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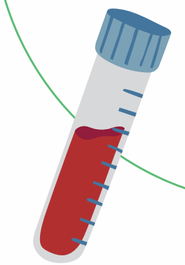
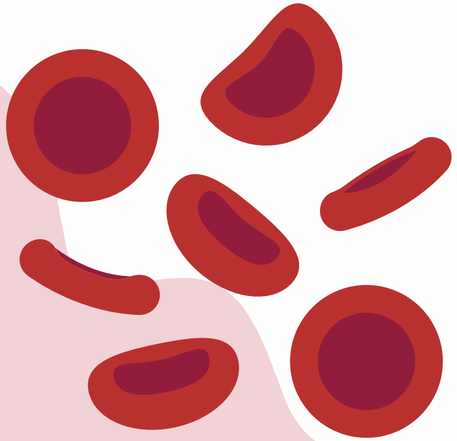


HAEMOGLOBINOPATHIES: THE BASICS FOR HAEM TRAINEES

Dr Amy Cooper

Haemoglobinopathy QI Fellow



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ACKNOWLEDGEMENT

Haembase and LearnHaem!

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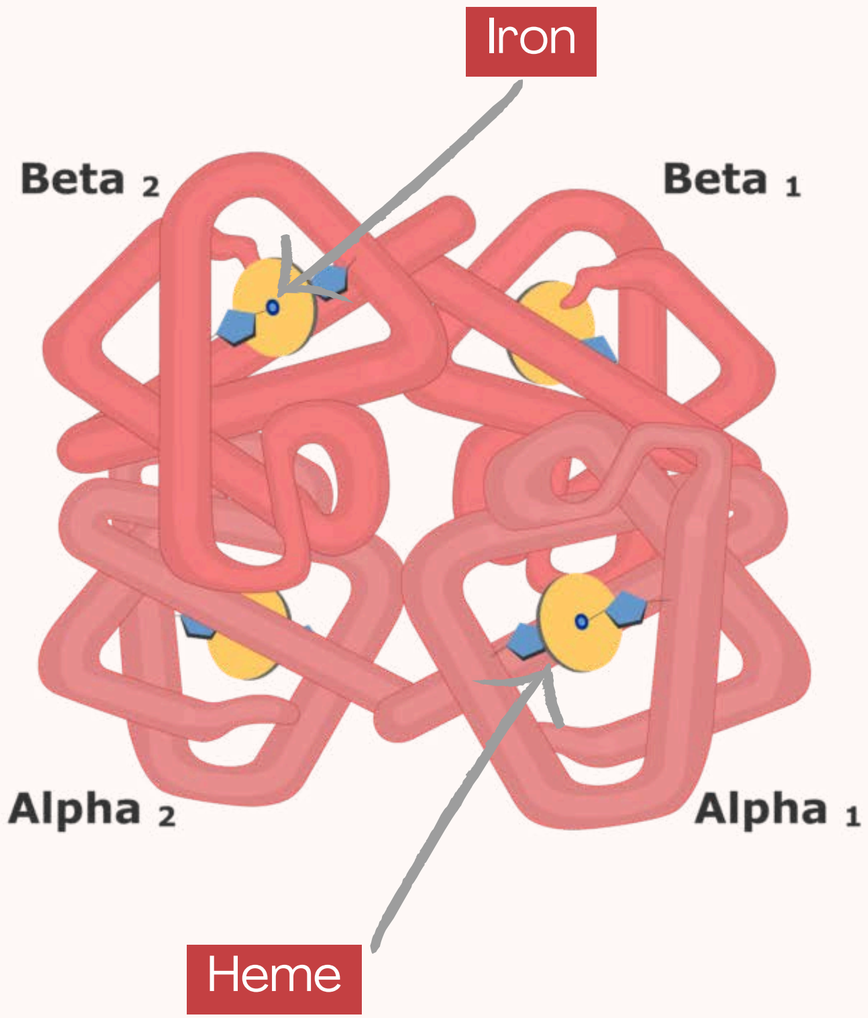
HAEMOGLOBIN

- Consists of two alpha and two beta globin chains
- Heme sits inside the globin chain and holds one iron molecule (4 per haemoglobin)
- The iron molecule reversibly binds oxygen (allowing it to carry and give up the O2 molecule)

Reminder - this is what Hb measures!



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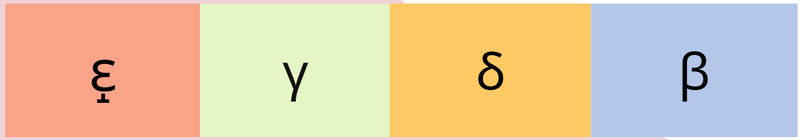
NORMAL HAEMOGLOBIN SYNTHESIS

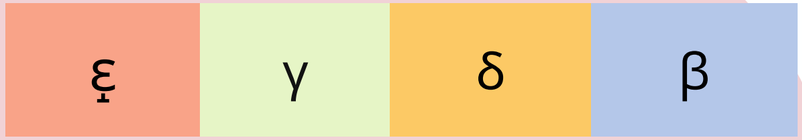
Chromosome 16

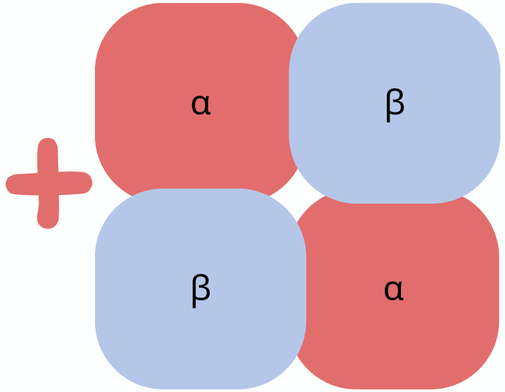
Chromosome 16

Chromosome 11

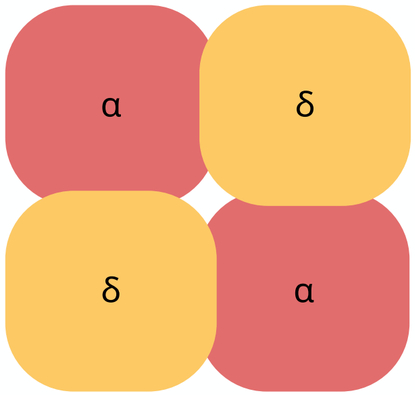


Chromosome 11

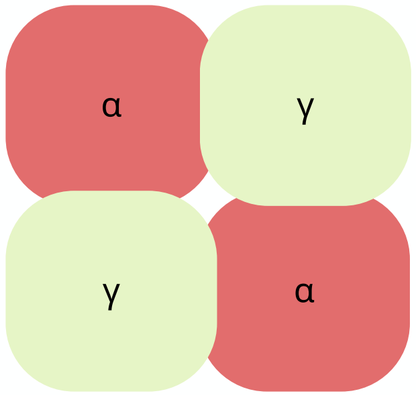




HbA



HbA2



HbF

Normal values:
HbA 97%
HbF 1%
HbA2 2%

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MEASURING TYPES OF HAEMOGLOBIN

- HPLC most commonly done for routine samples
- Other ways include using electrophoresis
  - Gel (acid/alkali)
  - Capillary
  - Isoelectric focussing - newborn blood spots
- There are also other ways of detecting abnormal haemoglobin - e.g. sickle solubility test

Two samples are required to confirm diagnosis - select the second modality based on the suspected variant haemoglobin

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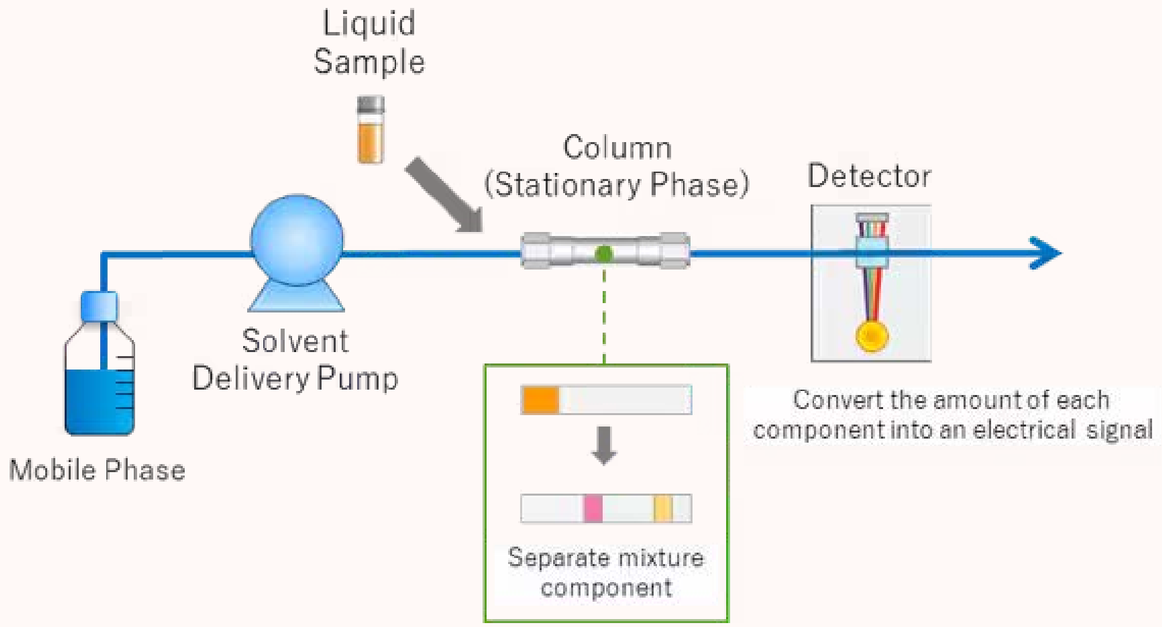
HPLC

- Sample is lysed to release haemoglobin from red cells
- **Mobile phase** - sample is added to a solvent to allow it to pass through the column
- **Stationary phase -** there are negatively charged molecules which attract the positively charged haemoglobin molecules at different points depending on their affinity for the column
- This is detected and turned into a graph



Red cells are LYSED before analysis

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Pitfalls

- Cannot distinguish between HbE and HbA2 (remember your A2E)
- Glycated haemoglobins elute separately

Image credit - Haembase

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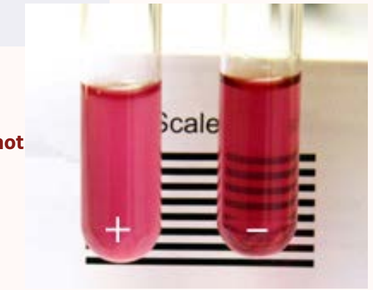
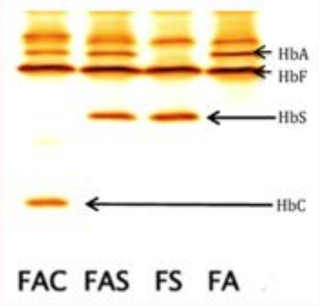
OTHER TYPES OF TESTING

SICKLE SCREEN

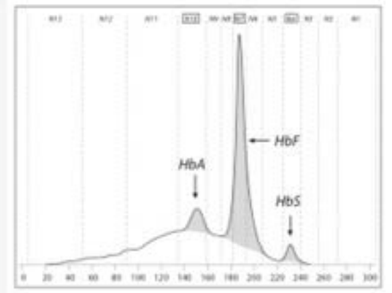
Sickle screen	*
Positive	
Please note, a negative test does not exclude the presence of a low percentage of haemoglobin S. Further testing by HPLC to follow.	

This is positive if there is any HbS present - cannot distinguish between trait and disease

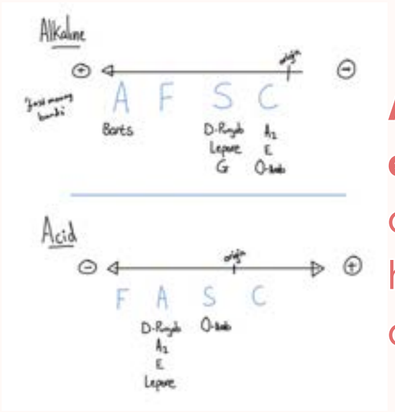




Isoelectric focussing - separates out glycosylated forms which can make interpretation difficult



Capillary electrophoresis - does not separate out glycosylated forms. Can distinguish between A2 and E



Acid/alkali gel electrophoresis - no longer commonly used, but can be helpful in diagnostic conundrums

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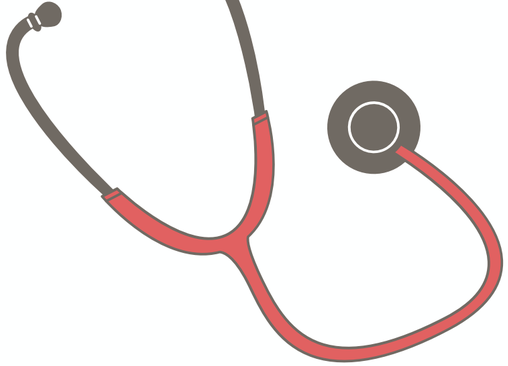

HOW CAN HAEMOGLOBIN SYNTHESIS GO WRONG

Structural abnormalities

Haemoglobin is made, but the structure is different to normal haemoglobin due to a genetic mutation (usually affecting the beta gene). Examples include:

- HbS
- HbC

Abnormalities in haemoglobin production

Mutations in alpha or beta genes reduce the production in alpha or beta chains. This reduces the amount of normal haemoglobin. These conditions are called thalassaemias.

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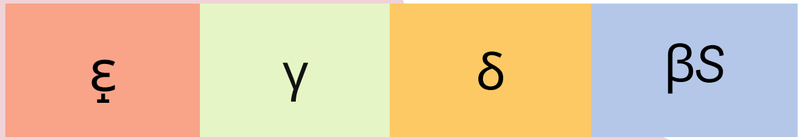
HBSS SICKLE CELL DISEASE

HbS has low oxygen affinity in hypoxic conditions

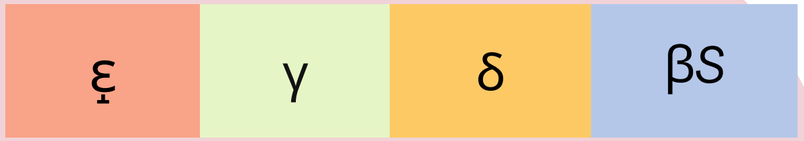
Chromosome 16

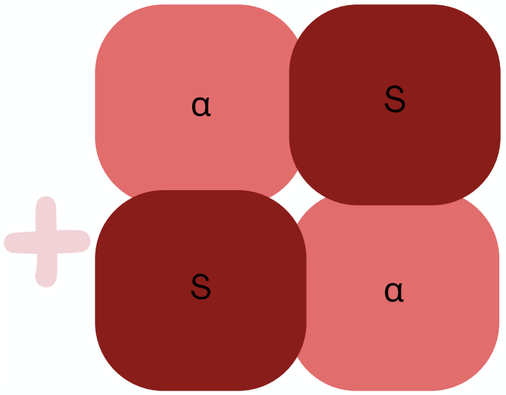
Chromosome 16

Chromosome 11

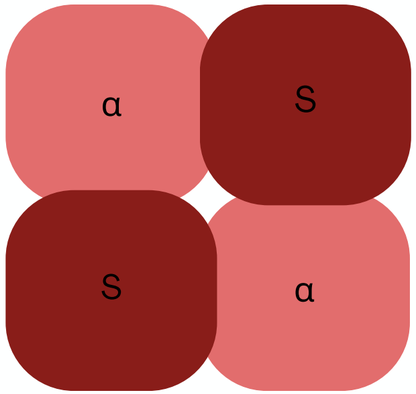


Chromosome 11

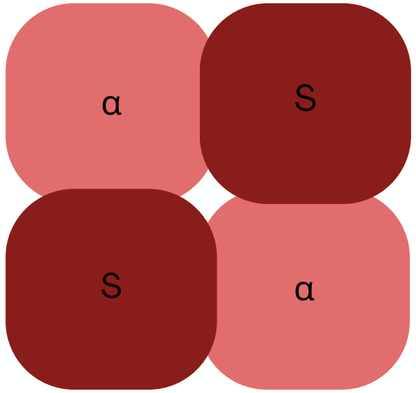




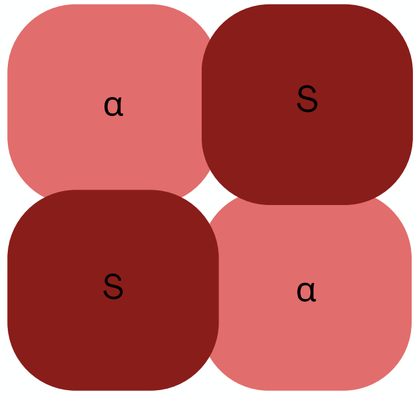
HbS



HbS



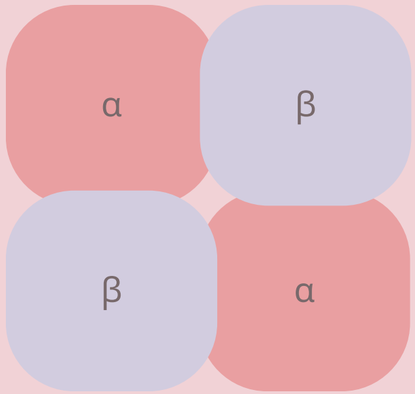
HbS



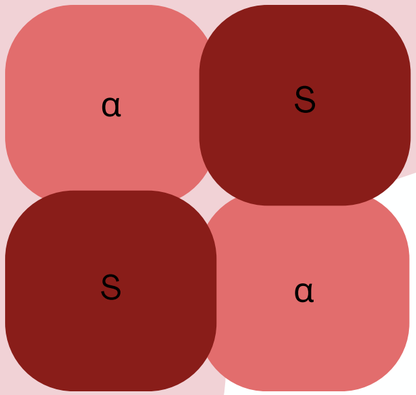
HbS

Results in around
90% HbS
Usual Hb 50-90

SICKLE CELL DISEASE (HBSS)

