Haemoglobinopathies in Clinical Genetic

Béatrice GULBIS M.D., PhD

LHUB-ULB - Department of Clinical Chemistry

ULB – Center of Human Genetics

Co-coordinator ERN EuroBloodNet

18.04.2023

Training objectives

- Mandatory elements for giving a genetic counselling for haemoglobinopathies
- Identifying a couple at risk for a major haemoglobinopathy
- Referring to available recommendations
- Genetic counselling for a haemoglobin S carrier

Haemoglobinopathies

JULES BORDET INSTITUUT

C H U | U V C BRUGMANN

Hôpital Erasme | ULB

Hôpital Universitaire des Enfants Reine Fabiola
Universitair Kinderziekenhuis Koningin Fabiola

CHU Saint-Pierre
UMC Sint-Pieter

Haemoglobinopathies

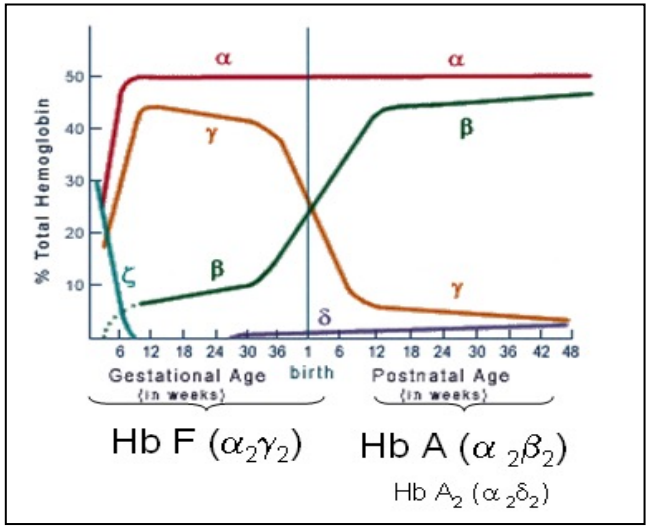
- Thalassaemias α et β

Decrease in globin chain production,
α or β

- Haemoglobin variants

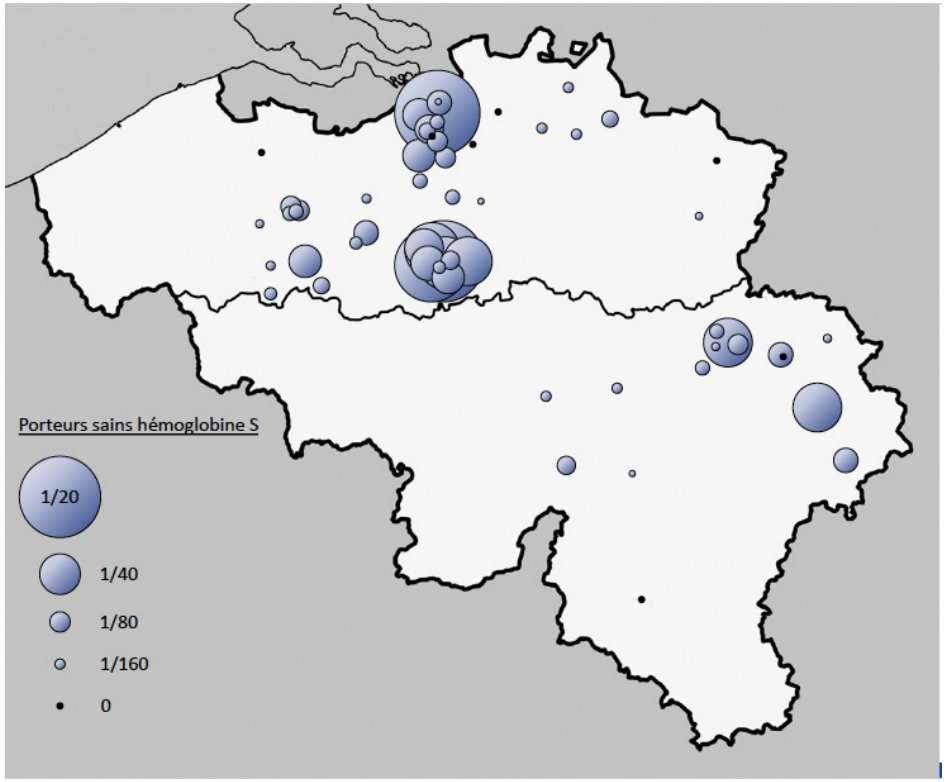
Abnormal globin chain
α , β or γ

N.B. Several variants are produced in less amount >> thalassaemia (e.g. Hb E, Hb Constant Spring)



Haemoglobinopathies: screening

- In Belgium = rare disease but not for heterozygotes (healthy carriers)
  ~~Haemolysis~~



