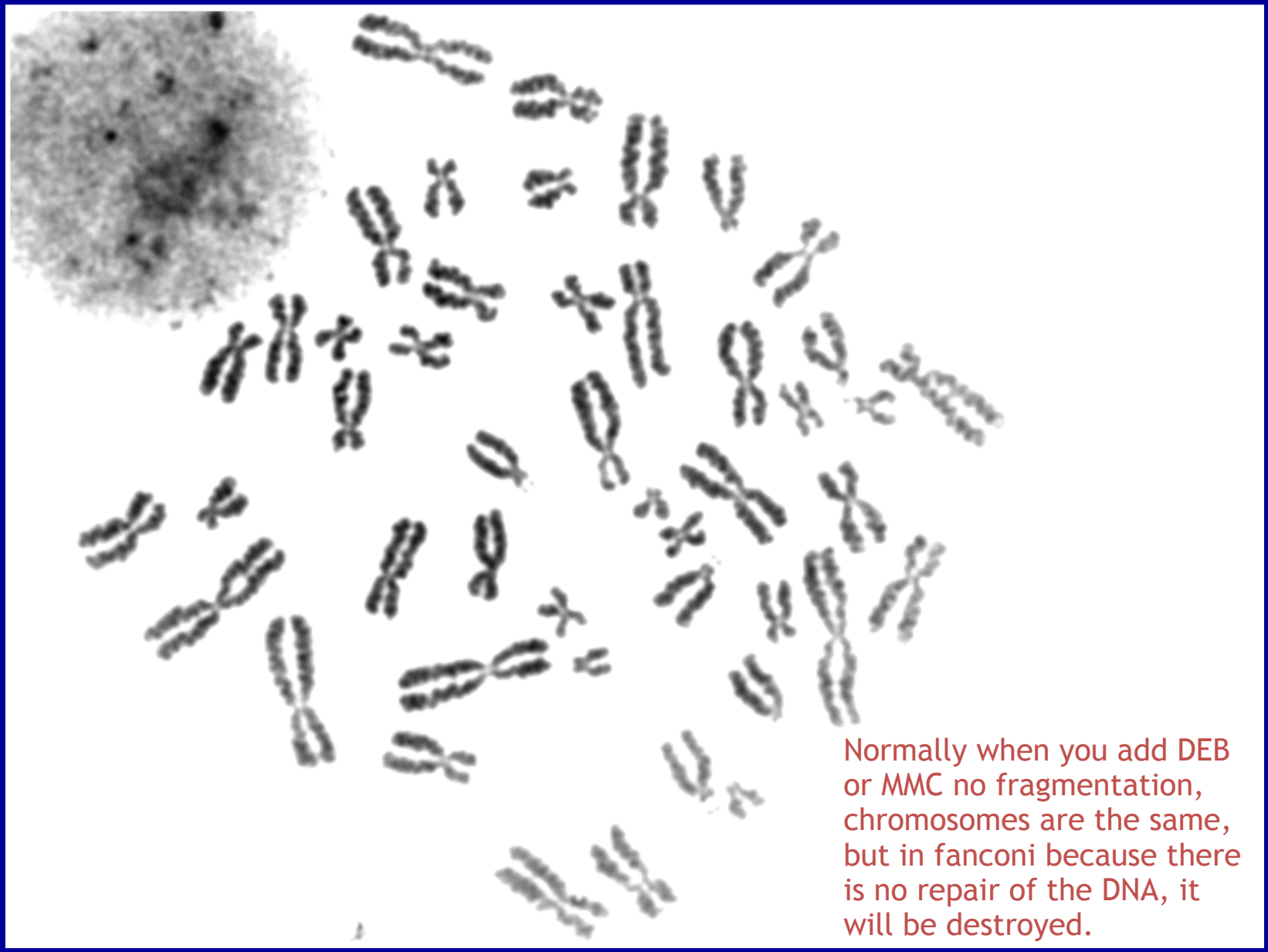
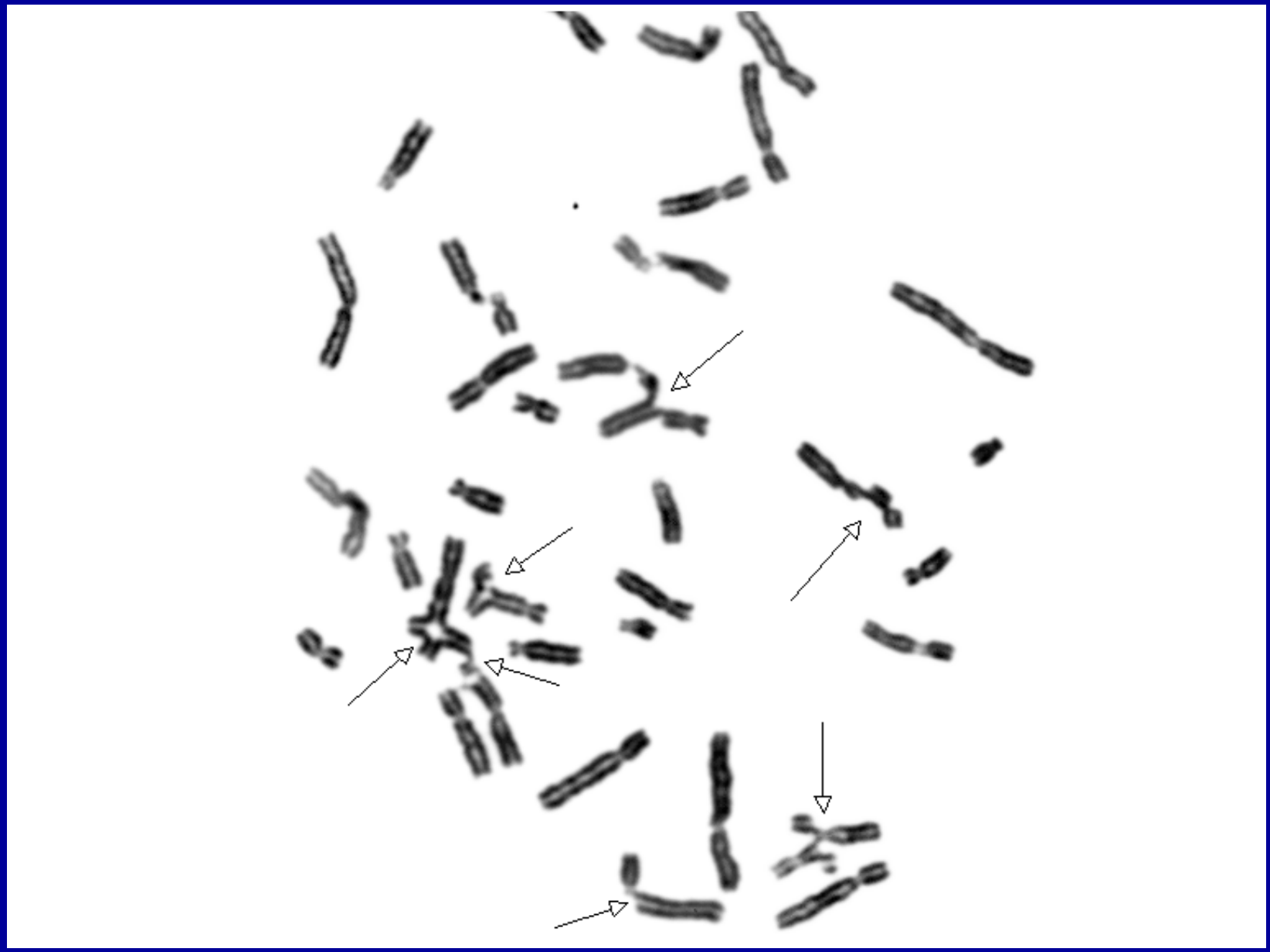
FA Cells Incubated without DEB or MMC



