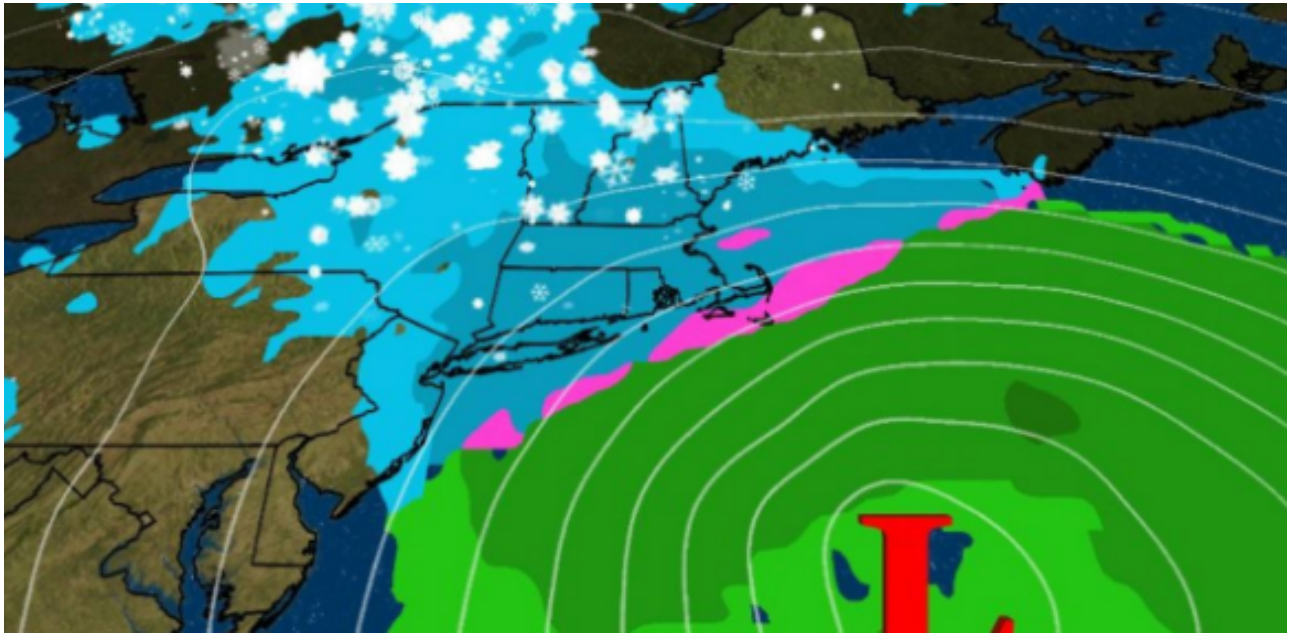
Heme Questions and Derivatives for the USMLE Step One Exam



Winter Storm Skylar Edition

Howard J. Sachs, MD
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Patient presents for routine preoperative evaluation prior to cataract sugery. In reviewing her data, you note the following:

Test	Result
White Blood Cell Count	7.2 th/mm3
Red Blood Cell Count	**5.86 mil/mm3**
Hemoglobin	**11.9 g/dL**
Hematocit	38.5 %
MCV	**65.7 fl**
MCH	**20.3 pg**
MCHC	**30.8 g/dL**
RDW	**19.9 %**
Platelet count	420 th/mm3

The patient states she's always been anemic.

What would expect to find on her blood smear?