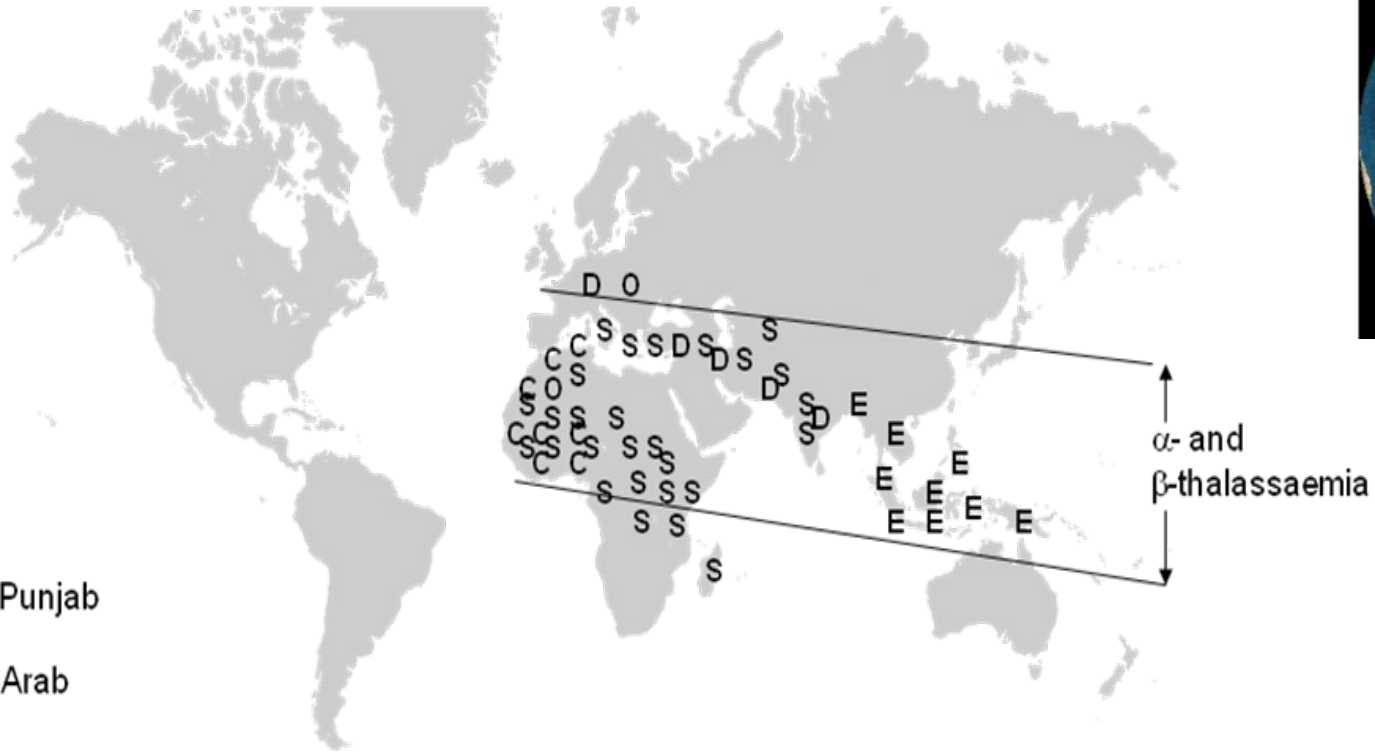
Ketelslegers O. et al. Belg J Hematol 2015;6(4):135-41

See newborn screening that is included in the newborn screening for metabolic disorders since first January 2023 in Fédération Wallonie Bruxelles

No date given for Flanders Region.

Haemoglobinopathies: population at risk

Malaria



Variants

- C= Hb C
- D= Hb D-Punjab
- E= Hb E
- O= Hb O-Arab
- S= Hb S

Autosomal recessive disorders

GENE
Normal

Variant

PARENTS

Mother
Heterozygote

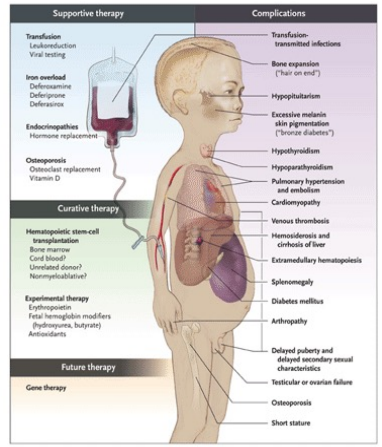
Father
Heterozygote

Risk

Normal | Trait | Trait | Disease

Healthy carrier

Thalassaemia
transfusion-dependent



Sickle cell anaemia/disorder

Message

- Preconceptionnal or antenatal screening for haemoglobinopathies is useful for the patient, the couple and the descendants

What is mandatory to screen for, who and how?

JULES BORDET INSTITUUT

CHU | UVC BRUGMANN

Hôpital Erasme ULB

Hôpital Universitaire des Enfants Reine Fabiola
Universitair Kinderziekenhuis Koningin Fabiola

CHU Saint-Pierre
UMC Sint-Pieter

Risk Thalassaemia

European Journal of Human Genetics (2015) 23, 426–437

Genotype interaction	*Disorder expected*	*Appropriate to offer PND*
Homozygous		
β° or severe β^{+}-thalassaemia	Thalassaemia major	Yes
Mild β^{+}-thalassaemia	Thalassaemia intermedia	Occasionally[a]
Mild β^{++}-thalassaemia (silent)	Very mild thalassaemia intermedia	No
$\delta\beta^{\circ}$-thalassaemia	Thalassaemia intermedia	Occasionally[a]
Hb Lepore	Thalassaemia intermedia to major (variable)	Occasionally[a]
HPFH	Not clinically relevant	No
Hb C	Not clinically relevant	No
Hb D-Punjab	Not clinically relevant	No
Hb E	Not clinically relevant	No
Hb O-Arab	Not clinically relevant	No
Compound heterozygous		
β°/severe β^{+}-thalassaemia	Thalassaemia major	Yes
Mild β^{+}/β° or severe β^{+}-thalassaemia	Thalassaemia intermedia to major (variable)	Occasionally[a]
Mild β^{++}/β° or severe β^{+}-thalassaemia	Mild thalassaemia intermedia (variable)	Occasionally[a]
$\delta\beta^{\circ}/\beta^{\circ}$ or severe β^{+}-thalassaemia	Thalassaemia intermedia to major (variable)	Occasionally[a]
$\delta\beta^{\circ}$/mild β^{+}-thalassaemia	Mild thalassaemia intermedia	Occasionally[a]
$\delta\beta^{\circ}$/Hb Lepore	Thalassaemia intermedia	Occasionally[a]
Hb Lepore/β° or severe β^{+}-thalassaemia	Thalassaemia major	Yes
Hb C/β° or severe β^{+}-thalassaemia	β-thalassaemia trait to intermedia (variable)	Occasionally[a]
Hb C/mild β^{+}-thalassaemia	Not clinically relevant	No
Hb D-Punjab/β° or severe β^{+}-thalassaemia	Not clinically relevant	No
Hb E/β° or severe β^{+}-thalassaemia	Thalassaemia intermedia to major (variable)	Yes
Hb O-Arab/β°-thalassaemia	Severe thalassaemia intermedia	Yes
$\alpha\alpha\alpha/\beta^{\circ}$ or severe β^{+}-thalassaemia	Mild thalassaemia intermedia	No
$\alpha\alpha\alpha\alpha/\beta^{\circ}$ and $\alpha\alpha\alpha\alpha\alpha\alpha/\beta^{\circ}$-thalassaemia	Mild to severe thalassaemia intermedia (variable)	Occasionally[a]

Note: The decision to have prenatal diagnosis belongs to the couple, once they have had comprehensive counselling.
[a]Couples with genotypes that may lead to offspring with unpredictable phenotypes occasionally select to have prenatal diagnosis or PGD.

