Webinars for patients

Sickle Cell Disease

Topic on Focus EuroBloodNet

Genetic Counselling

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ERN-EuroBloodNet subnetwork : Red Blood Cell
Coimbra – Portugal
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the Health Programme
of the European Union

European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

Webinar rules

- **30-35min presentation + 15 min Q&A session**
- **Microphones will be muted by host to avoid back noise**
- **Please, stop your video to improve internet conexion**
- **Send your questions during the presentation through the chat**

Conflicts of interest

I have no conflicts of interest to declare.

Why are you interested in Genetic Counselling for Sickle Cell Disease?

1. I'm are carrier of HbS (Sickle cell trait)
2. I'm a person with Sickle cell disease / I'm close to a person with SCD
3. We are a couple at risk for Sickle cell disease
4. I don't know if I'm a carrier, I've never been tested
5. I want to learn more about the genetics of SCD

Learning objectives

After this webinar on Genetic Counselling will be able to:

1. **Understand the genetic basis and pattern of inheritance of sickle cell disease**
2. **Understand how and who should do the diagnosis for Sickle cell trait (HbS carriers)**
3. **Be aware of the usefulness of identification of couples at risk for SCD and their options**

Definition

Sickle Cell disease:

a genetic disorder that affects red blood cells (erythrocytes) causing them to become sickle or crescent shaped.

Healthy red blood cells are round shaped, and they move through small blood vessels to carry oxygen to all parts of the body.

SCD red blood cells are C-shaped and are called “sickle.” The sickle cells die early, which causes anemia. When they travel through small blood vessels, they get stuck and clog the blood flow. This can cause strong pain and other serious complications such as infection, acute chest syndrome and stroke.

https://www.appdh.org.pt/drepanocitose

Sickle Cell disease is a severe disorder

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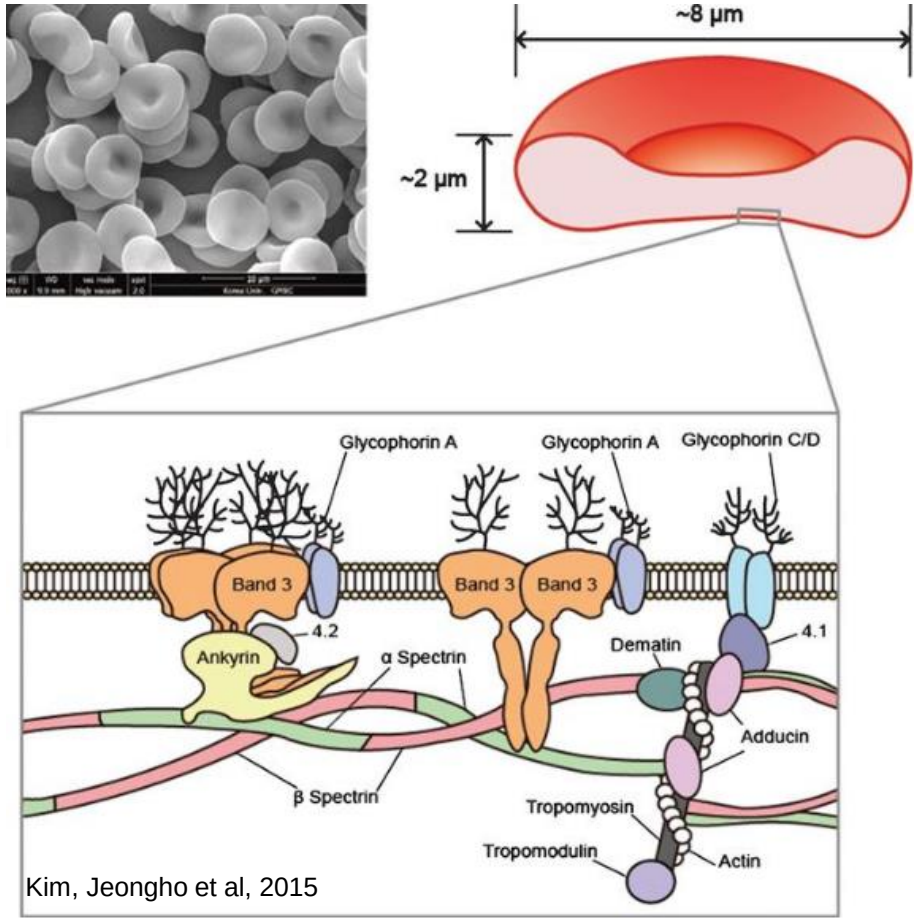
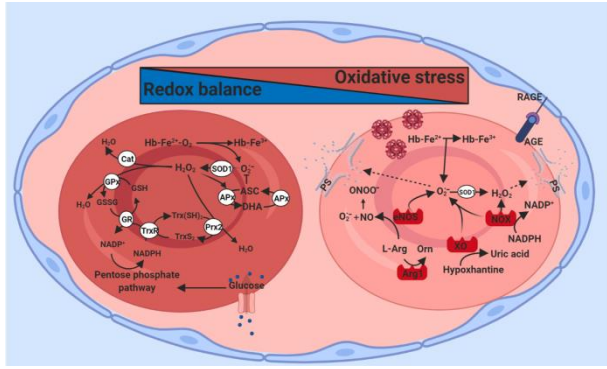
Red blood cells



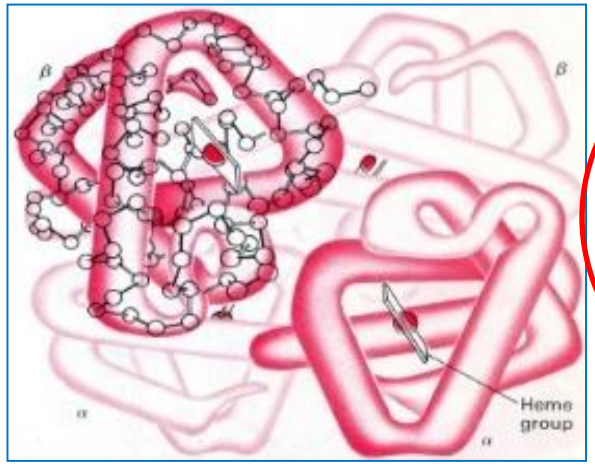
Kim, Jeongho et al, 2015

Membrane



Ali Mahdi et al, 2021

Enzymes



Hemoglobin

a protein that carries oxygen.

