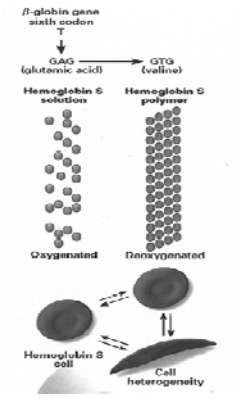
2015 Alabama Newborn Screening Conference

Alabama Newborn Screening Program

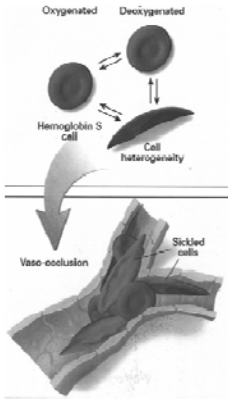
Marriott Hotel and Conference Center
Prattville, Alabama
Friday, September 18, 2015

Family Presentations: Timeline of Newborn Screening Disorders

Sickle Cell - Hendricks Family



Pathophysiology of Sickle Hemoglobin (HbS) From Gene to Cell to Organ Damage in Sickle Cell Disease



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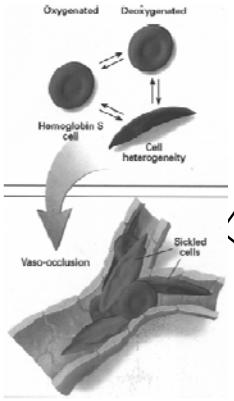
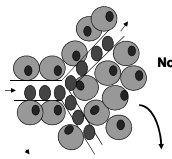


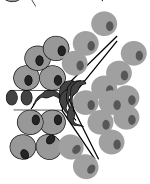
Hemolysis
- Anemia
- Plasma Hemoglobin
- ↑Bilirubin
- ↓Nitric Oxide (NO)

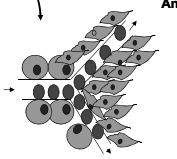
End Organ Damage

Transient	Irreversible
•Painful VOC	•Stroke
•Spleen infarct and sequestration	•Renal Pillary Necrosis
•ACS	•Anatomic asplenia
•Priapism	•Lung fibrosis
•Renal Injury	•Impotence
	•Renal Failure



Repetitive Injury to Tissue In Vaso-Occlusive Crisis (VOC) In Sickle Cell Disease Leads to End Organ Failure





SCD: Clinical Manifestations due to occlusion of microvasculature (**acute problems**) and end organ damage (**chronic problems**)

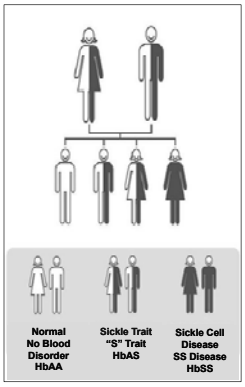
Bone Marrow	bone marrow infarction	painful crisis, dactylitis
	avascular necrosis	femur, humerus, clavicle
	osteomyelitis	bacterial bone infection
Spleen	splenomegaly	
	functional asplenia	bacterial sepsis
	anatomic asplenia	abdominal pain
Lungs	acute chest syndrome	chest pain, pneumonia
	lung fibrosis	lung infarction
	pulmonary hypertension	RHF, death
Brain	stroke	paralysis, aphasia
	silent cerebral infarct	brain scan abnormality
	decreased IQ	learning problems

SCD: Clinical Manifestations due to occlusion of microvasculature (**acute problems**) and end organ damage (**chronic problems**)

Kidney	papillary necrosis	hematuria
	hyposthenuria	inability to concentrate
	glomerular disease	hematuria, proteinuria
	pyelonephritis	bacterial kidney infection
Heart	cardiomegaly	mitral insufficency
	subendothelial infarcts	LV failure
	cor pulmonale	RV failure
Penis	priapism	acute pain erection
	sexual dysfunction	
Skin	leg ulcers	sores over malleoli

The Common Sickle Cell Diseases Inheritance

- = sickle (S) hemoglobin gene
- = beta^0 (β^0) thalassemia gene
- = C hemoglobin gene
- = beta^0 (β^0) thalassemia gene



Sickle Cell Disease,
Sickle Cell Anemia
Homozygous Sickle Cell Disease

The Common Sickle Cell Diseases Inheritance

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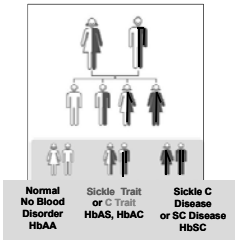

Sickle C Disease,
SC Disease

The Common Sickle Cell Diseases Inheritance

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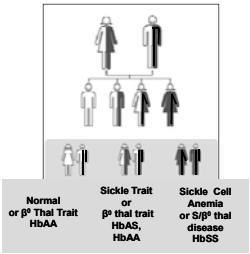

Sickle C Disease,
Sickle Cell Anemia
Sickle Beta Zero Thal Disease

The Common Sickle Cell Diseases Inheritance

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- = C hemoglobin gene
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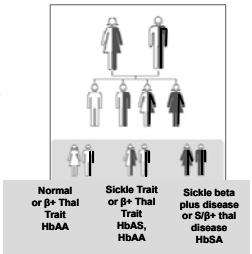

Sickle Beta Plus Disease,
Sickle Beta Plus Thal Disease

SCD: Clinical Manifestations due to occlusion of microvasculature (acute problems) and end organ damage (chronic problems)

