Pitfalls in the premarital testing for thalassaemia

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Case 1

Husband and Wife are not related

Husband	**Wife**
• Hb 13gm • MCV 82 • RDW 17 • MCH 31	Hb 10.5gm MCV 63.5 RDW 13 MCH 23

Case 1

Husband and Wife are not related

Husband	Wife	Baby
• Hb 13gm • MCV 82 • RDW 17 • MCH 31	Hb 10.5gm MCV 63.5 RDW 13 MCH 23	• Hb 6.5gm • MCV 72.5 • RDW 19 • MCH 23

Case 1

Husband and Wife are not related

Husband	Wife	Baby
• Hb 13gm • MCV 82 • RDW 17 • MCH 31	Hb 10.5gm MCV 63.5 RDW 13 MCH 23	• Hb 6.5gm • MCV 72.5 • RDW 19 • MCH 23 • **A 0%** • **A2 3.0%** • **F+S 97%**

Case 1

Husband and Wife are not related

Husband	Wife	Baby
• Hb 13gm • MCV 82 • RDW 17 • MCH 31 • **A2 2.3%** • **S 36%**	Hb 10.5gm MCV 63.5 RDW 13 MCH 23 **A2 4.3%**	• Hb 6.5gm • MCV 72.5 • RDW 19 • MCH 23 • **A 0%** • **A2 3.0%** • **F+S 97%**

Diagnosis

Sickle thalassemia

Hb S/B

Case 2

Husband and Wife are first degree relatives

Husband	**Wife**	**Baby** 6 month
• Hb 13gm • MCV 63 • RDW 13 • MCH 23 • A2 2.8% • 2.9% • 3,0%	Hb 10.5gm MCV 63.5 RDW 13 MCH 23 A2 4.8%	• Hb 5.5gm • MCV 85.5 • RDW 19 • MCH 23 • A2 3.0%

Diagnosis

Alpha thalassemia silent

with

beta thalassemia minor

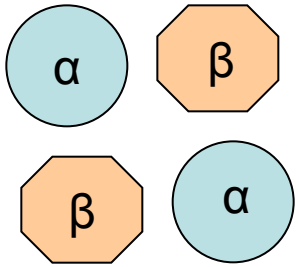
Haemoglobin

- ***Haem***
  - Iron
  - portoporphyrins
- ***Globin***
  - Two alpha with either

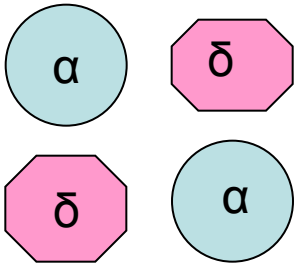
    +
  - Two beta (Hb A)
  - Two gamma (Hb F)
  - Or two delta (Hb A2)