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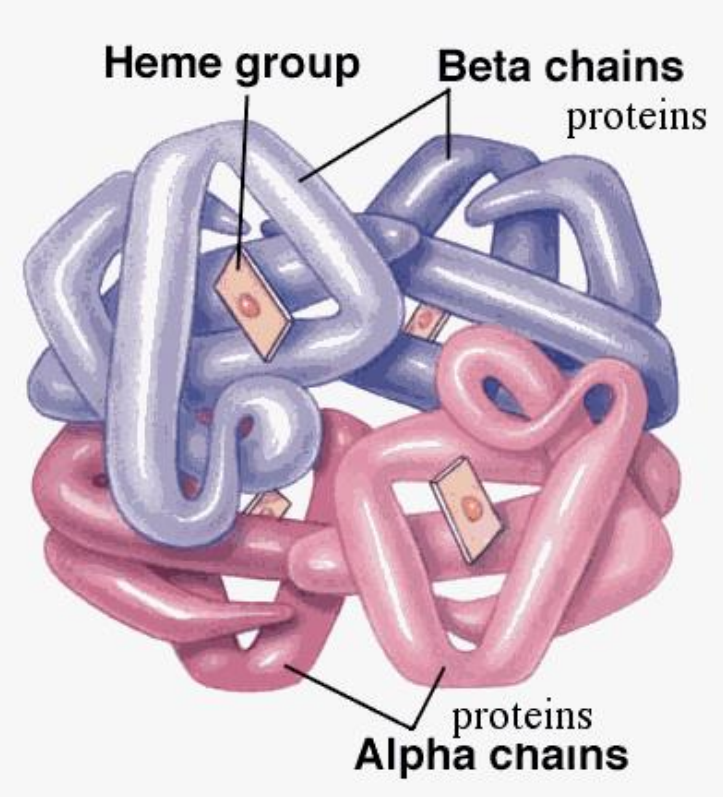
Hemoglobin



Normal hemoglobin in adults: **HbA** $\alpha_2\beta_2^A$

Normal hemoglobin in fetus: **HbF** $\alpha_2\gamma_2$

Hemoglobin in Sicke Cell: **HbS** $\alpha_2\beta_2^S$

β-globin gene: *HBB*

β-globin gene: HBB

Chromossome 11

HbA **HBB:c.20A**

HbS **HBB:c.20A>T**

β^S chain: Glu7Val

.....gcaggagccagggctgggcataaaagtcagggcagagccatctattgctt

ACAT A>T CACAACTGTGTTCACTAGCAACCTCAAACAGACACCATGGTGCATC
TGAC AAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAG
TTGG CTGGGCAG

gttggtatcaaggttacaagacaggtttaaggagaccaatagaaactgggcatgtggaga
cagagaagactcttgggtttctgataggcactgactctctctgcctattggtctattttc
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TCCAACTACTAAACTGGGGGATATTATGAAGGGCCTTGAGCATCTGGATTCTGCCTAATA
AAAAACATTTATTTTCATTGCAA

tgatgtatttaaattatttctgaatattttactaaaaagggaatgtggga.....

https://www.ensembl.org

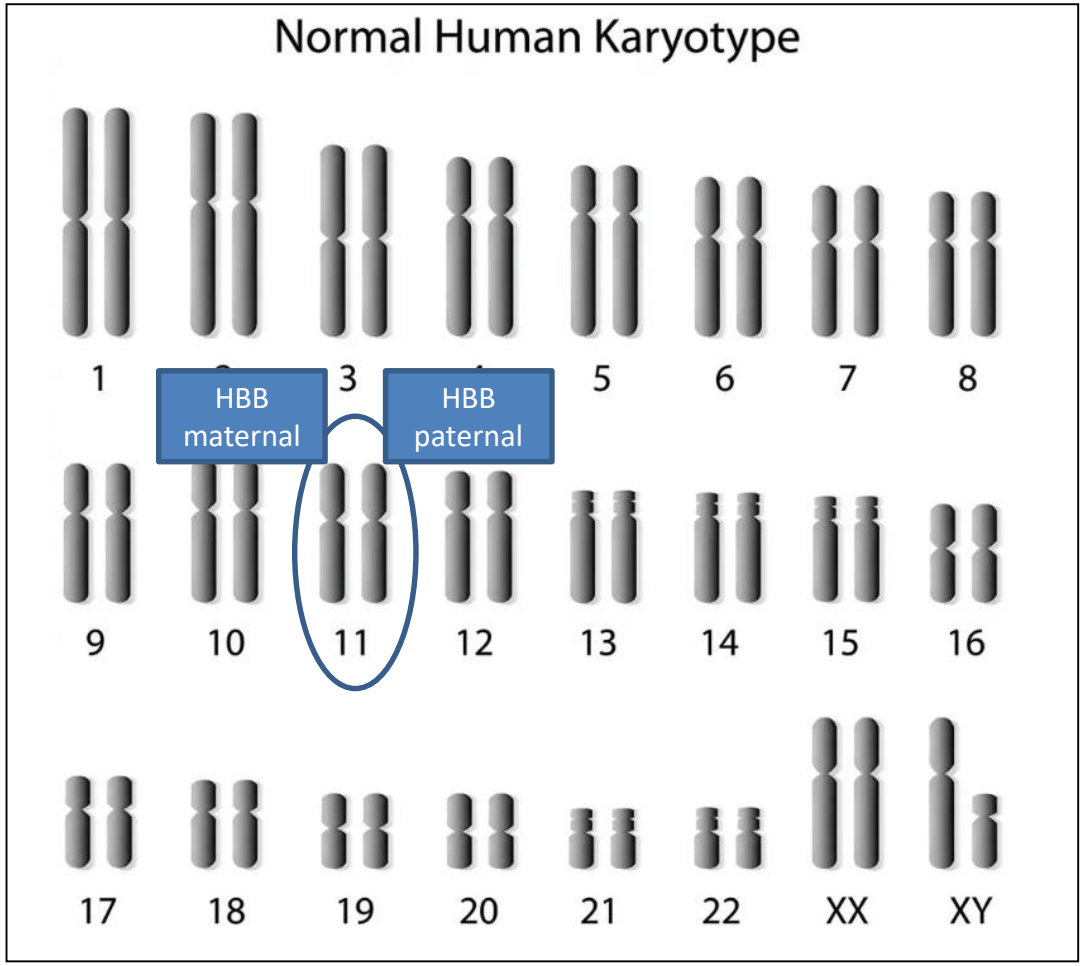
Learning objectives

After this webinar on Genetic Counselling will be able to:

