# 2017 Alabama Newborn Screening Conference

ALABAMA Newborn Screening PROGRAM

**Marriott Hotel and Conference Center**
**Prattville, Alabama**
**Friday, August 18, 2017**

## Newborn Screening for Sickle Cell Disease

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## Disclosures

- **Medical Consultant and Speaker Bureau for Novartis Pharmaceuticals, Inc.**
- **Grant funding from the Children's Oncology Group**
- **Grant funding from the Alabama Department of Public Health**

## Disclosures

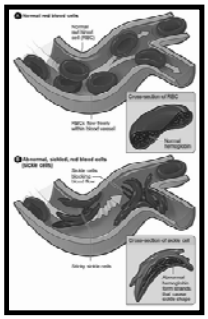
- **Clinical trial agreement with Selexys Pharmaceuticals Corporation with Quintiles providing clinical research organization services**
- **I will discuss off label use or investigational uses**

## Sickle Cell Disease

- **Sickle cell disease is a genetic blood disorder that affects the hemoglobin protein within the red blood cells that carries oxygen to all parts of the body**

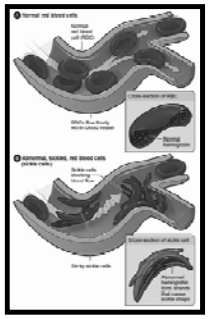
## Sickle Cell Disease

- **Normal red blood cells are flexible and flow freely within a blood vessel**
- **They last an average of 120 days in the bloodstream**



## Sickle Cell Disease

- Sickle cells are rigid and tend to stick to the blood vessel which blocks blood flow to areas of the body
- They last an average of 19 days in the bloodstream

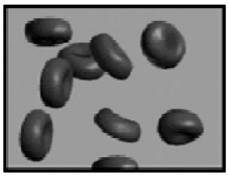


## Sickle Cell Disease

- This abnormality can result in chronic anemia, serious infections, severe painful episodes, strokes, damage to body organs, and early death

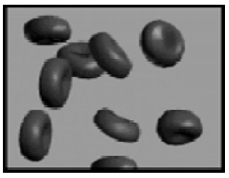
## Sickle Cell Disease

- In the 1970s, SCD was recognized as a major public health concern
- 20% children were dead by age 3



## Sickle Cell Disease

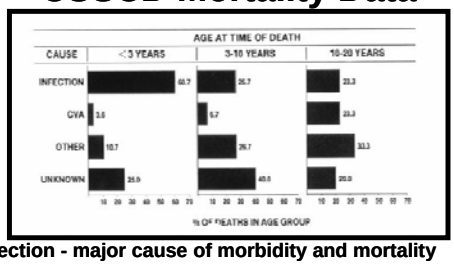
- 50% died before the age of 20 years
- The average lifespan was only 14 years



## Cooperative Study of Sickle Cell Disease

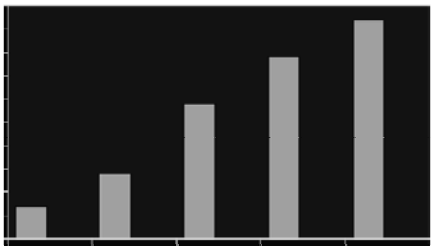
- Initiated in 1978 by the National Institutes of Health to gather data prospectively on the natural history of SCD
- Cohort of 2824 patients registered, followed, and managed (4007 registered)
- 23 clinical centers in the US

## CSSCD Mortality Data



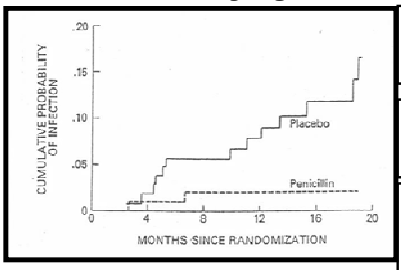

**Infection - major cause of morbidity and mortality**
**S. pneumoniae - most common during early childhood. Enteric organisms emerge as important pathogens in older patients**
**Leinken et al. Pediatrics. 1989;84:500.**

