Diagnostic difficulties in Thalassaemia

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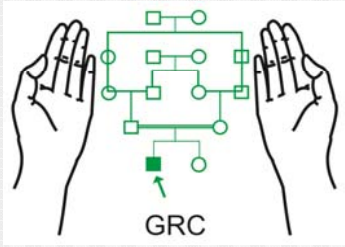
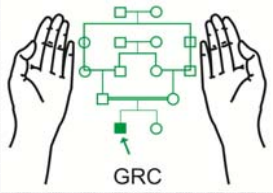




Genetic Haemoglobin Disorders

Thalassaemia Syndromes

α-Thalassaemias:

- α^{o}-Thalassaemias
- α^{+}-Thalassaemias
  - Deletion
  - Non-deletion
- With α-chain Hb variants
- With β-chain Hb variants
- With β-Thalassaemia

β-Thalassaemias:

- β^{o}-Thalassaemias
- β^{+}-Thalassaemias
- With β-chain Hb variants
- With α-chain Hb variants
- With α-Thalassaemia

δβ-Thalassaemia:

- $(\delta\beta)^{o}$-Thalassaemia
- $(^{A}\gamma\delta\beta)^{o}$-Thalassaemia
- $(\varepsilon\gamma\delta\beta)^{o}$-Thalassaemia
- δ-Thalassaemia
- γ-Thalassaemia

Hereditary Persistence of Fetal Haemoglobin (HPFH):

- Deletion
  - $(\delta\beta)^{o}$-HPFH
- Non-deletion
  - Linked to β-globin gene cluster
  - Unlinked to β-globin gene cluster

Structural Hb Variants

Sickling Disorders:

- With β-Thalassaemia
- With α-chain Hb variants
- With β-chain Hb variants

Other Structural Variants (Hb-E, C, D etc.):

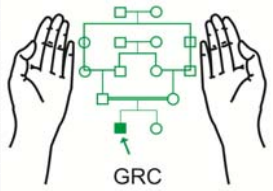
- With β-Thalassaemia
- With α-Thalassaemia

Unstable Haemoglobins:

M Haemoglobins:

Altered Affinity Haemoglobins:

Investigations for a Genetic Haemoglobin Disorder



History and Examination

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Complete Blood Counts

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Haemoglobin Electrophoresis

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Quantitative Estimation of Hb Fractions

↓

Other related Investigations

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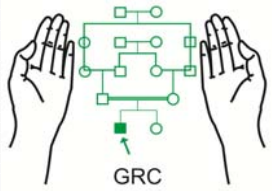
PCR



β-Thalassaemia Trait

- Typical form
- Silent β-thalassaemia trait
- Interaction with α-thalassaemia
- Interaction with structural Hb variants