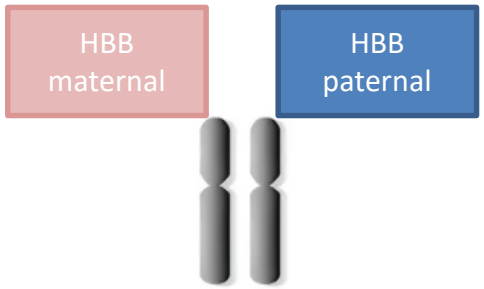
1. **Understand the genetic basis and the pattern of inheritance of sickle cell disease**
2. **Understand how and who should do the diagnosis for Sickle cell trait (HbS carriers)**
3. **Be aware of the usefulness of identification of couples at risk for SCD**

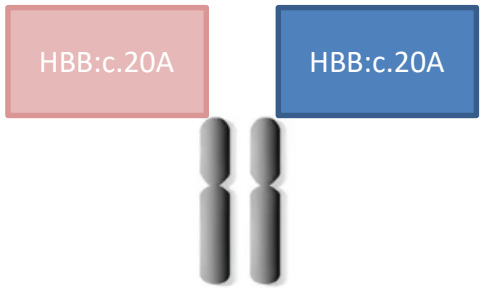
Pattern of Inheritance

- Human cell contain 23 pairs of chromosomes. 22 pairs autosomal and one pair sex chromosomes.
- 23chromosomes inherited from mother and 23 chromosomes from father.
- Sex chromosomes: XX for female and XY for male.



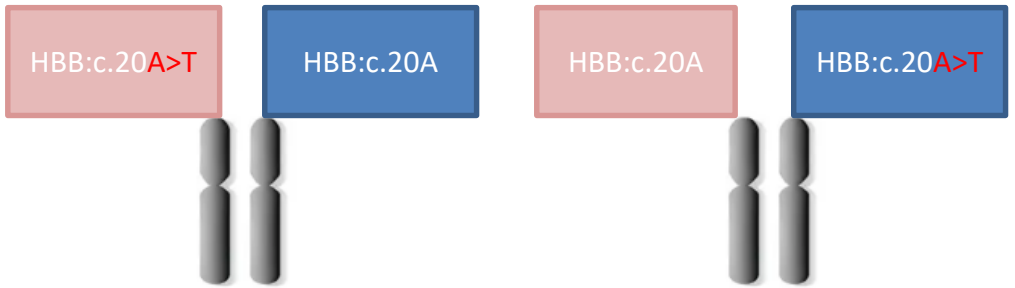
Pattern of Inheritance





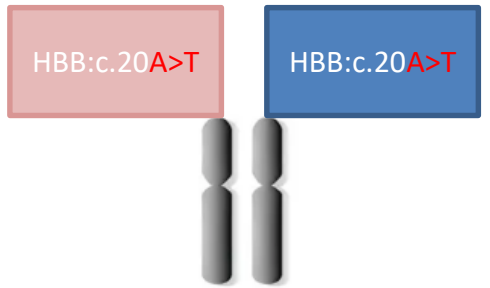
Homozygous normal

Hb A



Heterozygous AS

Hb A + Hb S



Homozygous S

Hb S (SS)

Normal

Sickle Cell disease

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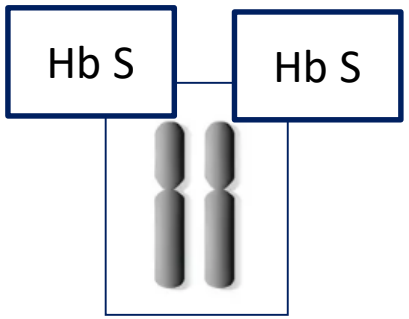
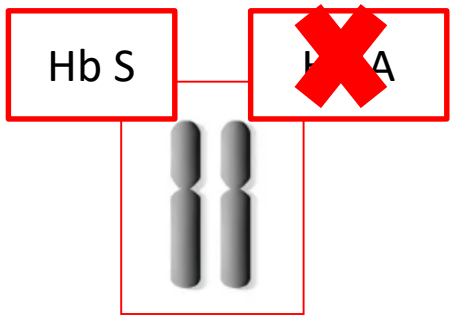
Autossomic recessive

HbS / Hb S

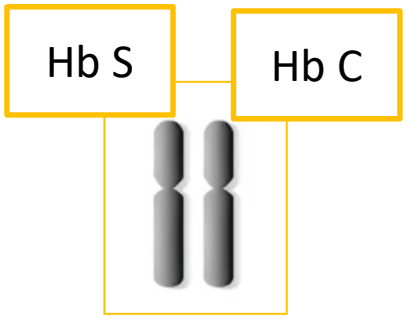
Hb S / other hemoglobinopathie



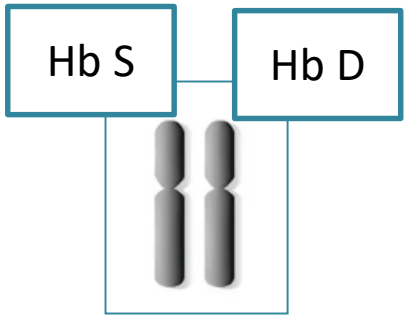
S/S



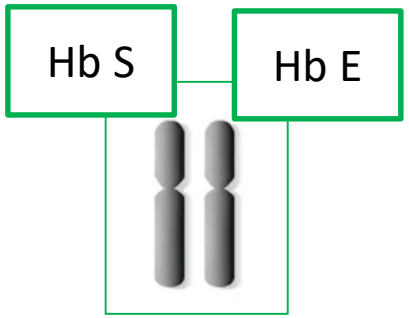
S/βthal



S/C



S/D



S/E

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Learning objectives

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1. Understand the genetic basis and the pattern of inheritance of sickle cell disease
2. Understand how and who should do the diagnosis for Sickle cell trait (HbS carriers)
3. Be aware of the usefulness of identification of couples at risk for SCD

Diagnosis of carriers – Hb S and other Hemoglobinopathies

Hemogram

- Normal hematological parameters
- Moderate anemia with hypochromic mycrocitic RBC

