Newborn Screening for Hemoglobinopathy

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April 17, 2009

I have no actual or potential conflict of interest in relation to this program

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Subject: Neonatal hemoglobinopathy screening

Method: Universal, HPLC

Purpose: Identify infants with homozygous sickle cell disease and begin penicillin prophylaxis

Secondary effects: Identifies infants with other hemoglobinopathies whom require follow-up

Identifies infants with hemoglobinapothy traits whose families should receive counseling

What are “normal” hemoglobins

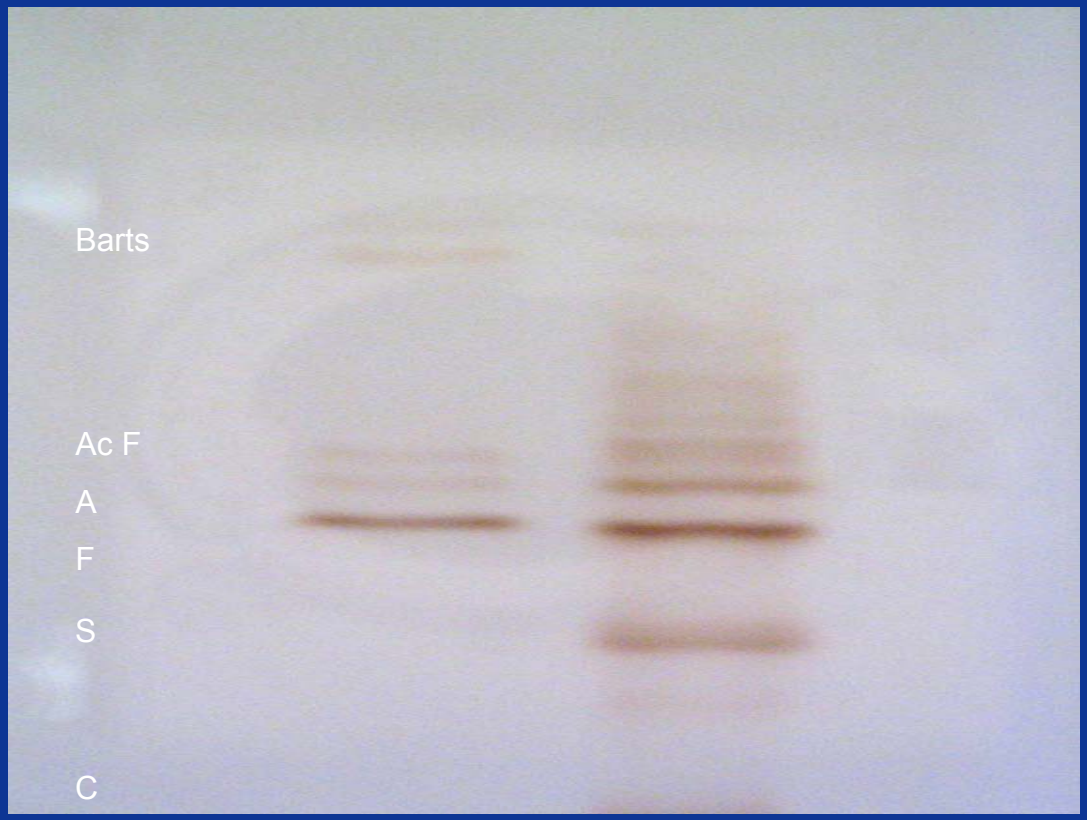
Hb F α_2 γ_2

Hb A α_2 β_2

Hb A_2 α_2 δ_2

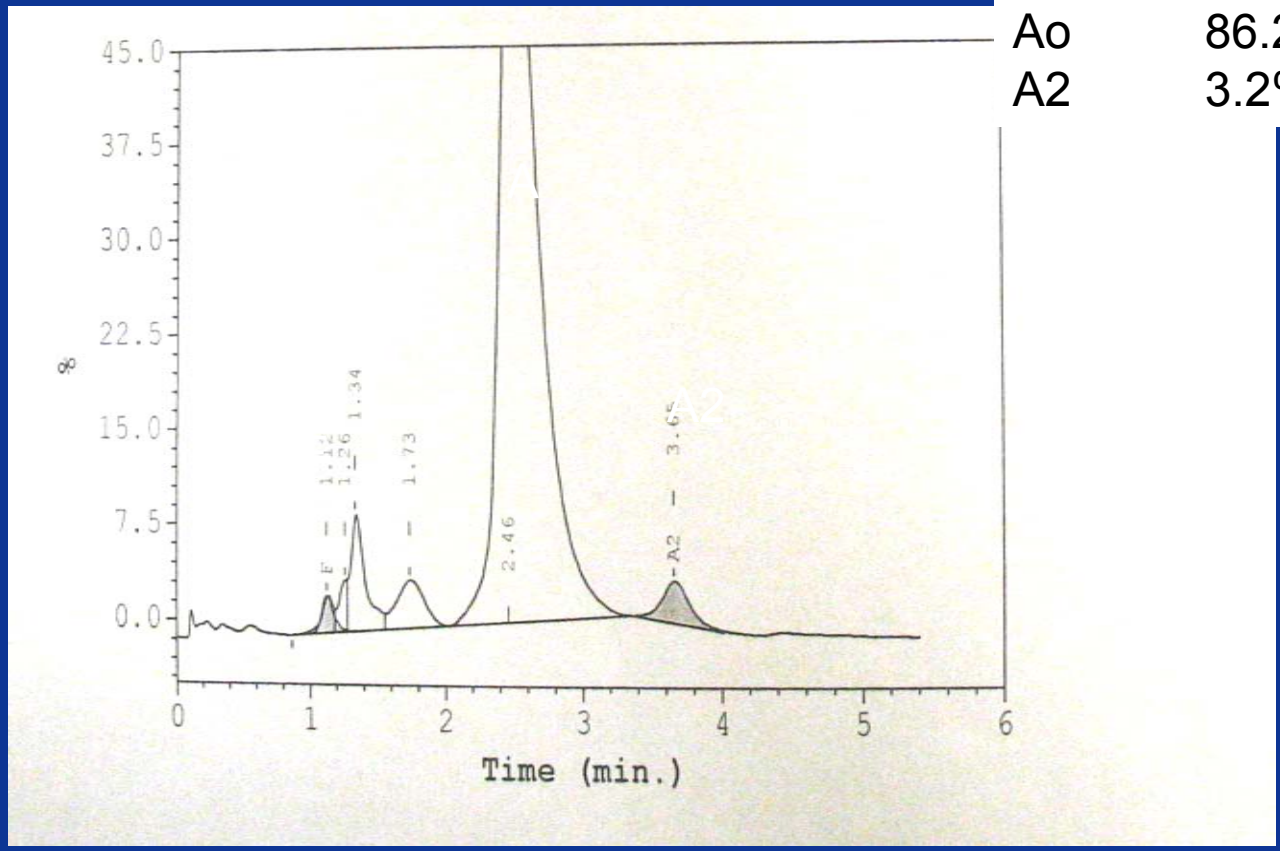
Newborns	Adults
80-90%	1-2%
10-20%	~95%
~1%	<3.5%

Isoelectric Focusing
Hb Barts + acetylated F, A and F
Control lane on right with aged bands, A, F, S (C at bottom)