Normally when you add DEB or MMC no fragmentation, chromosomes are the same, but in fanconi because there is no repair of the DNA, it will be destroyed.

FA Cells Incubated with DEB



Management and Treatment of Fanconi Anemia

- Careful evaluation of congenital anomalies
- Careful monitoring
  - Gynecologic, Hematologic, GI
- Supportive care for marrow failure
  - Androgen therapy
  - Hematopoietic growth factors
  - Transfusion support
- Bone marrow transplantation
  - Matched related donors
  - Alternative donors

Fanconi Anemia

Differential Diagnosis: (Inherited BM failure syndromes)

- Diamond-Blackfan anemia (isolated anemia, ribosomal patheies)
- Dyskeratosis congenita (works on telemire which protects the chromosoms)
- Shwachman-Diamond Syndrome (
- Amegakaryocytic thrombocytopenia.

Diamond Blackfan Anemia
vs
Transient Erythroblastopenia of Childhood

	DBA	TEC
eADA increased	YES	NO
MCV increased	YES	NO
HbF increased	YES	NO

Doctor skipped it

Severe Acquired Aplastic Anemia Definition

Two of three cytopenias as defined:

- Absolute neutrophil count (ANC) ≤ 500/µl*
  *<200 /µl -very severe aplastic anemia
- Platelet count (Plt) < 20K /µl
- Reticulocyte count < 40 x 10^9/L

and

- Bone marrow cellularity <25%

Doctor skipped it

Case 6

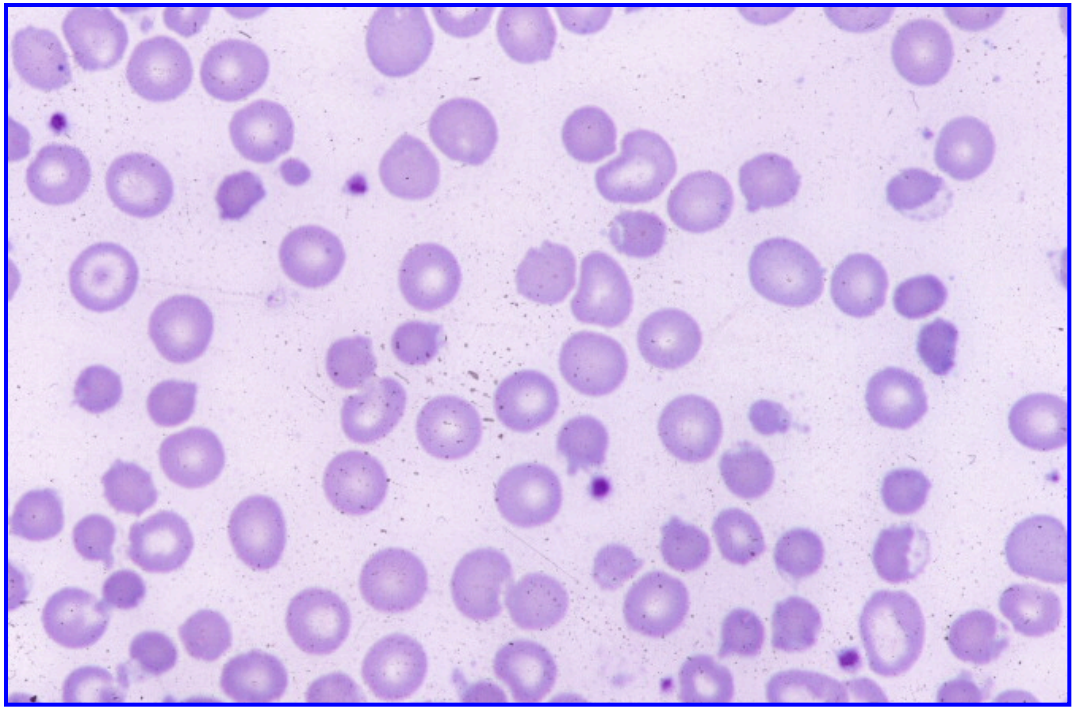
- Faisal is a 6-year-old boy who is admitted to the hospital for acute onset of dark urine and anemia after eating fava beans. He has significant indirect hyperbilirubinemia and requires a transfusion for Hgb 5 g/dl.