Gene on chr 16

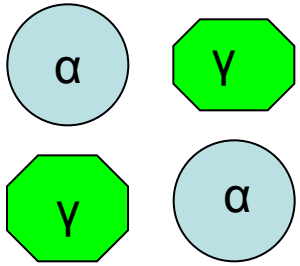
Gene on chr 11



2α 2β ⟶ HbA



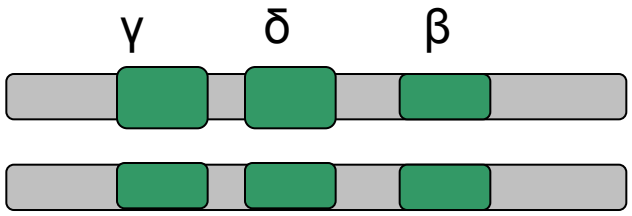
2α 2 δ ⟶ HbA2



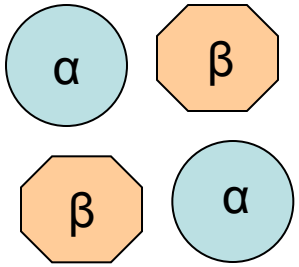
2α 2 γ ⟶ HbF

Beta gene defects

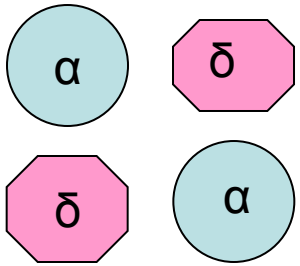
Chromosome 11



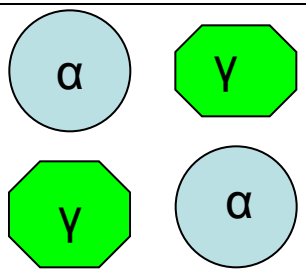
Normal



HbA 95.5 – 99%



HbA2 < 3.5%



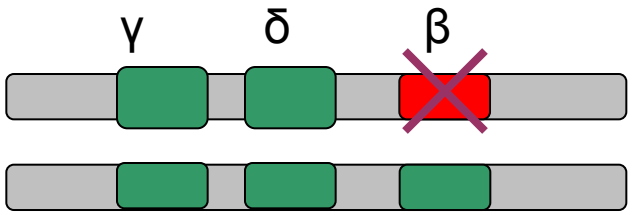
HbF < 1% (after one year age)

Types of defects on β gene

- Decrease OR absent production
  - Thalassemia
    - β+ decrease production
    - β○ Absent production
- Abnormal production
  - Sickle cell disease and others
    - Hb S, C^{H}, C ,E, D, J, O, I and others

Beta Thalassemia minor

Chromosome 11

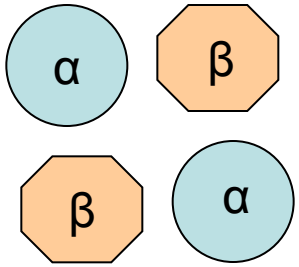


Beta thalassaemia minor

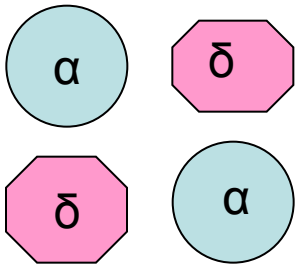
β + decreased production

or

β○ absent production

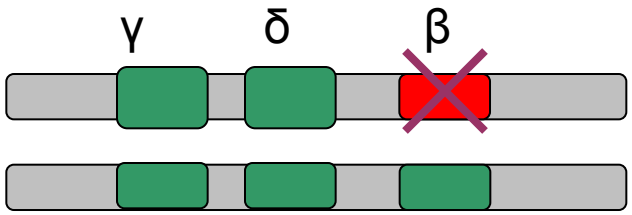


HbA



HbA2 > 3.5%

Chromosome 11

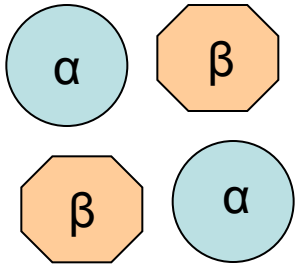


Beta thalassaemia minor

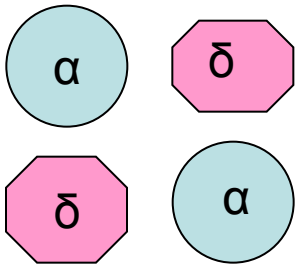
β + decreased production

or

β○ absent production



HbA



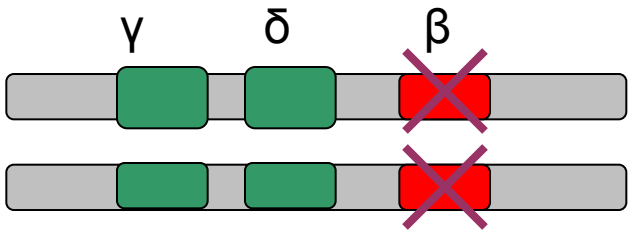
HbA2 > 3.5%

Features:

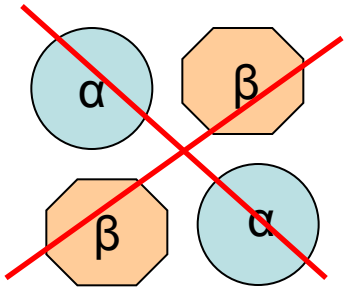
- Asymptomatic
- Mild anaemia
- Microcytosis
- Normal RDW
- Low MCH
- Normal MCHC
- At least one parent has microcytosis