HPLC Normal 5 year old

F	1.3%
Ao	86.2%
A2	3.2%



What are some “abnormal” hemoglobins

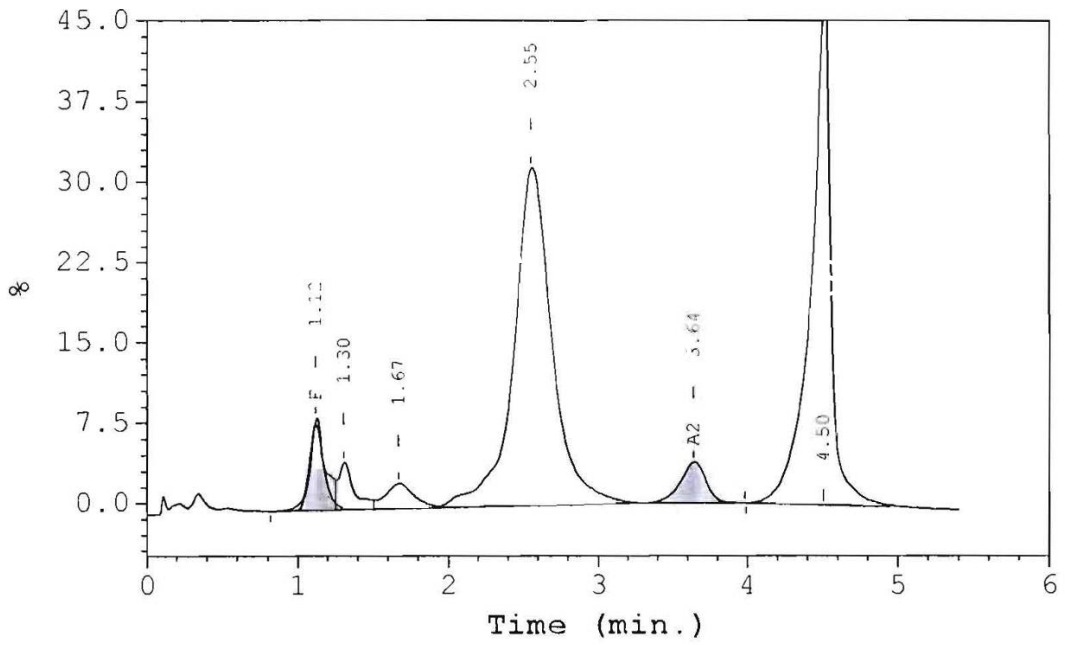
- HbS $\alpha_2 \beta_2^5$
- HbC $\alpha_2 \beta_C$
- HbE $\alpha_2 \beta_E^2$
- Hb Barts γ^4

12 month old S-trait

F Concentration = 4.8* %
A2 Concentration = 3.9* %

*Values outside of expected ranges

Analysis comments:

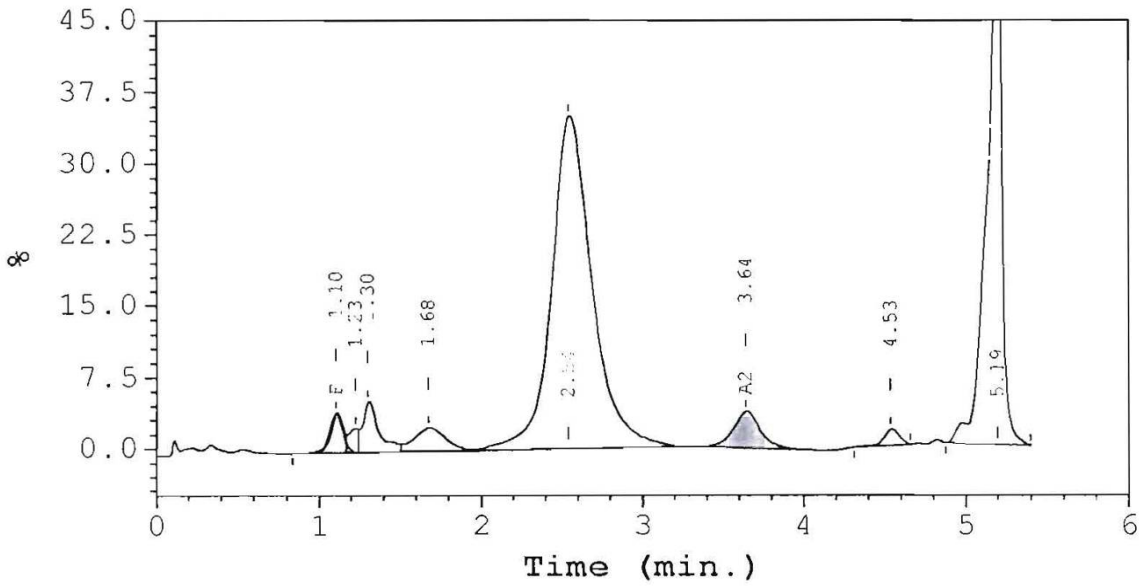


11 year C-trait

F Concentration = 2.1* %
A2 Concentration = 3.9* %

*Values outside of expected ranges

Analysis comments:

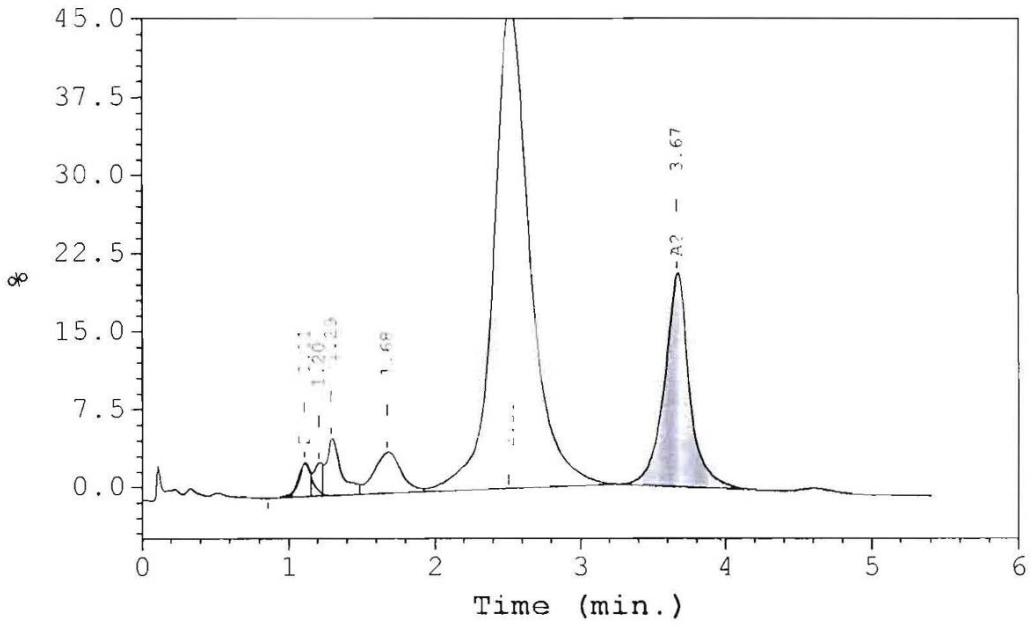


22 month old Hb E-trait

F Concentration = 1.8* %
A2 Concentration = 20.6* %

*Values outside of expected ranges

Analysis comments:

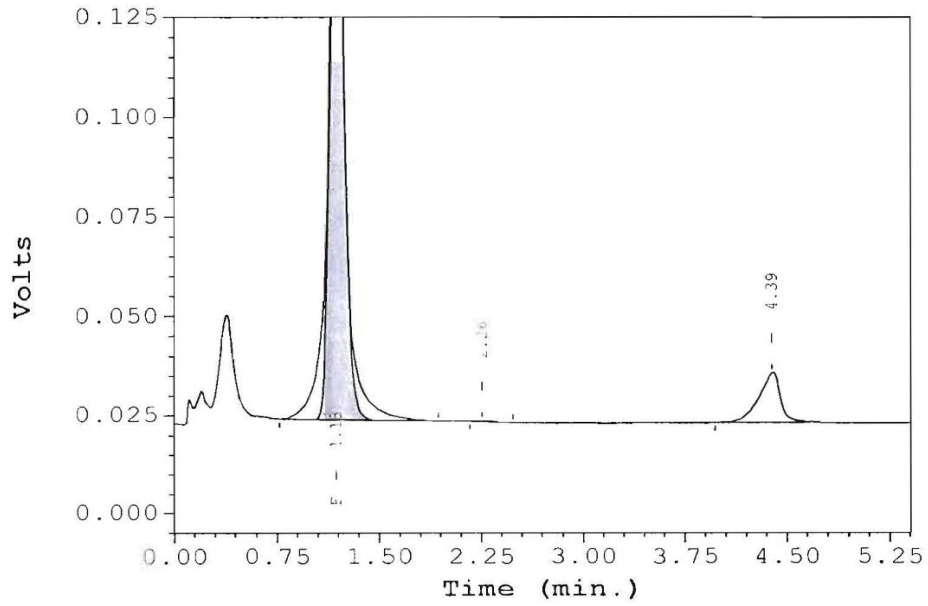


1 week old with F, Acetylated F and S (?SSD, Sbeta Zero, S-HPFH)