Case 6

- Which of the following labs will you order? (anemia + dark urine = destruction is intravascular)
  - Direct antiglobuiln test. (always check for it if intravascular)
  - Peripheral smear.
  - Reticulocytes.
  - Urinalysis.
  - All of the above.

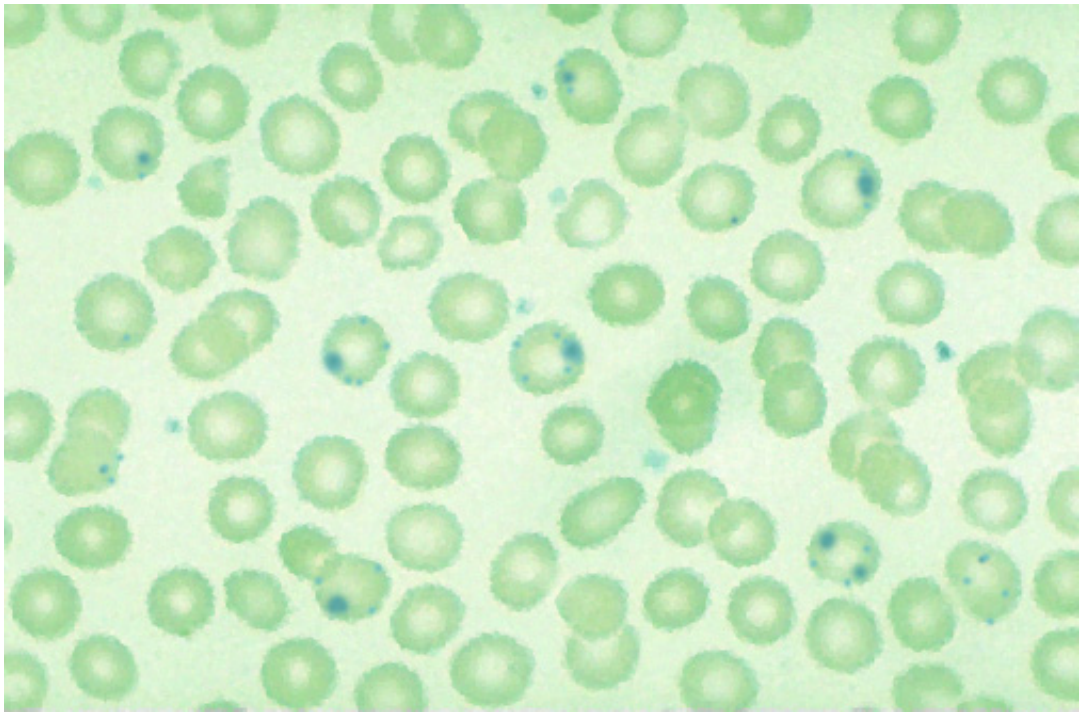
Case 6

- DAT negative, high retics, and peripheral smear showed blister cells.



Case 6

- Heinz bodies (denatured hemoglobin) on crystal violet staining



Case 6

- To confirm the diagnosis of G6PD deficiency, you will do the following:
  - Osmotic fragility test.
  - G6PD level assay during the acute phase.
  - Hgb electropheresis.
  - Wait until patient recovers from the acute illness and then check G6PD level (Becuse the reticulocytes will have normal G6PD, and this is a common exam question! in practice we do measure it but in mcqs they want you to see normal and wait)

G6PD Deficiency
common in sharjah and janoub

- Most common red cell enzymopathy
- X linked inheritance
- Decreased production of NADPH with inability to maintain reduced glutathione levels
- Hemolysis occurs in response to oxidative stresses such as infections, drugs, fava beans (“favism”), naphthalene (moth balls)
- Anemia may be low grade and chronic (CNSHA) or acute after exposure to oxidant

