Sickle Cell Disease

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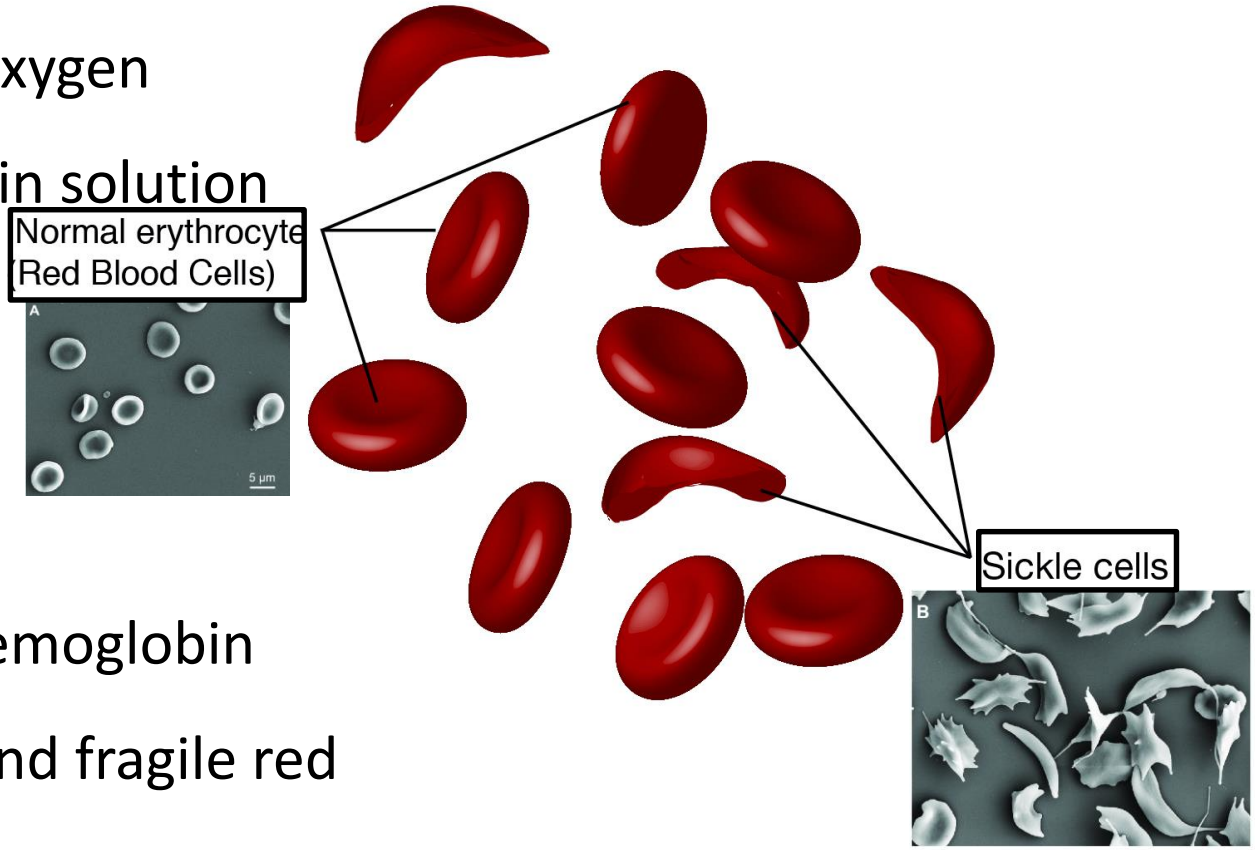
Sickle Cell Disease: An Inherited Disorder of the Red Blood Cell

- Red blood cells carry oxygen bound to hemoglobin in solution
- 'doughnut shaped'
- Genetic abnormality
- Abnormal clumping (polymerization) of hemoglobin
- Sickle-shaped, sticky and fragile red blood cells