F Concentration = 90.9* %
A2 Concentration = %

*Values outside of expected ranges

Analysis comments:



1 month old Hb F, acety F, S, and Barts

Total Area: 25

F Concentration = 92.2* %
A2 Concentration = %

*Values outside of expected ranges

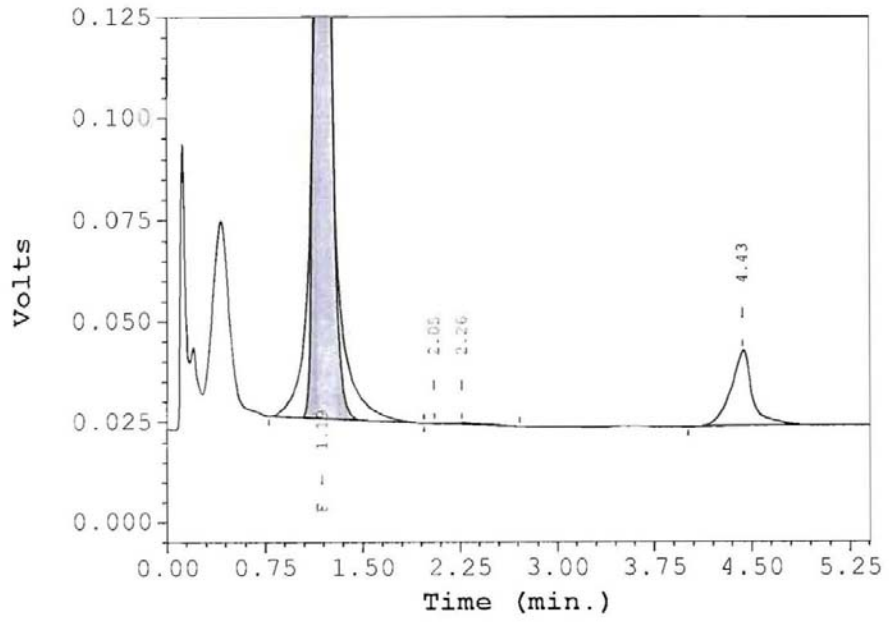
Analysis comments:

1-13-0

NB: Low

Barts

AcF



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2008 Missouri Newborn Hemoglobinopathy Screening Results

Hemoglobin Result	Cases	%
ALL	81,028	100
FA	79,334	97.9
FAS	978	1.2
FAC	292	0.36
FAX	140	0.17
FSA INC	106	0.13
FAE	49	0.06
FCA INC	37	0.05
FAD	36	0.04
FASX	2	0.002

2008 Missouri Newborn Hemoglobinopathy Screening Results

Hemoglobin Result	Cases	%
FS	20	0.02
FSC	11	0.01
High ↑ Barts	2	0.002
FSA	3	0.003
sl ↑ Barts	10	0.01
FC	3	0.003
FSX	2	0.002
FCX	2	0.002
FDA	1	0.001

2008 Missouri **Abnormal** (1694) Hemoglobinopathy Screening Results

Hemoglobin Result	Cases	%
FS (HbSS or SB°thal or S/HpFH	20	1.2
FSC (Hb SC Disease)	11	0.6
FSA (Sβ+ thal)	3	0.2
FSX	2	0.1
High ↑ Barts (? Hb H)	2	0.1
sl ↑ Barts (α thal trait)	10	0.6
FC (Hb CC disease or CB°thal)	3	0.2
FCX	2	0.1
FAS (sickle trait)	978 +	57.7
FAC (Hb C trait	292 +	17.2
FAX [variant trait (not Barts)]	140	8.3
FAE (Hb E trait)	49	2.9
FAD (Hb D trait)	36	2.1