Complete Blood Counts

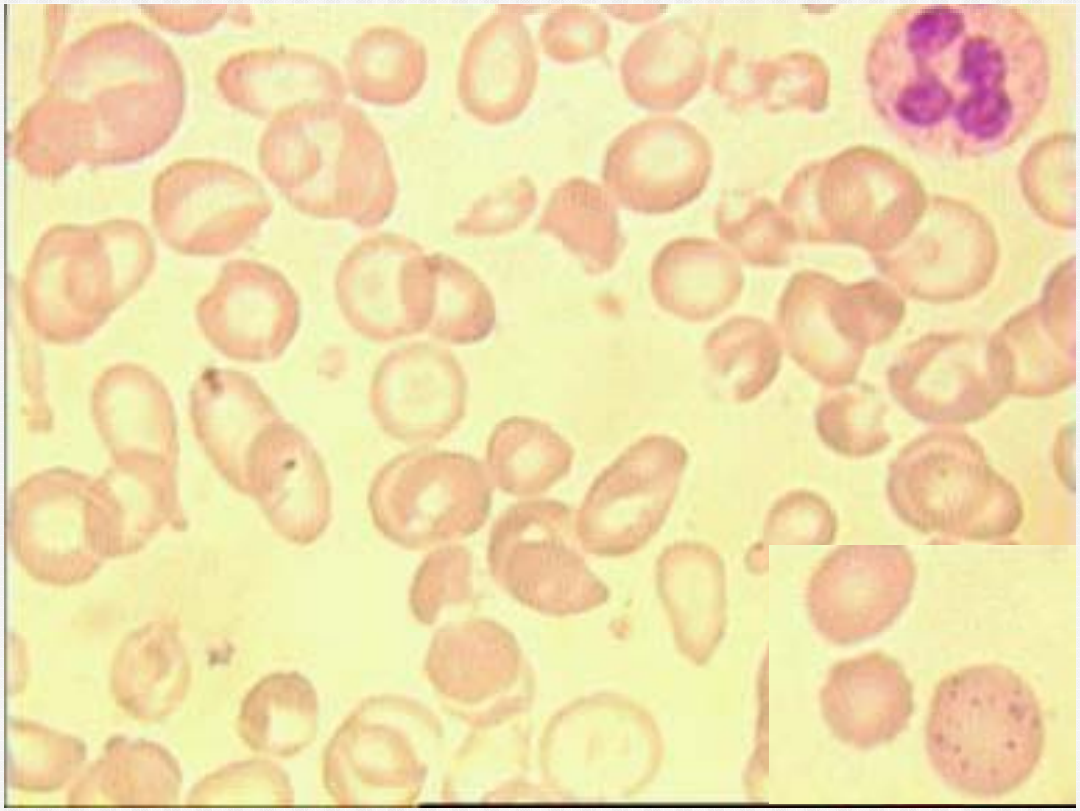
No. 28
DATE: 22/ 3/95
MODE: WHOLE BLOOD

WBC		6.7	$\times 10^3/\mu\ell$
RBC		5.45	$\times 10^6/\mu\ell$
HGB	-	10.5	g/dℓ
HCT	-	33.4	%
MCV	-	61.3	fℓ
MCH	-	19.3	pg
MCHC		31.4	g/dℓ
PLT		318	$\times 10^3/\mu\ell$

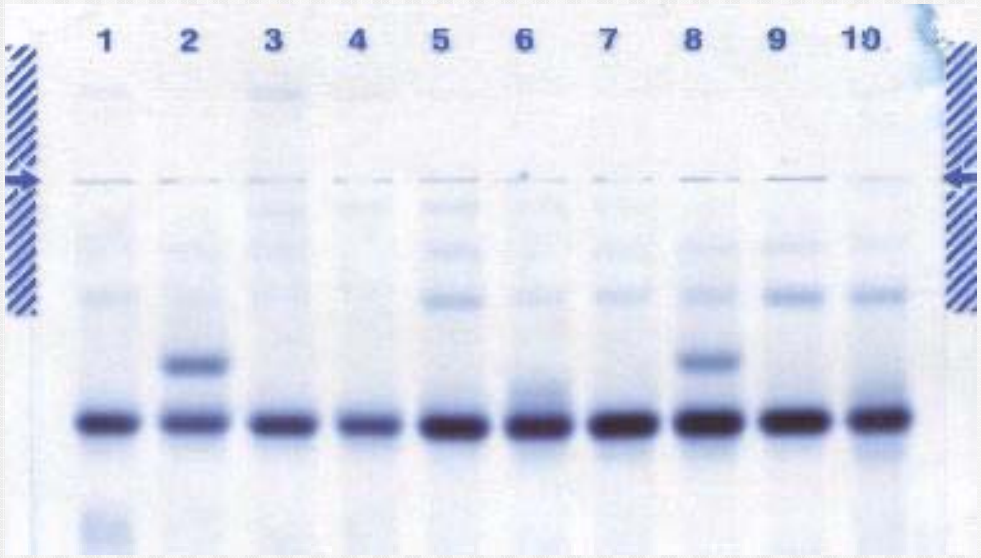
No. 32
DATE: 22/ 3/95
MODE: WHOLE BLOOD

WBC		8.9	$\times 10^3/\mu\ell$
RBC		4.86	$\times 10^6/\mu\ell$
HGB		14.4	g/dℓ
HCT		41.8	%
MCV		86.0	fℓ
MCH		29.6	pg
MCHC		34.4	g/dℓ
PLT		271	$\times 10^3/\mu\ell$

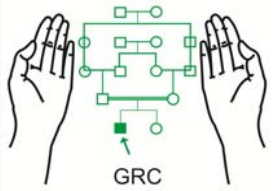
Peripheral Blood Film



Typical β-thalassaemia Trait



Hb-A2: ≥ 3.5%

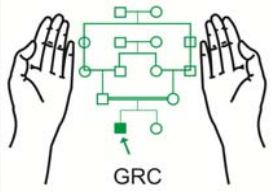


β-Thalassaemia Trait (atypical forms)

- Silent β-thalassaemia trait
- Interaction with α-thalassaemia
- Interaction with structural Hb variants