AND

Hemoglobin study

- Quantification and identification of Hb variants

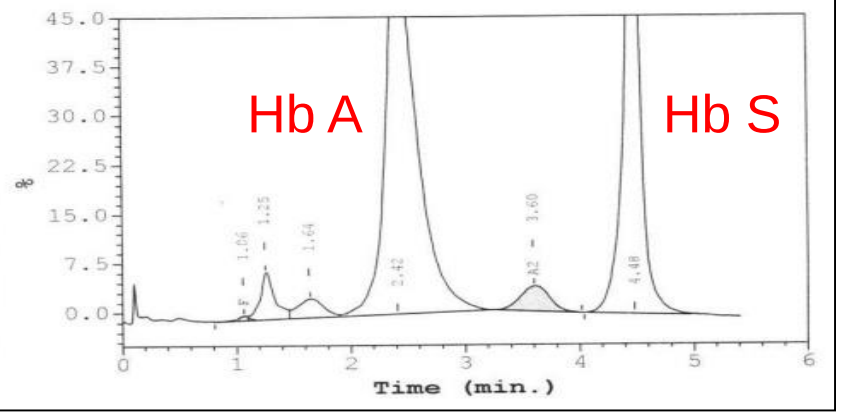
Hb S carrier

Hemoglobin study

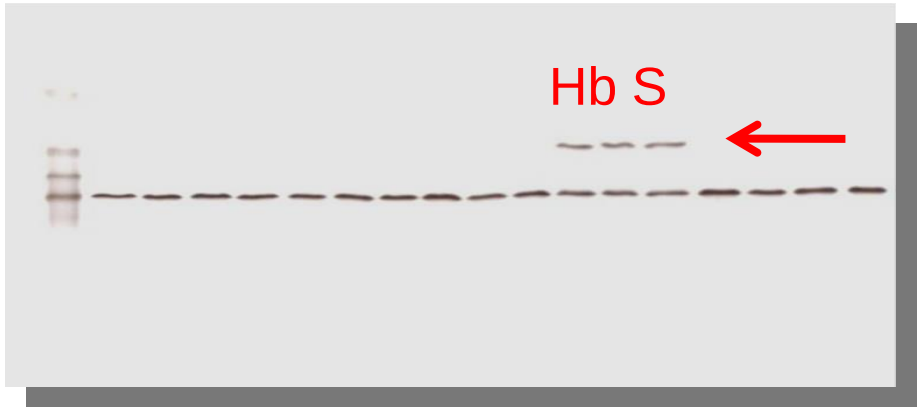
HPLC

Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
F	0.3	---	1.06	572
Unknown	---	3.2	1.25	8632
P3	---	2.2	1.64	6072
Ao	---	52.4	2.42	142319
A2	3.8*	---	3.60	9030
S-window	---	38.7	4.48	105043

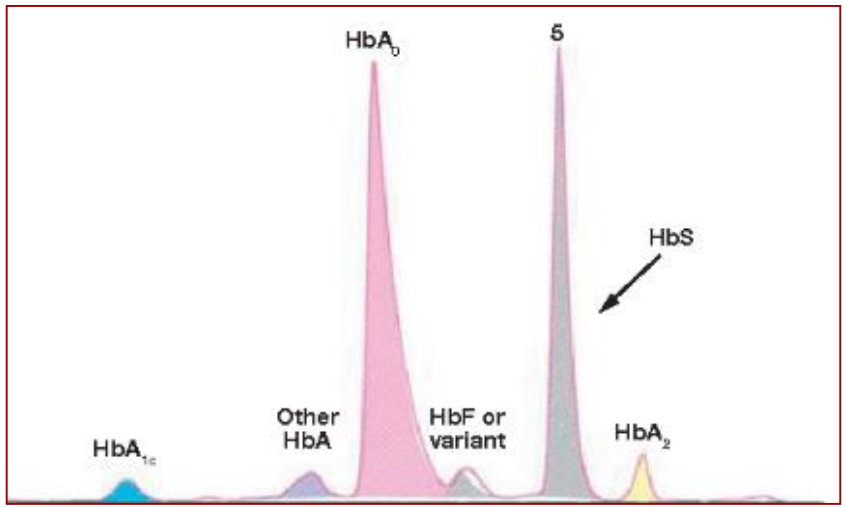
F Concentration = 0.3 %
A2 Concentration = 3.8* %



- Isoeletric Focusing (IEF)



Capillary Electrophoresis



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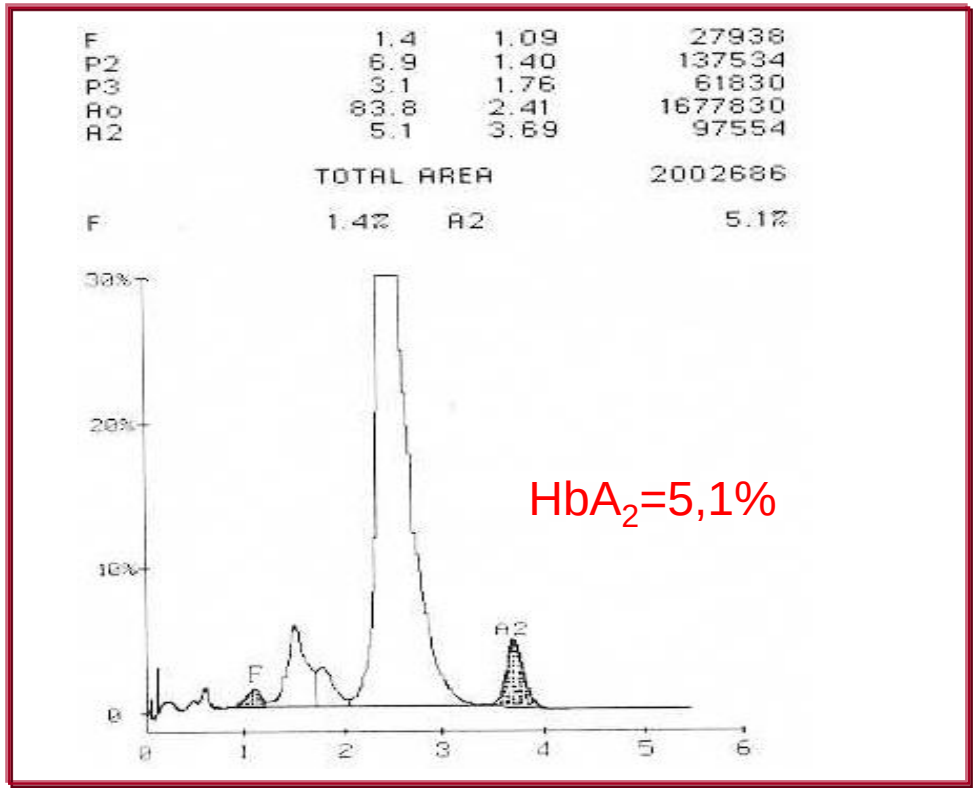
β-thalassemia carrier