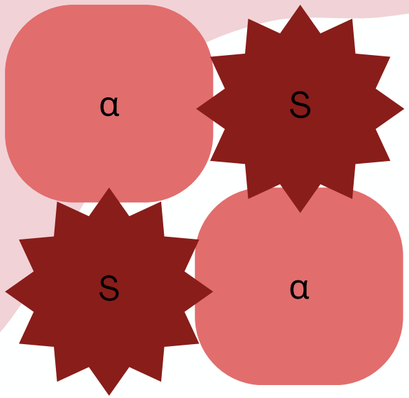


HbA

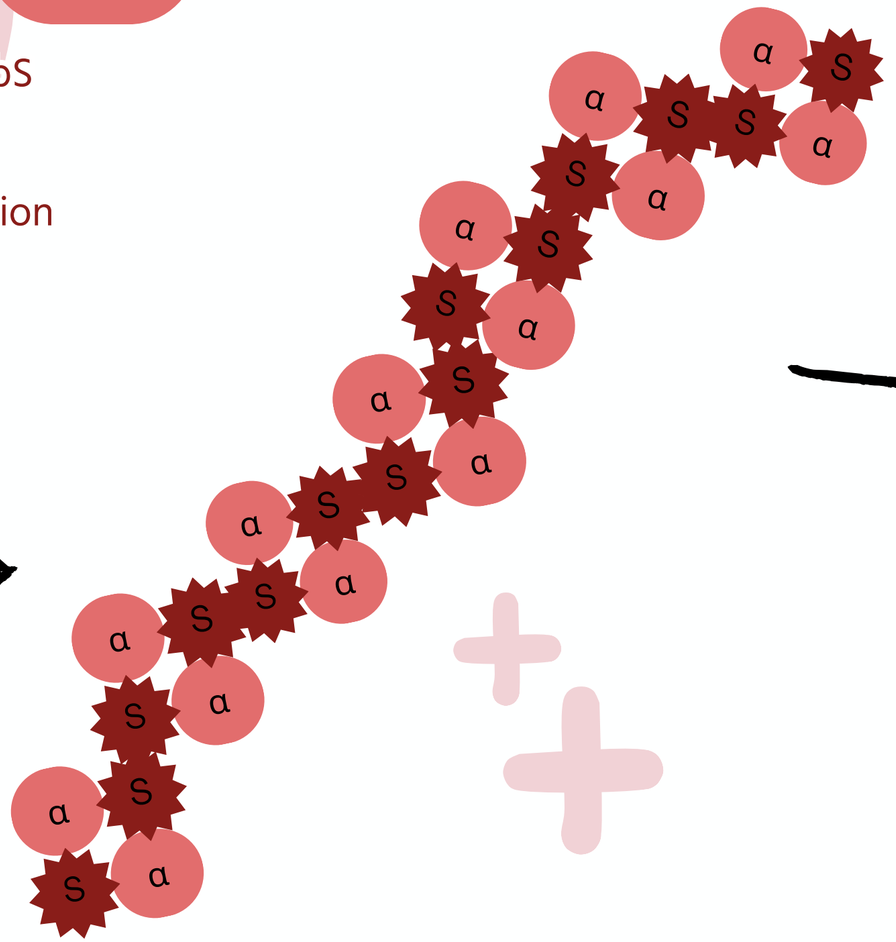


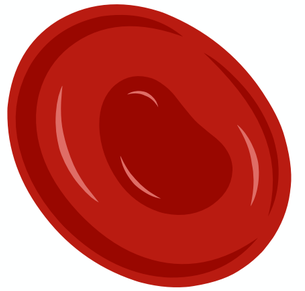
HbS

Deoxygenation



Polymerisation





Sickling

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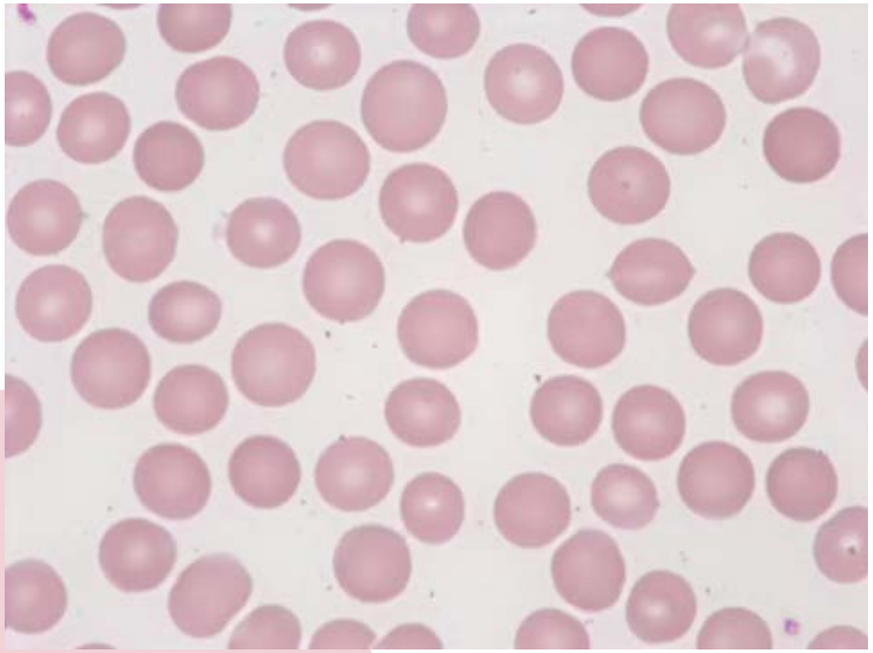
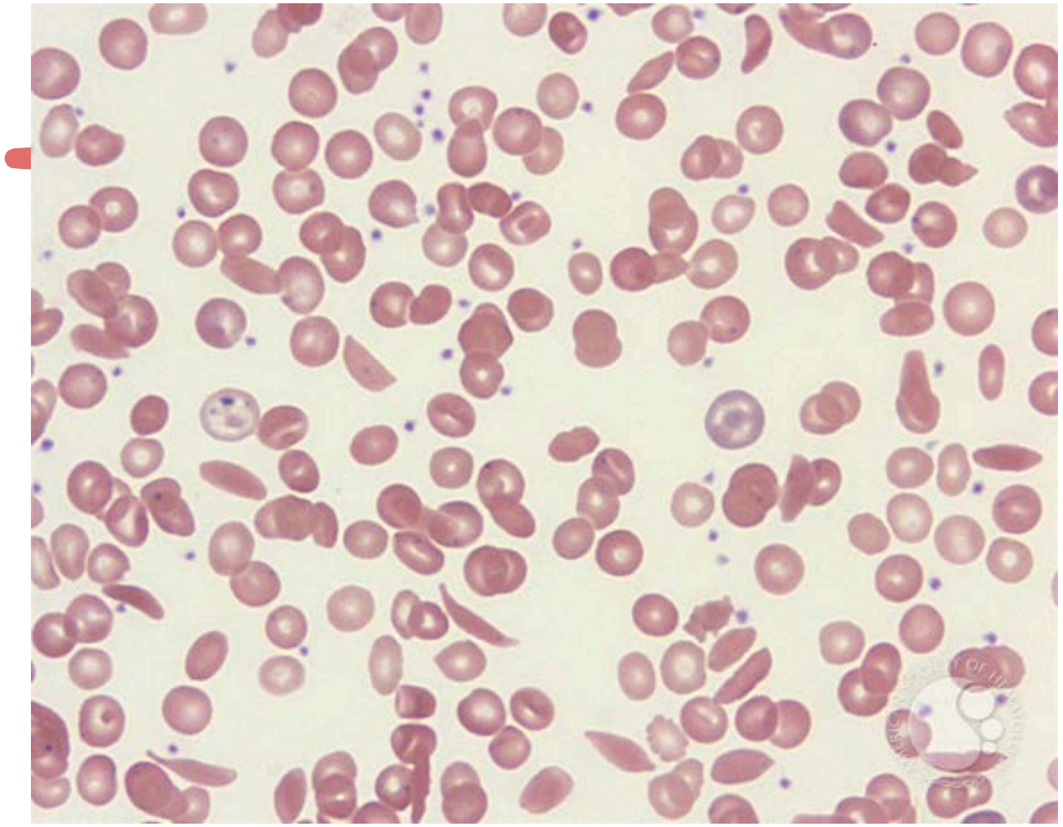
Low haemoglobin
Low RBC
Often normal MCV (unless co-existing thalassaemia trait - more on this later)



Normal



Sickle cell disease

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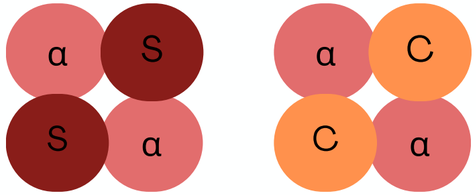
OTHER TYPES OF SICKLE CELL DISEASE

Chromosome 11

Chromosome 11

HbC crystallises at high oxygen concentrations - but does not polymerise

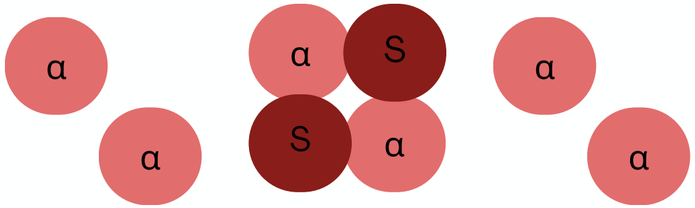
= HbSC disease



Chromosome 11

Chromosome 11

= HbS/beta thalassaemia



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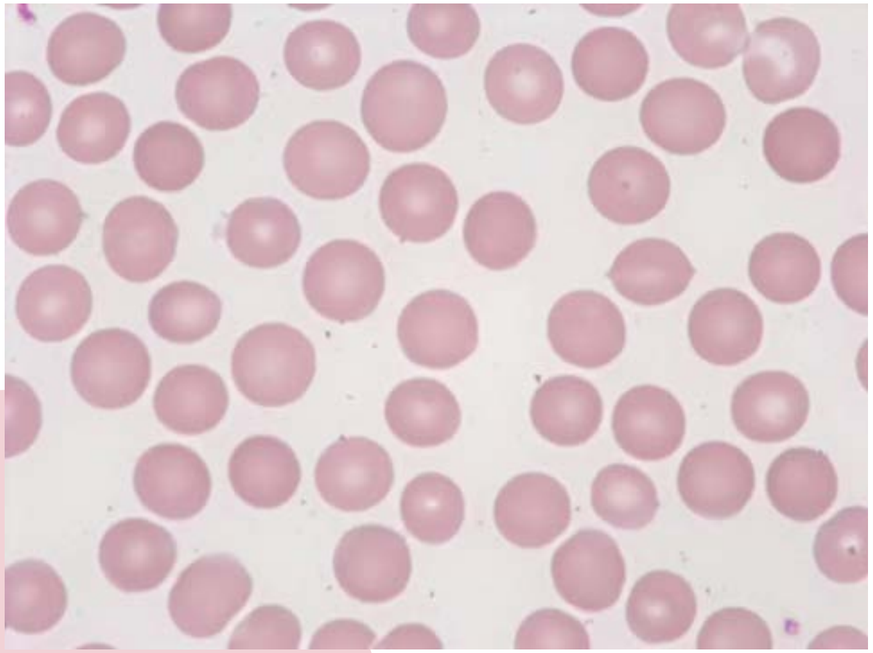
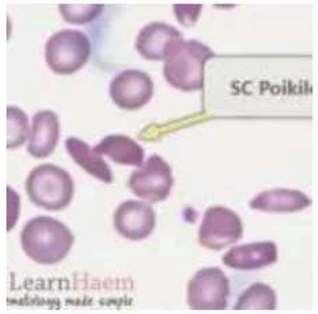
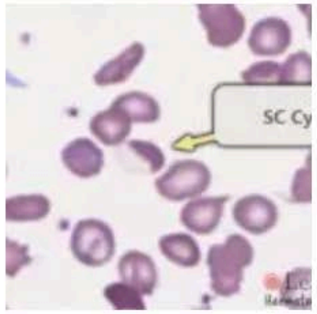
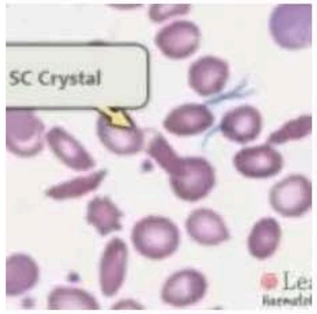
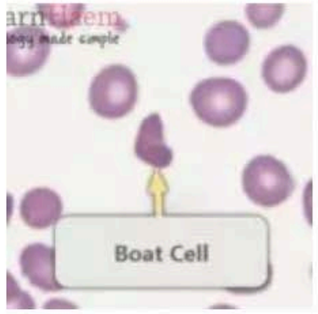


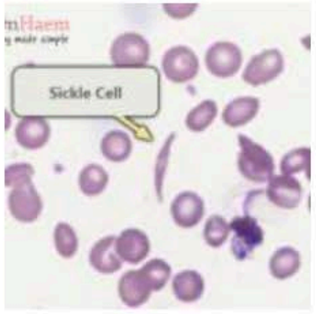
Normal

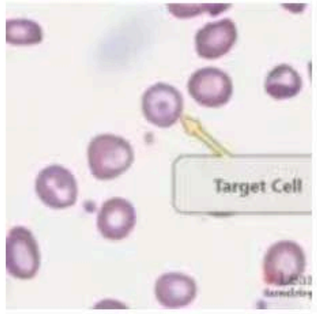












HbSC disease

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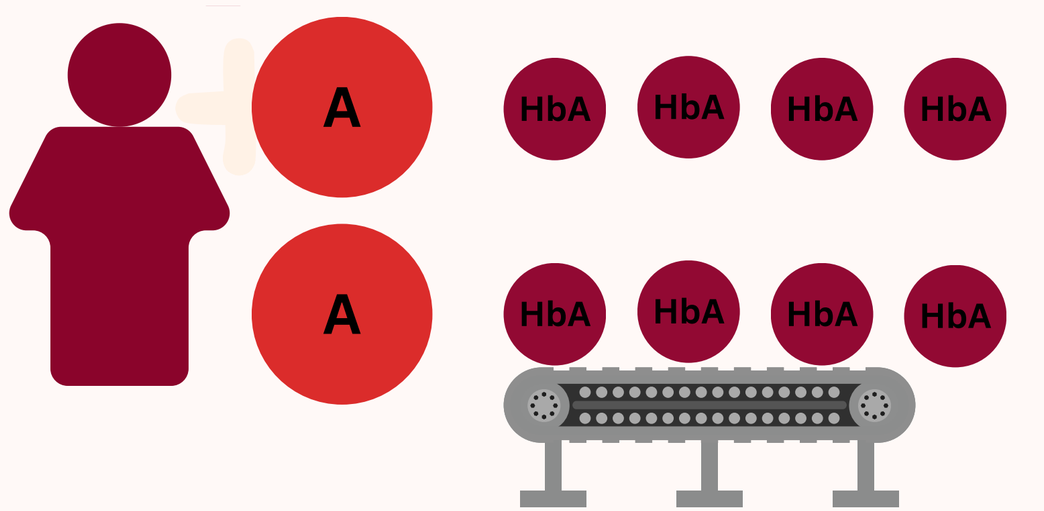
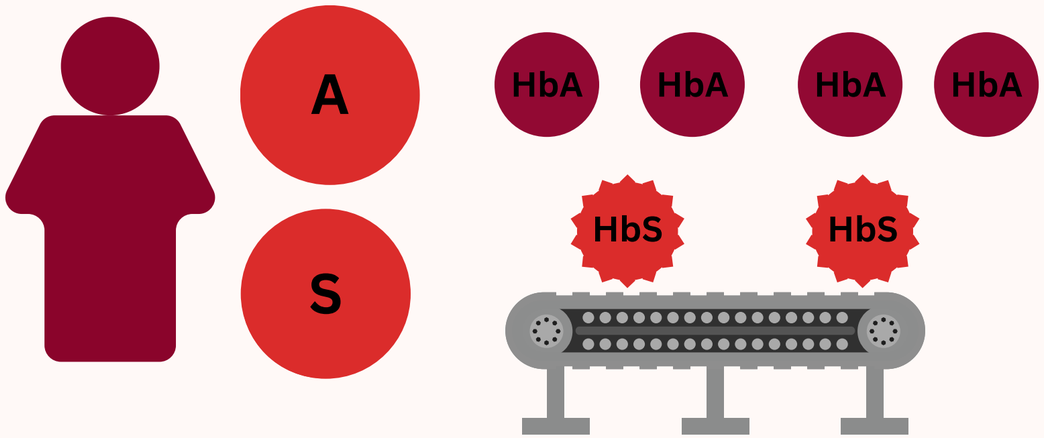
ARE CARRIERS UNAFFECTED?