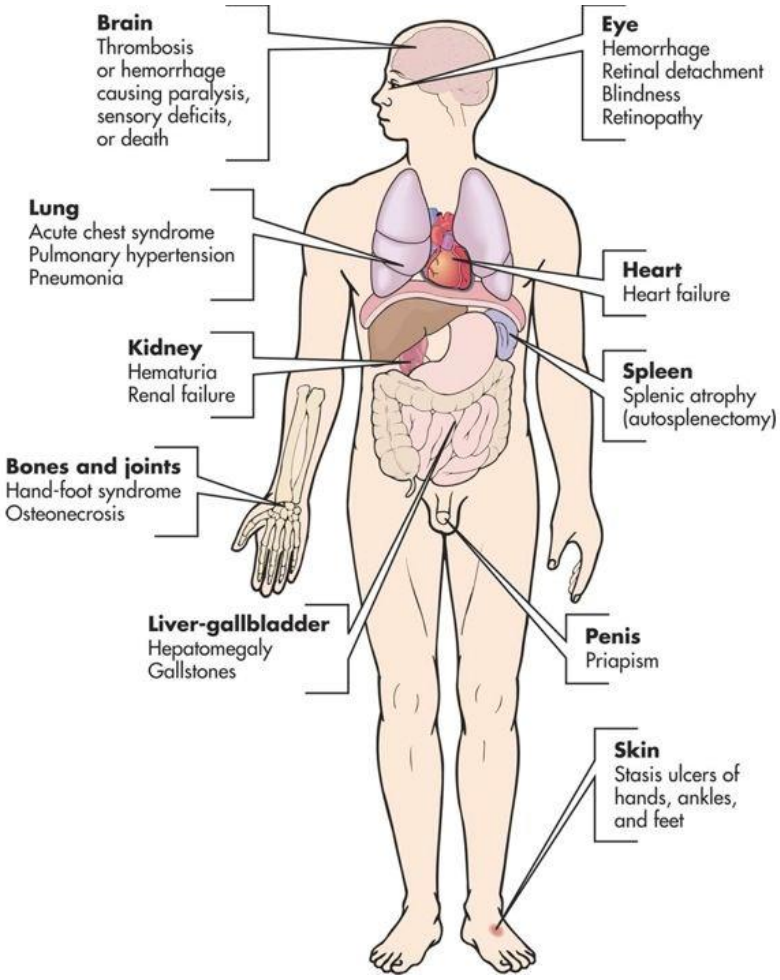
SCD Starves Tissues of Oxygen

- Abnormal red blood cells clog the small blood vessels
- Obstructs smooth flow of blood
- Impedes delivery of Oxygen to tissues
- Lack of oxygen causes tissue damage

Pain, Organ Damage, Impaired Quality of Life and Premature Death

- Stroke, and eye problems impair cogniti
- Pain, and anemia impair quality of life
- Bone and joint damage
- Kidney failure may need dialysis
- Premature death due to Infections,