Pyruvate kinase deficiency

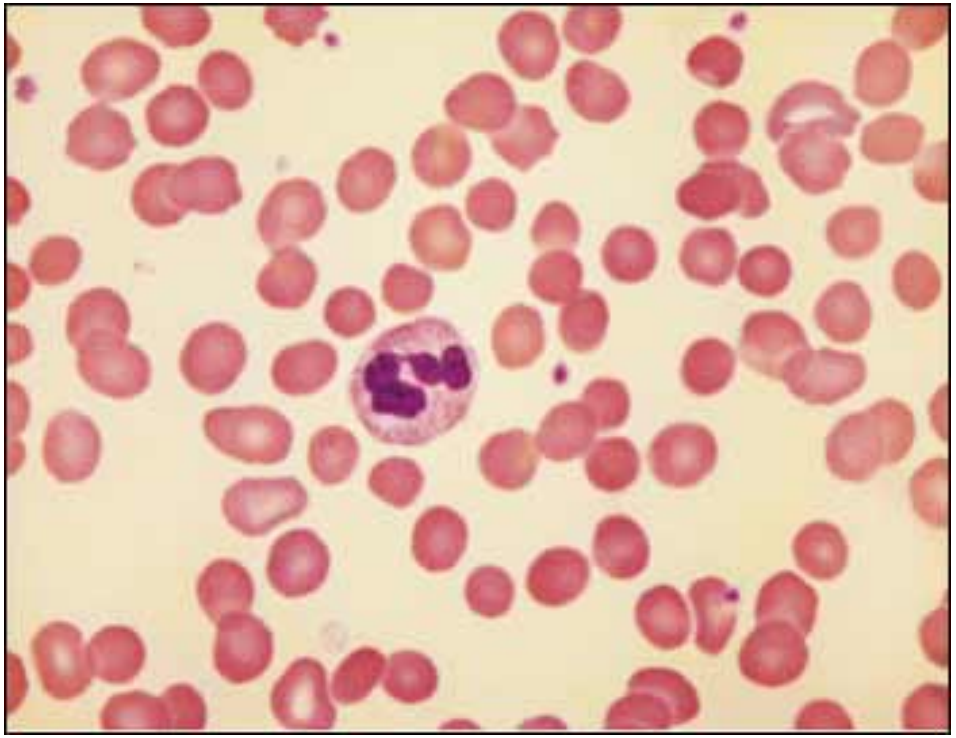
- Glycolytic pathway defect leading to decease in ATP production.
- Autosomal recessive.
- Both genetically and phenotypically heterogeneous.
- Severe cases: present as neonatal jaundice or in early childhood with jaundice, splenomegaly, and failure to thrive.
- Mild cases: mild compensated hemolytic anemia.
- High 2,3 DPG and no Heinz bodies.

Case 7

- Sarah is 2 month-old infant who you are seeing in your clinic for the first time for a well-child check. According to her mother, the neonatal period was complicated by prolonged hyperbilirubinemia requiring several days of phototherapy. Otherwise, she has done well and has been growing and thriving. Her mother has history of splenectomy and GB removal. Exam is remarkable for mild jaundice and spleen is 4 cm below costal margin.

Case 4

- CBC showed : Hgb 6.5 g/dl (normochromic normocytic), high MCHC, Retics 11%. Peripheral blood smear is shown below. DAT is negative.