1. Target cells
2. Red cells with basophilic remnant
3. Crescent shaped cells
4. Red cells with cytoplasmic inclusions
5. Microcytic cells without central pallor

MCHC, normal 33-36 g/dL

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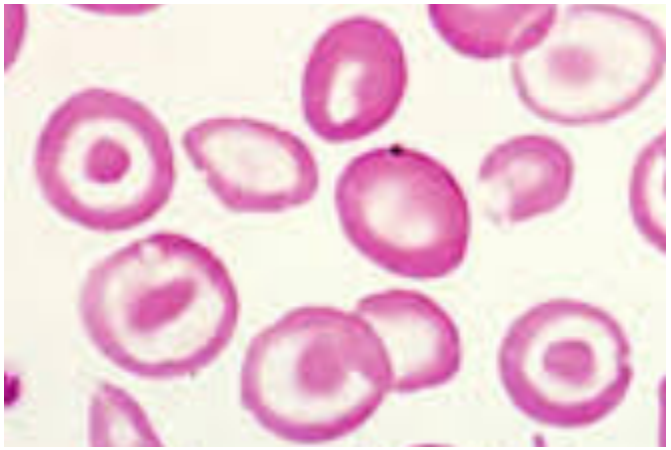

The patient states she's always been anemic. Smear shown.

A hemoglobin electrophoresis is obtained. Result: normal pattern.

Which of the following diagnoses are most likely?

1. α-thalassemia
2. β-thalassemia
3. Sickle cell trait
4. Iron deficency anemia

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1. Target cells: membrane in excess of hemoglobin (defective globin)
2. Red cells with basophilic remnant: Howell-Jolly Body (asplenia)
3. Crescent shaped cells: SCD
4. Red cells with cytoplasmic inclusions: Heinz bodies → Bite Cells
5. Microcytic cells without central pallor: Spherocytes

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1. Target cells: membrane in excess of hemoglobin (defective globin)

Differential Diagnosis of Microcytosis with Hypochromic Cells (low MCHC):

- Iron Deficiency
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- Longstanding nature and failure to mention a condition associated with chronic blood loss. Further, that MCV is very low with only minor anemia.
- Devoid of inflammatory signs or symptoms; Very low MCV.
- Thalassemia most likely dx

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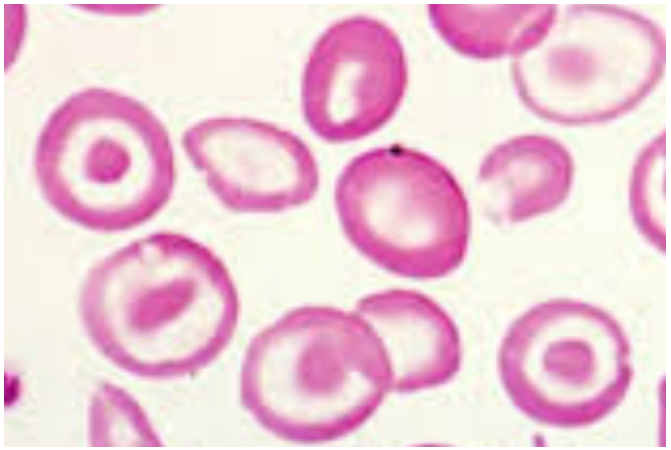

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2. β-thalassemia: defective $\beta \rightarrow$ other Hgb (A2-δ; F - γ)
3. Sickle cell trait: Hgb S (abnormal electrophoresis)
4. Iron deficency anemia: iron studies, not phoresis.

$\alpha 2\beta 2$
HbA

$\alpha 2\delta 2$
HbA2

$\alpha 2\gamma 2$
HbF

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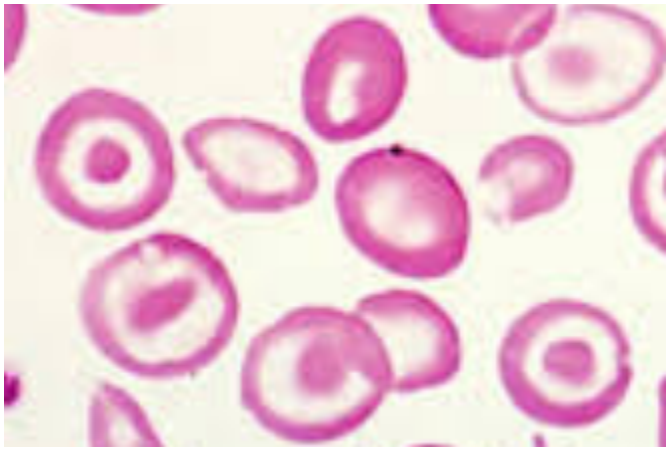