- Hemograma

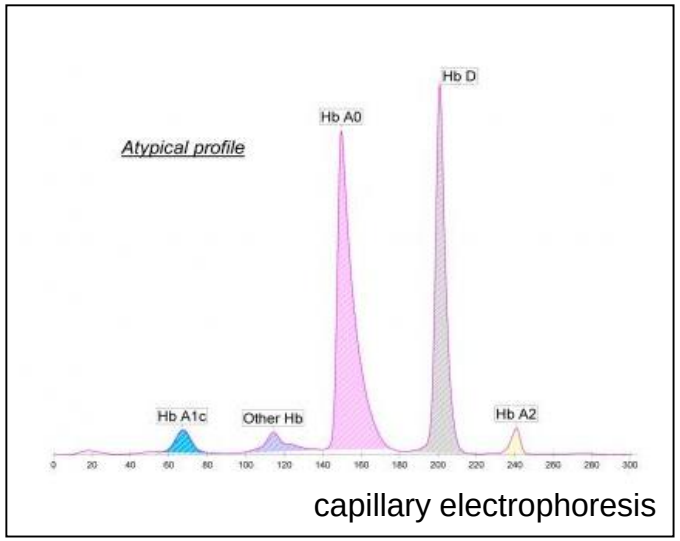
Hb (g/dL)	Normal or low
MCV (fL)	Low
MCH (pg)	Low

HbA_2 >3.5%

- Hemoglobin study (HPLC):



Other Hb variants

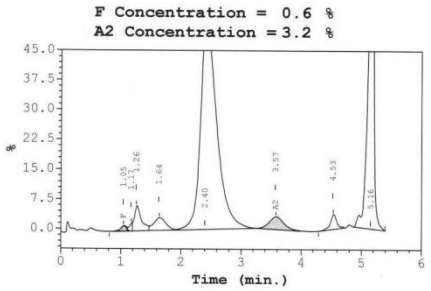


capillary electrophoresis

Hb D

Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
F	0.6	---	1.05	14146
Unknown	---	0.4	1.17	11459
P2	---	2.7	1.26	80459
P3	---	2.3	1.64	70364
Ao	---	51.3	2.40	1547410
A2	3.2	---	3.57	86114
S-window	---	1.5	4.53	43905
C-window	---	38.5	5.16	1161799

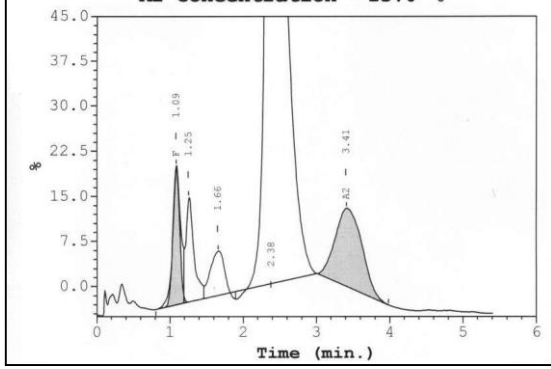
F Concentration = 0.6 %
A2 Concentration = 3.2 %



Hb C

Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
F	6.3*	---	1.09	117579
Unknown	---	4.6	1.25	104408
P3	---	3.4	1.66	76880
Ao	---	75.2	2.38	1695546
A2	13.0*	---	3.41	260310

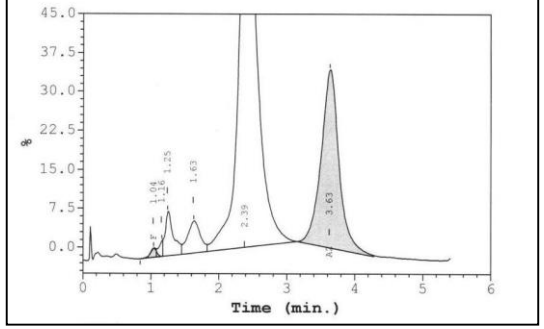
F Concentration = 6.3* %
A2 Concentration = 13.0* %



Hb Lepore

Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
F	0.6	---	1.04	10127
Unknown	---	0.6	1.16	11204
Unknown	---	3.2	1.25	64424
P3	---	3.6	1.63	72141
Ao	---	64.1	2.39	1290207
A2	34.3*	---	3.63	564500

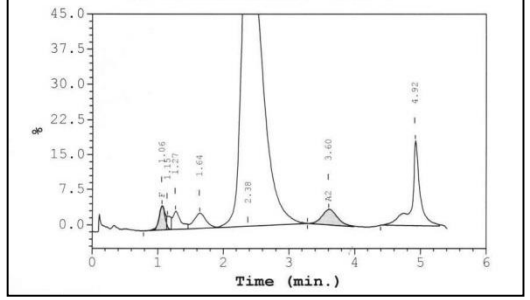
F Concentration = 0.6 %
A2 Concentration = 34.3* %



Hb E

Peak Name	Calibrated Area %	Area %	Retention Time (min)	Peak Area
F	2.2*	---	1.06	40816
Unknown	---	0.7	1.15	15271
P2	---	1.8	1.27	40091
P3	---	2.3	1.64	51723
Ao	---	81.4	2.38	1798418
A2	3.3	---	3.60	66748
C-window	---	8.8	4.92	195130