- Inheritance of sickle cell disease is **autosomal recessive**

- The genes are **codominant**
- Both alleles are expressed independently, which means they both create haemoglobin





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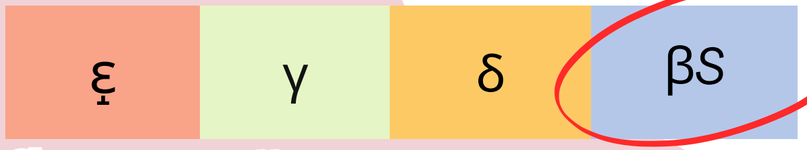
SICKLE CELL TRAIT

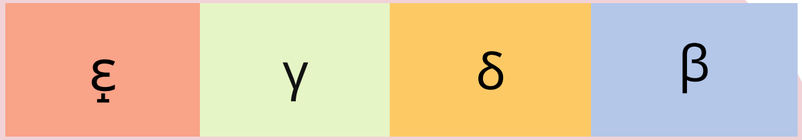
Chromosome 16

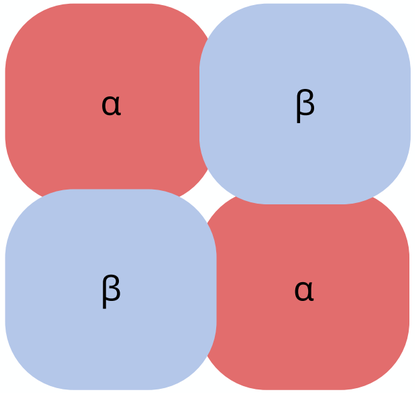
Chromosome 16

Chromosome 11

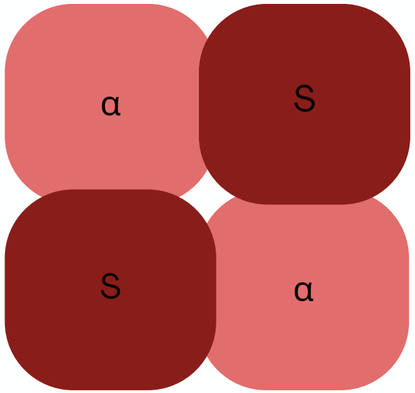


Chromosome 11

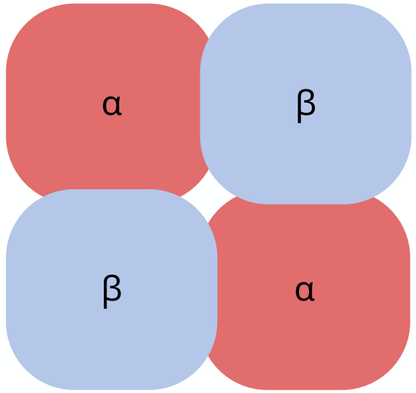




HbA



HbS



HbA

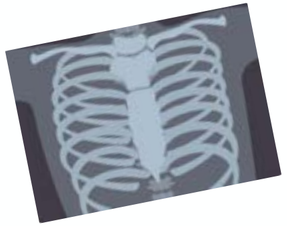
Translates to:
70% HbA
30% HbS
Normal haemoglobin
Normal MCV

WHAT DO SICKLED CELLS DO IN THE BODY?

Vaso-occlusion

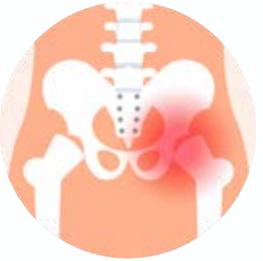
Sickled cells are rigid and non-deformable. They can get stuck in small vessels leading to ischaemia, organ damage and pain

Painful crisis



Acute chest syndrome

Avascular necrosis



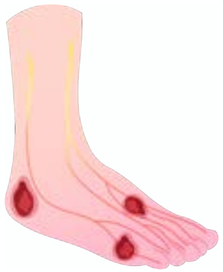
WHAT DO SICKLED CELLS DO IN THE BODY?

Haemolysis

The abnormal sickled cells are destroyed through intravascular haemolysis. The lifespan of a sickle cell is around 10-20 days.

Haemolysis depletes nitric oxide, causes local vascular damage and promotes systemic inflammation

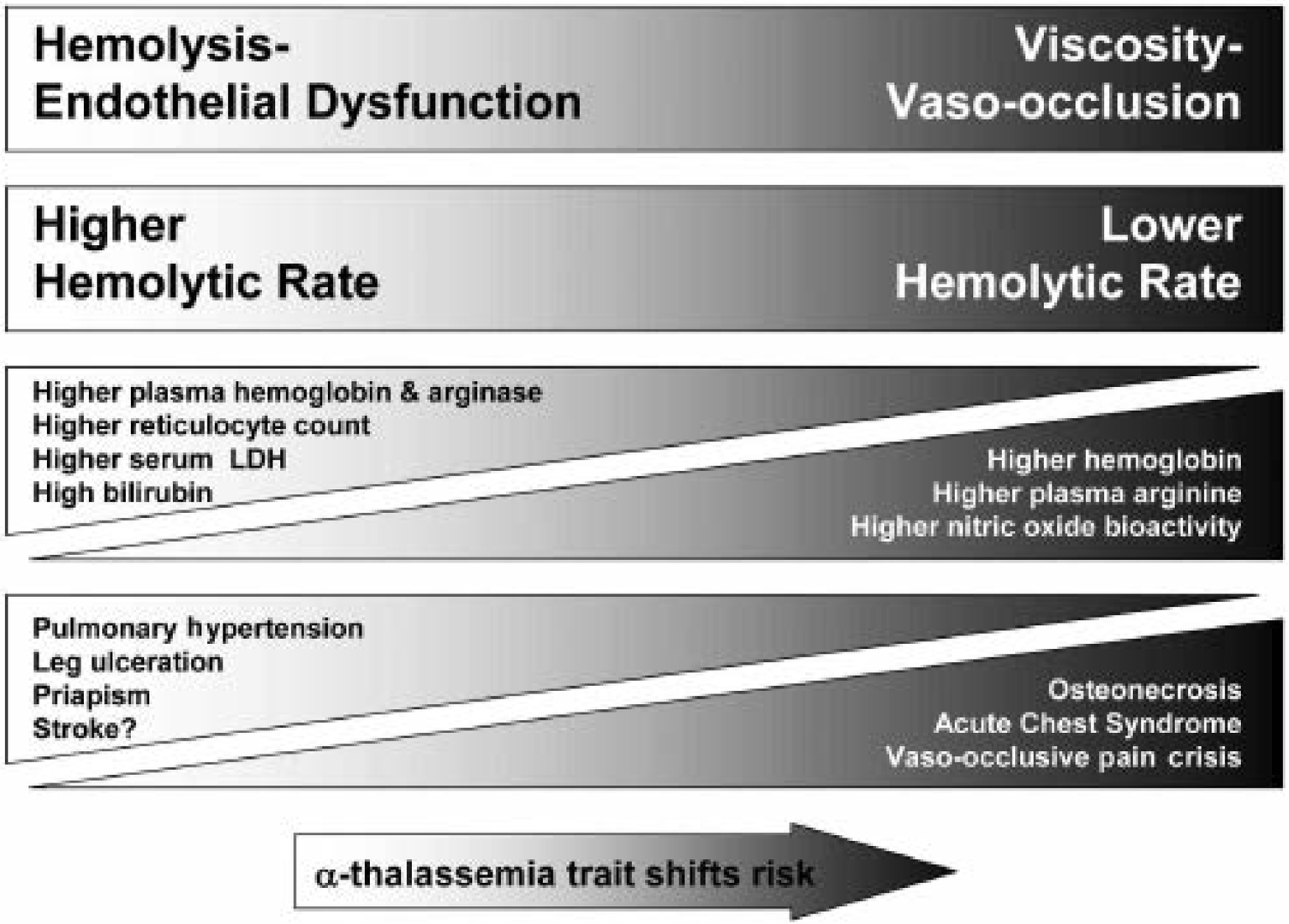
Leg ulceration

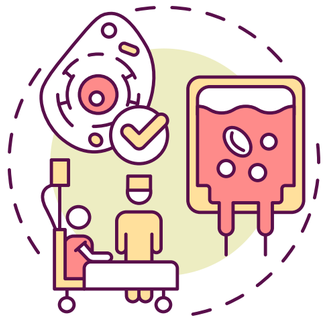


Priapism

Stroke

Spectrum of Sickle Cell Complications





TREATMENT OPTIONS

TRANSFUSION

Chronic transfusion

Remains a common long-term treatment option for the indications listed opposite. Decision to transfuse is usually made by the paediatric haematology consultant who knows the patient.

Risks of transfusion

The benefit of transfusion should be weighed against the risks of alloimmunisation, a common complication seen frequently in transfused adults. Red cells should be matched for ABO, Rh (D,C,c,E,e) and Kell blood groups as a minimum.

Also consider risk of iron overload and need for chelation.

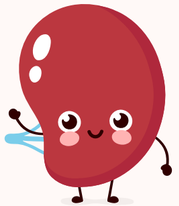
Exchange vs top up

Simple top-up exchange more commonly used in paediatrics, exchange transfusion is more common in adults.

Primary stroke prevention - if abnormal TCDs - STOP and STOP2 trial

Secondary stroke prevention - long term transfusion programme (very high risk of recurrence without transfusion)

Secondary prevention of recurrent painful crisis or acute chest syndrome



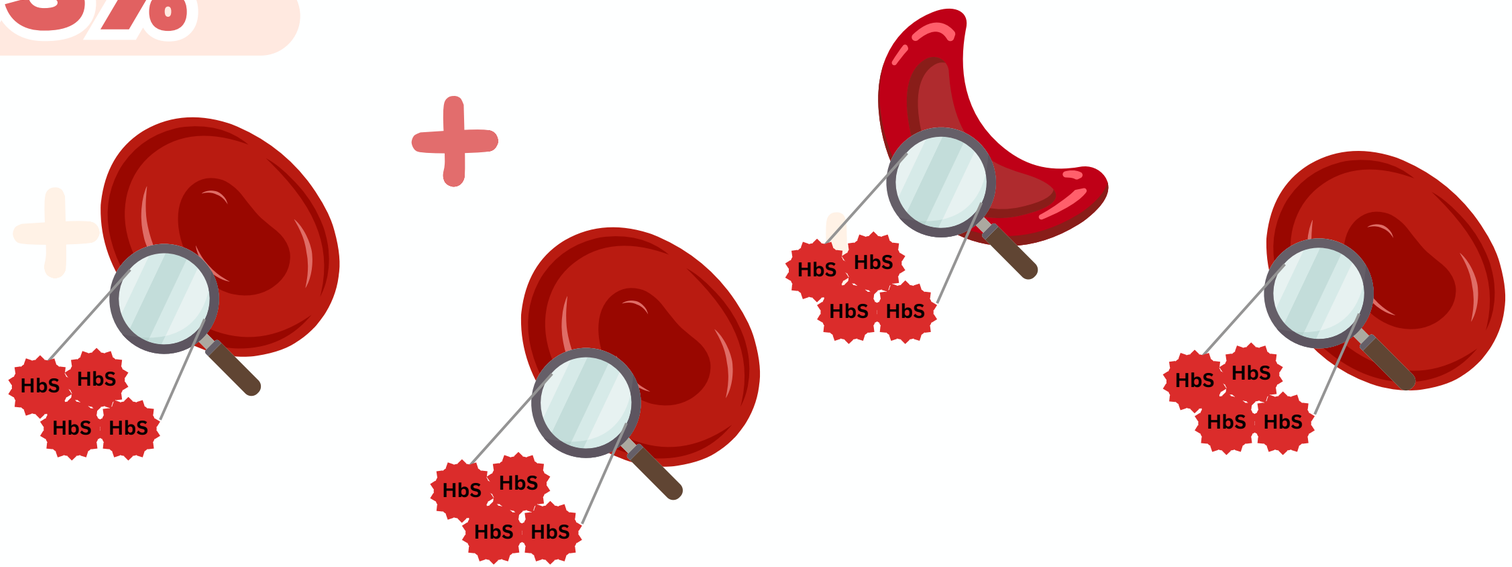
Other indications **may** include managing symptomatic splenomegaly, priapism, chronic organ damage... but not evidence based

HOW TRANSFUSION IMPACTS HBS%

Red cells are lysed in the analyser and haemoglobin is counted.

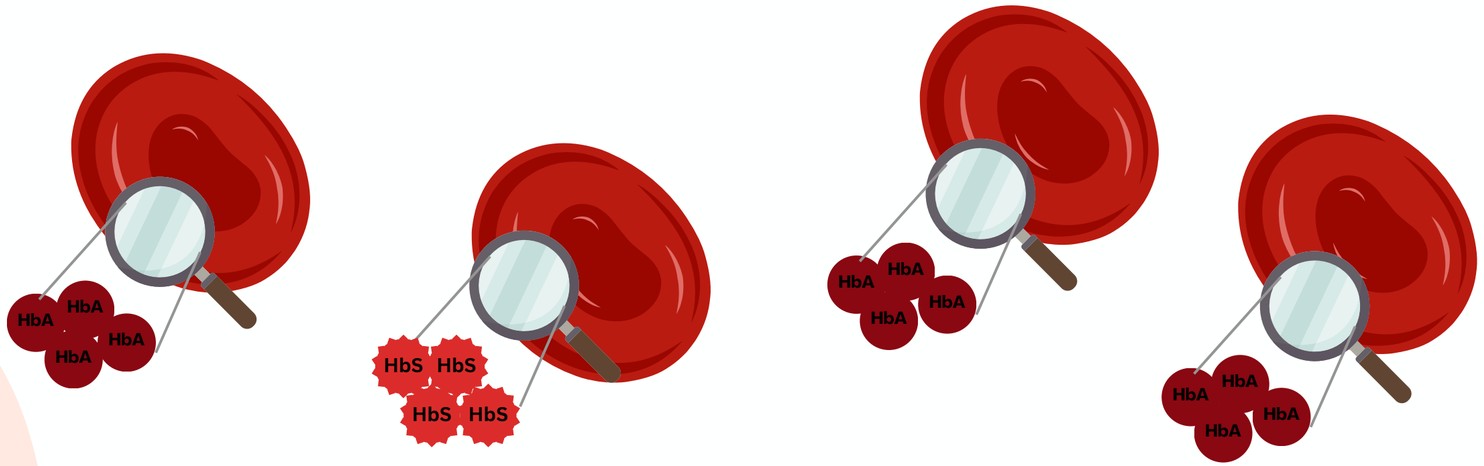
Untransfused

HbS % usually 80-90%



Transfused

HbS % lower - often aim <30%



HbS negative blood is given so this post-transfusion value is not impacted

HYDROXYCARBAMIDE

Who can have it?

Hydroxycarbamide can be used in all patients with a sickling disorder from age 9 months onwards (**BABYHUG** trial)

How does it work?

There are many proposed mechanisms of action...

HYDROXYCARBAMIDE

Who can have it?

Hydroxycarbamide can be used in all patients with a sickling disorder from age 9 months onwards (**BABYHUG** trial). HbSS, HbS/beta thalassaemia in particular, but also for other genotypes depending on their disease phenotype

How does it work?

There are many proposed mechanisms of action...

What are the benefits?

- Potential reduction in vaso-occlusive crisis
- Long term primary stroke prevention after initial period of transfusion
- Potential prevention of chronic sickling complications (e.g. nephropathy, pulmonary hypertension etc) but no strong evidence

Transiently inhibits DNA synthesis - acts for 1-4 hours. Daily transient erythroid precursor suppression recruits more erythroid progenitors with **increased HbF**

Reduced marrow production of white cells --> less inflammation? Less vascular ashesion = less vaso-occlusion?

Lower platelet count --> less thrombotic?

NO

Hydroxycarbamide carries a nitric oxide molecule which can be released --> local vasodilation, offset haemolysis related NO consumption

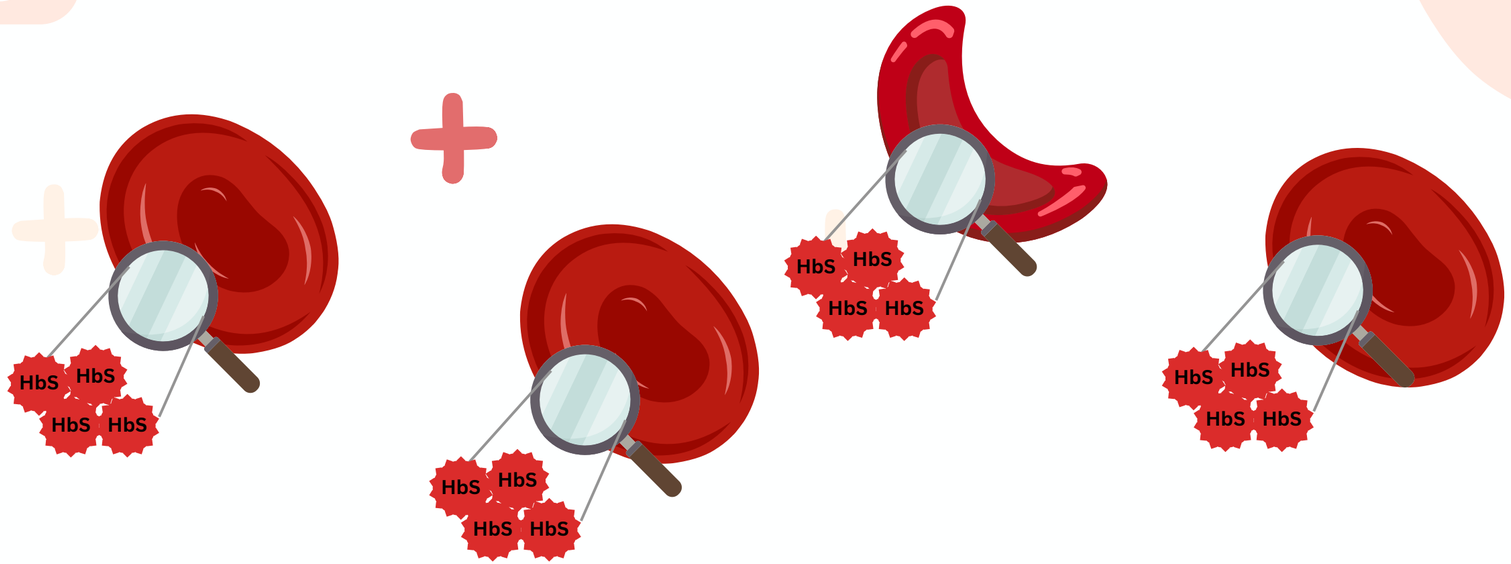
HOW HYDROXYCARBAMIDE IMPACTS HBS%

Red cells are lysed in the analyser and haemoglobin is counted.