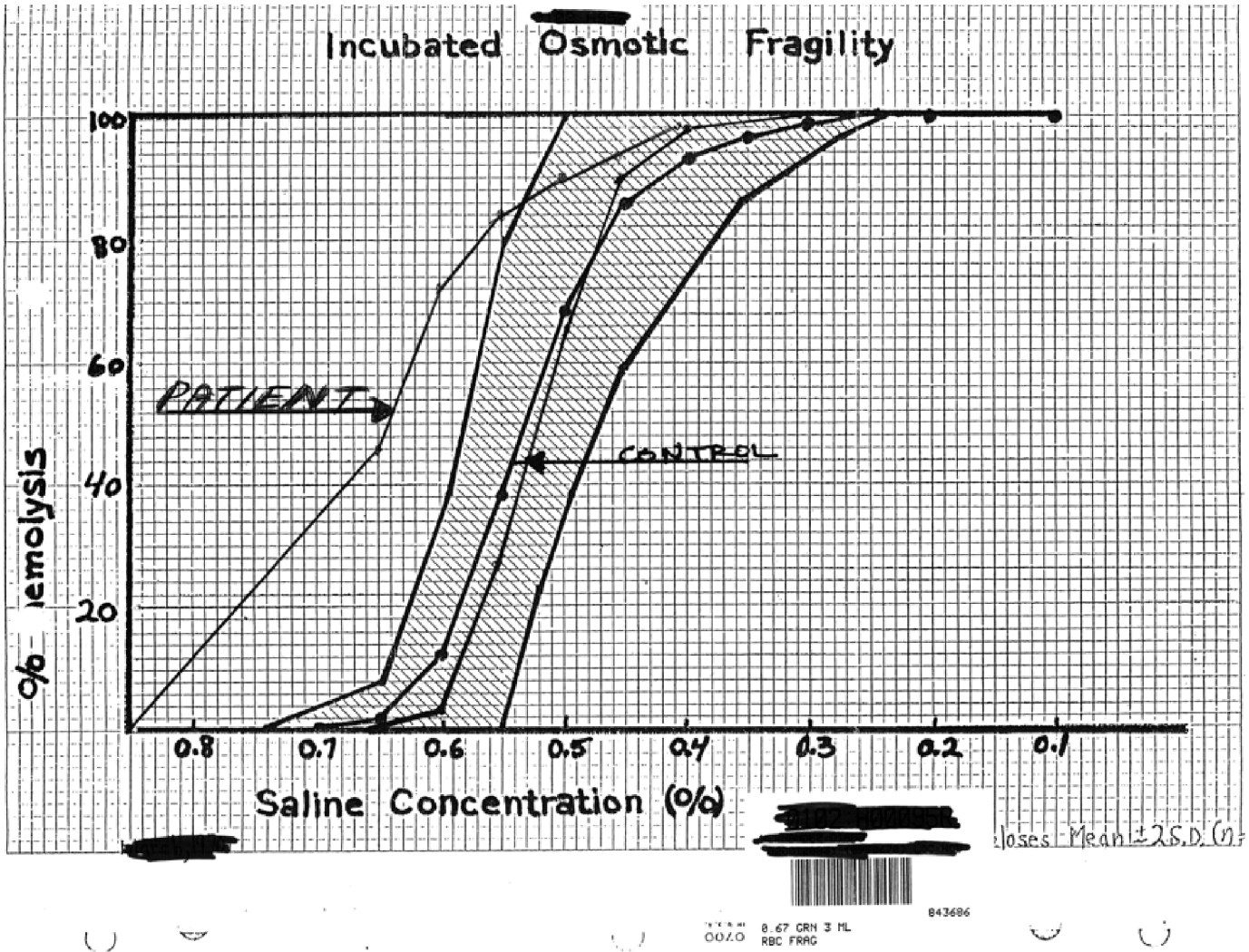
Case 7

- What is your diagnosis?
  - Autoimmune hemolytic anemia.
  - Hereditary spherocytosis.
  - Thalassemia.
  - Iron deficiency anemia.

Case 7

- You suspected hereditary spherocytosis, what will you order to confirm your diagnosis:
  - Hgb electropheresis.
  - Iron studies.
  - Osmotic fragility test.
  - Bone marrow study.

Case 7

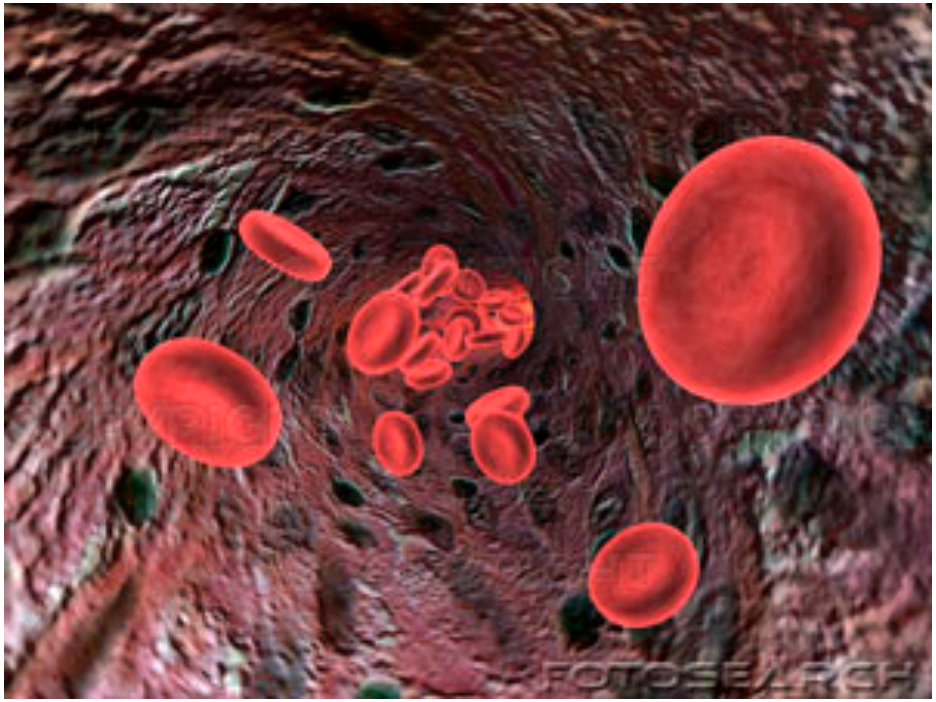

Incubated Osmotic Fragility
100
80
60
40
20
% Hemolysis
PATIENT
CONTROL
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
Saline Concentration (%)
Doses Mean ± 2S.D. (n
843686
0.67 GRN 3 ML
RBC FRAG