pneumonia heart-lung complications

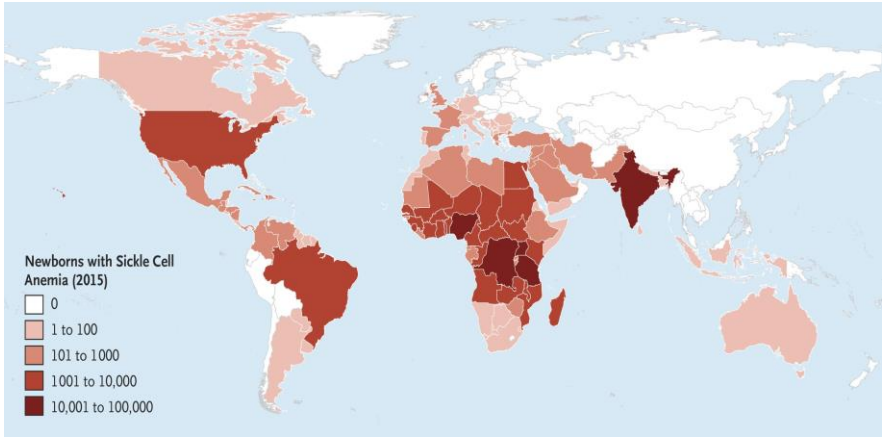


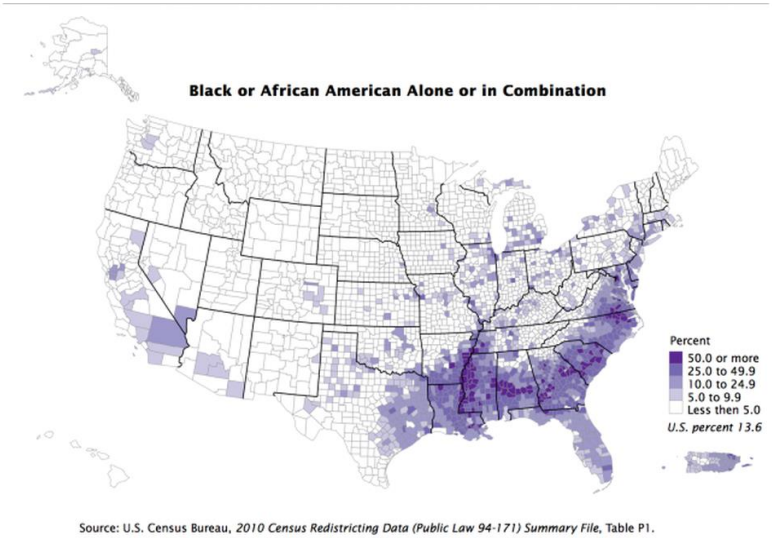
Sickle Cell and the COVID Pandemic

- Increased rate of severe covid needing admission to hospital (65-70% vs 17%)
- Severe pain is the main presentation
- Acute chest syndrome/Pneumonia (60% hospitalized patients0
- Higher death rate (3.2-10% vs. 1.75%)
- Eligible to receive antibody therapy for prevention of severe disease
- African-Americans have more severe economic impact of COVID
- COVID vaccination rates in GA 41% Whites, 36% Blacks, 74% Asians

Sickle Cell Disease is a Global Public Health Problem

- 312, 000 births affected by SCD each year
- 4000 births in the USA affected by SCD, 100, 000 patients in US
- More than half live in southern USA
- 70% on Medicaid/Medicare.
- Costs of care exceed $2.98 billion/year