Without hydroxycarbamide

HbS % usually 80-90%

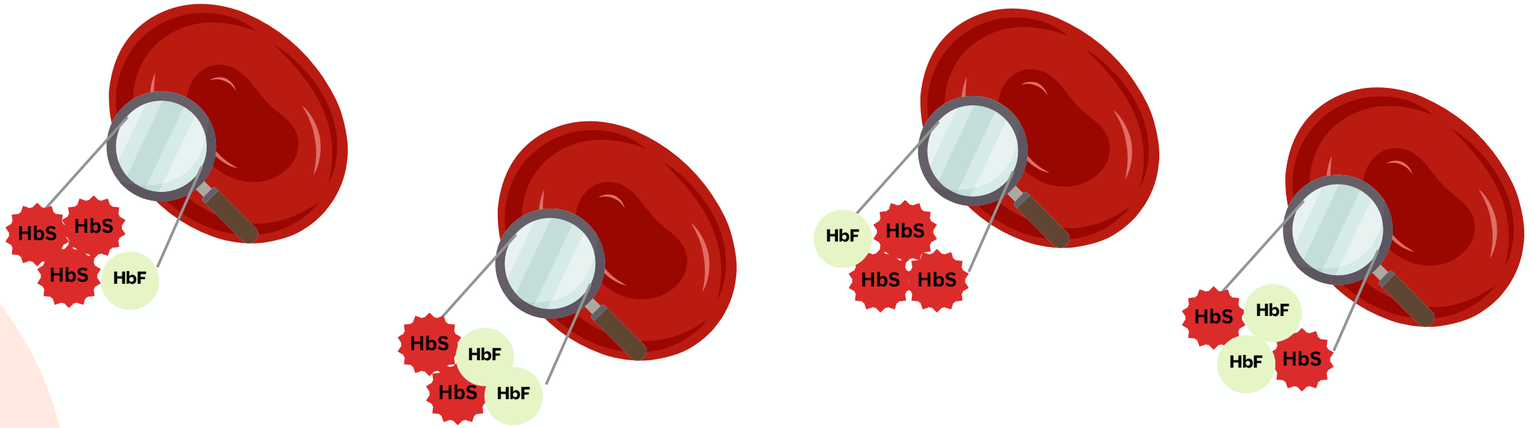
HbF% usually <1%



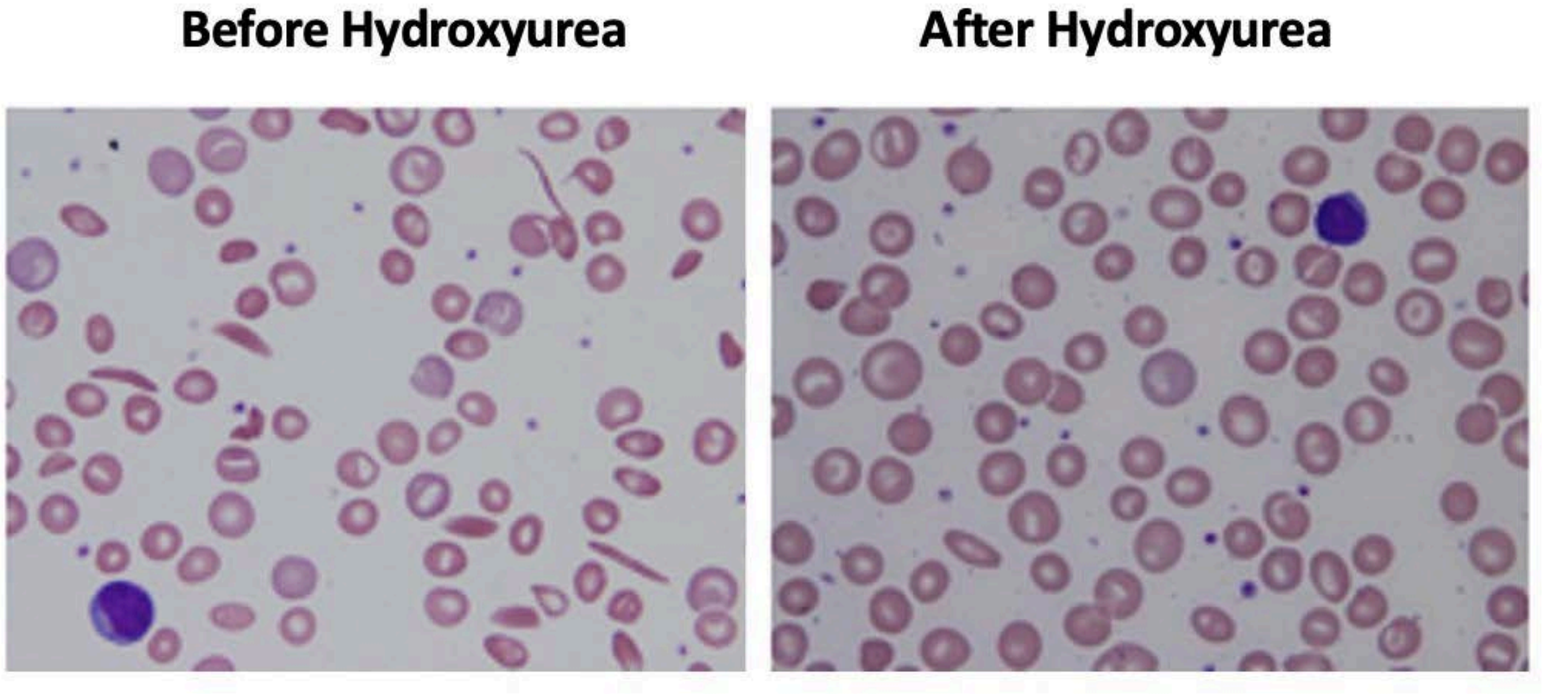
With hydroxycarbamide

HbS % 60-80%

HbF% - 10-30%



HOW HYDROXYCARBAMIDE IMPACTS THE BLOOD FILM



- Higher MCV
- More hydrated, deformable cells
- Less terminally sickled forms

HYDROXYCARBAMIDE

How should we be prescribing hydroxycarbamide?

- Aim for a target of:
  - HbF >20% if possible
  - Neutrophils over 1
- Escalate doses gradually up until the maximum tolerated dose (MTD) (based on blood counts)

Why escalate?

A study from Africa showed that those on the MTD had:

- 60% reduction in VOC
- 70% reduction in ACS
- 70% reduction in transfusions
- 80% reduction in hospitalisation

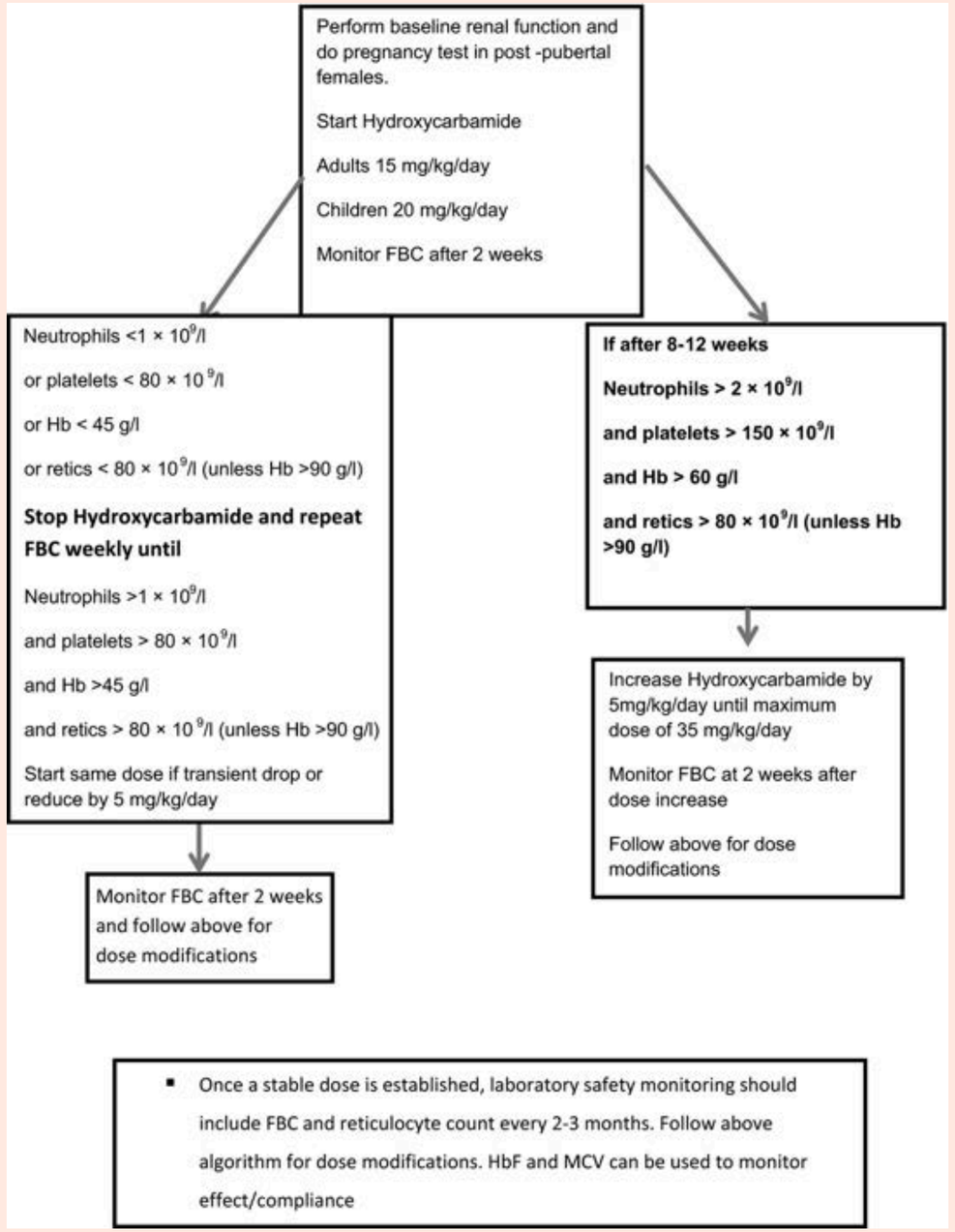
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

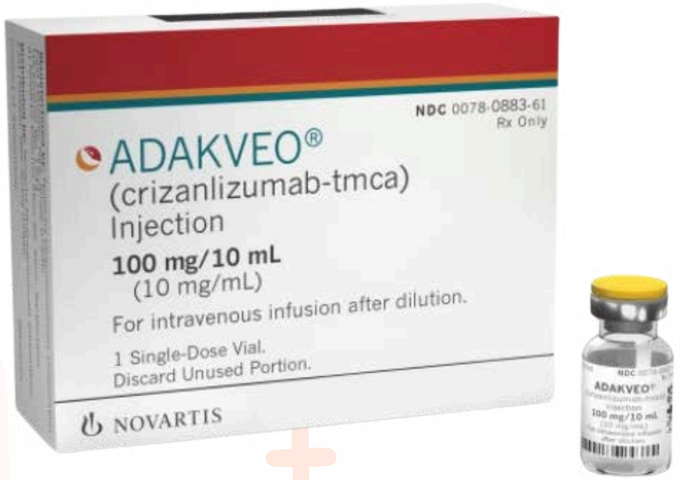
Hydroxyurea Dose Escalation for Sickle Cell Anemia in Sub-Saharan Africa

Authors: Chandy C. John, M.D., Robert O. Opoka, M.Med., Teresa S. Latham, M.A., Heather A. [illegible], Catherine Nabaggala, M.B., B.S., Phillip Kasirye, M.Med., Christopher M. Ndugwa, M.Med., Adam Lane, Russell E. Ware, M.D., Ph.D. Author Info & Affiliations

Published June 24, 2020 | N Engl J Med 2020;382:2524-2533 | DOI: 10.1056/NEJMoa2000146



OTHER MEDICAL OPTIONS?



Prevents endothelial adhesion

Decrease HbS polymerisation

OTHER MEDICAL OPTIONS?

On **January 10th 2024**, the Crizanlizumab licence was revoked by the Medicines and Healthcare products Regulatory Agency (MHRA). 1 Feb 2024

Sickle Cell Society
https://www.sicklecellsociety.org › News

Crizanlizumab - end of NHS supply - Sickle Cell Society

OTHER MEDICAL OPTIONS?


THE LANCET
Haematology

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ARTICLES · Volume 12, Issue 4, E248-E257, April 2025 Download Full Issue

Crizanlizumab with or without hydroxyurea in patients with sickle cell disease (STAND): primary analyses from a placebo-controlled, randomised, double-blind, phase 3 trial

Prof Miguel R Abboud, MD [a] · Rodolfo D Cançado, PhD [b] · Prof Mariane De Montalembert, PhD [c] · Prof Wally R Smith, MD [d] · Prof Hala Rimawi, FRCP-UK [e] · Ersi Voskaridou, MD [f] · et al. Show more

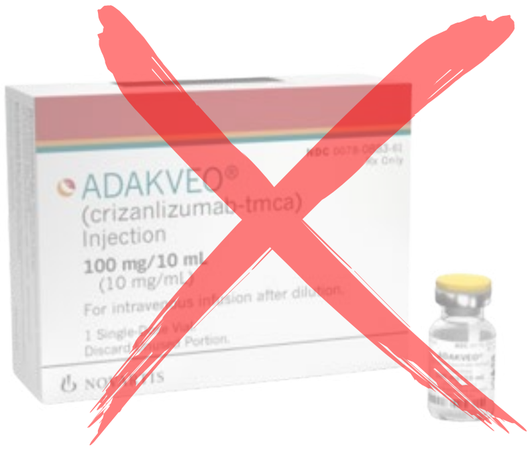
Affiliations & Notes Article Info Linked Articles (1)

1. Annualized Rate of Vaso-occlusive Crisis (VOC) Events Leading to a Healthcare Visit

Type: Primary | Time Frame: 1 year

Arm/Group Title	Crizanlizumab (SEG101) at 5.0 mg/kg	Crizanlizumab (SEG101) at 7.5 mg/kg	Placebo
Arm/Group Description	Participants received Crizanlizumab (SEG101) 5.0 mg/kg IV infusions on day 1, day 15 and every 4 weeks thereafter.	Participants received Crizanlizumab (SEG101) 7.5 mg/kg IV infusions on day 1, day 15 and every 4 weeks thereafter.	Participants received 0.5r placebo by IV infusions or day 15 and every 4 weeks thereafter.
Overall Number of Participants Analyzed	84	83	85
Mean (Standard Deviation) | Unit of Measure: number of events per year	2.5 (2.98)	1.9 (2.30)	2.1 (2.81)

OTHER MEDICAL OPTIONS?



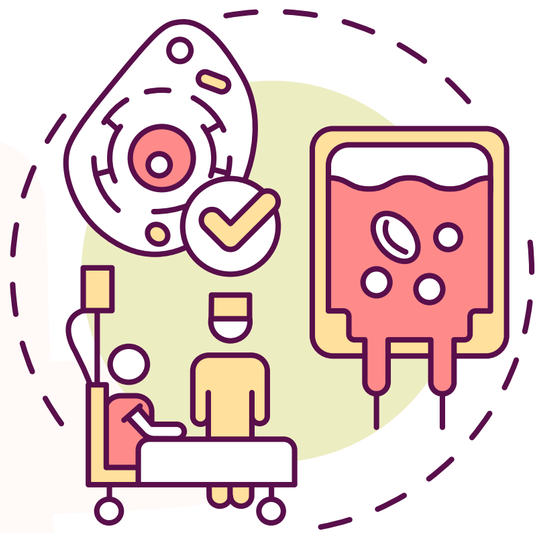
Pfizer Voluntarily Withdraws All Lots of Sickle Cell Disease Treatment OXBRYTA® (voxelotor) From Worldwide Markets

On September 25, 2024, Pfizer announced the voluntary withdrawal of voxelotor from the global market for adults and pediatric patients 4 years of age and older based on clinical data indicating that the overall benefit of the drug no longer outweighed the risks.[2]

"The data suggest an imbalance in vaso-occlusive crises and fatal events, which require further assessment. Consequently, Pfizer is voluntarily withdrawing the product from the market at this time. Pfizer is also discontinuing all ongoing Oxbryta studies and early access programs," the company said in a letter to health care providers that was dated one day after the public announcement.[3]

There were reports of deaths in two clinical studies being conducted outside of the U.S. In a study of 236 children with SCD and a higher risk of stroke in Africa, the Middle East, and the United Kingdom, there were eight deaths in the voxelotor group, mainly related to malaria or sepsis. A separate study of 88 adolescents and adults in Brazil, Kenya, and Nigeria who had SCD and leg ulcers saw eight deaths occur in the voxelotor group, with malaria being identified as a cause or a factor in some of those cases.[4]

POTENTIAL CURES



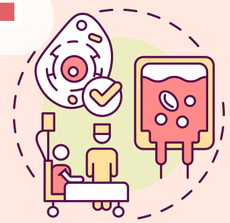
ALLOGENEIC STEM CELL TRANSPLANT

Who can have it?