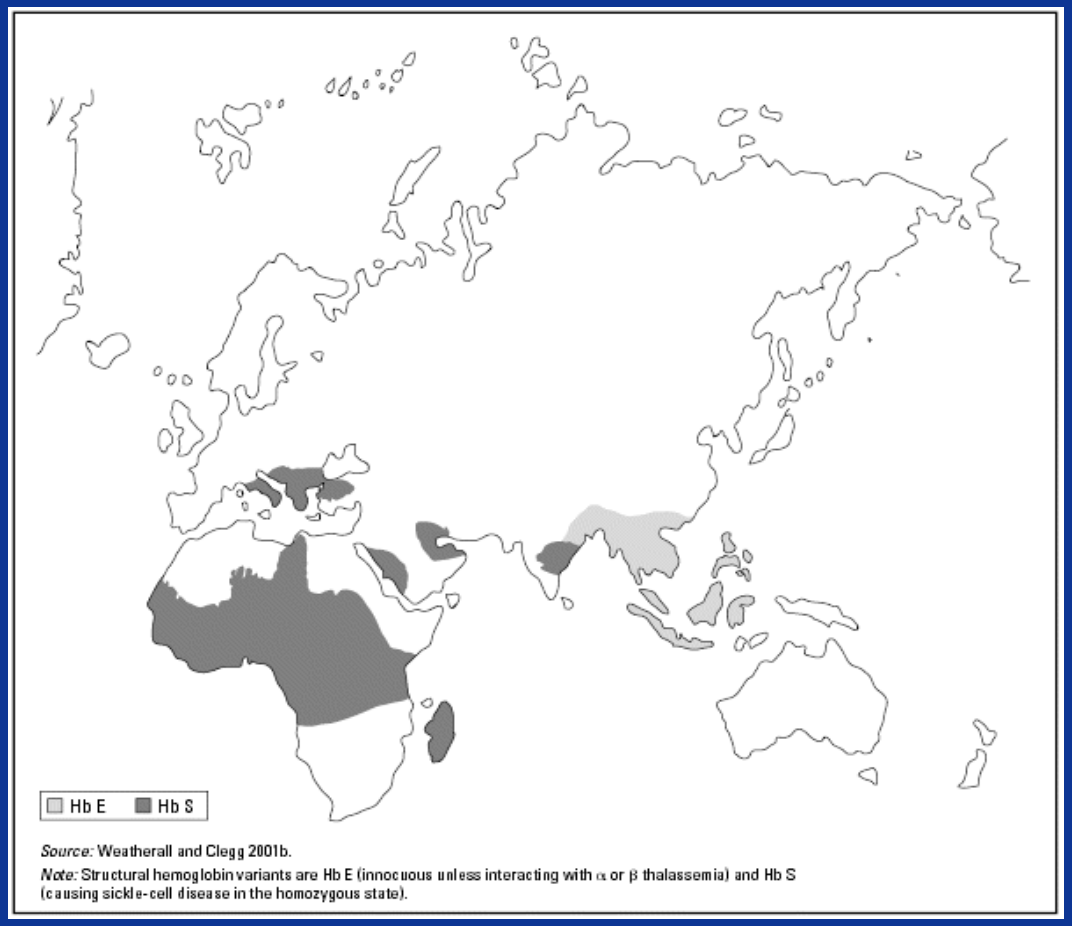
What do you do with abnormal hemoglobin screen?

- Call hematologist
- Obtain confirmatory hemoglobin electrophoresis
- Review family history

Hb S

- Occurs in approximately 8% of African-Americans
- Occurs in other populations that migrated from near Mediterranean sea
- Same pattern on Hgb electrophoresis (cellulose) as Hgb D

Old world distribution of Hb S and Hb E



Source: Weatherall and Clegg 2001b.

Note: Structural hemoglobin variants are Hb E (innocuous unless interacting with α or β thalassemia) and Hb S (causing sickle-cell disease in the homozygous state).

Hb E

- Occurs in >15% of people of Southeast Asian descent
- Significant clinical condition when double heterozygote with β˚thalassemia
- Most common abnormal hemoglobin in the world

Hb C

- Occurs in 2-3% of African Americans
- Same pattern or Hgb electrophoresis (cellulose) as Hgb E and Hgb A2
- Most significant clinical condition when double heterozygote with Hgb S.