## CSSCD Functional Asplenia



**Age in years**

## Prophylactic Penicillin Study PROPS - I



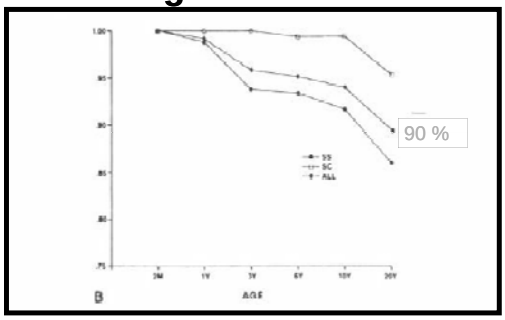

13/110 Infections, 3 deaths

2/105 infections, No deaths

Study was terminated 8 months early

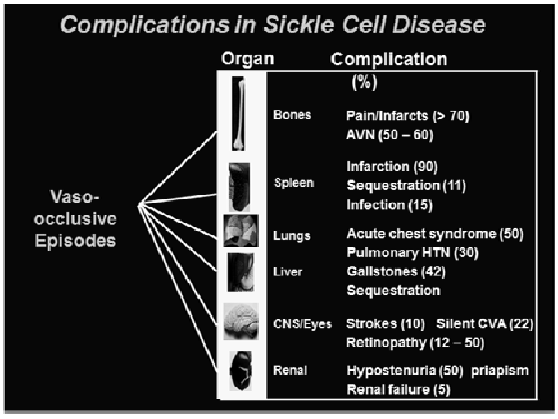
NEJM, 1986 314:1593-9

## Probability of Survival to Age 20 Years




## Newborn Screening

- **This study provided the greatest impetus for widespread implementation of newborn screening for SCD to**
  - **Provide early dx and referral**
  - **Ensure prompt delivery of care starting with penicillin prophylaxis**
  - **Permit education and counseling**




## Newborn Screening

- **Learning about risk can help with**
  - **Early diagnosis**
  - **Better treatment**
  - **Understanding the chances of passing a disease on to future generation**
- **Allows opportunity to discuss the availability of therapeutic and potentially curative interventions**

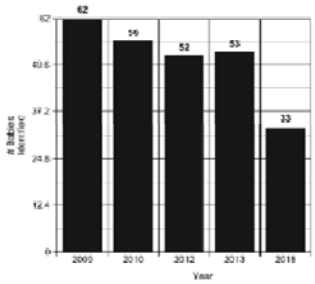
## Sickle Cell Trait and Disease

- **3.5 million Americans are genetic carriers of SCD and have SCT**


## Sickle Cell Trait and Disease

- **Incidence of SCD**
  - **1 in 375 African**
  - **Americans**
  - **1 in 1,200 Hispanics**
  - **1 in 3000 Native Americans**
  - **1 in 60,000 Whites**

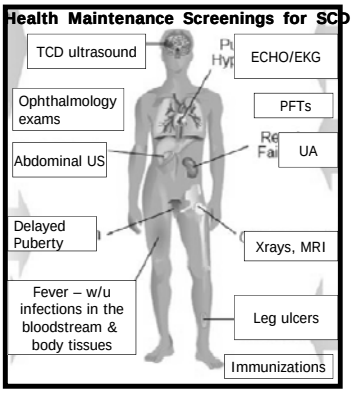

## Alabama NBS Statistics for SCD




**Screening for SCD in Alabama began in 1988**

## 2016 Confirmed NBS Primary Disorders

| Newborn Screening Primary Disorder | 2016 Confirmed |
|---|---|
| Classical Galactosemia | 3 |
| Congenital Adrenal Hyperplasia (CAH) | 4 |
| Congenital Hypothyroidism | 29 |
| Critical Congenital Heart Defect (CCHD) | 3 |
| Cystic Fibrosis | 16 |
| Hearing Loss | 52 |
| Hgb S/Beta Thalassemia | 2 |
| Hgb SC Disease | 14 |
| Hgb SS Disease | 30 |
| Hyperphenylalaninemia (secondary condition) | 3 |
| MCADD | 2 |
| PKU | 2 |
| VLCADD | 3 |
| TOTAL | 160 |



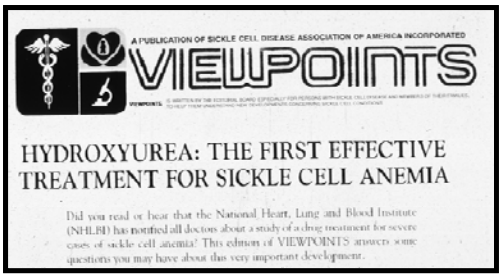

## RBC Transfusions Play a Major Role in the Management of SCD Complications

**Regular, Long-Term (Chronic) Transfusions**

- Stroke prevention
- *Recurrent acute chest* syndrome that is not helped by hydroxyurea*
- Frequent acute pain*
- Recurrent splenic sequestration*
- Leg ulcers*
- *Progressive organ failure* (hepatic, renal, cardiac, and pulmonary)*
- Other indications (eg, priapism, complicated pregnancy)*