Allo SCT is available to patients with a fully matched sibling donor **ONLY** who have a severe disease phenotype. Both patient and donor should be aged 2 or above.

- History of >= 3 severe pain crises or other acute complications per year despite institution of supportive care measures (optimal treatment with hydroxycarbamide (HC) or transfusion therapy). Other acute complications would include acute hepatopathy or splenic sequestration or acute priapism
- Recurrence of acute chest syndrome despite optimum treatment with hydroxycarbamide (HC) or transfusion therapy
- Clinically significant neurologic vascular event or deficit lasting over 24 hours and confirmed radiologically (i.e. stroke) or progressive cerebral vasculopathy
- Administration of regular transfusion therapy, either by simple transfusion or exchange transfusion with the aim to prevent severe sickle complications by maintaining a low HbS%. Severe sickle complications include a history of >= 2 chest syndromes, >= 3 painful crises or severe recurrent priapism
- Patients assessed as requiring transfusion but with red cell alloantibodies/very rare blood type, rendering it difficult to continue/commence chronic transfusion
- Patients requiring hydroxycarbamide/transfusion for treatment of SCD complications who cannot tolerate either therapy due to significant adverse reactions
- Established end organ damage relating to SCD including but not limited to progressive sickle vasculopathy and hepatopathy.

ALLOGENEIC STEM CELL TRANSPLANT



Who can have it?

Allo SCT is available to patients with a fully matched sibling donor **ONLY** who have a severe disease phenotype. Both patient and donor should be aged 2 or above.

Clinical Trial > Br J Haematol. 2021 Feb;192(4):761-768. doi: 10.1111/bjh.17311. Epub 2021 Feb 3.

Non-myeloablative human leukocyte antigen-matched related donor transplantation in sickle cell disease: outcomes from three independent centres

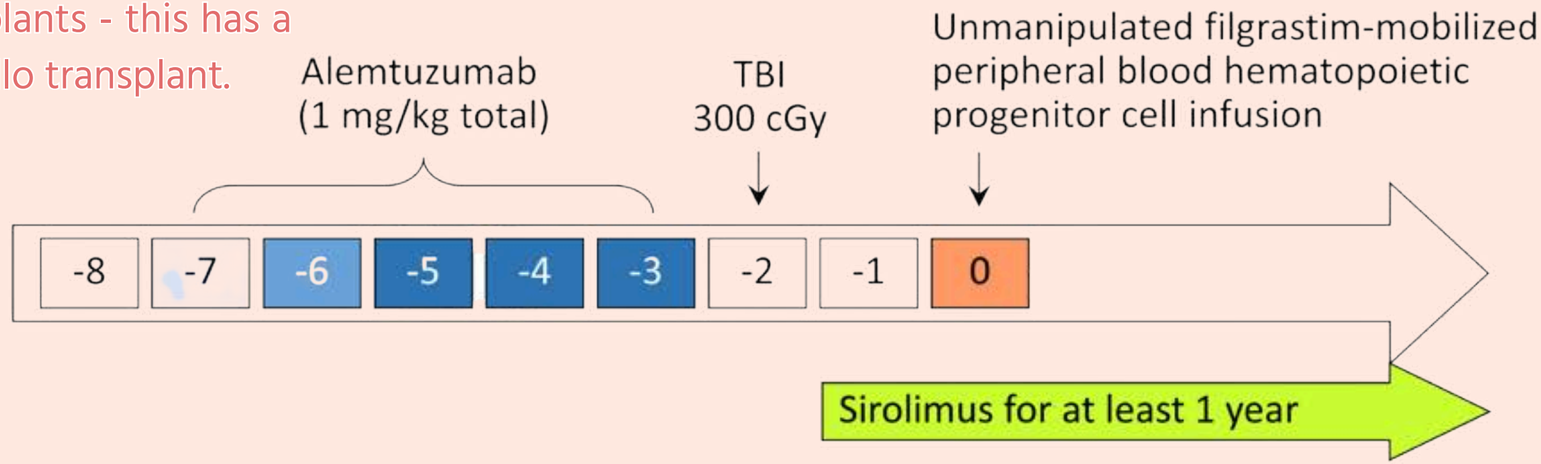
Mohsen Alzahrani [1], Moussab Damlaj [1], Neal Jeffries [2], Bader Alahmari [1], Avani Singh [3], Damiano Rondelli [3], John F Tisdale [4], Santosh L Saraf [3], Matthew M Hsieh [4]

Affiliations + expand

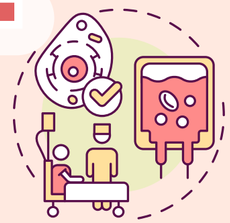
PMID: 33534948 PMCID: PMC8582053 DOI: 10.1111/bjh.17311

What kind of conditioning is used?

A 'chemotherapy free' conditioning protocol using alemtuzumab and TBI is being used for matched sibling transplants - this has a lower toxicity profile than the traditional MAC allo transplant.



ALLOGENEIC STEM CELL TRANSPLANT



Who can have it?

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What kind of conditioning is used?

A ‘chemotherapy free’ conditioning protocol using alemtuzumab and TBI is being used for matched sibling transplants - this has a lower toxicity profile than the traditional MAC allo transplant.

How effective is this?

- OS rate of around 95% aged <16
- EFS 73-96%
- Mixed donor chimerisms are intended and can still result in cure

Low rates of GvHD - 2% acute, no chronic GvHD cases

If no matched sibling - haploidentical transplant being studied in adults (REDRESS)

Matched unrelated donor (MUD) transplant not used as the chance of finding a match is low - <20%.

21 successful pregnancies recorded in 14 patients (7 male, 7 female)

GENE THERAPY

Approved for use in SCD in January 2025!

Who can have it?

Gene therapy is only available to the following patients over the age of 12:

- No available matched sibling donor

AND

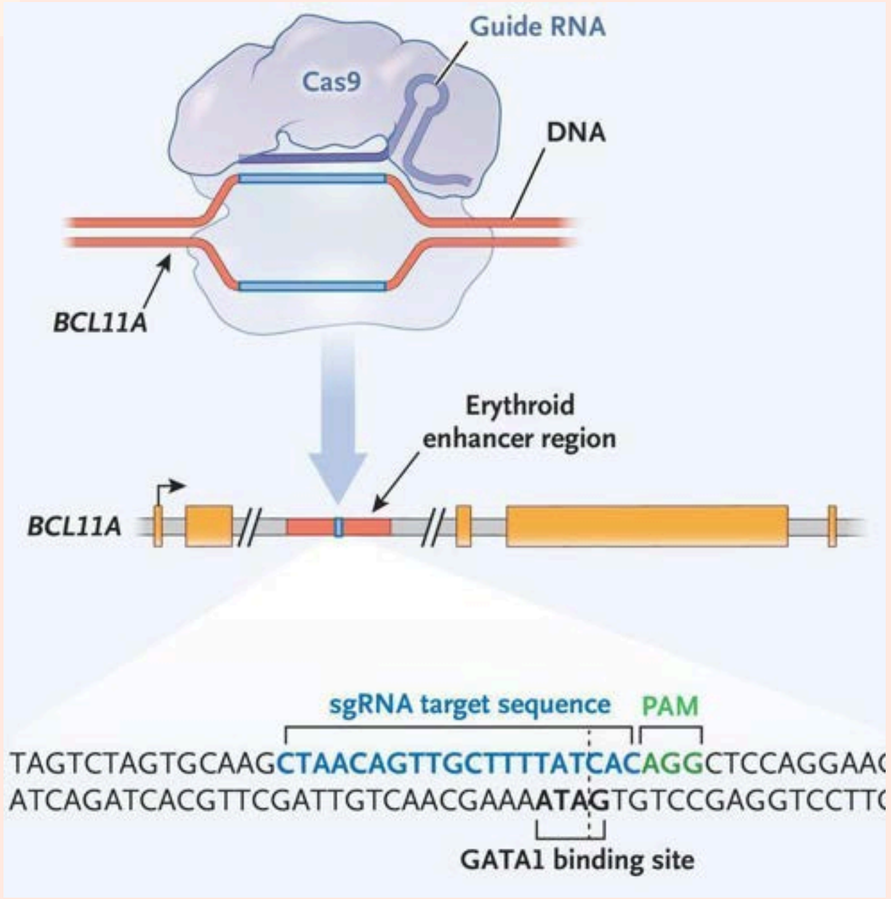
- Two or more vaso-occlusive crisis requiring hospital attendance in the two years prior to referral

What kind of procedure is this?

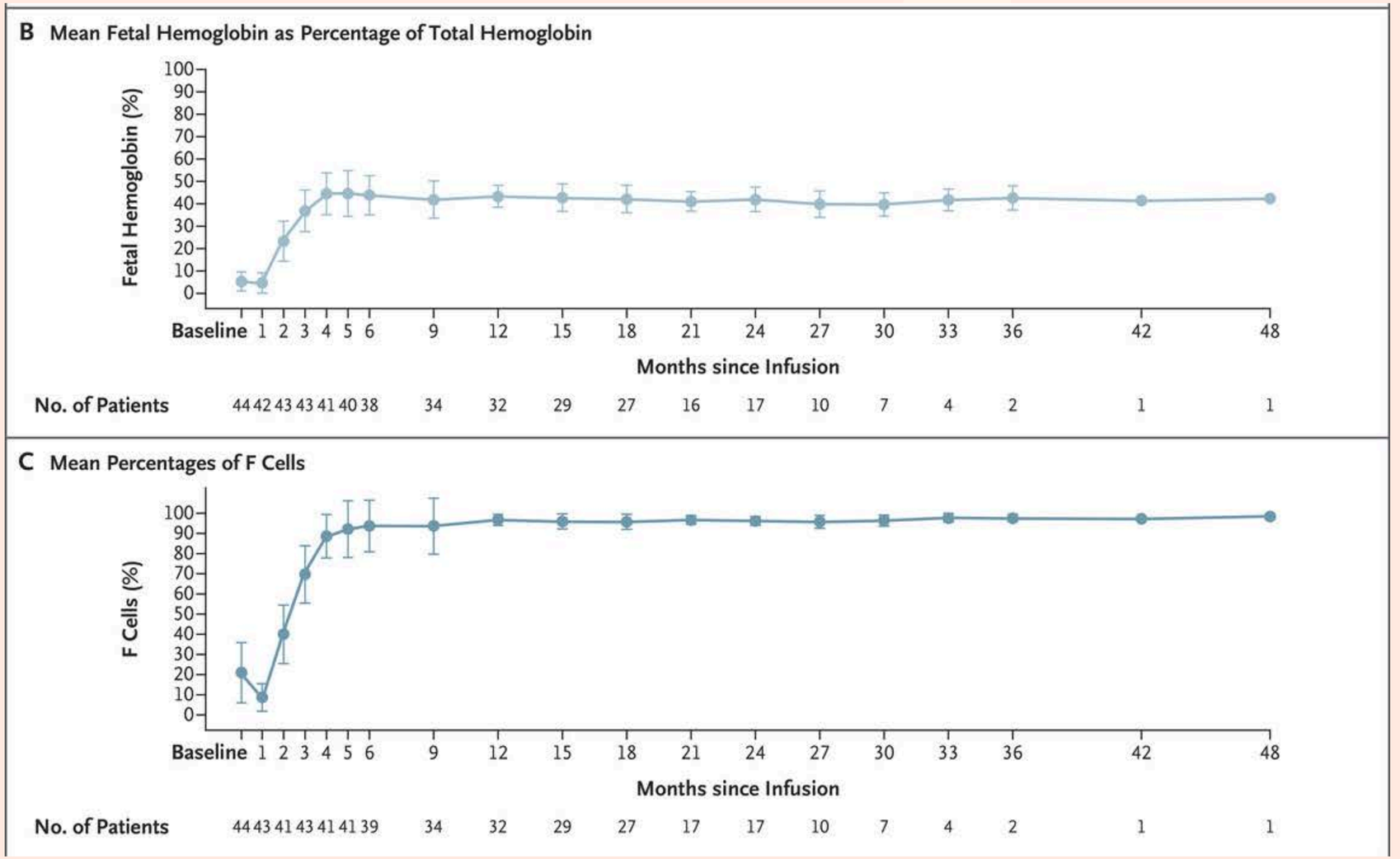
Autologous, gene edited stem cells are reinfused after the administration of myeloablative conditioning.

Is this a cure?

This treatment has the potential to offer a functional/clinical cure - however we currently do not have enough follow up data to say this with certainty.



BCL11A normally suppresses HbF production - this can be inhibited using gene therapy to allow HbF to be produced again.


B Mean Fetal Hemoglobin as Percentage of Total Hemoglobin
Fetal Hemoglobin (%)
100
90
80
70
60
50
40
30
20
10
0
Baseline 1 2 3 4 5 6 9 12 15 18 21 24 27 30 33 36 42 48
Months since Infusion
No. of Patients 44 42 43 43 41 40 38 34 32 29 27 16 17 10 7 4 2 1 1
C Mean Percentages of F Cells
F Cells (%)
100
90
80
70
60
50
40
30
20
10
0
Baseline 1 2 3 4 5 6 9 12 15 18 21 24 27 30 33 36 42 48
Months since Infusion
No. of Patients 44 43 41 43 41 41 39 34 32 29 27 17 17 10 7 4 2 1 1

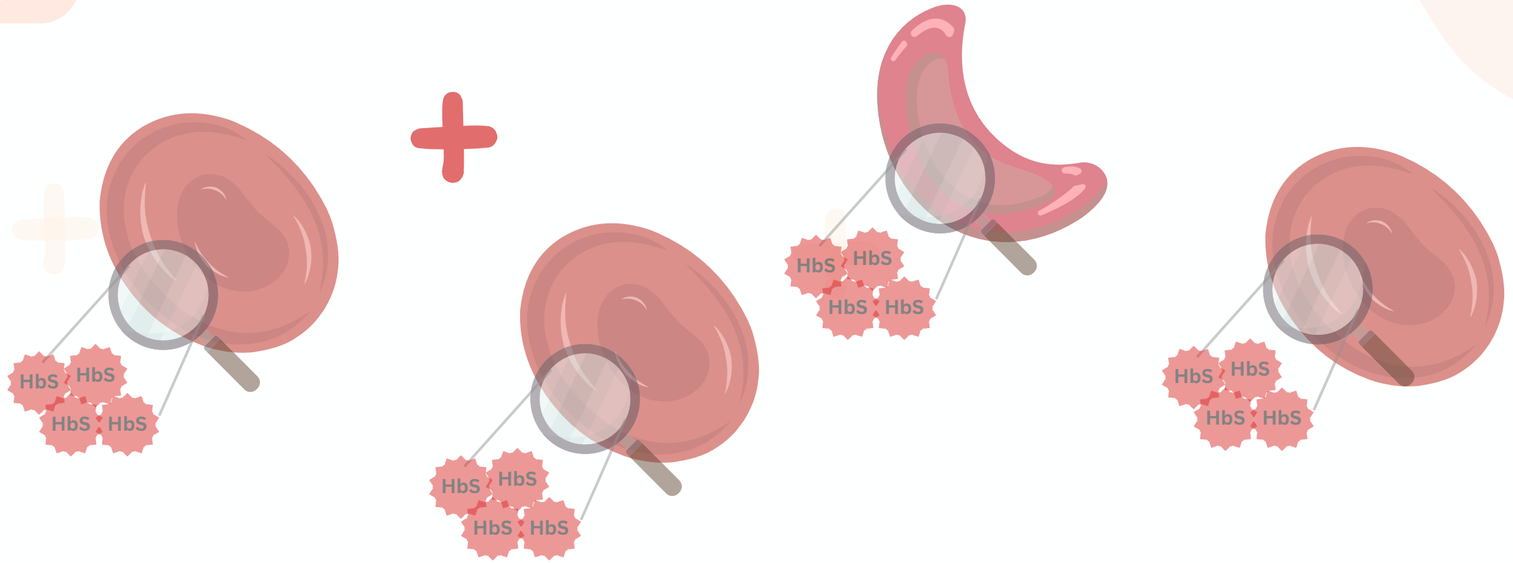
HOW GENE THERAPY IMPACTS HBS%

Red cells are lysed in the analyser and haemoglobin is counted.