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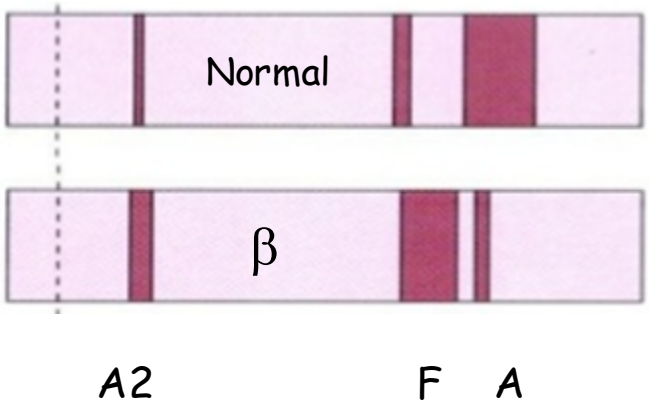
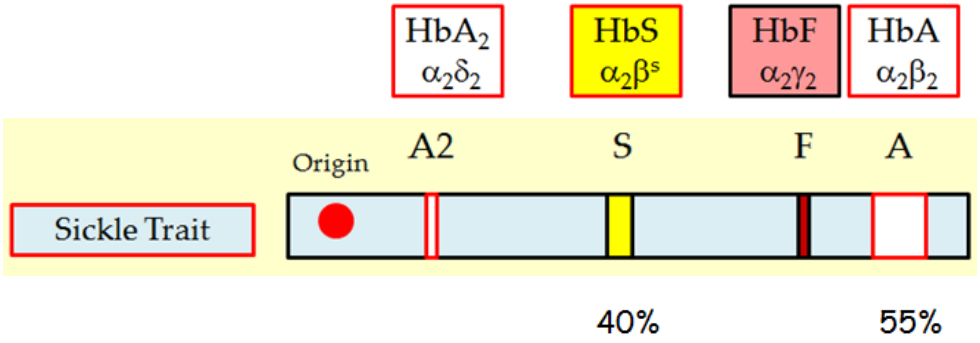
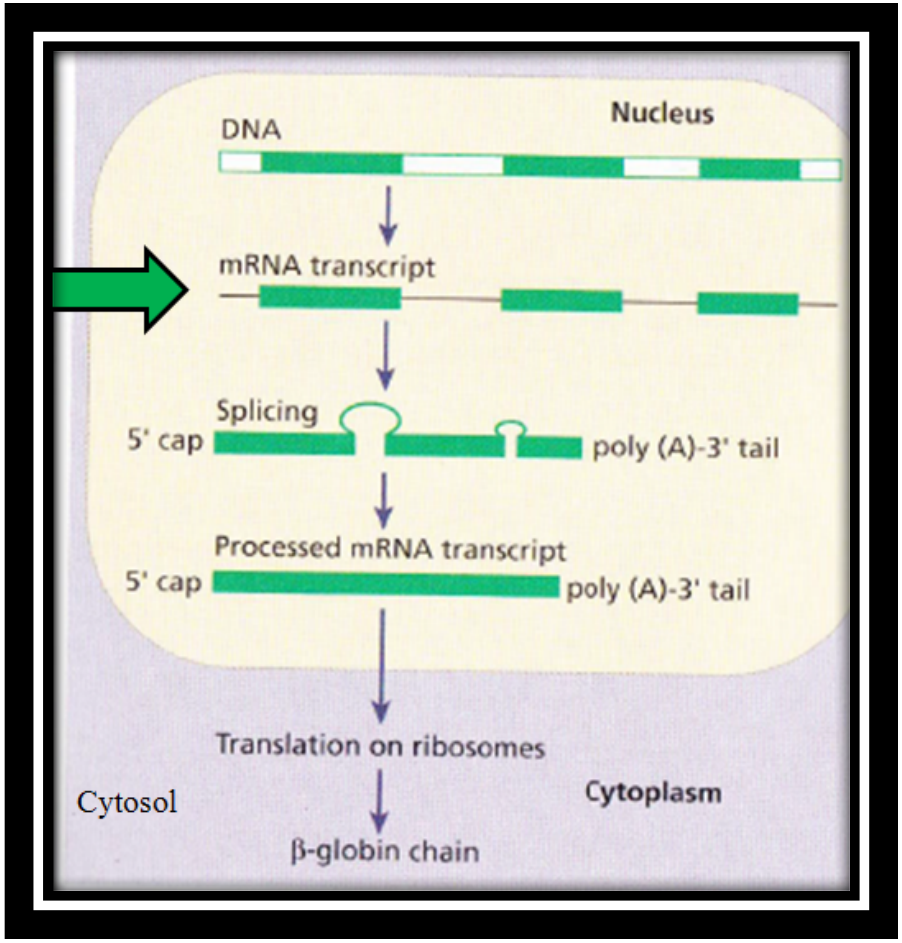