F Concentration = 2.2* %
A2 Concentration = 3.3 %



Hb Koln

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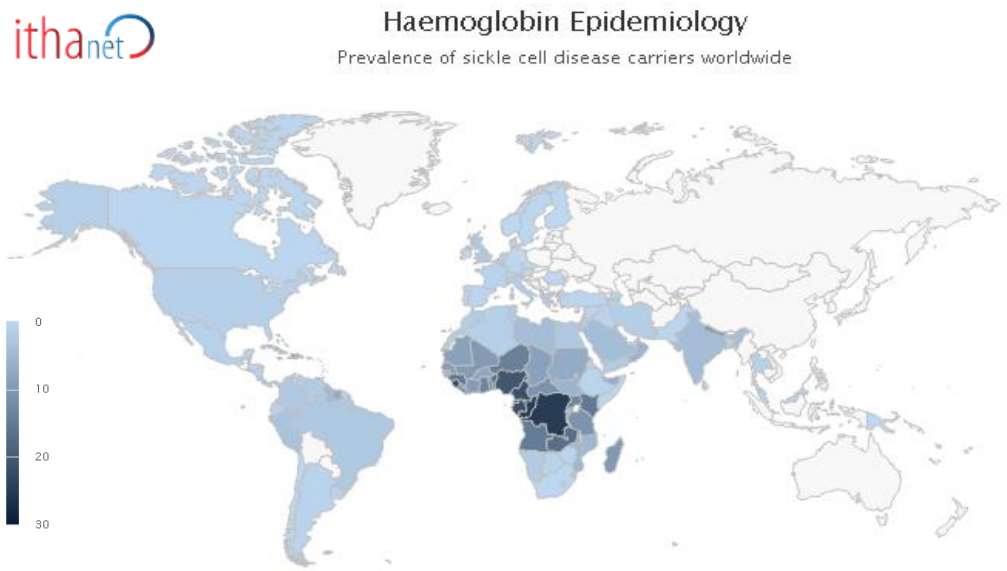
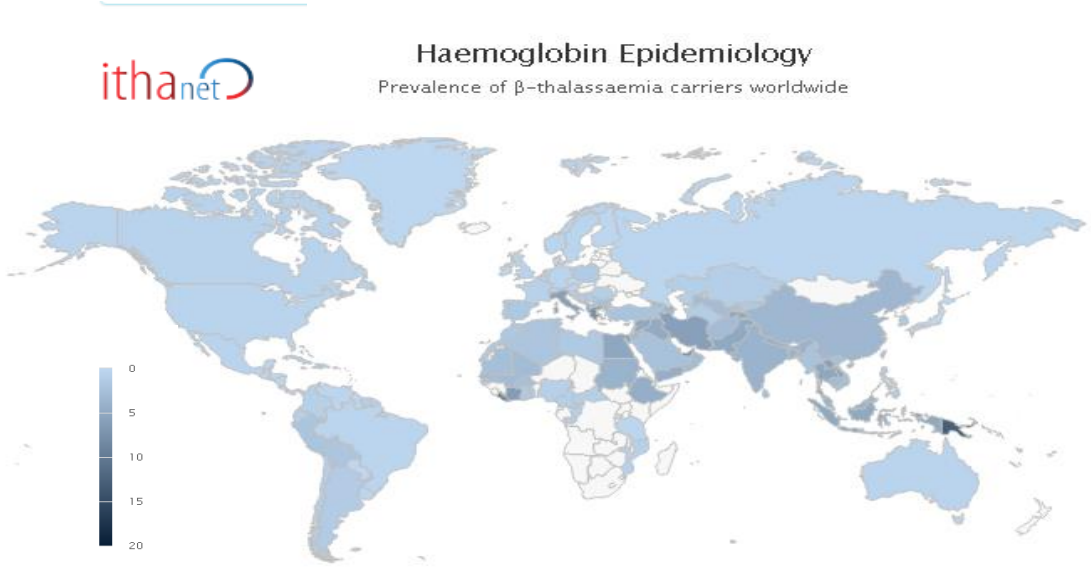
Who should be tested?

Sickle cell trait (SCT) is one of the most common hemoglobin mutations in the world because of its protective effects against severe malaria.



Sickle cell trait



Beta thal trait

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https://www.ithanet.eu/db/ithamaps

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Who should be tested?

SCT carriers are at risk for having children with sickle cell disease (SCD)

SCT screening should be universal and done at the age of 13-to18-years old or at pre-conception counseling

https://www.appdh.org.pt/

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3. Be aware of the importance of identification of couples at risk for SCD and their options

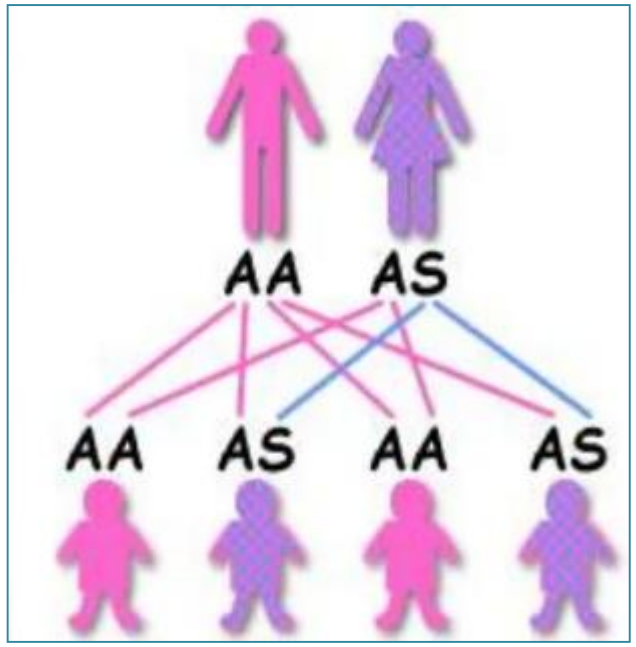
I’m a carrier, and now?

People who inherit one sickle cell gene and one normal gene have sickle cell trait (SCT). People with SCT usually do not have any of the symptoms of sickle cell disease (SCD), but they can pass the trait on to their children, therefore, pre- and postconception counseling is of significant importance.

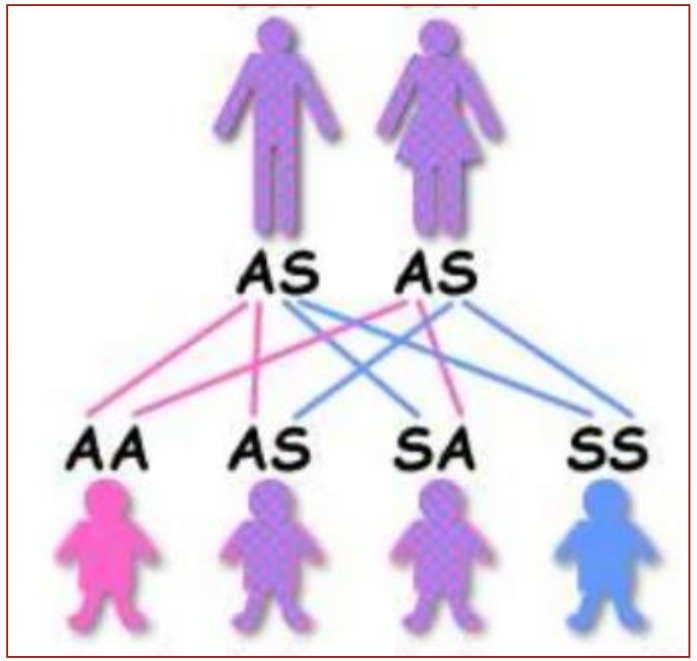
When you start planning to have a child your partner should be tested for Hb S and other Hemoglobinopathies

I’m a carrier, and now?