Without gene therapy

HbS % usually 80-90%

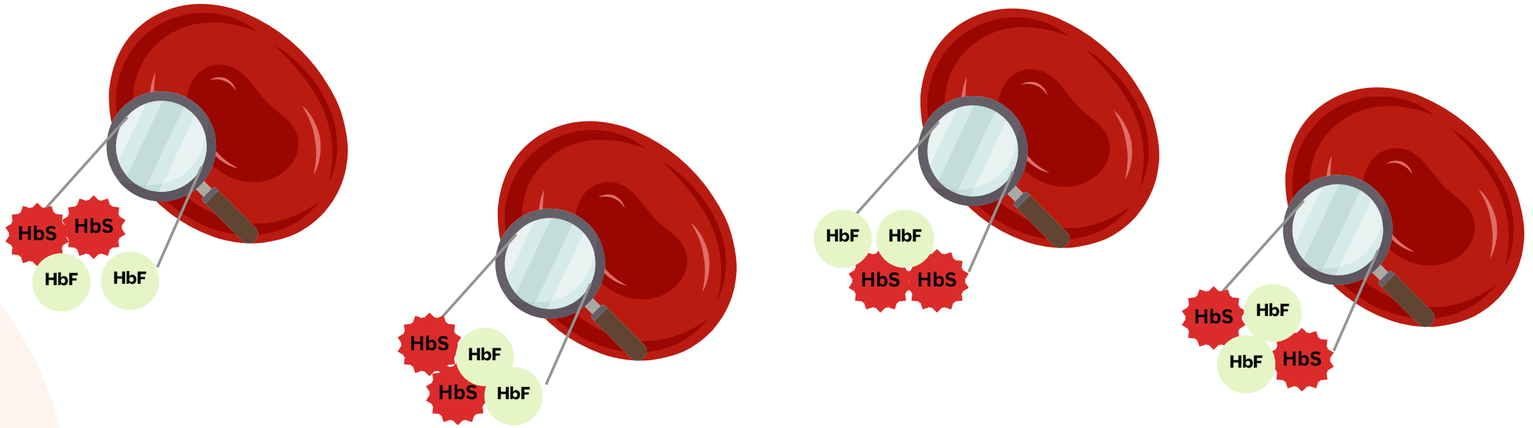
HbF% usually <1%



With gene therapy

HbS % 50%

HbF% - 40-50%



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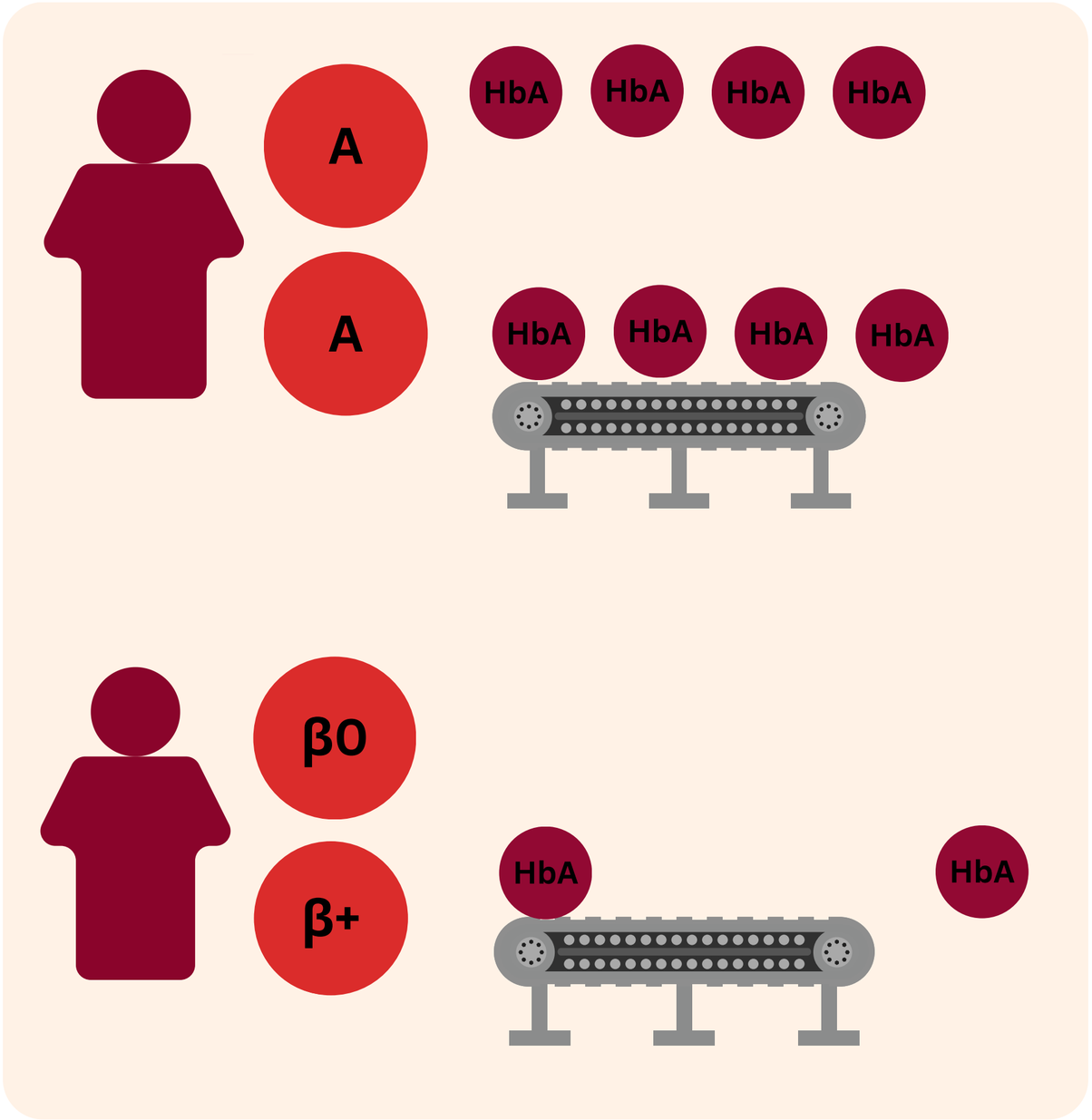
Coordinating Centre

THALASSAEMIA

South West Haemoglobinopathy Coordinating Centre

Haemoglobin production in thalassaemia



Chromosome 11

ε	γ	δ	βO

+

Chromosome 11

ε	γ	δ	β+

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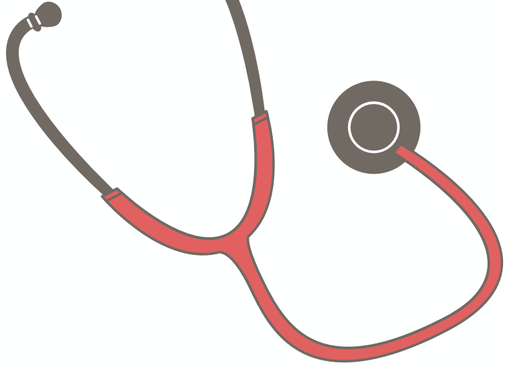

HOW CAN HAEMOGLOBIN SYNTHESIS GO WRONG

Structural abnormalities

Haemoglobin is made, but the structure is different to normal haemoglobin due to a genetic mutation (usually affecting the beta gene). Examples include:

- HbS
- HbC

Abnormalities in haemoglobin production

Mutations in alpha or beta genes reduce the production in alpha or beta chains. This reduces the amount of normal haemoglobin. These conditions are called thalassaemias.

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BETA THALASSAEMIAS

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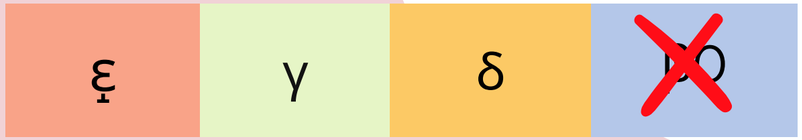
Coordinating Centre

BETA THALASSAEMIA MAJOR

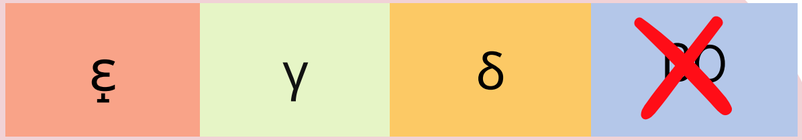
Chromosome 16

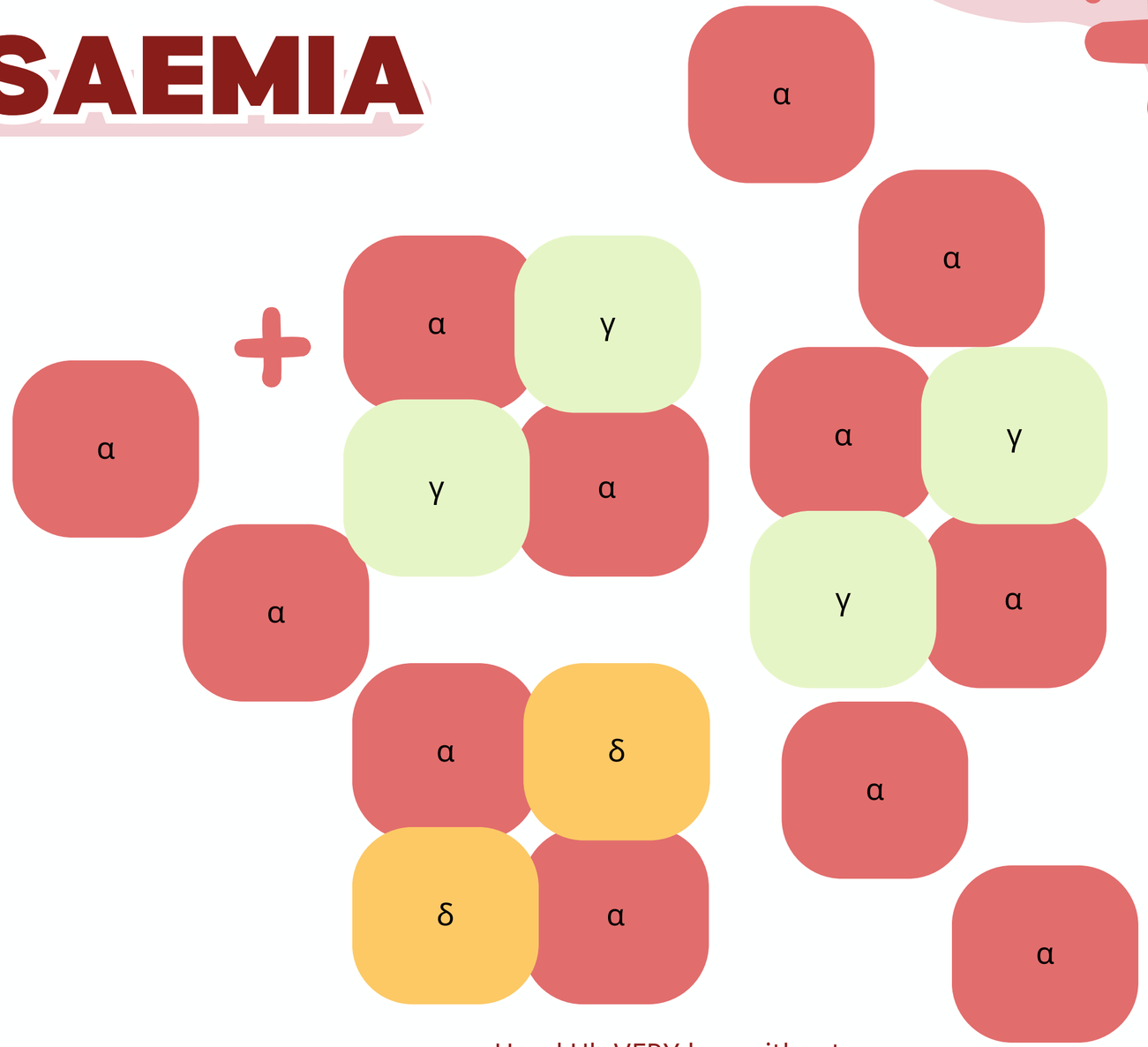
Chromosome 16

Chromosome 11



Chromosome 11





Usual Hb VERY low without transfusion
Significant microcytosis

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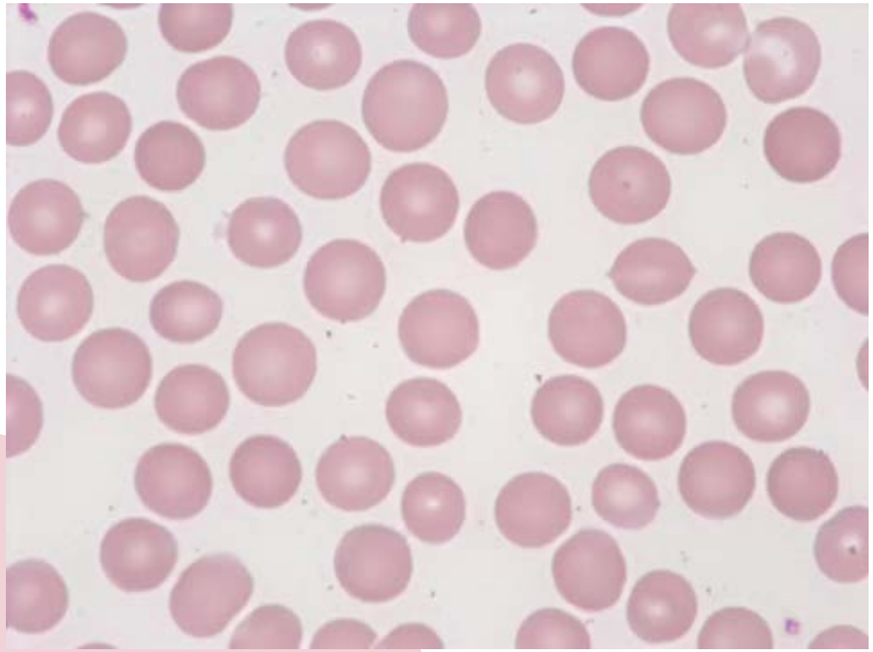
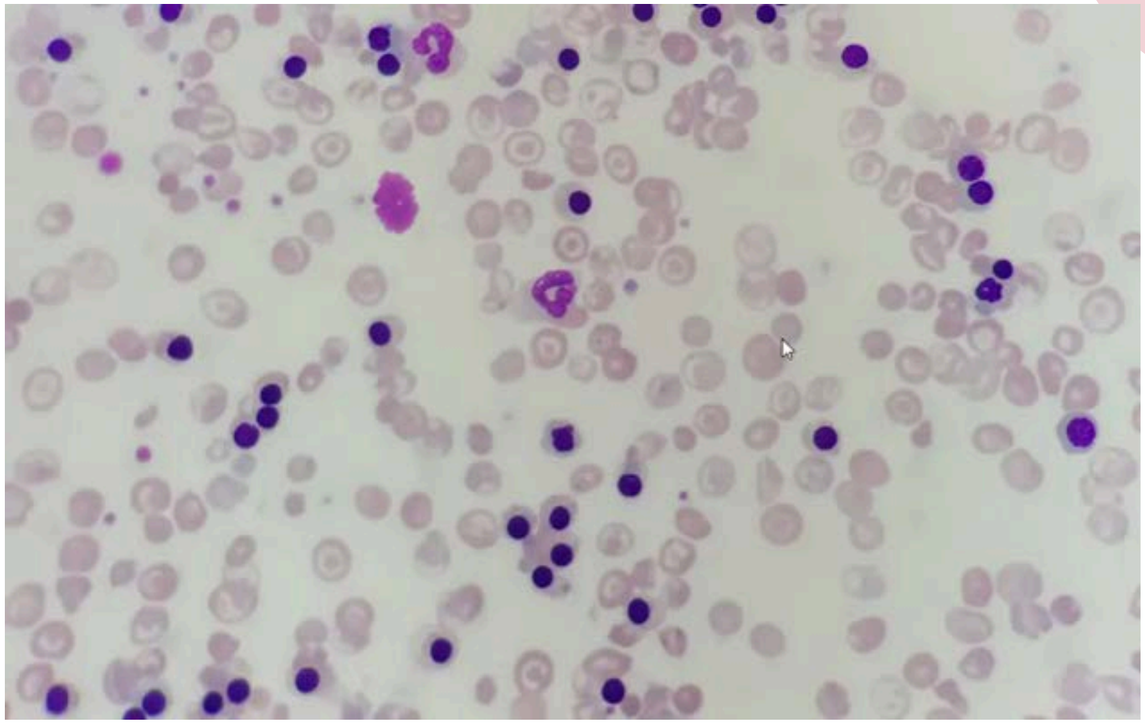


Normal



Thalassaemia major

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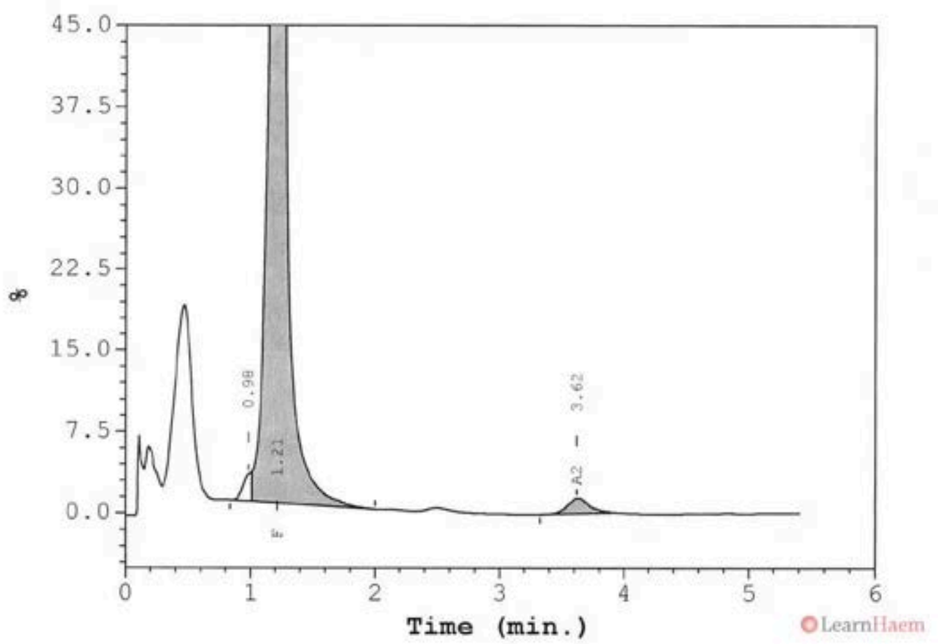
BETA THALASSAEMIA MAJOR - DIAGNOSIS

No HbA

Majority of haemoglobin is HbF

Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
Unknown	---	0.9	0.98	18087
F	93.8*	---	1.21	1908326
A2	1.4*	---	3.62	24705