Beta thalassemia major

Chromosome 11

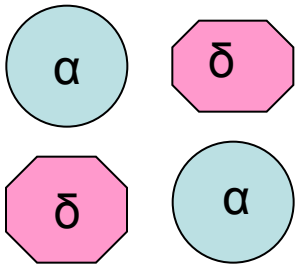


Beta thalassaemia major

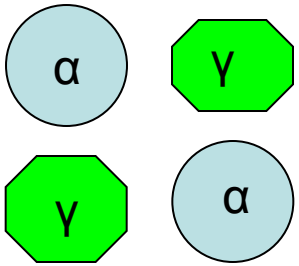


HbA absent or markedly reduced

β○ β○	Hb A = 0
β+ β○	Hb A ≈ 5%
β+ β+	Hb A ≈ 10%

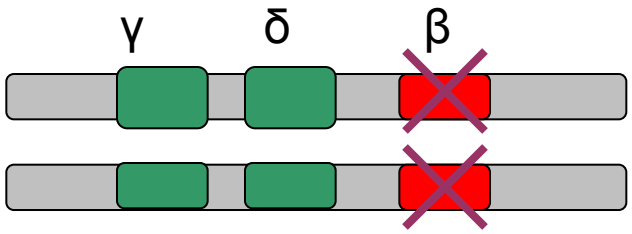


HbA2 variable amount

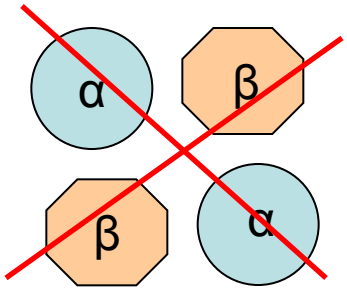


HbF up to 100%

Chromosome 11



Beta thalassaemia major



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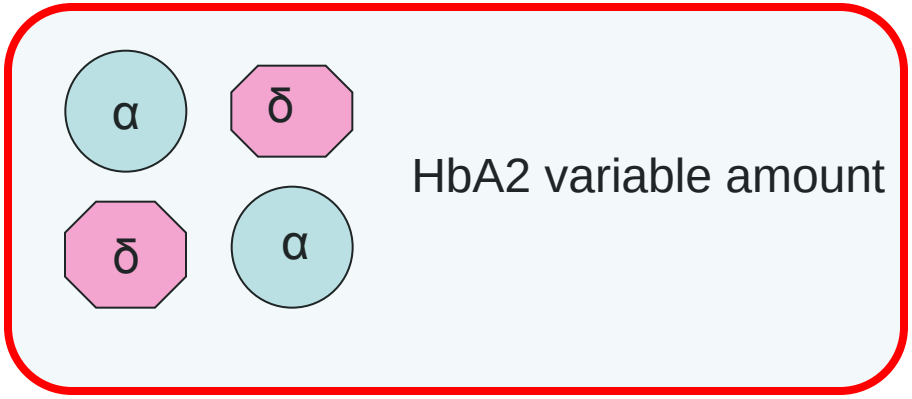
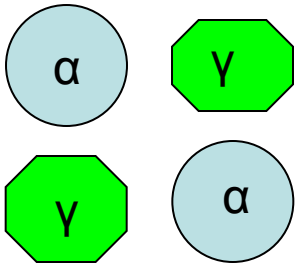


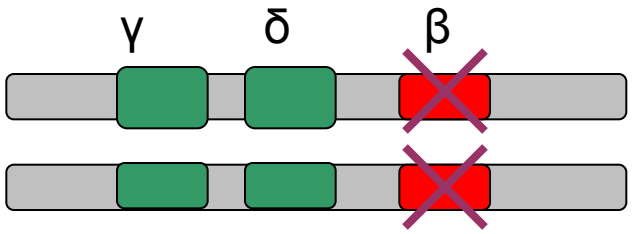
HbA2 variable amount



HbF up to 100%

Beta thalassaemia major

Chromosome 11



β○ β○	Hb A = 0
β+ β○	Hb A ≈ 5%
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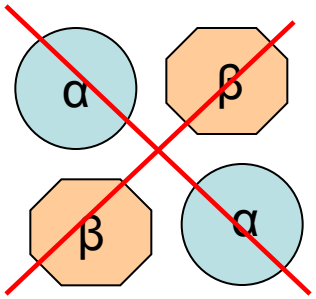
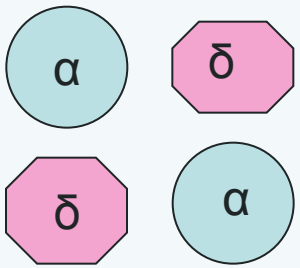