Risk
Sickle cell disease

European Journal of Human Genetics (2015) 23, 426–437

Genotype interaction	Disorder expected	Appropriate to offer PND
Homozygous		
Hb S	Sickle cell disease	Yes
Compound heterozygous		
Hb S/β^0 or severe β^+-thalassaemia	Sickle cell disease	Yes
Hb S/mild β^+-thalassaemia	Mild sickle cell disease	Occasionally[a]
Hb S/$\delta\beta^0$-thalassaemia	Mild sickle cell disease	Occasionally[a]
Hb S/Hb Lepore	Mild sickle cell disease	Occasionally[a]
Hb S/HbC	Sickle cell disease (variable severity)	Yes
Hb S/Hb D-Punjab	Sickle cell disease	Yes
Hb S/Hb O-Arab	Sickle cell disease	Yes
Hb S/Hbs C-Harlem, S-Southend, S-Antilles	Sickle cell disease	Yes
Hb C/Hb S-Antilles	Sickle cell disease	Yes
Hb S/Hbs Quebec-Chori, C-Ndjamena, O-Tibesi	Sickle cell disease	Yes
Hb S/Hbs I-Toulouse, Shelby, Hope, North Shore	Haemolytic anaemia	No
Hb S/Hb E	Mild to severe sickle cell disease	Occasionally[a]
Hb S/HPFH	Very mild sickle cell disease	No

Note: The decision to have prenatal diagnosis belongs to the couple, once they have had comprehensive counselling.

[a] Couples with genotypes that may lead to offspring with unpredictable phenotypes occasionally select to have prenatal diagnosis or PGD.

Guidelines Belgian Hematology Society – RBC committee

Figure 2. Antenatal screening: (combinations that give rise to the risk of a foetus affected by a severe haemoglobinopathy *(adapted from the work of Prof. B. Modell and published by the UK National Screening Committee)*

Serious risk: Counselling and prenatal diagnosis to be offered

Less serious risk: Counselling to be offered and further investigation maybe required

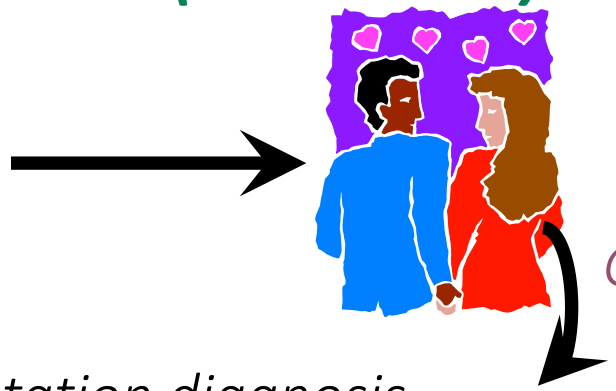
No risk

		Mother										
	Carrier of:	Hb S	β-thalassaemia	δβ-thalassaemia	Hb Lepore	Hb E	Hb O_{Arab}	Hb C	Hb D_{Punjab}	HPFH*	α^{0}-thalassaemia	α^{+}-thalassaemia
Father	Hb S	■	■	▒	▒	▒	■	■	■	▒		
	β-thalassaemia	■	■	■	■	■	▒					
	δβ-thalassaemia	▒	■	▒	■	▒	▒					
	Hb Lepore	▒	■	■	■	▒	▒					
	Hb E	▒	■	▒	▒							
	Hb O_{Arab}	■	▒	▒	▒							
	Hb C	■										
	Hb D_{Punjab}	■										
	HPFH*	▒										
	α^{0}-thalassaemia										■	▒
	α^{+}-thalassaemia										▒	

*HPFH : *Hereditary Persistence of Foetal Haemoglobin*

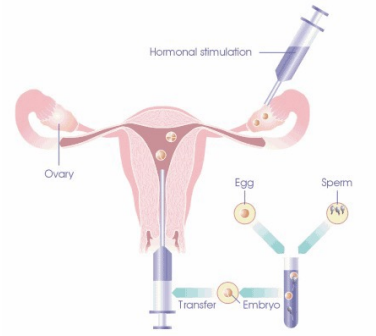
Many other haemoglobinopathies combinations exist and cannot be presented
In case of an unexplained microcytosis or in any doubt, please take the advice of an expert in the field

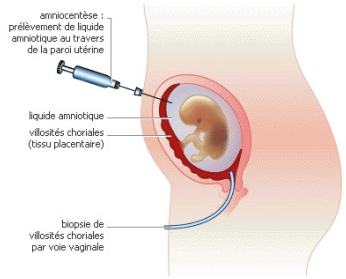
Screening in Belgium pre-conceptionnal or antenatal targeted *not universal (all women)*



Genetic counselling

Prenatal, preimplentation diagnosis





Be aware of the evolution of the treatments (new drugs, gene therapy)

How and for whom? Recommendations

(KCE, BHS, Guide de consultation prénatale 2022 ONE/CRGOLFB)

Screening at distance from blood transfusion	
All women	Complete blood count, ferritin (CRP)
If at least one of risk factor • MCH< 27 pg in absence of iron deficiency • Clinical signs, diagnosis of a major haemoglobiopathy • Population at rik • Partner (Progenitor) – population at risk*	Complete blood count, ferritin (CRP) Separation of Hb fractions and, Hb A_2 and Hb F quantification

(*) Item not present in **KCE report 248BS– 2015**:

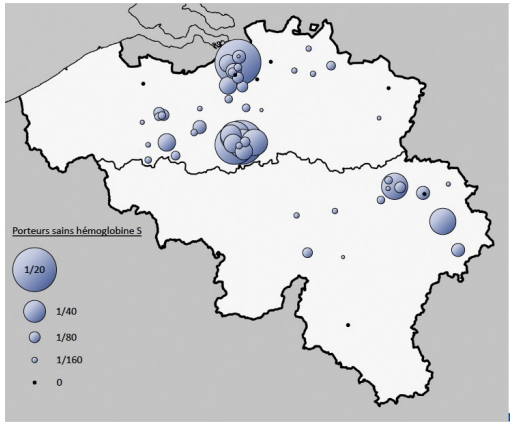
4.4.3. Hémoglobinopathies – actualisation

KCE 2004	Recommandation	Force de la Recommandation	Niveau de preuve
	• Ne proposez pas à chaque femme enceinte une détection des hémoglobinopathies par électrophorèse. Proposez de pratiquer un dépistage sélectif sur base des facteurs de risque.**	Faible	NA (CBR)*

** Niveau de preuve provenant du guideline australien de 2014: CBR=Recommandation consensuelle en raison d'éléments de preuve insuffisants pour appuyer la recommandation*
*** Facteurs de risque = antécédents familiaux d'anémie, de thalassémie ou d'autres variantes anormales de l'hémoglobine; femmes originaires d'autres régions que l'Europe du Nord ; symptômes cliniques suggérant un trouble lié à l'hémoglobine (comme des syndromes de douleurs aiguës récurrentes ou une susceptibilité accrue aux infections); résultats anormalement faibles de MCV ou de MCH.*

Message

- Preconceptionnal or antenatal screening for haemoglobinopathies
  - Simple and routinely available tests can be used for screening
  - To be done in the population at risk if can be defined (third generation …), otherwise universal (systematic)



Screening tests for haemoglobinopathies?