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Coordinating Centre

BETA THALASSAEMIA INTERMEDIA

Chromosome 16

ζ	α	α

Chromosome 16

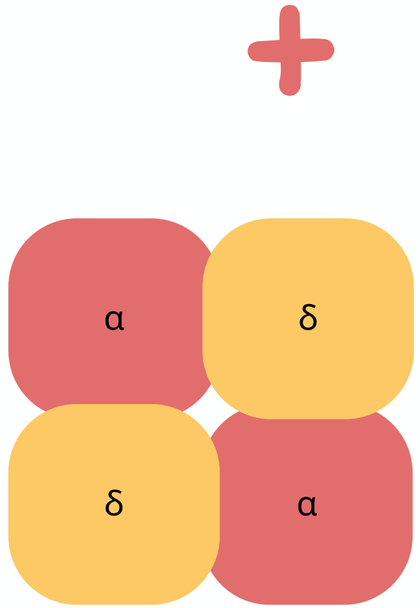
ζ	α	α

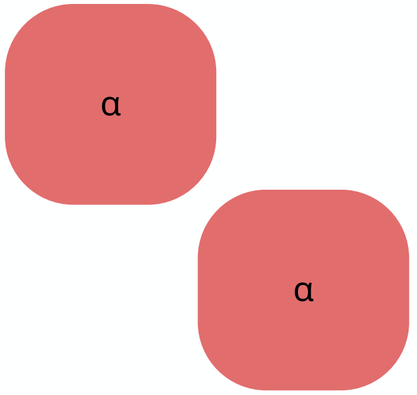
Chromosome 11

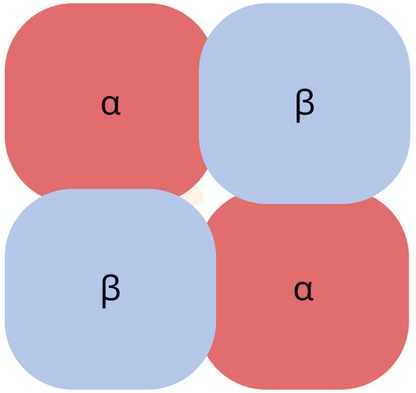
ε	γ	δ	~~β0~~

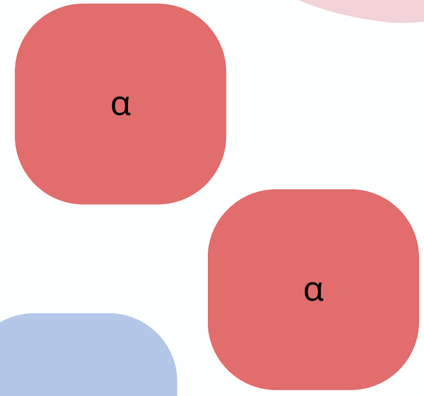
Chromosome 11

ε	γ	δ	β+

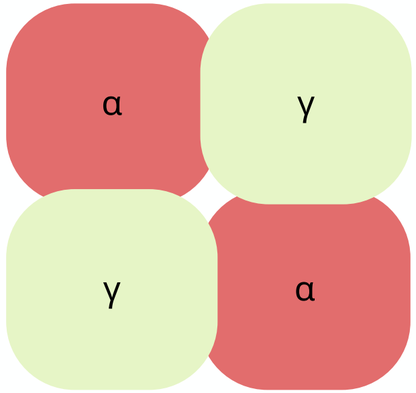








Usual Hb around
70-80
Microcytosis
Haemolysis



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BETA THALASSAEMIA INTERMEDIA

Raised HbA2

Most Hb is HbF

Small amount of HbA only

Peak Name	Calibrated Area%	Area%	Retention Time (min.)	Peak Area
F	71.6*	---	1.16	987082
P3	---	1.6	1.72	24279
Ao	---	30.1	2.48	468719
A2	4.6*	---	3.65	78429

Total Area : 1558508

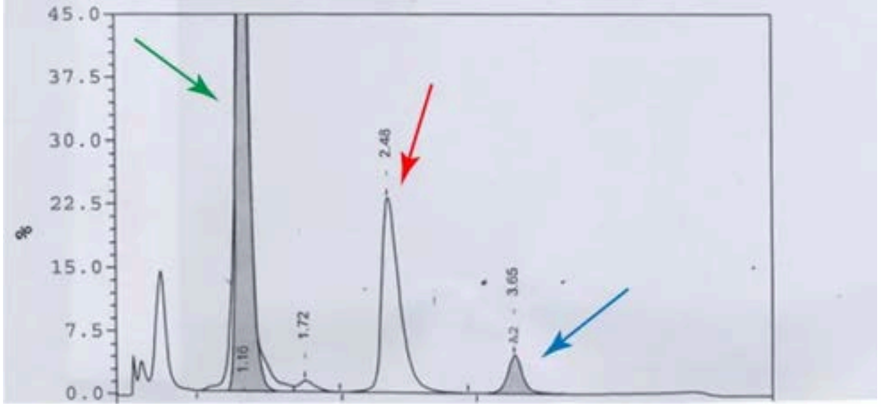
F Concentration = 71.6* %

A2 Concentration = 4.6* %

LearnHaem

Analysis comments:

*Values outside of expected ranges



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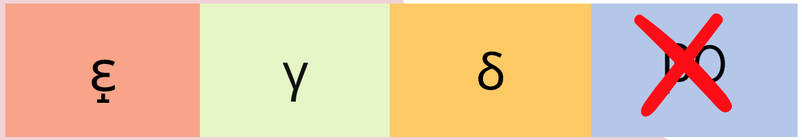
BETA THALASSAEMIA TRAIT

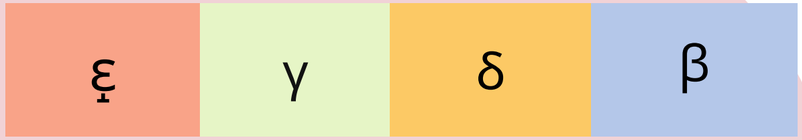
Chromosome 16

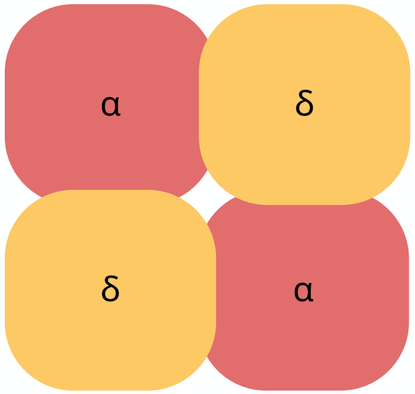
Chromosome 16

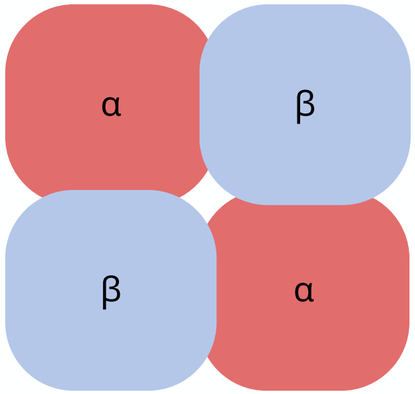
Chromosome 11

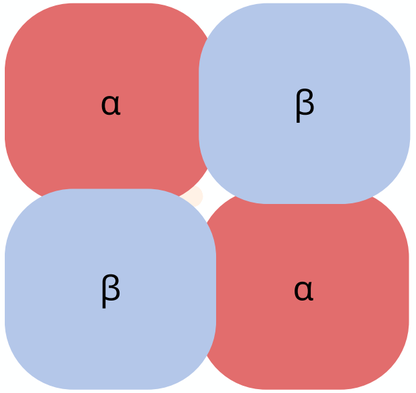


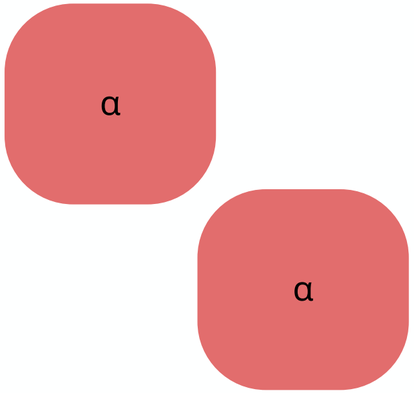
Chromosome 11

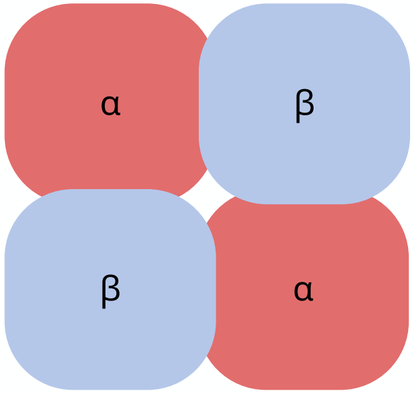












Usual Hb around
100-130
Microcytosis

South West
Haemoglobinopathy
Coordinating Centre

BETA THALASSAEMIA TRAIT

FULL BLOOD COUNT					
White Cell Count		6.05	10^9/L	4.0 - 11.0
RBC	*	5.55	10^{12}/L	3.80 - 5.30
Haemoglobin	*	110	g/L	120 - 150
Haematocrit	*	0.361	L/L	0.37 - 0.45
MCV	*	65.0	fL	83 - 100
MCH	*	19.8	pg	27.0 - 32.0
MCHC	*	305	g/L	310 - 350

South West
Haemoglobinopathy
Coordinating Centre

BETA THALASSAEMIA TRAIT

Raised HbA2 only abnormality

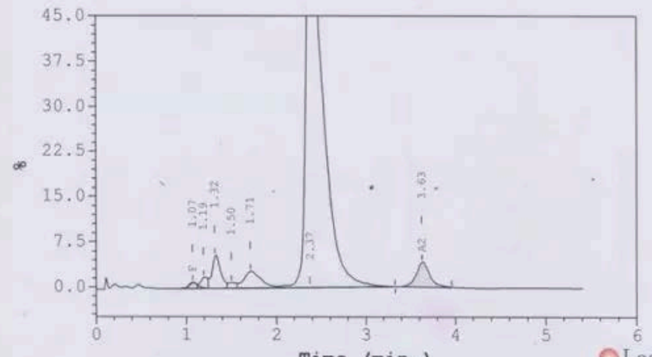
Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
F	0.8	---	1.07	13523
Unknown	---	1.1	1.19	19337
P2	---	3.7	1.32	65657
Unknown	---	0.6	1.50	11157
P3	---	3.8	1.71	66683
Ao	---	85.5	2.37	1517347
A2	4.2*	---	3.63	81884

Total Area: 1,775,589

F Concentration = 0.8 %
A2 Concentration = 4.2* %

*Values outside of expected ranges

Analysis comments:



LearnHaem

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ALPHA THALASSAEMIAS

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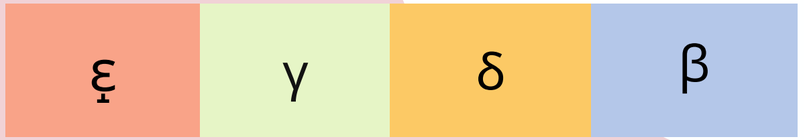
ALPHA THALASSAEMIA MAJOR

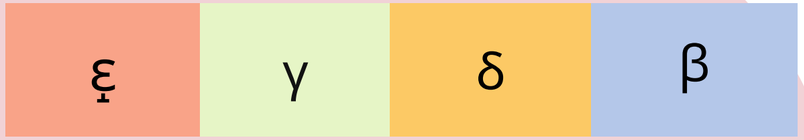
Chromosome 16

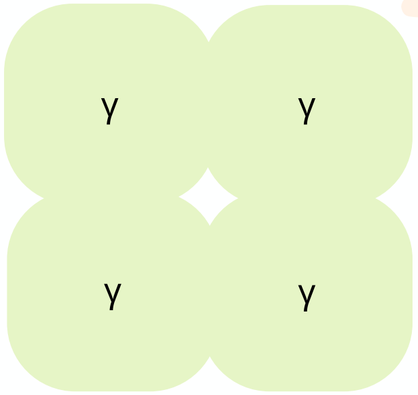
Chromosome 16

Chromosome 11

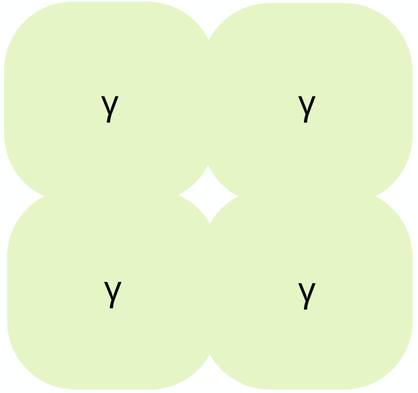


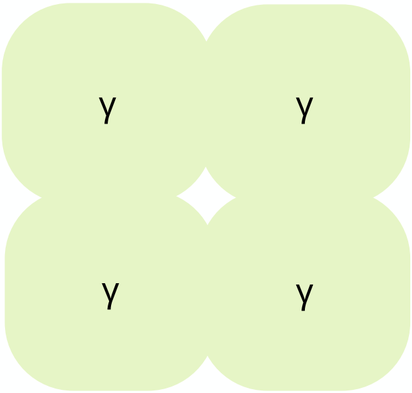
Chromosome 11





Hb Barts





- Very high O2 affinity - will not give up O2 into tissues of fetus
- Accumulates in red cells

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Haemoglobinopathy
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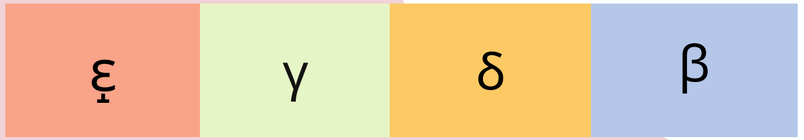
ALPHA THALASSAEMIA MAJOR

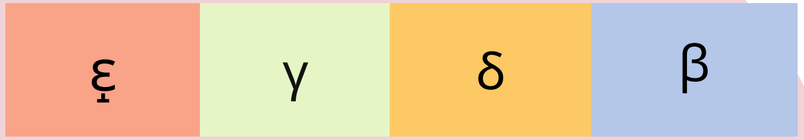
Chromosome 16

Chromosome 16

Chromosome 11



Chromosome 11



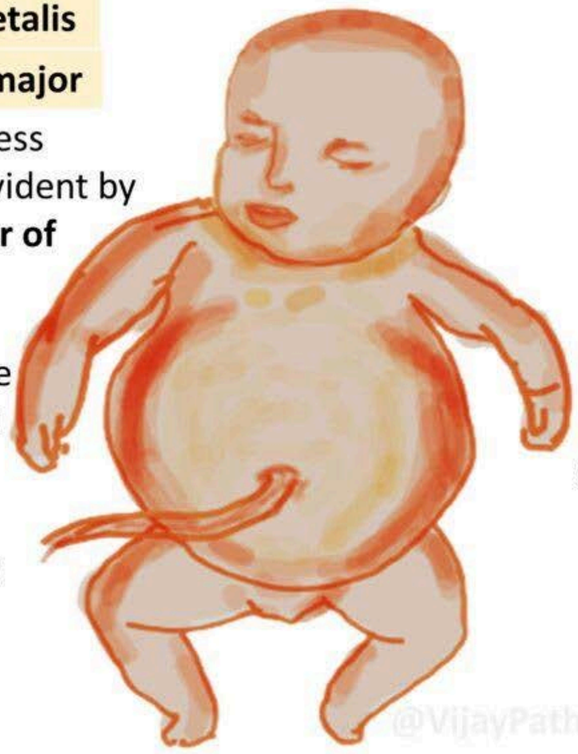
Hb Bart's hydrops fetalis

alpha thalassemia major

Signs of fetal distress usually become evident by the **third trimester of pregnancy**

fetus shows severe pallor, generalized edema, and massive hepatosplenomegaly

similar to that seen in hemolytic disease of the newborn



Why NOT before 3rd month?

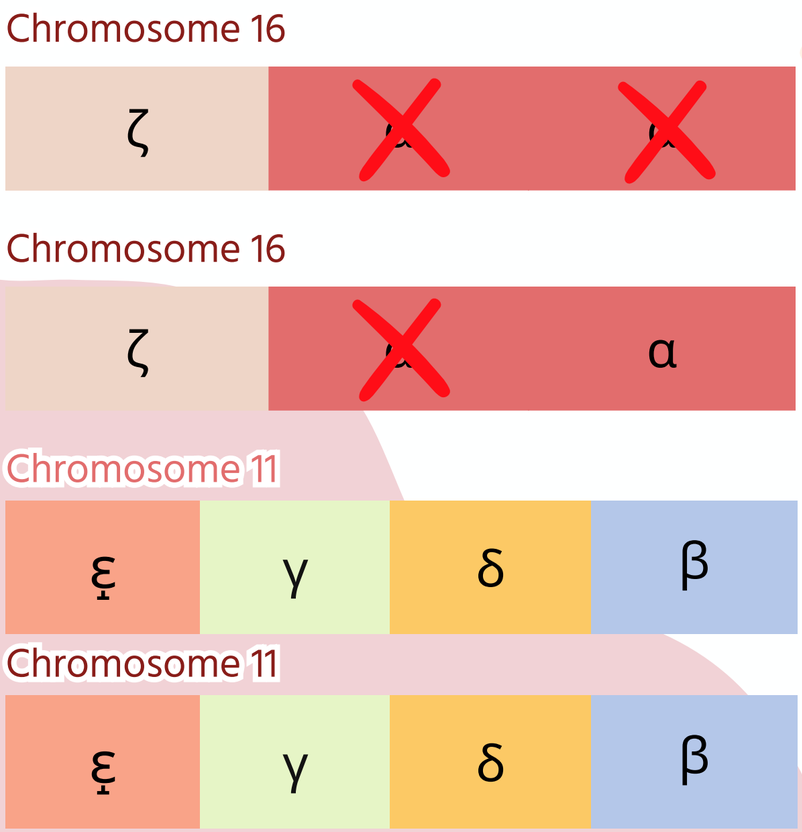
due to the expression of ζ chains, an embryonic globin that pairs with γ chains to form a functional ζ2γ2 Hb tetramer.