Case 7

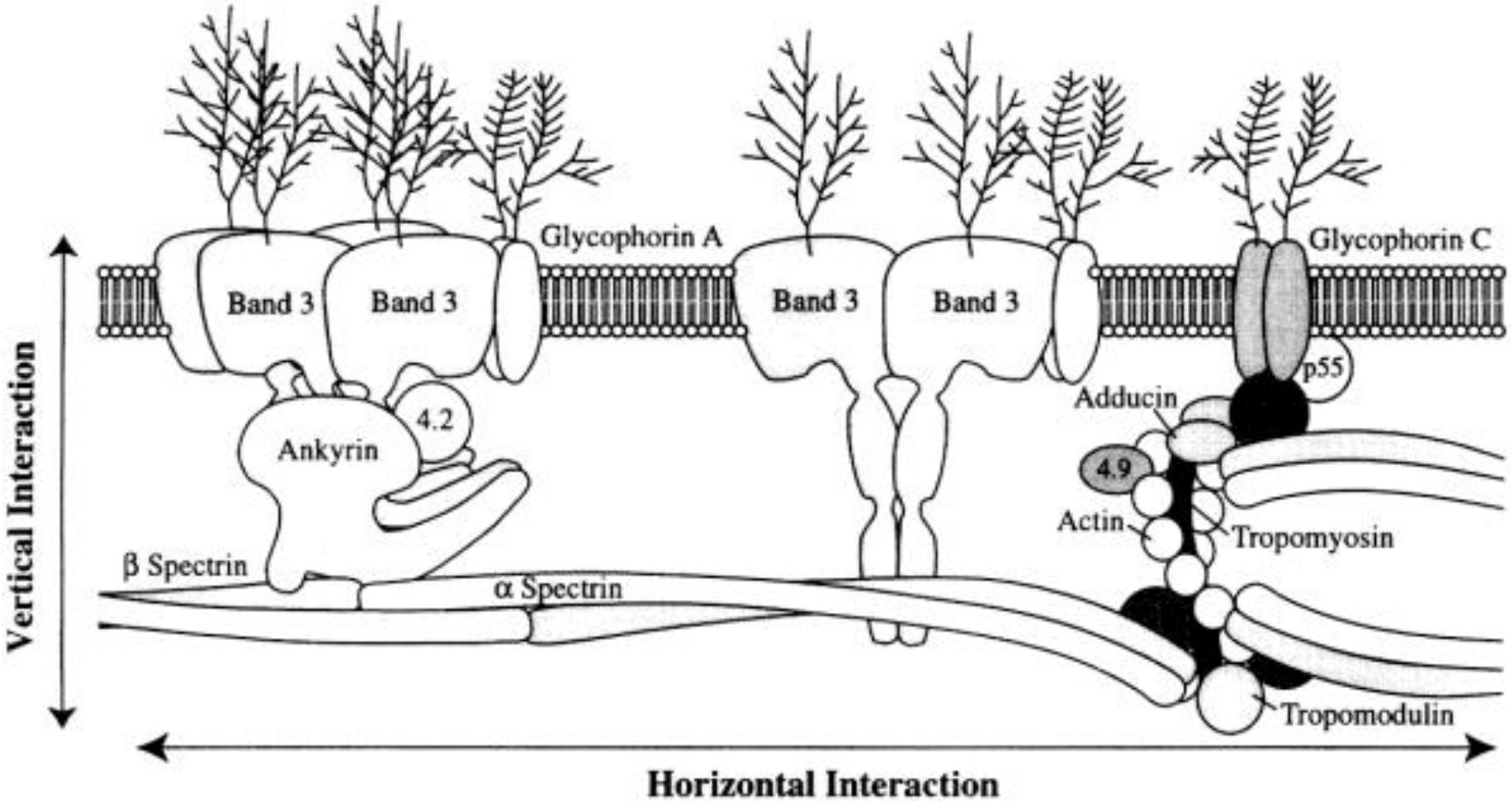
- How will you manage this patient?
  - Immediate splenectomy to prevent further hemolysis.
  - Start iron supplement.
  - Start folic acid and explain to her mother that she may need splenectomy at 5 years of age. (any hemolytic anemia we give folic acid) why wait till 5 years? till fully vaccinated!
  - Refer patient for bone marrow transplantation.

Red Cells

- Biconcave disc with diameter of 7.5 μm
- Efficient transport vehicle for oxygen exchange
- Shape also allows deformability as the erythrocytes move through capillaries
- Normal life span 120 days



Red Cell Membrane Structure



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Hereditary Spherocytosis

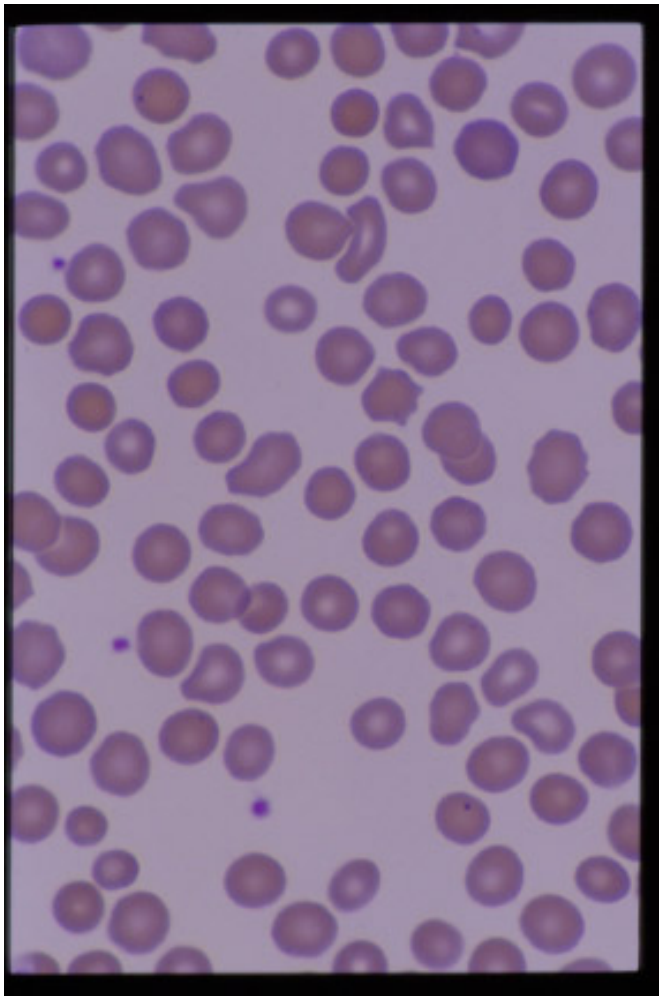
- Most common cause of non-immune hemolytic anemia
- Autosomal dominant transmission
  - 25-30% sporadic mutations
- Loss of membrane surface area relative to intracellular volume → spheres and decreased deformability
- Abnormalities of spectrin and/or ankyrin, and less commonly Protein 4.2 or Band 3