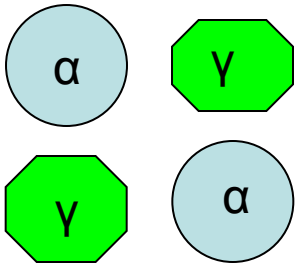
HbA absent or markedly reduced

Features:

- Transfusion dependant
- Both parents must have beta thal minor-
- Both have low MCV



HbA2 variable amount



HbF up to 100%

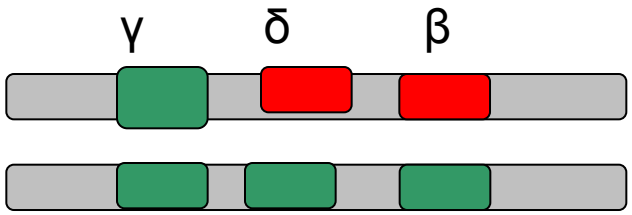
Beta thalassemia intermedia

Beta thalassemia intermedia

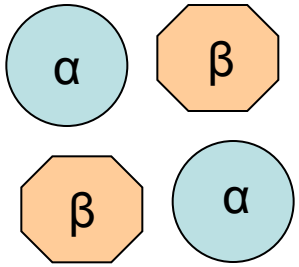
- Same genetics as in thal major
- But milder symptoms and less transfusion requirement
- Usually benefit from splenectomy
- Causes may include:
  - β+ β+
  - HPHF
  - Concomitant alpha thalassemia defect
  - Others

δ β Thalassemia

Chromosome 11



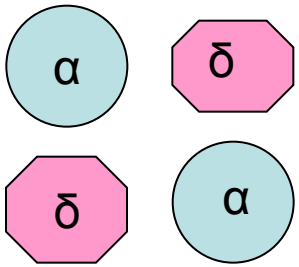
δ β Thalassemia



HbA →

Features:

- Mild/moderate anaemia
- Microcytosis
- Splenomegaly

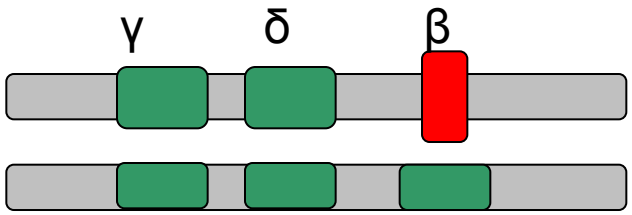


HbA2 < 3.5% →

Abnormal chain production

Sickle and others

Chromosome 11

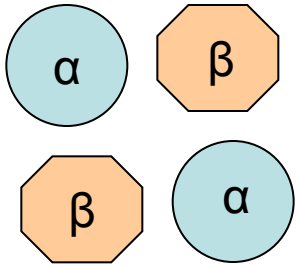


Abnormal gene

Abnormal chain production

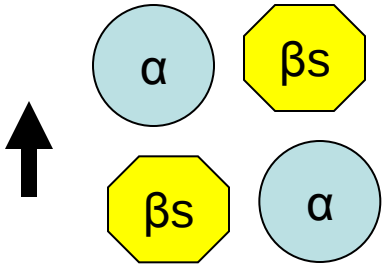
S, C^H , C ,E, D, J, O, I

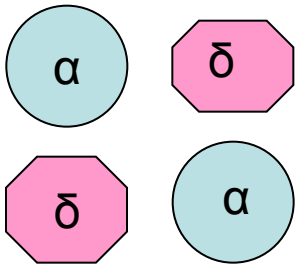
MCV might be normal



HbA

Hb **S , C ,E, D, J, O, I**





HbA2 < 3.5%

Premarital counseling

β+	β+
β○	β○
δ β	δ β
S	S
C^H	C^H
C	C
E	E
D	D
J	J
O	O
I	I

Alpha thalassemia

Haemoglobin

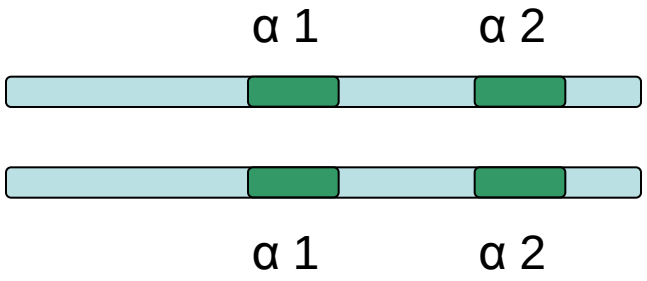
- ***Haem***
  - Iron
  - portoporphyrins
- ***Globin***
  - Two alpha with either
  - Two beta (Hb A)
  - Two gamma (Hb F)
  - Or two delta (Hb A2)