JULES BORDET INSTITUUT

C H U | U V C B R U G M A N N

Hôpital Erasme | ULB

Hôpital Universitaire des Enfants Reine Fabiola
Universitair Kinderziekenhuis Koningin Fabiola

CHU Saint-Pierre
UMC Sint-Pieter

Recommended tests

- Thalassaemias α et β
  - Carriers

➢ CBC normal or not
  - ❑ ± MCH < 27 pg (25 pg)
  - ❑ ± Microcytose
  - ❑ ± Anaemia

- Hb variants
  - Carriers

➢ CBC most often normal

- Separation – quantification Hb fractions (Hb A_2 et Hb F)

- Molecular biology

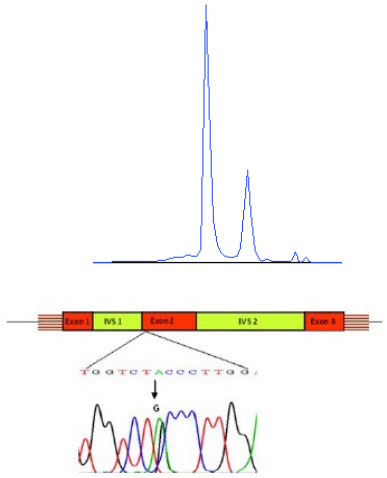


Fig. 1 Schematic representation and sequence chromatogram of the novel beta-globin mutation (HBB:c.107A>G)

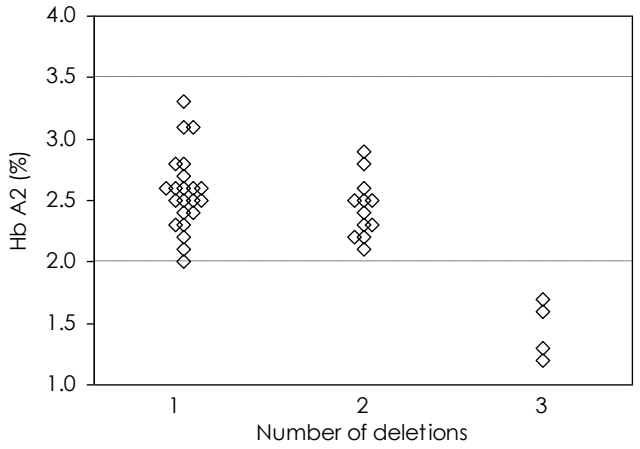
Separation –quantification Hb fractions

- *Molecular biology(prenatal diagnosis, rare Hb variant)*

Separation and quantification Hb fractions:

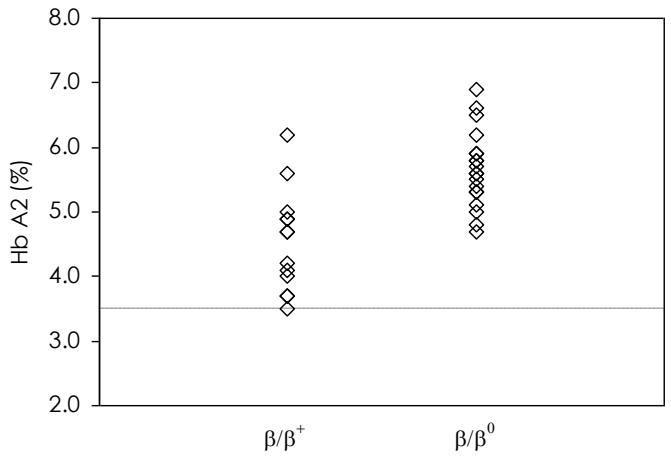
% Hb A_2/% Hb F + interpretation by the clinical biologist

α- thalassaemia



Risk ++ of α°- thalassaemia
(MCH < 25 pg)

β- thalassaemia



+ risk $\delta\beta$ – thalassaemia with
Low Hb A_2 and high Hb F

NHS Sickle Cell and Thalassaemia Screening Programme

Handbook for antenatal laboratories

First screening test must detect

(confirm with a second test, same sample, other technique)

Significant maternal haemoglobinopathies

The following maternal haemoglobinopathies should be detected by antenatal screening and are important for maternal care:

- Hb SS
- Hb SC
- Hb SD^{Punjab}
- Hb SE
- Hb SO^{Arab}
- Hb S/Lepore and Hb Lepore/β thalassaemia
- Hb S/β thalassaemia
- Hb S/δβ thalassaemia
- HbH disease (--/-α)
- β thalassaemia major/intermedia
- Hb E/β thalassaemia