Clinical Manifestions of HS

- Hemolytic anemia
  - Degree of anemia varies with different mutations
  - 25% with compensated hemolysis and no anemia
- Pallor, fatigue
- Jaundice
  - Neonatal jaundice in first 24 hours of life
- Splenomegaly
- Gallstones (any hemolytic anemia)
- Positive family history
- May present with parvovirus associated aplasia

Laboratory Manifestations of HS

- Spherocytes on peripheral blood smear
- Reticulocytosis
- Increased incubated osmotic fragility
- Negative DAT
- Increased MCHC > 36% due to relative cellular dehydration
- Increased bilirubin, LDH



Case 8

- Abdullah is 12 y/o boy who was referred to KKUH because of acute onset of pallor, jaundice, dark urine. Patient is hemodynamically stable. CBC showed normochromic normocytic anemia (hgb 10 g/dl), high retics. LFT is otherwise unremarkable.

Case 8

- Which of the following investigations will most likely be abnormal? (think of autoimmune and g6pd)
  - DAT (or direct coombs test).
  - G6PD level
  - Haptoglobin level (finds to free hb, so if no hb it will be low)
  - Any of the above can be abnormal.

Case 8

- DAT:
  IgG negative
  Complement +ve (means igm mediated=intravascular hemolysis=cold autoimmune hemolytic anemia=less sever than warm ha (igg +))

-Warm will be active at normal body temperature, so always attacking! But the cold will be active at cold temperature, so easier to manage! Supportive management + blankets and thats it!)

So the patient has cold autoimmune hemolytic anemia.

-(Steroids not very effective in intravascular)
-Rule out sle and lymphoma when you see a pt with warm AIHA.

Extravascular vs Intravascular Hemolysis

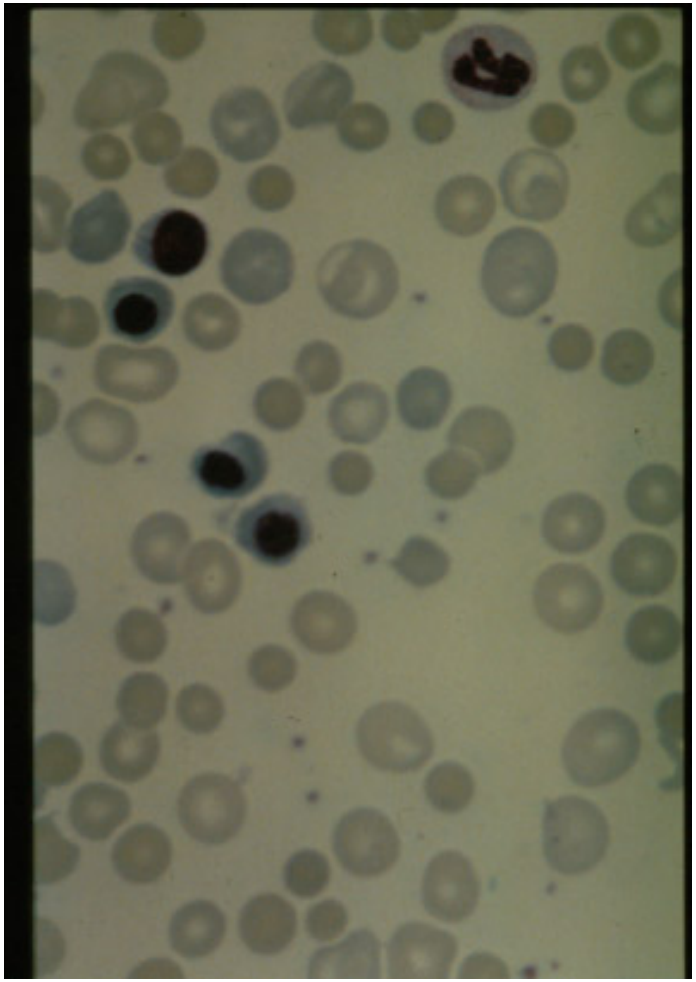
	Intravascular	Extravascular
Location of RBC Clearance	Inside vessels	In spleen and or liver (RES)
Antibody Type*	IgM (occ. IgG)	IgG
Mechanism of Hemolysis	Complement mediated/liver	Macrophages digest RBCs
Lab Findings	Hgbinemia Hgbinuria ↓ Haptoglobin	↑ Bilirubin ↑ LDH
Example	Cold Agglutinin Disease	Warm AIHA, HDN, HS