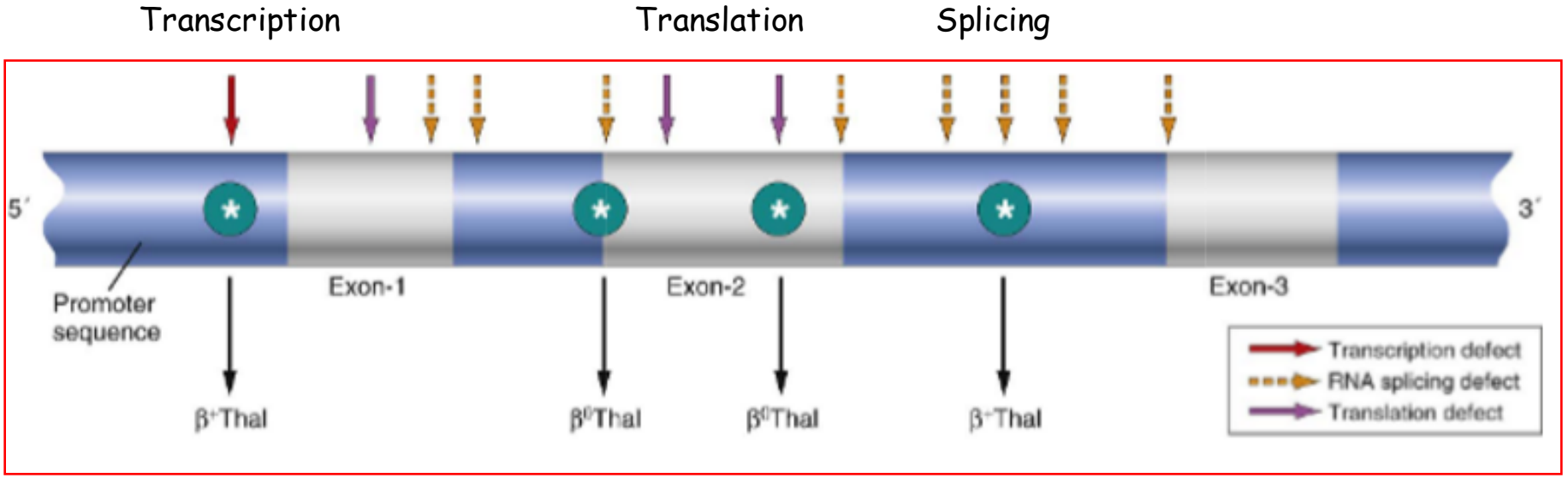


1. α-thalassemia: imbalance with normal β-chains
2. β-thalassemia: defective β → other Hgb (A2-δ; F - γ)

β-thalassemia: Mutation with abnormal mRNA → splicing, transcription and translation



β-Thalassemia = Point Mutatation



Whereas α-thalassemia is a disease of gene deletions, β-thalassemia is a disease of gene mutations (mRNA splicing, transcription, translation).