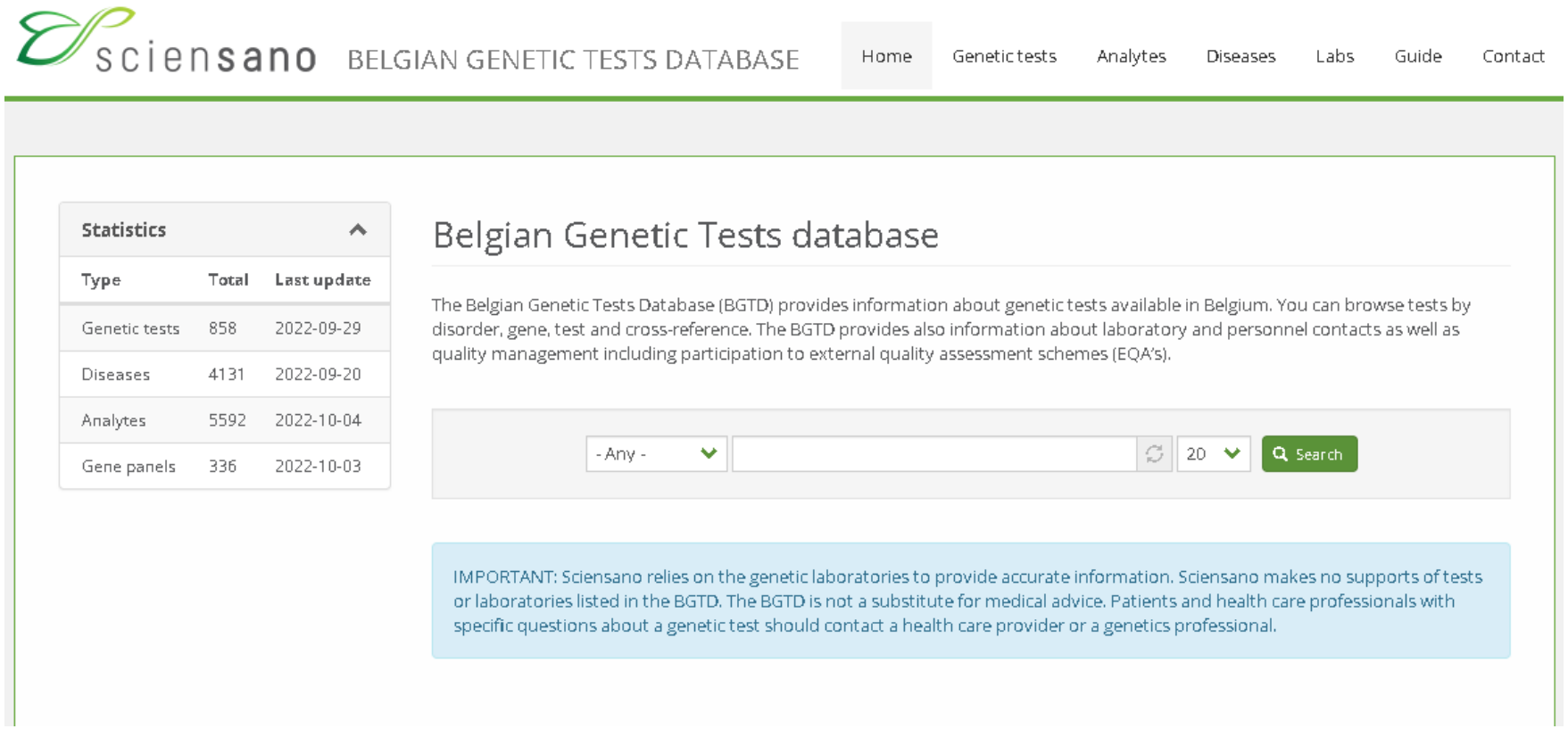
Carrier states in biological mother:

- HbS
- HbC
- HbD^{Punjab}
- HbE
- HbO^{Arab}
- Hb Lepore
- β thalassaemia
- δβ thalassaemia
- α^0 thalassaemia (--/αα)
- Hereditary Persistance of Fetal Haemoglobin (HPFH)

Any compound heterozygote state including one or more of the above conditions.
Any homozygous state of the above conditions.

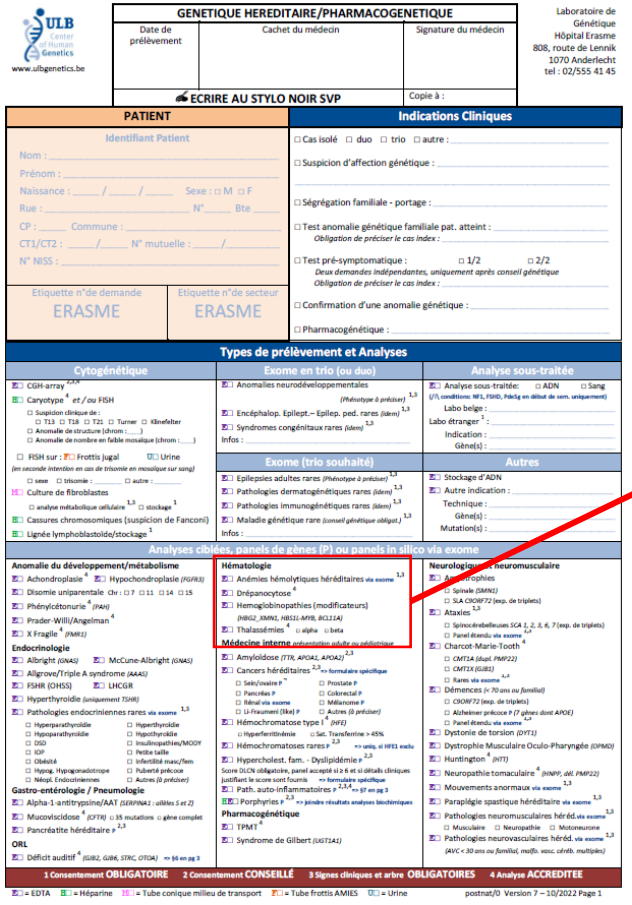
October 2017
Public Health England leads the NHS Screening Programmes

Genetics in Belgium



https://gentest.healthdata.be/

Request for a test



GENETIQUE HEREDITAIRE/PHARMACOGENETIQUE

Date de prélèvement | Cachet du médecin | Signature du médecin

ECRIRE AU STYLO NOIR SVP — Copie à :

Laboratoire de Génétique
Hôpital Erasme
808, route de Lennik
1070 Anderlecht
tel : 02/555 41 45

www.ulbgenetics.be

PATIENT

Identifiant Patient

Nom :
Prénom :
Naissance : / / Sexe : ☐ M ☐ F
Rue : N° Bte
CP : Commune :
CT1/CT2 : / N° mutuelle : /
N° NISS :

Etiquette n°de demande: ERASME
Etiquette n°de secteur: ERASME

Indications Cliniques

☐ Cas isolé ☐ duo ☐ trio ☐ autre :
☐ Suspicion d'affection génétique :
☐ Ségrégation familiale - portage :
☐ Test anomalie génétique familiale pat. atteint :
Obligation de préciser le cas index :
☐ Test pré-symptomatique : ☐ 1/2 ☐ 2/2
Deux demandes indépendantes, uniquement après conseil génétique
Obligation de préciser le cas index :
☐ Confirmation d'une anomalie génétique :
☐ Pharmacogénétique :