Bone Marrow	bone marrow infarction	painful crisis, dactylitis
	avascular necrosis	femur, humerus, clavicle
	osteomyelitis	bacterial bone infection
Spleen	splenomegaly	
	functional asplenia	bacterial sepsis
	anatomic asplenia	abdominal pain
Lungs	acute chest syndrome	chest pain, pneumonia
	lung fibrosis	lung infarction
	pulmonary hypertension	RHF, death
Brain	stroke	paralysis, aphasia
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	decreased IQ	learning problems

History of Newborn Screening (NBS) for Sickle Cell Anemia (SCA)

- 1948: Pauling shows SCA is due to and abnormal hemoglobin (hemoglobin S); separates it by electrophoresis
- 1954: Ingram shows SCA is due to a single amino acid substitution in beta chain of hemoglobin
- 1960s -1970s: Simple inexpensive methods, developed to detect hemoglobin S; appropriate for NBS

History of Newborn Screening (NBS) for Sickle Cell Anemia (SCA)

- 1972: Sickle Cell Anemia Control Act established The National Sickle Cell Disease Program within HEW under The NHLBI in 1972. Funds 41 sickle cell centers and clinics, over 250 general screening programs, 69 research grants and contracts for screening, education, and counseling clinics. Despite Federal efforts NBS for hemoglobinopathies not embraced

History of Newborn Screening (NBS) for Sickle Cell Anemia (SCA)

- 1978: The National Genetic Disease Act passed additional funds for SCD. Via HRSA developed community-based education, screening and counseling. NIH funds 23 Comprehensive Sickle Cell Centers (CSCC) (down to 10 by 1986). Estab screening/education center in 40 states. Despite Federal efforts NBS for hemoglobinopathies not embraced.

History of Newborn Screening (NBS) for Sickle Cell Anemia (SCA)

- 1983 - 86: Prophylactic Penicillin Study (NHLBI) assesses efficacy of oral penicillin in preventing severe bacterial infections in children with SCD. 7-8 cases pneumococcal sepsis/100 pt yrs with 20% fatalities reduced by 84% with >95% reduction in fatalities mostly of babies <2 years old

History of Newborn Screening (NBS) for Sickle Cell Anemia (SCA)

- 1987: "Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies. Conference" (NIH) convened. All states must offer universal screening for SCA to lower the mortality of the disease.
- 2006: US universal NBS for SCD

History and Current Status of Newborn Screening for Hemoglobinopathies Jane M. Benson, BA, Bradford L. Therrell Jr, PhD; *Sem. Perinatology* 34: 134 ff, 2010

2013 ADPH Newborn Screening Diagnoses: Number Newborns Identified

Hearing Loss	58
Sickle and other Hemoglobinopathies*	53
Congenital Hypothyroidism	36
Cystic Fibrosis	13
Phenylketonuria	4
Hyperphenylalaninemia	3
Medium Chain Acyl CoA Dehydrogenase Deficiency	3
Congenital Adrenal Hyperplasia	2
Critical Congenital Heart Defect	2
Carnitine Uptake Defect	1
Classical Galactosemia	1
Long Chain Acyl CoA Dehydrogenase Deficiency	1
Maple Syrup Urine Disease	1
Methylmalonic Acidemia	1
Very Long Chain Acyl CoA Dehydrogenase Deficiency	1

What Happens When a Newborn Has An Abnormal NBS for a Sickle Hemoglobinopathy

- NBS positive for a sickle cell disorder (FS,FSA, FSC)

1. Notification of: Parents, Primary Care Physician (PCP), Hematologist at Comprehensive Sickle Cell Center (CSCC), Community Based Organization - Area Chapter SCD Association of America (SCDAA)

What Happens When a Newborn Has An Abnormal NBS for a Sickle Hemoglobinopathy

2. Initiation of prophylactic penicillin
3. Referral to Hematologist at CCSC at UAB or USA, Confirmation of diagnosis, Sickle Cell Disorder Specific Education, Preventive Care (stroke, renal disease, gallstones, Fe overload, decreased pain episodes etc.), State of the Art Treatment (e.g. hydroxyurea, bone marrow transplant etc.)

What Happens When a Newborn Has An Abnormal NBS for a Sickle Hemoglobinopathy

- NBS positive for sickle cell trait (FAS)

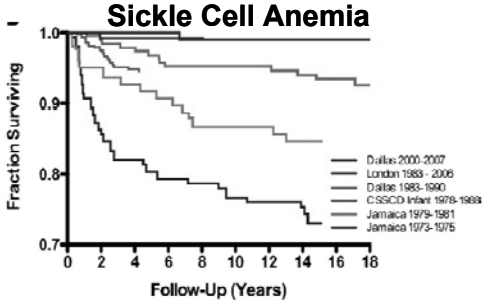
1. Notification of: Parents, Primary Care Physician (PCP), Community Based Organization - Area Chapter SCD Association of America (SCDAA)
2. Genetic counseling and education, Per PCP and Area SCDAA Chapter

What Happens When a Newborn Has An Abnormal NBS for a Sickle Hemoglobinopathy

- NBS positive for other abnormal hemoglobin "X" (FX, FAX,FXA, F):

1. Notification of: Parents, Primary Care Physician (PCP)

Impact of Newborn Screening, Education and Comprehensive Care on Survival of Patients with Sickle Cell Anemia



Hendricks Family