Point: 100's of mutations lead to varying degrees of β-chain synthesis.
Clinical manifestations of β-thalassemia
depend on degree of residual chain synthesis.

Implication: imbalance between α- and β-chain synthesis

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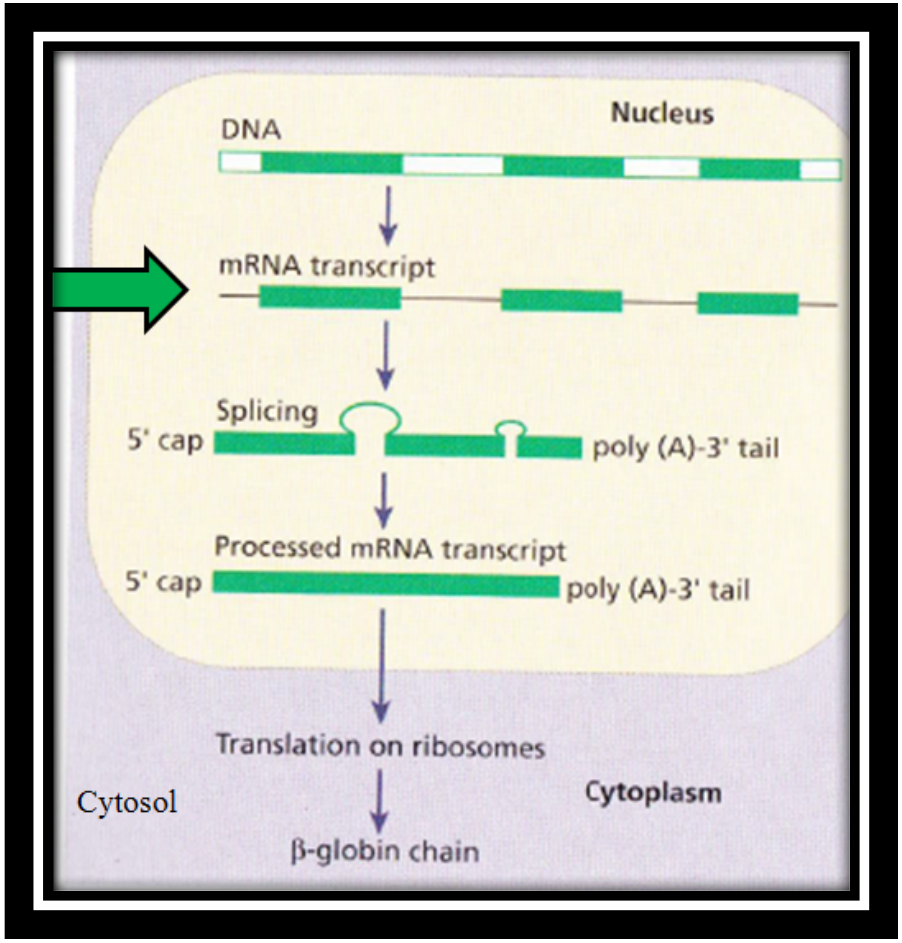
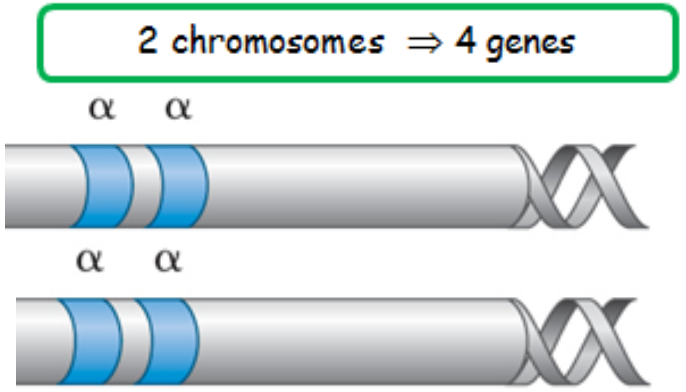
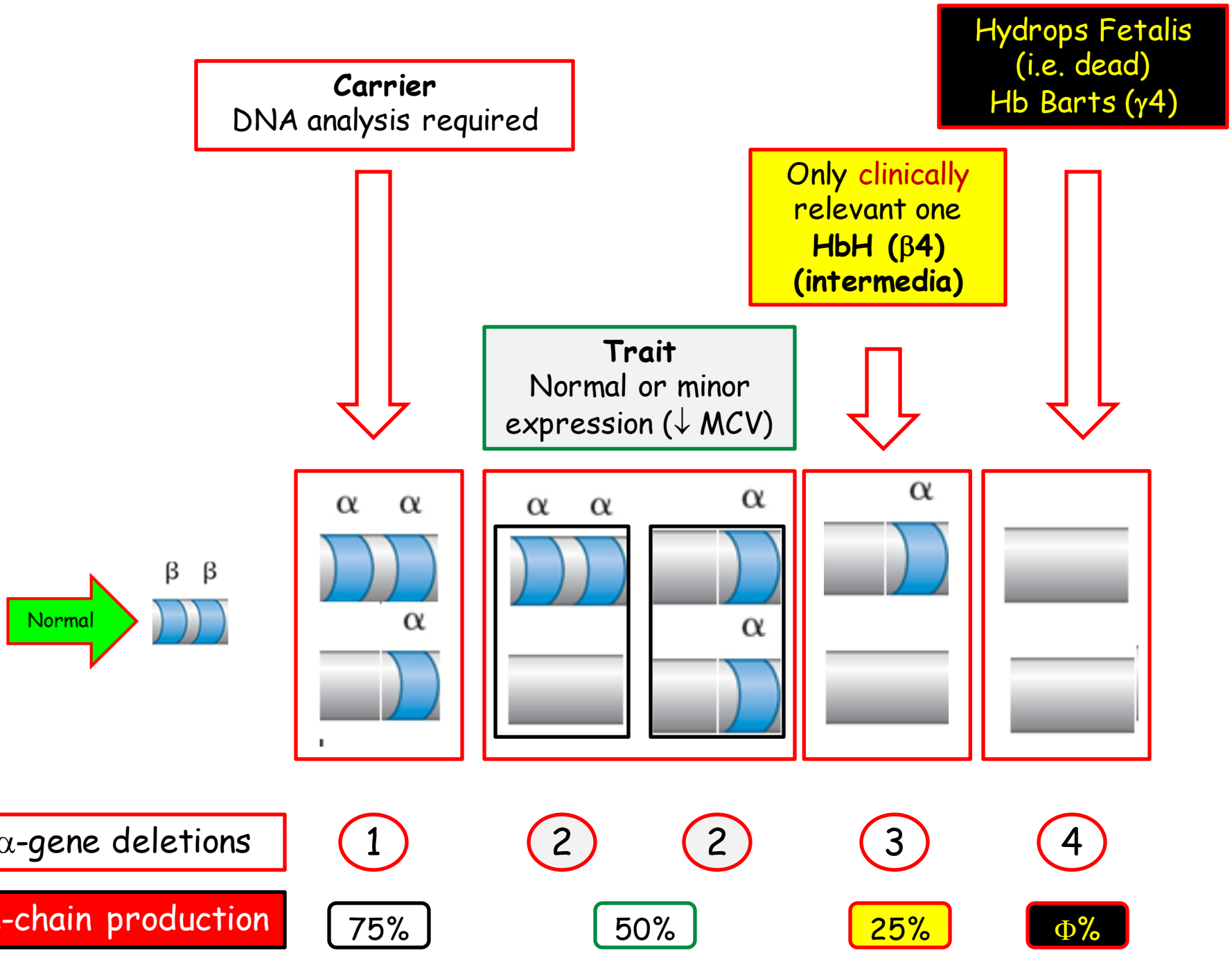