Types de prélèvement et Analyses

Cytogénétique

- CGH-array
- Caryotype et / ou FISH
  - ☐ Suspicion clinique de : ☐ T13 ☐ T18 ☐ T21 ☐ Turner ☐ Klinefelter ☐ Anomalie de structure (chrom :) ☐ Anomalie de nombre en faible mosaïque (chrom :)
  - ☐ FISH sur : ☐ Frottis jugal ☐ Urine
  - *(en seconde intention en cas de trisomie en mosaïque sur sang)*
  - ☐ sexe ☐ trisomie : ☐ autre :
- Culture de fibroblastes
  - ☐ analyse métabolique cellulaire ☐ stockage
- Cassures chromosomiques (suspicion de Fanconi)
- Lignée lymphoblastoïde/stockage

Exome en trio (ou duo)

- Anomalies neurodéveloppementales *(Phénotype à préciser)*
- Encéphalop. Epilept.– Epilep. ped. rares *(idem)*
- Syndromes congénitaux rares *(idem)*

Infos :

Exome (trio souhaité)

- Epilepsies adultes rares *(Phénotype à préciser)*
- Pathologies dermatogénétiques rares *(idem)*
- Pathologies immunogénétiques rares *(idem)*
- Maladie génétique rare *(conseil génétique obligat.)*

Infos :

Analyse sous-traitée

- Analyse sous-traitée: ☐ ADN ☐ Sang
  (/!\ conditions: NF1, FSHD, Pdérig en début de sem. uniquement)
- Labo belge :
- Labo étranger :
- Indication :
- Gène(s) :

Autres

- ☐ Stockage d'ADN
- Autre indication :
- Technique :
- Gène(s) :
- Mutation(s) :

Analyses ciblées, panels de gènes (P) ou panels in silico via exome

Anomalie du développement/métabolisme

- Achondroplasie (*FGFR3*) — Hypochondroplasie (*FGFR3*)
- Disomie uniparentale Chr : ☐ 7 ☐ 11 ☐ 14 ☐ 15
- Phénylcétonurie (*PAH*)
- Prader-Willi/Angelman
- X Fragile (*FMR1*)

Endocrinologie

- Albright (*GNAS*) — McCune-Albright (*GNAS*)
- Allgrove/Triple A syndrome (*AAAS*)
- FSHR (OHSS) — LHCGR
- Hyperthyroïdie (*uniquement TSHR*)
- Pathologies endocriniennes rares via exome
  - ☐ Hyperparathyroïdie ☐ Hyperthyroïdie
  - ☐ Hypoparathyroïdie ☐ Hypothyroïdie
  - ☐ DSD ☐ Insulinopathies/MODY
  - ☐ IOP ☐ Petite taille
  - ☐ Obésité ☐ Infertilité masc/fem
  - ☐ Hypog. Hypogonadotrope ☐ Puberté précoce
  - ☐ Néopl. Endocriniennes ☐ Autres (*à préciser*)

Gastro-entérologie / Pneumologie

- Alpha-1 antitrypsine/AAT (*SERPINA1 : allèles S et Z*)
- Mucoviscidose (*CFTR*) ☐ ≥ 35 mutations ☐ gène complet
- Pancréatite héréditaire P

ORL

- Déficit auditif (*GJB2, GJB6, STRC, OTOA*) => §6 en pg 3

Hématologie

- Anémies hémolytiques héréditaires via exome
- Drépanocytose
- Hemoglobinopathies (modificateurs)
  (HBG2_XMN1, HBS1L-MYB, BCL11A)
- Thalassémies ☐ alpha ☐ beta

Médecine interne *orientation adulte ou pédiatrique*

- Amyloïdose (*TTR, APOA1, APOA2*)
- Cancers héréditaires => formulaire spécifique
  - ☐ Sein/ovaire P ☐ Prostate P
  - ☐ Pancréas P ☐ Colorectal P
  - ☐ Rénal via exome ☐ Mélanome P
  - ☐ Li-Fraumeni (like) P ☐ Autres (*à préciser*)
- Hémochromatose type I (*HFE*)
  - ☐ Hyperferritinémie ☐ Sat. Transferrine > 45%
- Hémochromatoses rares P => uniq. si HFE1 exclu
- Hypercholest. fam. - Dyslipidémie P
  Score DLCN obligatoire, panel accepté si ≥ 6 et si détails cliniques justifiant le score sont fournis => formulaire spécifique
- Path. auto-inflammatoires P => §7 en pg 3
- Porphyries P => joindre résultats analyses biochimiques

Pharmacogénétique

- TPMT
- Syndrome de Gilbert (*UGT1A1*)

Neurologique / neuromusculaire

- Ataxies
  - ☐ Spinale (*SMN1*)
  - ☐ SLA *C9ORF72* (exp. de triplets)
- Ataxies
  - ☐ Spinocérébelleuses *SCA 1, 2, 3, 6, 7* (exp. de triplets)
  - ☐ Panel étendu via exome
- Charcot-Marie-Tooth
  - ☐ *CMT1A* (dupl. *PMP22*)
  - ☐ *CMT1X* (*GJB1*)
  - ☐ Rares via exome
- Démences (*< 70 ans ou familial*)
  - ☐ *C9ORF72* (exp. de triplets)
  - ☐ Alzheimer précoce P (*7 gènes dont APOE*)
  - ☐ Panel étendu via exome
- Dystonie de torsion (*DYT1*)
- Dystrophie Musculaire Oculo-Pharyngée (*OPMD*)
- Huntington (*HTT*)
- Neuropathie tomaculaire (*MNPP, dél. PMP22*)
- Mouvements anormaux via exome
- Paraplégie spastique héréditaire via exome
- Pathologies neuromusculaires héréd. via exome
  - ☐ Musculaire ☐ Neuropathie ☐ Motoneurone
- Pathologies neurovasculaires héréd. via exome
  (AVC < 30 ans ou familial, malfo. vasc. cérébr. multiples)

1 Consentement OBLIGATOIRE **2 Consentement CONSEILLÉ** **3 Signes cliniques et arbre OBLIGATOIRES** **4 Analyse ACCREDITEE**

= EDTA = Héparine = Tube conique milieu de transport = Tube frottis AMIES = Urine

postnat/0 Version 7 – 10/2022 Page 1

Hématologie

- Anémies hémolytiques héréditaires via exome
- Drépanocytose [4]
- Hemoglobinopathies (modificateurs)
  (HBG2_XMN1, HBS1L-MYB, BCL11A)
- Thalassémies [4] ☐ alpha ☐ beta

NEED to have the clinical phenotype and laboratory findings !