Gene on chr 16

Gene on chr 11

Chromosome 16

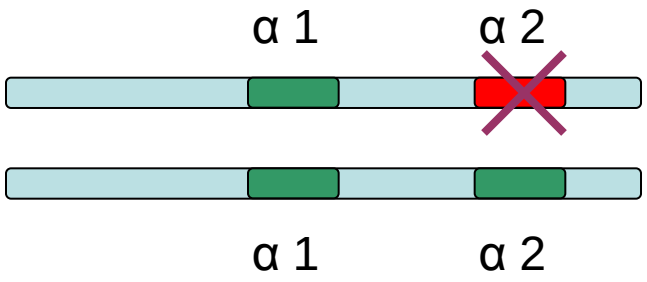
αα, αα



Normal

Chromosome 16

α-, αα



Alph Thalassaemia silent

•Around 15% of Palestinians

Example

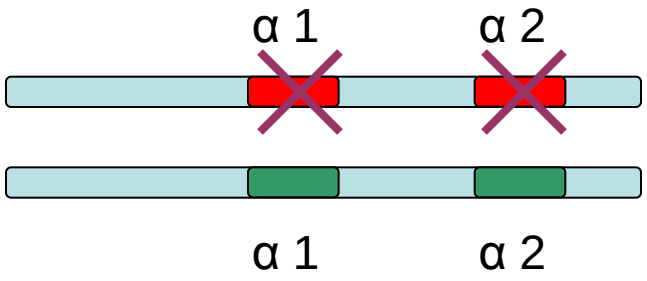
Hb 13 grm

MCV 81

RDW 14.5

Normal Hb electrophoresis

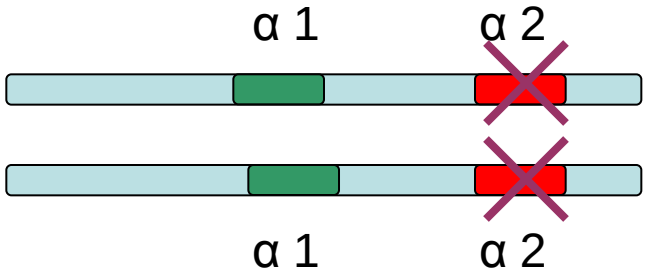
Chromosome 16



Alpha Thalassaemia trait

- -, αα

OR



Example

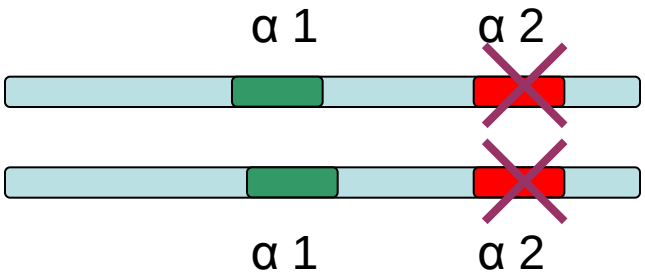
Hb 11 grm

MCV 70

RDW 18

α-, α-

Normal Hb electrophoresis



α-, α-

Alpha Thalassaemia trait

- Fairly common in Palestine
- Usually both parents have normal MCV (Silent)