α-thalassemia: Gene Deletion
Less α-chains but normal β-chains (↓ Hgb A)




Hydrops Fetalis
(i.e. dead)
Hb Barts (γ4)
Carrier
DNA analysis required
Only clinically
relevant one
HbH (β4)
(intermedia)
Trait
Normal or minor
expression (↓ MCV)
Normal
β β
α α
α α
α α
α
α
α
α-gene deletions
1
2
2
3
4
α-chain production
75%
50%
25%
Φ%

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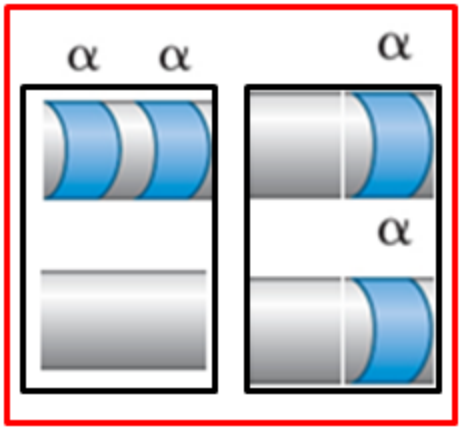

Microcytosis
Normal Hemoglobin Electrophoresis

Compatible with α-thalassemia trait

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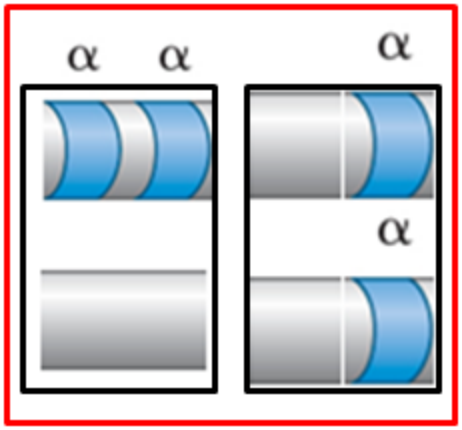

Microcytosis
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	Ref Range & Units	
Ferritin	11.0 - 306.0 ng/mL	22.0

	Ref Range & Units	
Iron Saturation	20 - 50 %	36
Iron	28 - 170 ug/dL	121
Transferrin	202 - 336 mg/dL	271
Total Iron Binding Capacity	255 - 450 ug/dL	339

65 y.o. alcoholic from Morocco presents to ER with episode of midepigastric pain. She reports a 6 month history of diarrhea. PE: 110/80; HR 108. Cor: S1S2 normal, no JVD or murmur. Abd: mild tenderness; Neuro: ataxic gait. Ext: 1+ bilateral edema
Data: WBC 6.4; HCT 32%. Smear below.
Which of the following best explains the basis of her anemia?

NA	135 - 145 mmol/L	138
K	3.5 - 5.3 mmol/L	3.9
Cl	97 - 110 mmol/L	100
CO2	24 - 32 mmol/L	27
BUN	7 - 23 mg/dL	13
Creatinine	0.60 - 1.30 mg/dL	0.95
Glucose	70 - 99 mg/dL	94
Calcium	8.7 - 10.7 mg/dL	9.5

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2. Abnormality of membrane cytoskeleton
3. Point mutation in the β-globulin chain
4. Portal hypertension
5. Failure of DNA synthesis
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Erythropoietin	2.6 - 18.5 mIU/mL	147.5 (H)