For molecular sequencing we need information

- [x] β-THALASSEMIE MINEURE ou MAJEURE
- [ ] α- THALASSEMIE MINEURE ou MAJEURE
- [ ] SYNDROME DREPANOCYTAIRE PARTICULIER (HbSβ+thalassémie)

Les prélèvements :

- sang - 7 cc tube EDTA

Remarque : l'ADN seul ne permet pas de confirmer certains diagnostics comme une persistance héréditaire de l'Hb F.

Les informations à joindre afin de permettre une interprétation correcte des analyses à réaliser ainsi que des résultats :

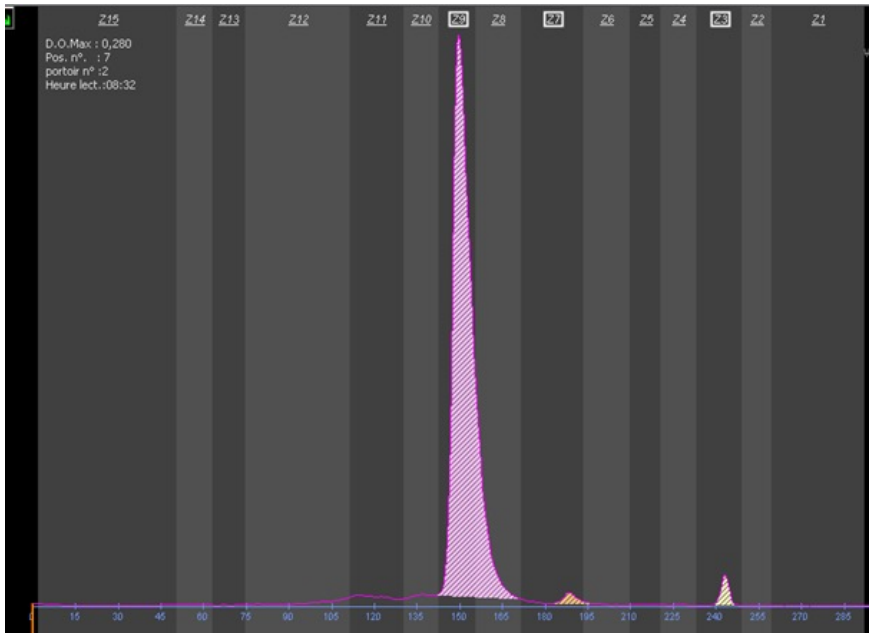
Transfusion	Oui / Non Date : ..../..../....	**Date de prélèvement**	
Grossesse	Oui / Non	**Hémoglobine g/dL**	10
Origine géographique		**GR 10^6/mm³**	5
Histoire familiale ?	Oui / Non	**MCV fL**	78
Anémie hémolytique ?	Oui / Non	**MCHC g/dL**	32
Splénomégalie ?	Oui / Non	**MCH pg**	25
Ictère néonatal?	Oui / Non	**RDW/HDW**	14,6
		Ferritine ng/mL	16
		Saturation transferrine %	11
		CRP mg/dL	3,2
		HbA_2 %*	2,6
		Hb F %	<0,5
		Hb(s) anormale(s) ? **Laquelle ?** Ex HbAS, Hb SS, Hb SC, ...	Oui / Non .....

??

Hb A_2 2.6%

Hb F < 0.5%

Case 1: a gynaecologist prescribes a Hb electrophoresis for a patient, 24 y.o. 6 weeks pregnancy, Asian origin

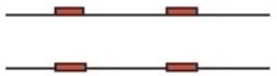
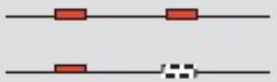
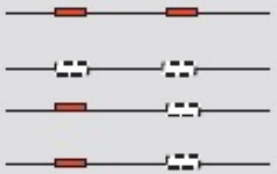
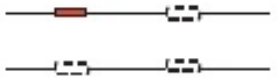
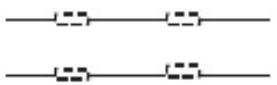


Do you have enough information for a genetic counselling?

CZE kit haemoglobin: HbA_2 2.2% (2.1% - 3.2%)
Hb F 0.6 % (< 1.5%)
Hb A 97 %
Absence of a Hb variant

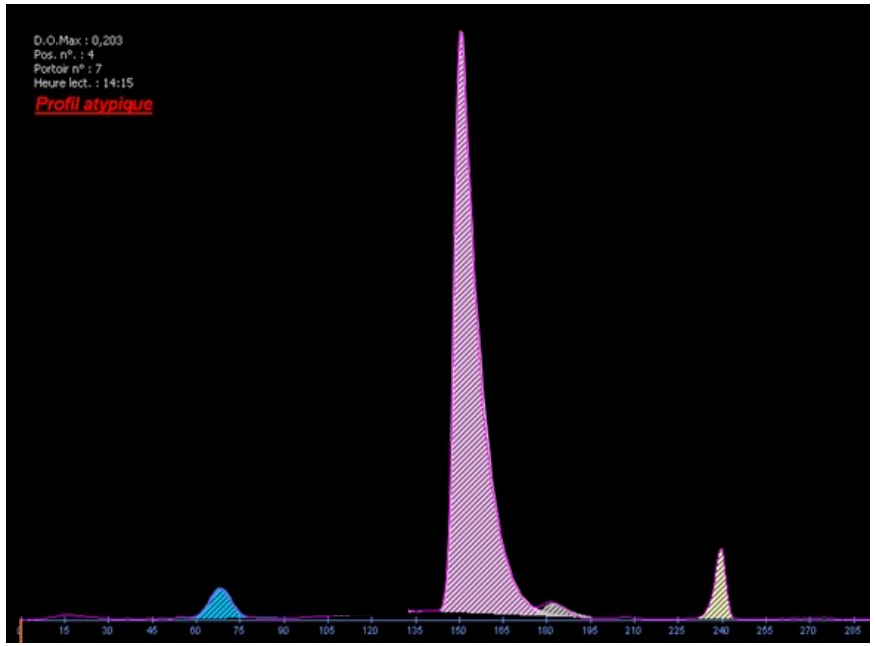
Screening for α-thalassaemia

Molecular genetics of alpha-thalassaemias P. Aguilar Martinez and B. Gulbis DOI: 10.1002/9780470015902.a0022439.pub2