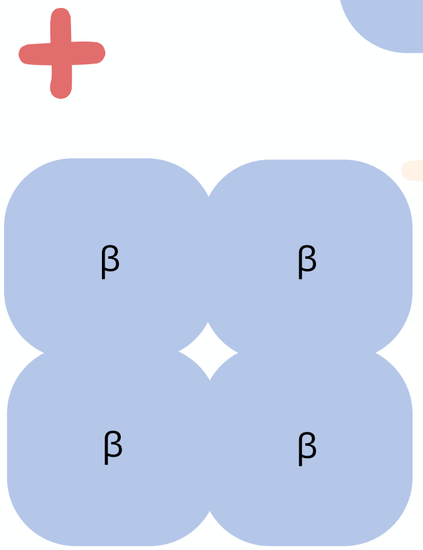
Hb Portland I

Survival in early development

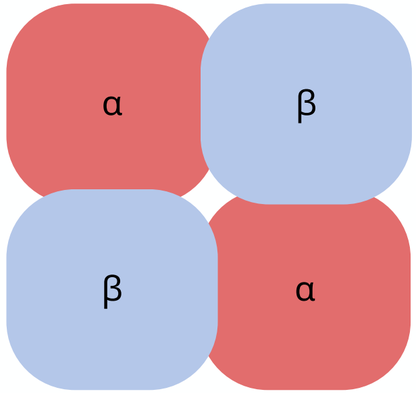
South West
Haemoglobinopathy
Coordinating Centre

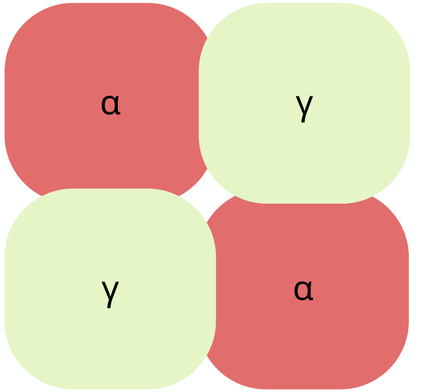
HBH DISEASE (ALPHA THALASSAEMIA DISEASE)

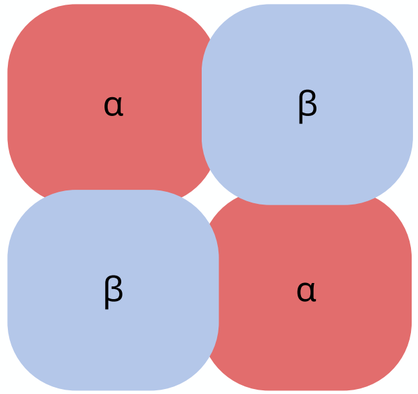




HbH







Usual Hb around 80
Microcytosis
HbH% usually 10-20%
Haemolysis, splenomegaly

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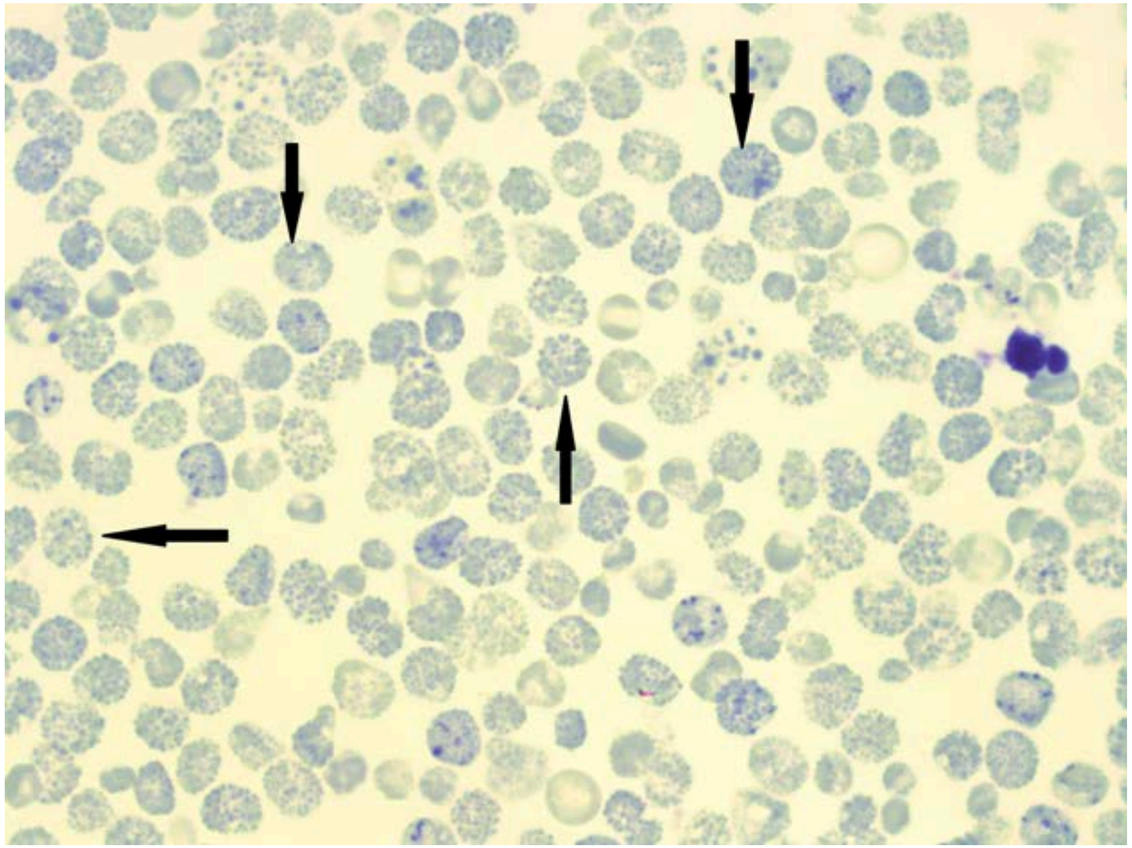
Haemoglobinopathy
Coordinating Centre

HBH DISEASE (ALPHA THALASSAEMIA DISEASE)



Classic ‘golf ball’ appearance can only be seen with supravital staining

Exam fodder: MDS can induce acquired HbH disease - ATRX mutation

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Haemoglobinopathy
Coordinating Centre

HBH DISEASE (ALPHA THALASSAEMIA DISEASE)

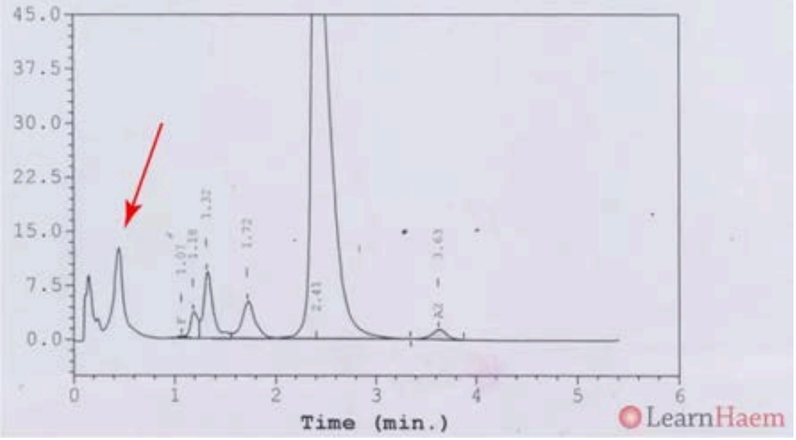
Peak Name	Area %	Area %	Time (min)	Area
F	0.2	---	1.07	3626
Unknown	---	2.1	1.18	33545
P2	---	6.4	1.32	102318
P3	---	5.0	1.72	79683
Ao	---	84.8	2.41	1361813
A2	1.4*	---	3.63	25346

Total Area: 1,606,332

Concentration = 0.2 %
Concentration = 1.4* %

alues outside of expected ranges

alysis comments:



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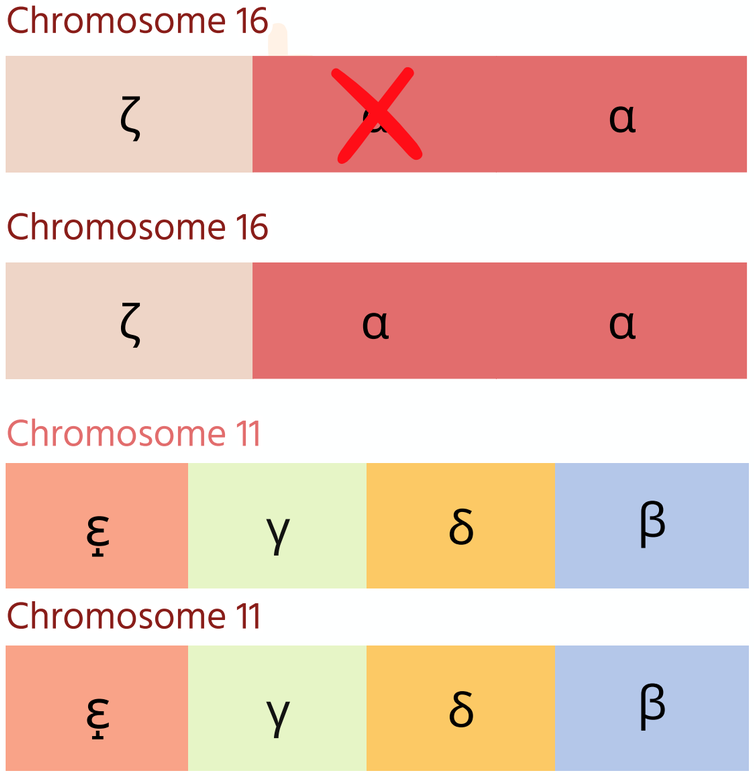
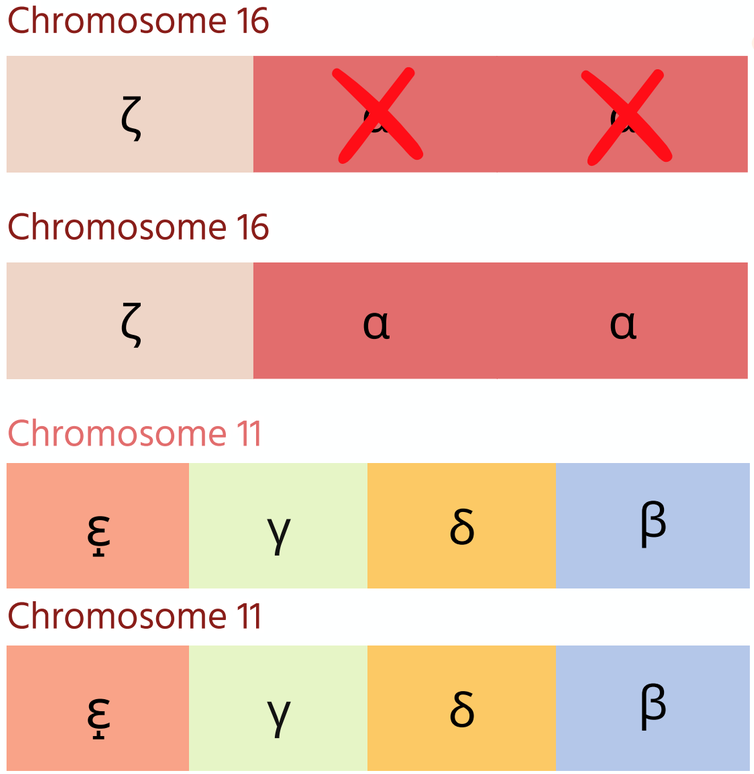
ALPHA THALASSAEMIA TRAIT

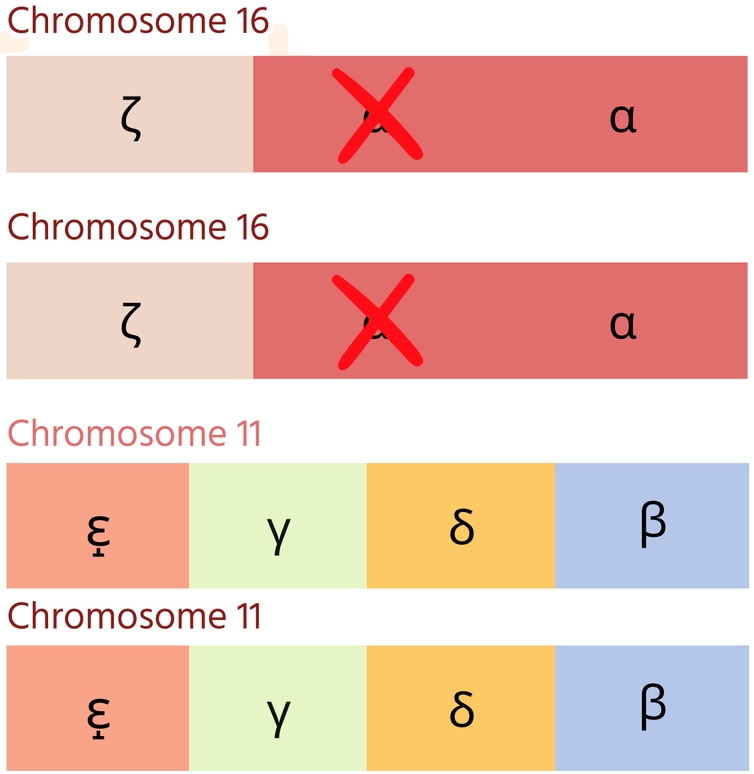
α_+ heterozygosity



α_0 heterozygosity



α_+ homozygosity



Essentially normal levels of HbA
Microcytosis
Possible mild anaemia

HPLC usually normal
MCH <27, or <25 in homozygous carriers or α_0 heterozygosity

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Coordinating Centre

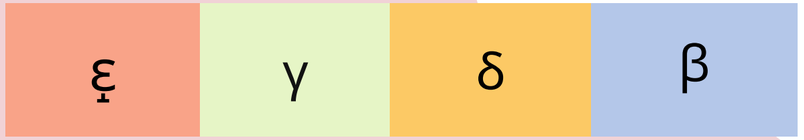
ALPHA THALASSAEMIA TRAIT - ARE ALL TRAITS EQUAL?

Chromosome 16

Chromosome 16

Chromosome 11

Chromosome 11



Chromosome 16

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South West Haemoglobinopathy Coordinating Centre

ALPHA THALASSAEMIA TRAIT - ARE ALL TRAITS EQUAL?

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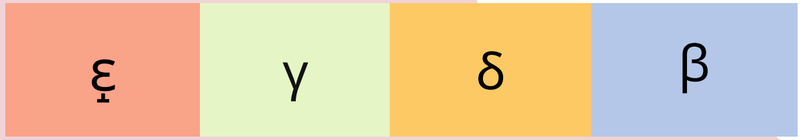

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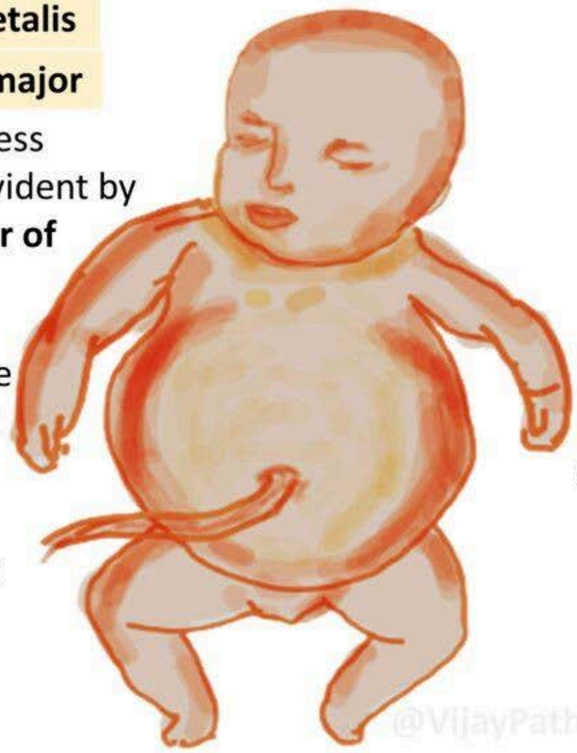

Why NOT before 3rd month?

due to the expression of ζ chains, an embryonic globin that pairs with γ chains to form a functional ζ2γ2 Hb tetramer.

Hb Portland I

Survival in early development

@VijayPatho

South West Haemoglobinopathy Coordinating Centre

CONSIDER GENETIC TESTING BASED ON ETHNICITY

Haemoglobin S	African including north African, African-Caribbean, African-American, black British and any other African ethnicity (e.g. central and south American of partly African ethnicity), Greeks, southern Italians including Sicilians, Turks, Arabs, Indians
Haemoglobin C	African including African-Caribbean, African-American, Black British and any other African ethnicity (e.g. Central and South American of partly African ethnicity)
α^0 thalassaemia	Chinese, Taiwanese, Southeast Asian (Thai, Laotian, Cambodian, Vietnamese, Myanmar, Malaysian, Singaporean, Indonesian, Filipino), Cypriot, Greek, Turkish and Sardinian
β thalassaemia	All ethnic groups other than Northern Europeans

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Haemoglobinopathy
Coordinating Centre

We have covered

- How to test for haemoglobin variants
- Sickle cell disease
  - The basics
  - Treatment options
- Thalassaemia types and testing.