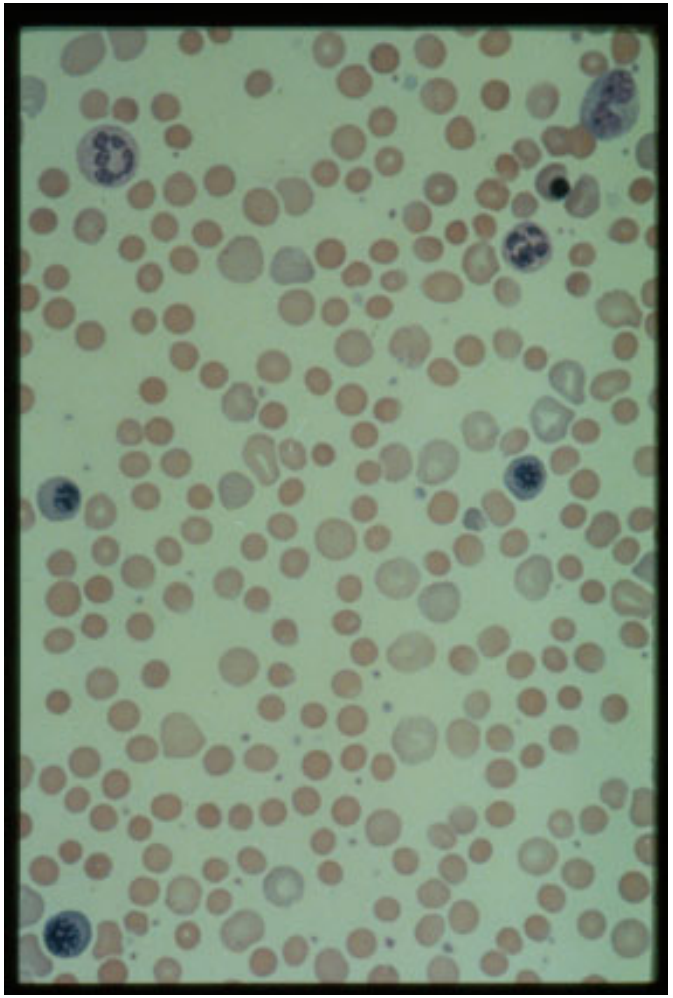
Warm Autoimmune Hemolytic Anemia

- May be idiopathic or associated with SLE, lymphoid malignancies, immunodeficiency
- Antibodies usually against “common” (Rh) antigens
- DAT positive (IgG ± C3)
- Treatment: Steroids, splenectomy, other immunosuppressive drugs, ± IVIG, transfusion with least incompatible blood

Autoimmune Hemolytic Anemia Peripheral Blood Smear

-You can see spherocytosis
-Big bluish cells: reticulocytes, because its hemolytic anemia, too many





Cold Agglutinin Disease

- IgM mediated
  - IgM-RBC immune complex forms at 4°C
  - Often react with I/i blood group system
- Can be associated with Mycoplasma, EBV
- DAT + for C3, thus intravascular lysis
- Treatment: Keep patient warm, supportive therapy, plasmapheresis for severe disease. Steroids, IVIG, and splenectomy not usually helpful since intravascular, complement mediated lysis.

Case 9

- Anas is 8 week-old male infant who is a former 30 wks premie and came to your clinic for routine check. He has been doing well and his exam was unremarkable. CBC showed Hgb 8 g/dl (normochromic and normocytic) and CBC otherwise unremarkable.

Case 9

- What will you do next?
  - Urgent PRBC transfusion.
  - Obtain iron studies and start iron Rx.
  - Start folic acid.
  - Reassure parents. (its normal in their age group)

Physiologic anemia

	Nadir of Hemoglobin Value	
	Age (wk)	Lower Limit of Normal
Term infant	12	9.5 gm/dl
Premature infant	6 - 8	7.0 gm/dl

(The smaller the premie, the earlier and lower the hemoglobin nadir)

-Still have to give iron supplementations in premature to reduce the risk

Case 10

- A six month old male infant was brought by his parents to ED because of increased irritability and swelling in both wrists and ankles for two days. CBC showed slight increase in total WBC count and Hb of 8 g/dl.

Case 10

- What is the most likely diagnosis?
  - Septic arthritis
  - Juvenile rheumatic arthritis
  - Sickle cell disease
  - Thalassemia
  - G6PD deficiency

Case 10

- What is the most important diagnostic investigation in SCA apart from molecular study?
  - Sickling test (will be positive even in trait thats why we don’t do it to differentiate)
  - Hemoglobin electrophoresis
  - Peripheral blood smear (same as sickling)

Case 10

- How can you differentiate between SA, SS, SB^+, and SB^0 on Hb electrophoresis?

  Hb A **Hb S** **HbF** **HbA_2**

  -Most sever is ss and sb0

Type	Hemoglobin HPLC					Severity
	HbA	HbA2	HbF	HbS	Other	
HbSS (sickle cell anemia)	0	<3.6	<10	90-95		Severe
HbSS-$\propto$ thalassemia	0	<3.6	<10	90-95	Low MCV	Severe
HbS-β^0 thalassemia	0	≥3.6	<10	90-95		Severe
HbS-β^+ thalassemia	5-30	≥3.6	<10	60-90		Moderate
HbSC disease	0	<3.6	<3	45-50	HbC 45-50	Moderate
HbS-O_{Arab}	0	<3.6	<3	45-50	Hb O_{Arab} 45-50	Severe
HbS-HPFH	0	<3.6	20-40	60-80		Mild

Phenotype of SCD in Saudi Arabia

SCD Phenotype	African American	Saudi SW	Saudi Eastern (Children)	Saudi Eastern (Adult)
Vaso-occlusive crisis	61%	70-100%	7%	96%
Osteonecrosis	10-21%	14-23%	4%	18%
Acute Chest syndrome	38-50%	10-40%	30%	47%
Splenic Sequestration	10-20%	7-23%	na	15%
Gall stones	28%	34%	14%	66%
Persistent splenomegaly	Majority had auto-splenectomy	11-30%	na	71%
Stroke	11%	2-10%	1%	6%
Priapism	13-35%	3%	1%	17%
Leg ulcers	10%	None	None	None
Serious infections	12%	11%	4%	17%

Majority of cases in shaqiah! around 40000 cases

Perrine et al. Ann Intern Med. 1978, Acquaye et al BJH 1985, Padmos et al. BJH 1991, Powars et al Medicine 2005, Alsultan et al. JPHO 2012, Alsultan et al. BJH 2014, others