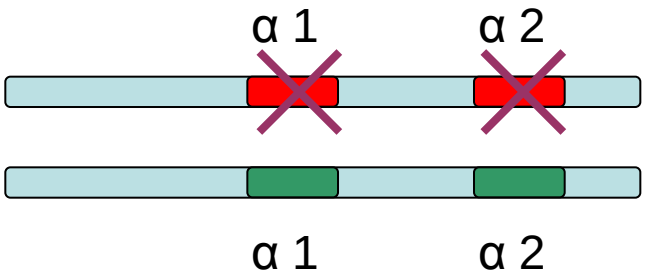
Example

Hb 11 grm

MCV 70

RDW 18

Normal Hb electrophoresis



- -, αα

Alpha Thalassaemia trait

- Very rare in Palestine
- One parent must have low MCV

Example

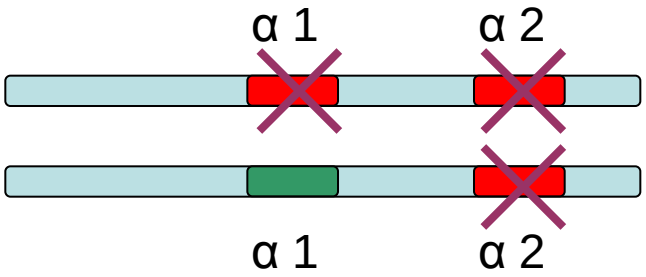
Hb 11 grm

MCV 70

RDW 18

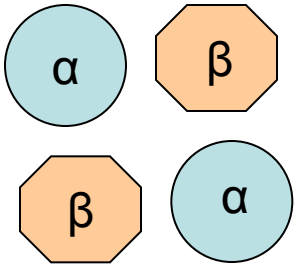
Normal Hb electrophoresis

Chromosome 16

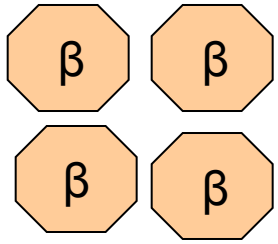


- -, α-

Alpha Thalassaemia – HBH disease

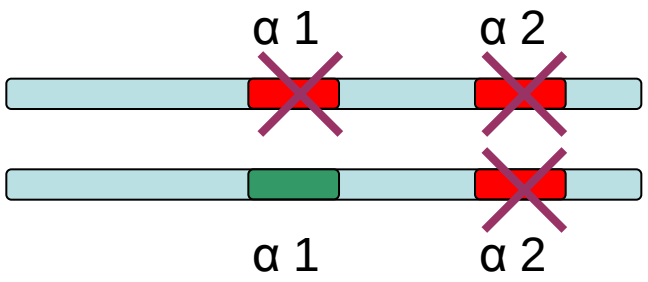


HbA



HbH

Chromosome 16

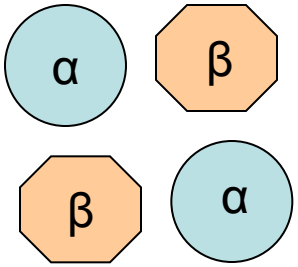


- -, α-

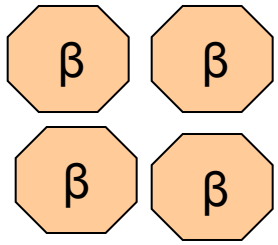
Alpha Thalassaemia – HBH disease

Features:

- Splenomegaly
- One parent has normal MCV and one parent has low MCV



HbA



HbH

Example

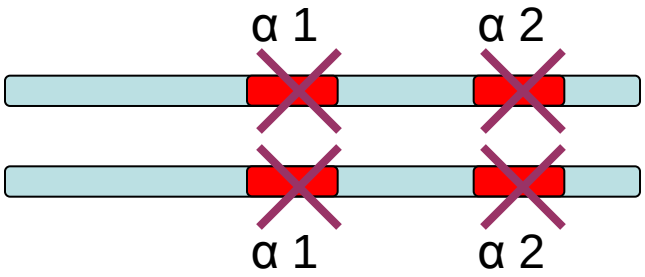
Hb 7.5grm

MCV 65

RDW 21

Chromosome 16

- -, - -



Alph Thalassaemia – HB Barts disease

Example

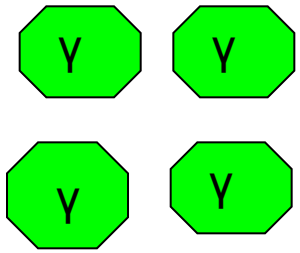
Hb 1-2grm

MCV --

RDW --

Incompatible with life

Death in utero due to hydrops fetalis



Hb Barts

Causes of Normal Hb A2 in
a patient with thalassaemic picture

- Lab error / technique
- Concomitant iron deficiency
- Concomitant alpha thalassaemia
- Alpha thalassaemia minor
- Delta Beta thalassaemia
- Hb Lepore
- Extreme love of couples ومن الحب ما قتل

Recommendations

- Study of all new cases of thalassemia major since the introduction of the premarital testing
- CBC on both couples(Not one as it is now) and proceed for Hb electrophoresis if one has low MCV (Needs cost analysis)

THANK YOU