β-Thalassaemia Major

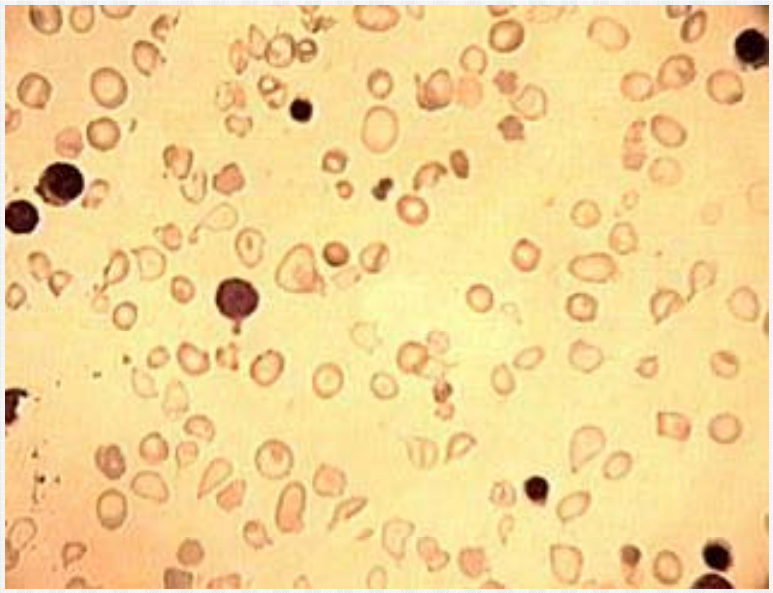
- Normal at birth
- Increasing pallor after 3 months of age
- Repeated infections



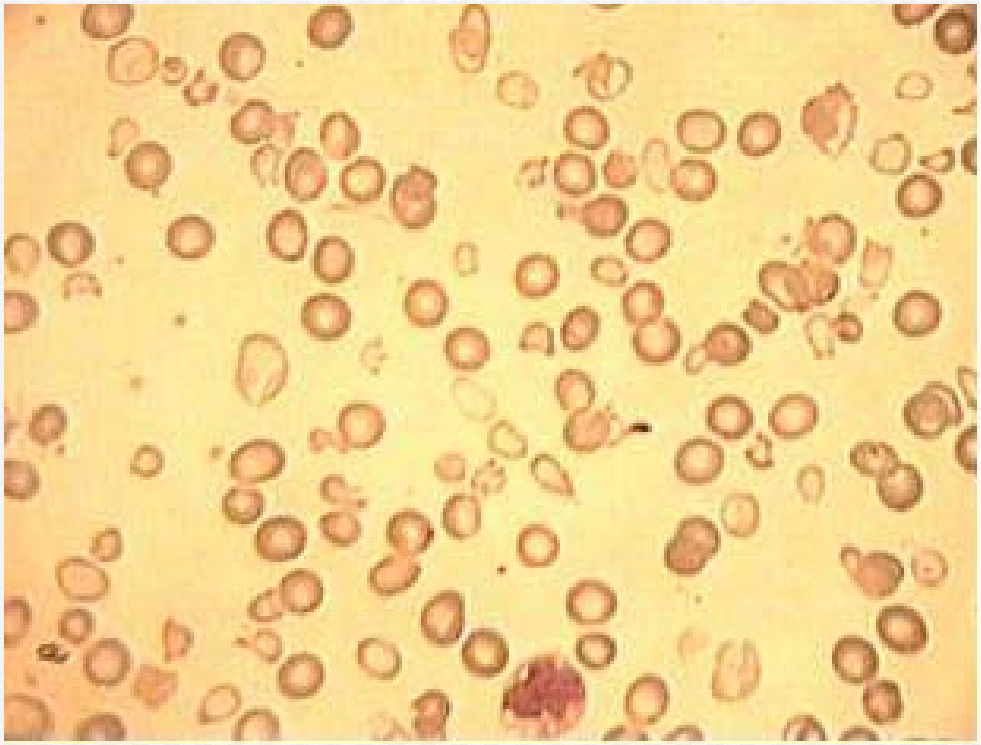
Blood Picture

- TLC: 37.0 X 109/L
- Hb: 3.5 g/dl
- TRBC: 2.7 X 1012/L
- MCV: 64.1 fl
- MCH: 21.2 pg
- Platelets: 270 X 109/L
- Reticulocytes: 4.5%
- ESR: 37 mm in 1st hour