Couple without risk
Only one is a carrier of Hb S



Couple at risk
Both of them are carriers of Hb S



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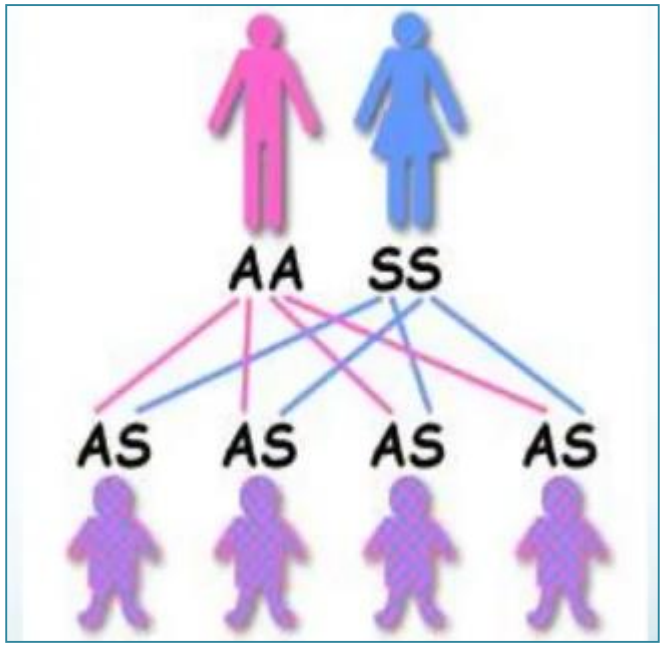
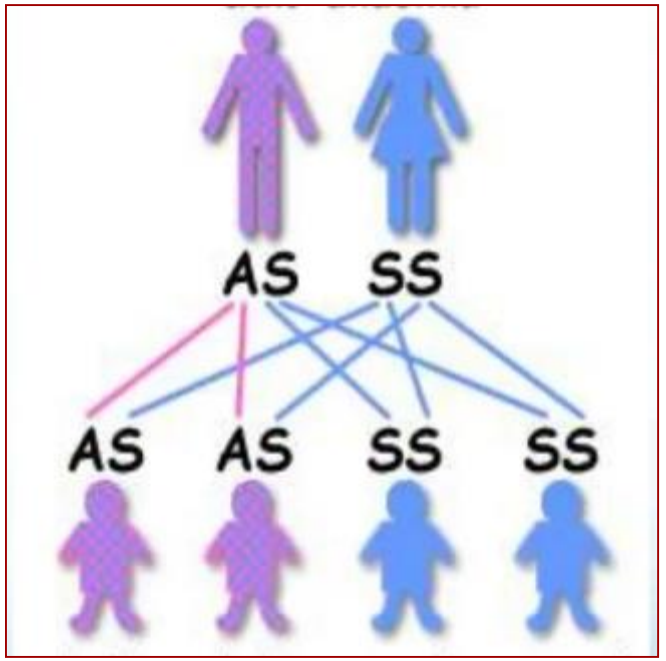
And if I have SCD?

Couple without risk
Partner is normal (Hb A/Hb A)



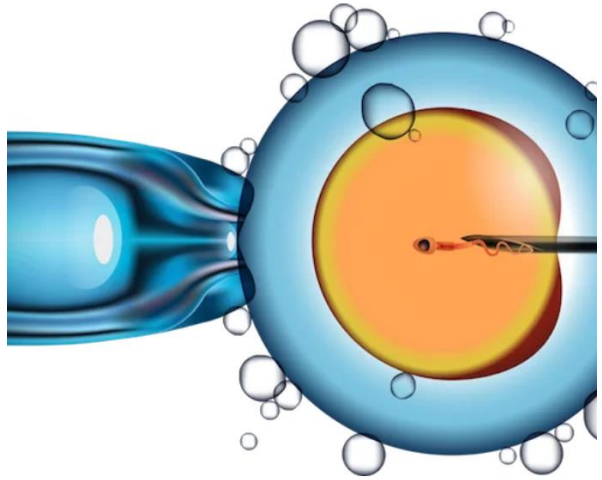
Couple at risk
Partner ia a carrier of Hb S (or other hemoglobinopathie)



Pre – conception

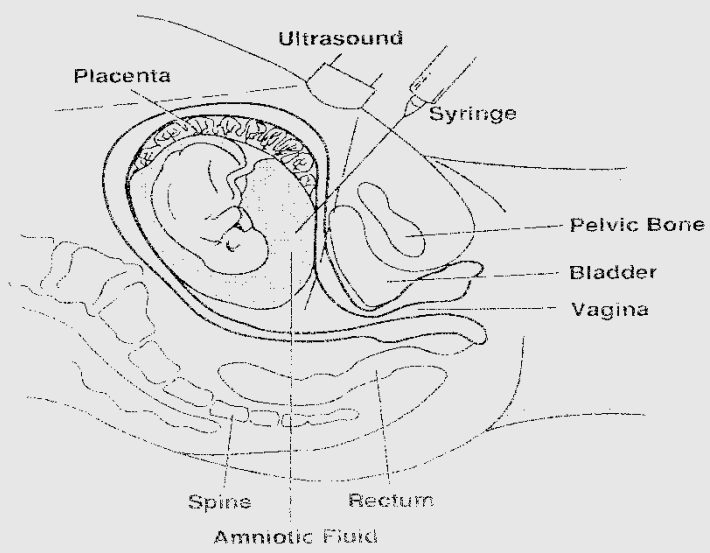
In vitro fertilization (IVF) with preimplantation genetic screening

- Method to prevent having a child with sickle cell before conception.
- Embryos are taken from the mother, fertilized, and then screened for sickle cell.
- The embryos that do not have the full sickle cell gene are selected.