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Data >> PE >> Verbiage

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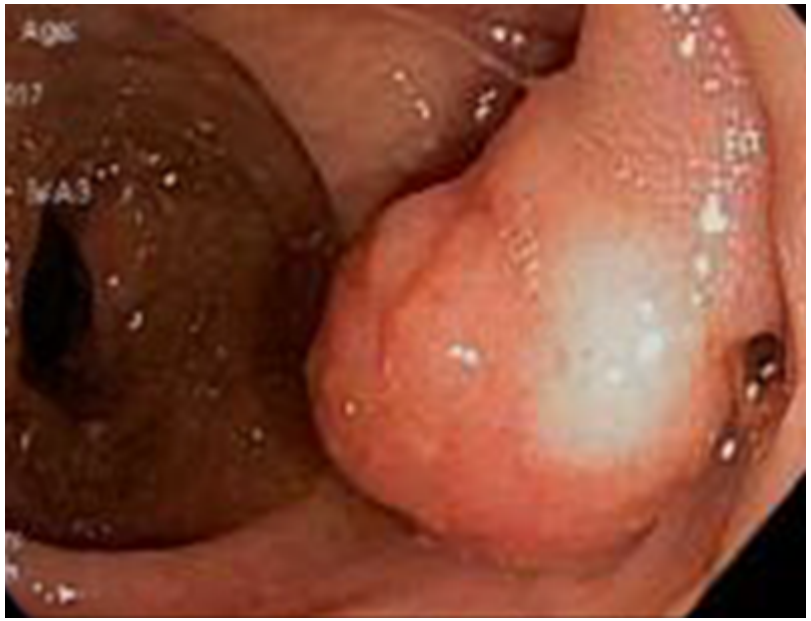

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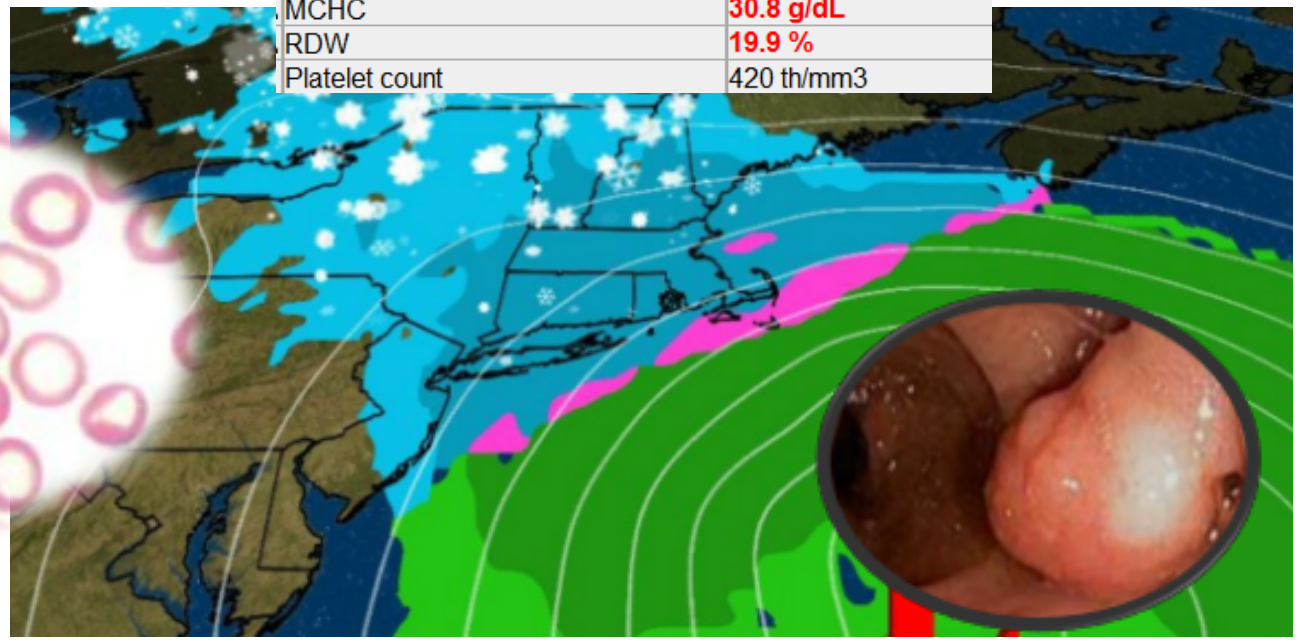

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