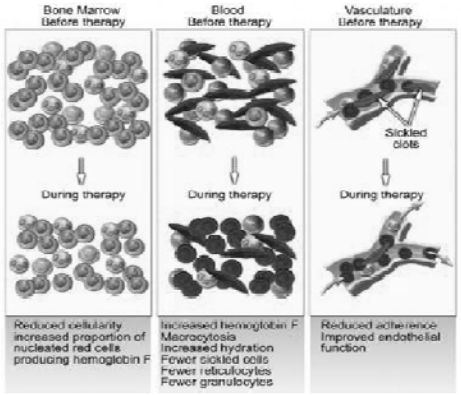
**Episodic Transfusions**

- Acute stroke
- Symptomatic anemia
- Acute chest syndrome
- Multiorgan failure
- Preoperative management




***Multicenter National Trial – 1991***

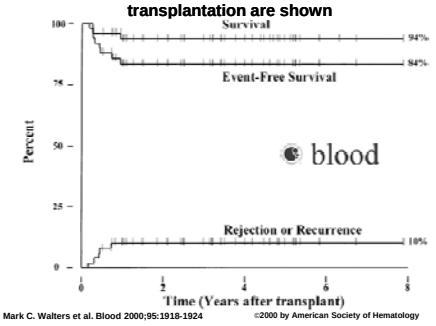
**FDA approved 1995 for age 18 years and older**
**50% reduction in pain crises, ACS and need for transfusion**
**40% reduction in deaths**




## The Cure


**To date, > 1000 Bone Marrow Transplants have been performed around the world for Sickle Cell Disease**

**Outcome after transplantation for 50 children with advanced, symptomatic sickle cell disease.Kaplan-Meier estimates for survival and event-free survival following marrow transplantation are shown**




Mark C. Walters et al. Blood 2000;95:1918-1924 ©2000 by American Society of Hematology

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Gene Therapy in a Patient with Sickle Cell Disease

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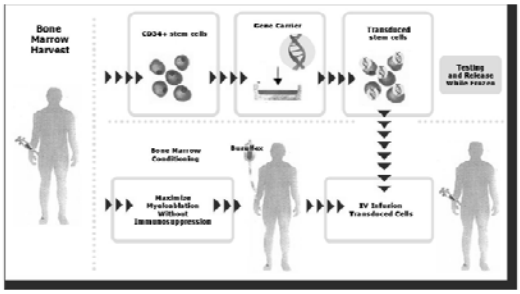
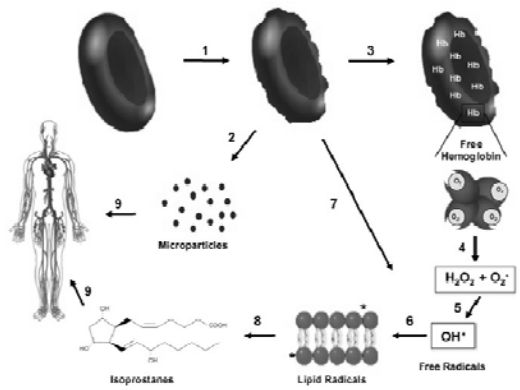
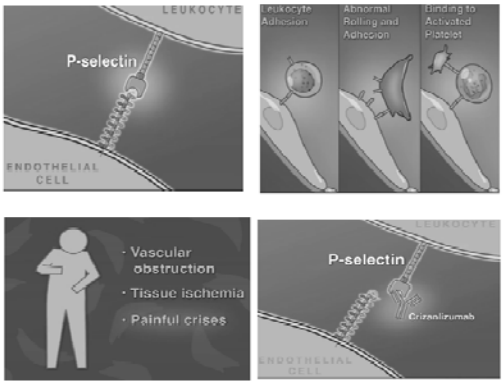







## The SUSTAIN Study Overview

- **In this yearlong trial involving patients with sickle cell disease, crizanlizumab, an antibody to P-selectin, was associated with a 45% lower rate of pain crises than placebo and a longer time to their onset**

The NEW ENGLAND JOURNAL of MEDICINE

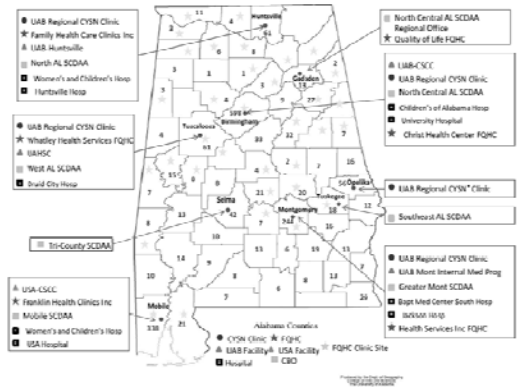
Ataga KI et al. N Engl J Med 2017;376:429-439

## The SUSTAIN Study Overview

- **Adverse events included arthralgia, diarrhea, and pruritus**

The NEW ENGLAND JOURNAL of MEDICINE

Ataga KI et al. N Engl J Med 2017;376:429-439





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