α thalassemia trait

- Results from a 2 out of 4 gene deletion
- Occurs in 2-3% of African-Americans (trans)
- Occurs in >5% of people with Southeast Asian descent (cis)

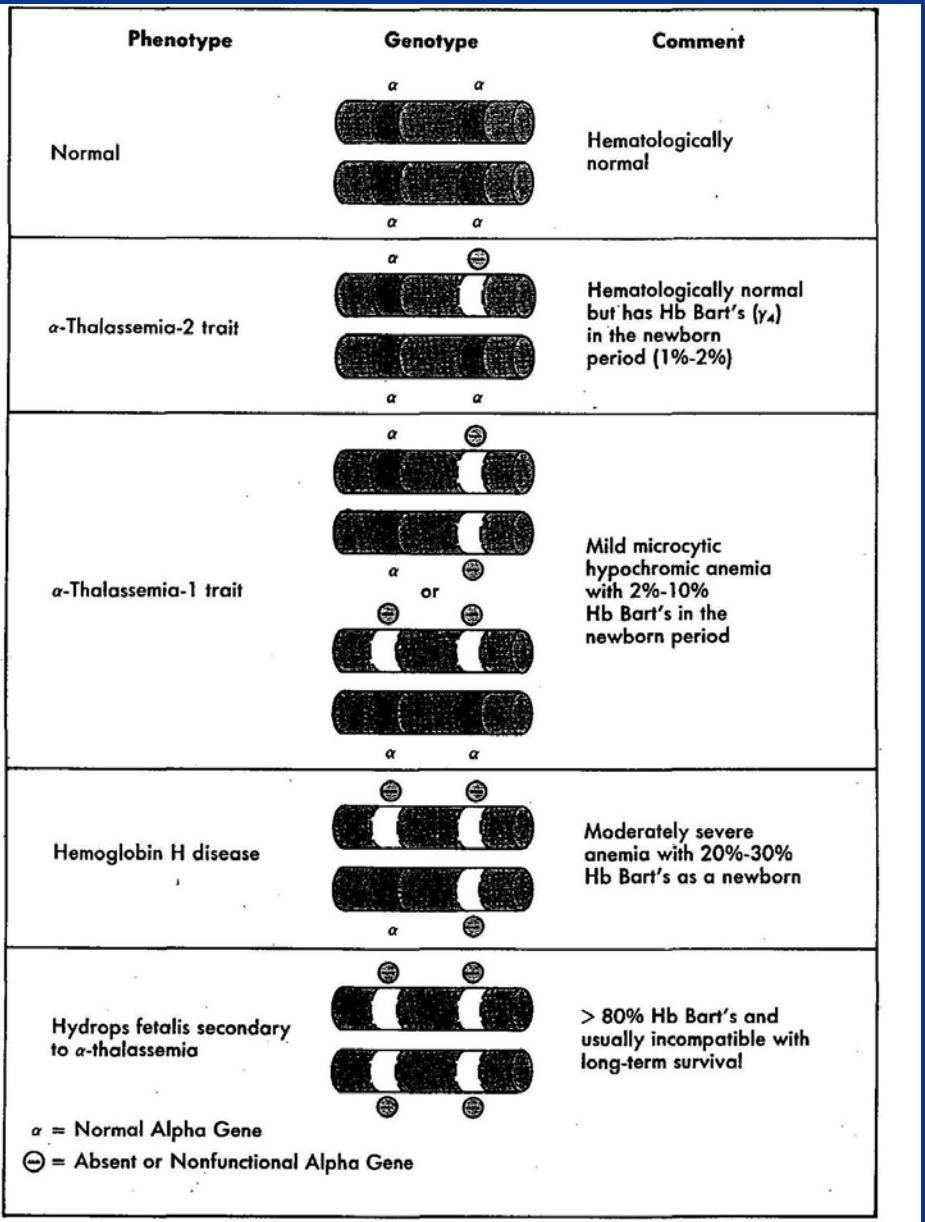
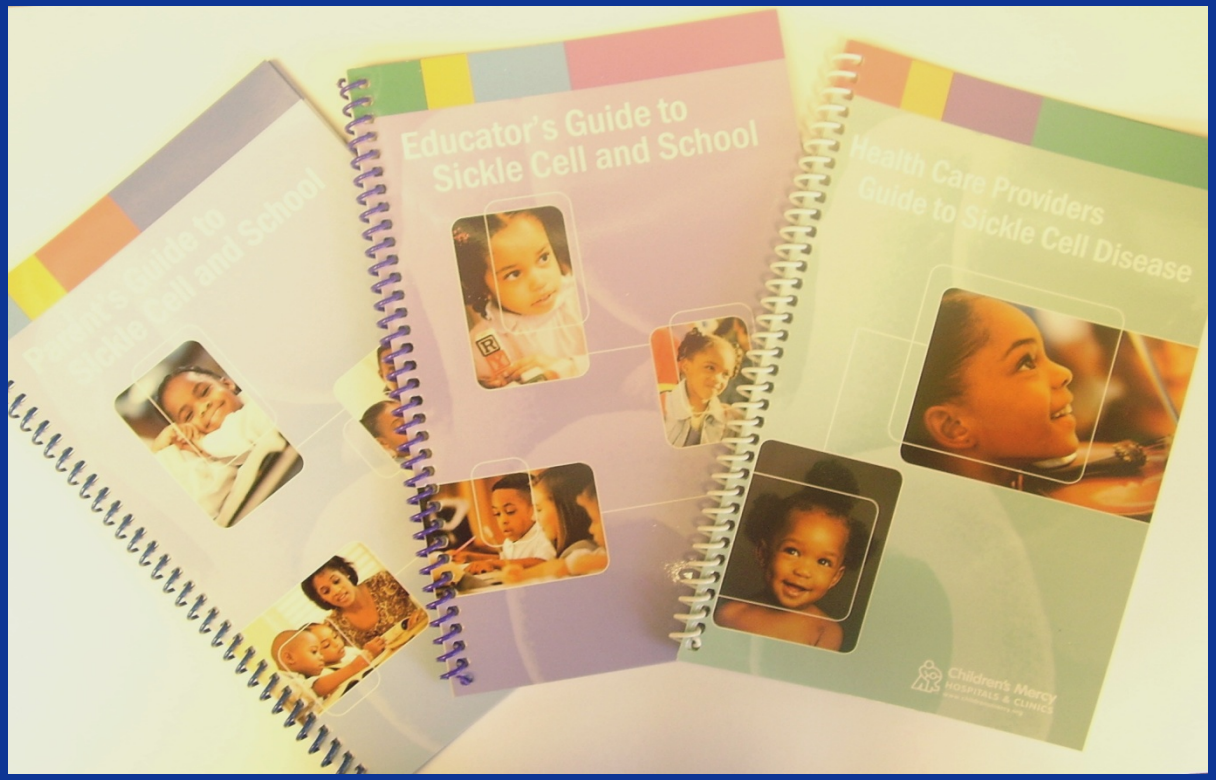


Fig. 13-5. Deletion of one or more of the four α genes results in an α-thalassemia syndrome. Examp of a normal α-globin gene complement and the phenotypes, genotypes, and clinical effects of vari deletions are shown. (From Schwartz E, Surrey S: *Hosp Pract* Sept. 15, 1986.)



Health Supervisor for Children with Sickle Cell Disease

Section on Hematology/Oncology and Committee on Genetics

Pediatrics 2002; 109; 526-535

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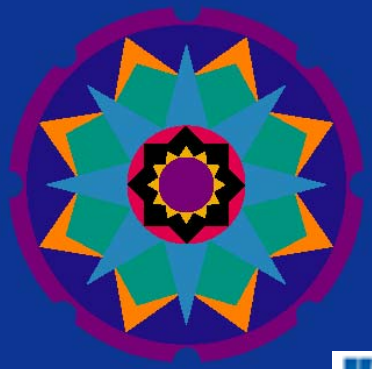

Centers for Disease Control and Prevention
Your Online Source for Credible Health Information

Sickle Cell Disease: 10 Things You Need to Know

http://www.cdc.gov/Features/Sickle Cell/

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