β-Thalassaemia Major



β-Thalassaemia Major in Previously Transfused Patients



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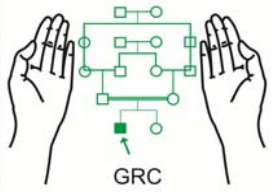
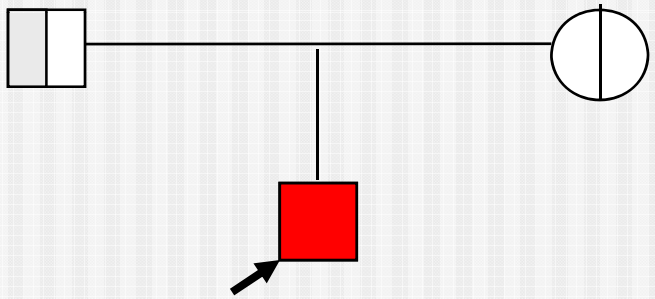
β-Thalassaemia Major in Previously Transfused Patients

	Untransfused (n=171)		Transfused (n=109)		*p* value
	Mean	Range	Mean	Range	
Hb (g/dl)	6.3	1.9 - 9.0	6.2	2.3 – 11.2	0.20
MCV (fl)	70	57 - 83	74	58 - 98	0.014
MCH (pg)	21	15 - 29	24	16 - 31	0.015
Hb-F (%)	95	35 - 97	31	0.5 - 97	< 0.001



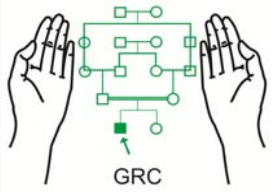
Diagnosis of β-Thalassaemia Major in Previously Transfused Patients

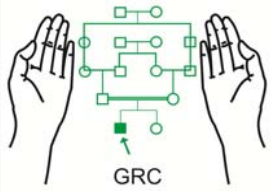
Hb: 12.7 g/dl
MCV: 66 fl
MCH: 19 pg



Hb: 10.4 g/dl
MCV: 64 fl
MCH: 18 pg

Transfusion Dependent Anaemia ??
Hb: 6.7 g/dl
MCV: 76 fl
MCH: 24 pg
Hb-F: 3.5%





Miscellaneous Investigations

- Sickling Test
- Heinz Body Test
- Test for Unstable Haemoglobins
- Test for Methaemoglobin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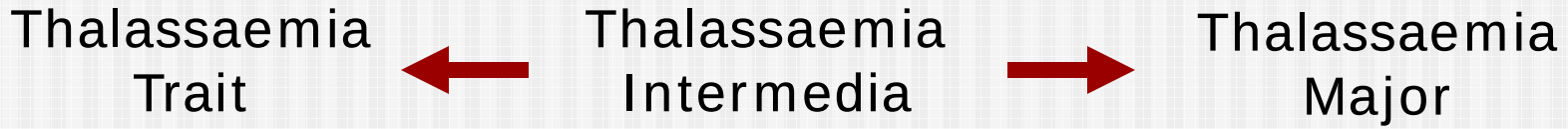
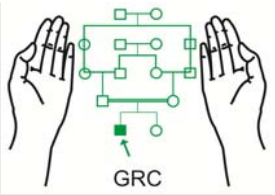
Thalassaemia Intermedia





	Thalassaemia Major	Thalassaemia Intermedia	Thalassaemia Minor
Severity	++++	++	+,±
Genetics	Homozygous/double heterozygous	Homozygous/double heterozygous	Heterozygous
Splenomegaly	++++	++,+++	+, 0
Jaundice	+	++	0
Bony changes	++++,++	+, 0	+, 0
Haemoglobin	<7 g/dl	7-10 g/dl	>10 g/dl
Hypochromia	++++	+++	++
Microcytosis	+++	++	+
Target cells	10-35%	++	+
Stippling	++	+	+
Reticulocytes	5-15%	3-10%	2-5%
Nucleated RBC	+++	+, 0	0
Hb-F	20->94%	30-100%	1-2%
Hb-A_2	1-8.7%	<1-10.0%	3.5-8.0%

Thalassaemia Intermedia in Pakistan

Cause of Thalassaemia Intermedia:	n (%):	Mean age:	
		At 1st transfusion:	At Examination:
Xmn-I +/+ genotype	14 36%)	6 years	13 years
β^+-mutation	6 (15%)	3 years	8 years
β^+-mutation and coincidental α-thalassaemia	6 (15%)	11¼ years	18 years
Unidentified thalassaemia mutation	2 (6%)	7½ years	12½ years
Coincidental α-thalassaemia	11 (28%)	9½ years	13½ years
Total	39	7 years	14 years

(Ahmed 1998)

PCR for Thalassaemia

- Prenatal Diagnosis
- Diagnosis in previously transfused patients
- Silent thalassaemia alleles
- Distinction between structural variants
- Thalassaemia intermedia
- α-thalassaemia
- β-Thalassaemia carriers in certain situations
- Rare thalassaemias
- Donor chimerism studies after SCT