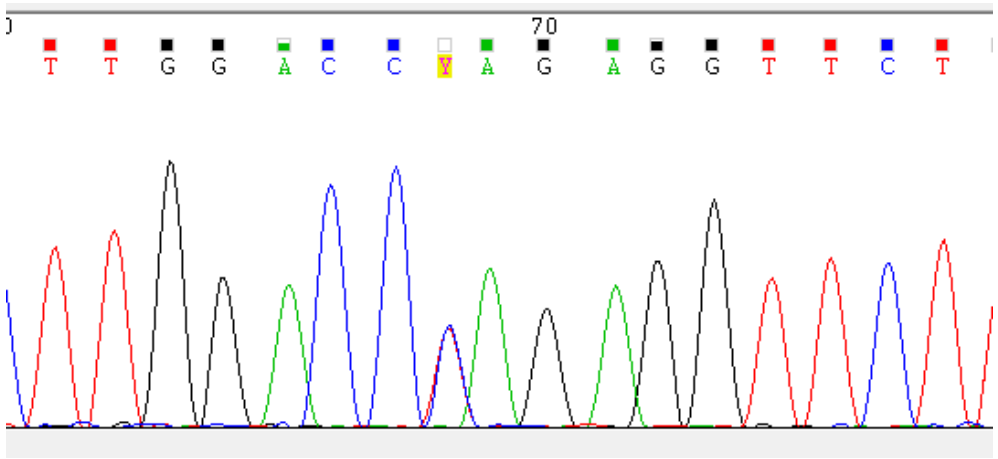


Pos – conception

Pre-natal diagnosis

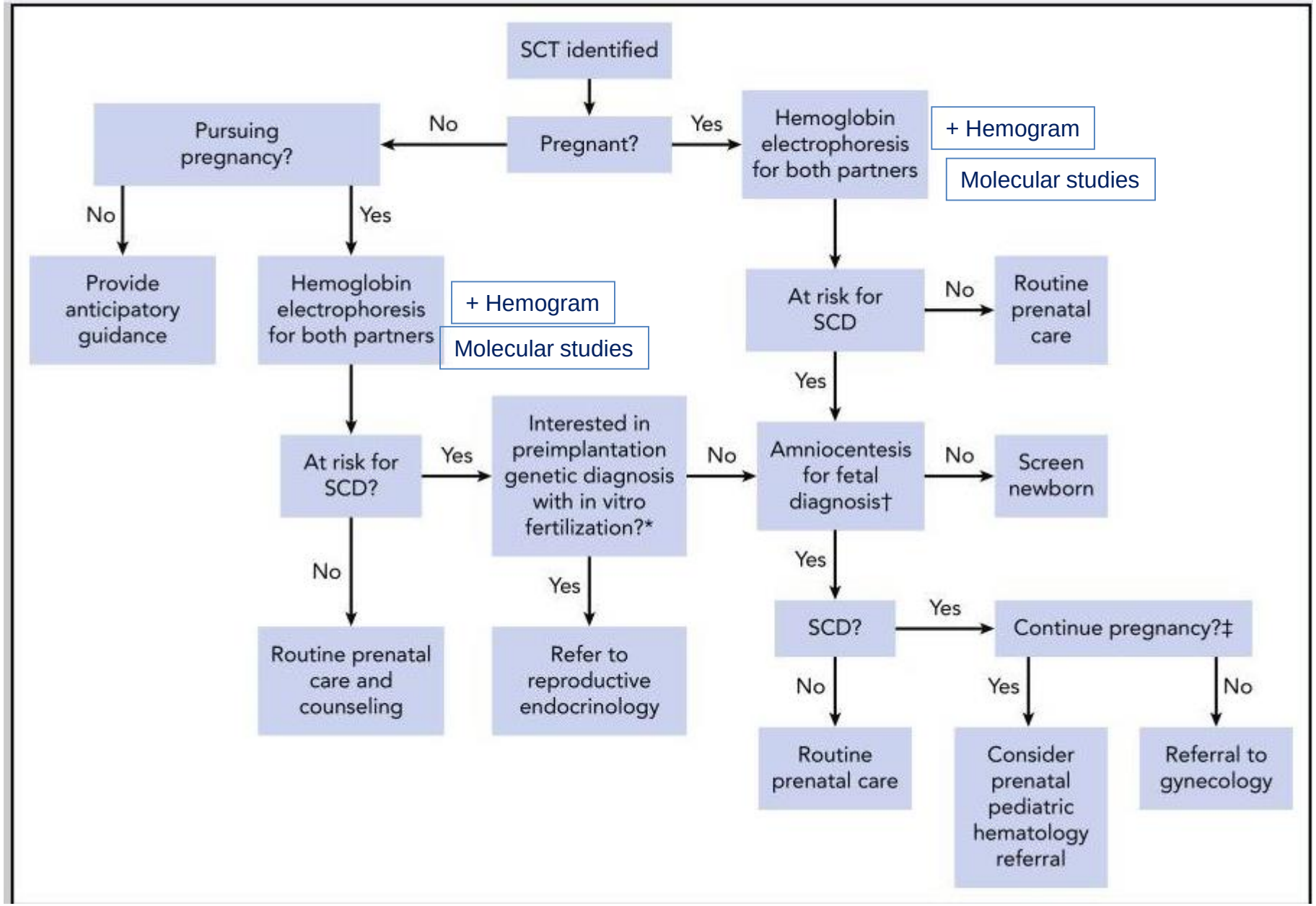


- Fetal DNA
- PCR/Sanger sequencing to look for the parents mutations



Amniocentesis
or cordocentesis at the first weeks of pregnancy

Reproductive decision-making tree for SCT carriers and their physicians



European Reference Network
for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

Pecker LH, Naik RP. The current state of sickle cell trait: implications for reproductive and genetic counseling. Blood. 2018 Nov 29;132(22):2331-2338.

Learning objectives

After this webinar on Genetic Counselling will be able to:

1. Understand the genetic basis and pattern of inheritance of sickle cell disease
2. Understand how and who should do the diagnosis for Sickle cell trait (HbS carriers)
3. Be aware of the importance of identification of couples at risk for SCD and their options

But,

If you need Genetic Counseling you should consult your doctor and a genetic counselor, only they know your condition and could give you the best advice.

Take-home message

1. SCD is a recessive disorder, but the carriers can be identified with an easy and cheap hemoglobin study. If you are at a reproductive age ask your doctor to do the test!

2. A couple at risk for SCD have different options to make the right decision.

It will always be a personal choice, but it's important to be informed.

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Webinars for patients
Sickle Cell Disease
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