	Name of the condition	Nb of functional α-globin genes	Clinical and biological phenotype	α-globin genotype	Alpha genes
	Normal	4	Normal individual	αα/αα	
Mild forms	α-thal2	3	Asymptomatic (or low MCH)	αα/α-	
Mild forms	α-thal1	2	Thalassemia trait	αα/ -- or α-/α-	 Alpha° = MCH < 25 pg; Alpha⁺ = MCH 25-26.9 pg
Severe forms	Haemoglobin H disease	1	Chronic haemolytic anaemia	α-/--	
Severe forms	Bart's hydrops foetalis syndrome	0	Death *in utero* or at birth	--/--	

Case 2: a general practitioner proposed an antenatal screening (9 w. pregnancy)

- Request/Results
  - Complete blood count MCH 24 pg; Hb 10.1 g/dL
  - Ferritin 105 ng/mL >> Ok
  - Separation Hb fractions



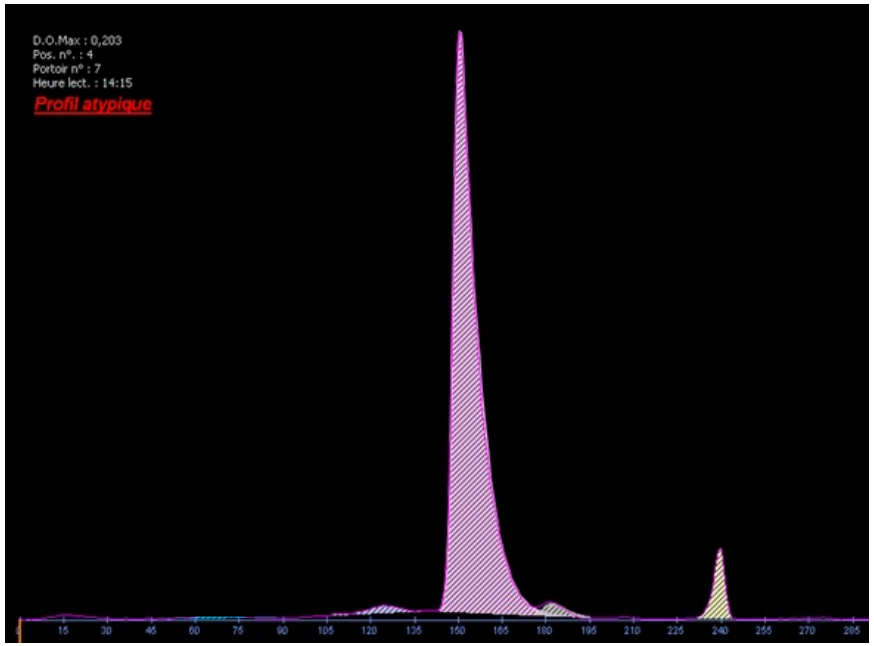
What do you propose to complete the assessment?

Risk of β-thalassaemia trait
>> partner to be tested;
final diagnosis= molecular biology

HbA_2 5.1 % (2.1 – 3.2%)

Case 3: a general practitioner proposed an antenatal screening (9 w. pregnancy)

- Request/Results
  - Complete blood count MCH 28 pg; Hb 12.1 g/dL
  - Ferritin 105 ng/mL >> Ok
  - Separation Hb fractions



Causes minor increase in Hb A_2:

- β-thalassaemia trait (silent)
- Alpha globin gene triplication
- Technical interference (+ Hb variant)
- Mutation KLF1

- Hyperthyroidism
- Megaloblastic anemia
- Antiviral treatment (HIV)
- Pseudoxanthoma

HbA_2 3.3 %

Message

- Pre-conception or prenatal counselling for haemoglobinopathies requires **complete information**: clinical and biological data (complete blood count, separation and quantification of Hb fractions)

Hb S carrier: counselling?

JULES BORDET INSTITUUT

C H U | U V C BRUGMANN

Hôpital Erasme | ULB

Hôpital Universitaire des Enfants Reine Fabiola
Universitair Kinderziekenhuis Koningin Fabiola

CHU Saint-Pierre
UMC Sint-Pieter

AS – clinical data

- Benign status, healthy individuals
- « Laboratory diagnosis » - screening – family study

AS – Recommendations?

Hematology 2018 ASH Education program
Blood 2018; 132: 2331-2338

- Genetic counselling (procreation)
- Confirmed complications
  - Rare exercise-related deaths, see general population
    - Systematic screening not necessary
    - Apply universal precautions related to strenuous exercise
  - Kidney
    - Progression to renal failure (15-35% > 45 y.; risk x 2; risk decreases if alpha-thal., risk increases if diabetes)
    - Renal medullary carcinoma (rare but imaging if haematuria)
    - Screening if child, young adult with micro – macro haematuria or renal imaging
    - Refer to a urologist if adult AS with unexplained haematuria
  - Splenic infarction
  - Reduced deaths from malaria

AS - Recommendations

- When there is significant hypoxia (high altitude, etc.), sickling of erythrocytes may occur
  - Hydration and mobilization if traveling by long-haul plane (valid for the general population…);
  - If surgery, notify the anaesthesiologist of the AS status
  - Hydration ++ during intensive physical exercises (valid for the general population…)

AS - Recommendations

- Specific situation : pregnancy
  - Probable associations: thromboembolic complications, spontaneous abortions? Pre-eclampsia? Asymptomatic bacteriuria?

- Special advice for AS complaining of pain
  - Consider the pain
  - Look for a cause unrelated to HbS
  - If necessary, refer the patient to a pain consultation

Message

- Mainly **benign condition**
- Some recommendations in situations of **severe hypoxia**

"I hear, I know.
I see, I remember.
I do, I understand."

(Confucius, 551BC - 479)

THE END …

A votre disposition

Beatrice.Gulbis@lhub-ulb.be
AnneSophie.Adam@lhub-ulb.be
Sara.Benyaich@lhub-ulb.be

Laboratoire Hospitalier Unviversitaire de Bruxelles
lhub-ulb.be

Centre de génétique humaine de l'ULB
ulbgenetics.be
Demandegenetique@hubruxelles.be

European Reference Network
for rare or low prevalence complex diseases

Network Hematological Diseases (ERN EuroBloodNet)

www.eurobloodnet.eu

JULES BORDET INSTITUUT

C H U | U V C BRUGMANN

Hôpital Erasme | ULB

Hôpital Universitaire des Enfants Reine Fabiola
Universitair Kinderziekenhuis Koningin Fabiola

CHU Saint-Pierre
UMC Sint-Pieter