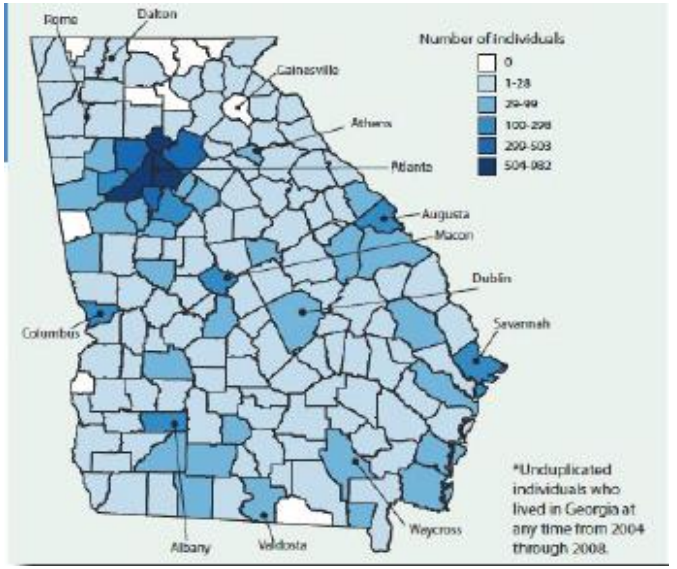


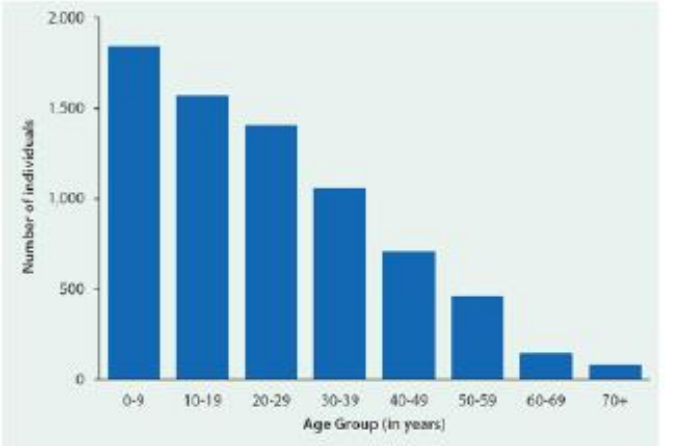


Source: U.S. Census Bureau, *2010 Census Redistricting Data (Public Law 94-171) Summary File*, Table P1.

Sickle Cell is a Major Public Health Problem in GA

- 7300 people with SCD in Georgia one of top three states for individuals with SCD
- 97% African American, 2% Hispanic
- One in every 295 births in African Americans
- Over 1900 patients, largest program in US
- 128 patients treated with bone marrow transplant at CHOA



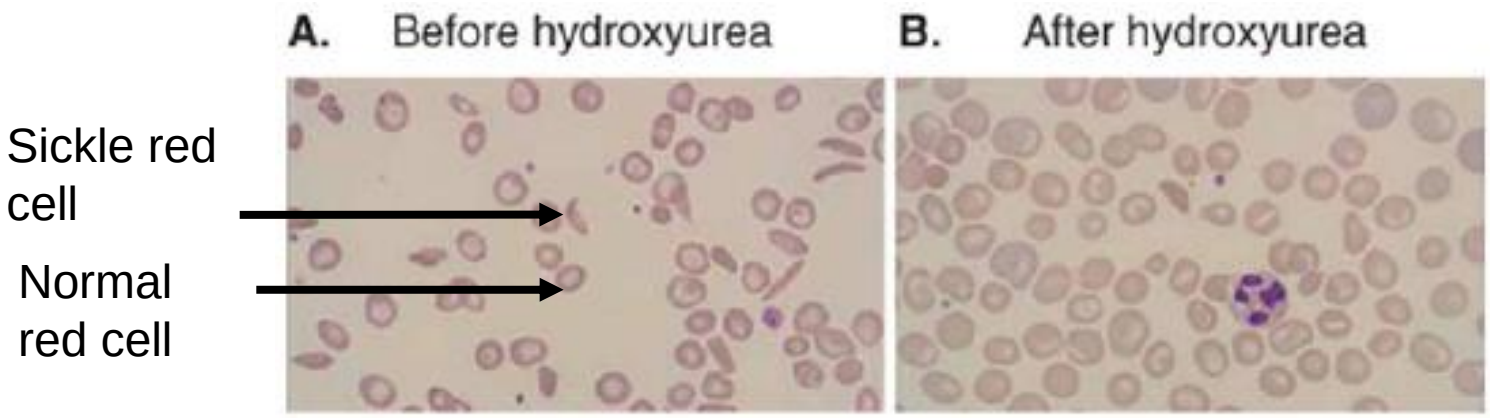


2004-2008 RuSH and PHReSH studies

Medical Advances Have Improved Care of SCD

- Newborn screening for SCD enables care before babies become sick
- Penicillin and pneumococcal vaccine can prevent deadly form of pneumonia
- Ultrasound of the brain can detect childre with increased risk for stroke
- New medications, bone marrow transplant for selected patients

Hydroxyurea: First FDA Approved Drug for SCD



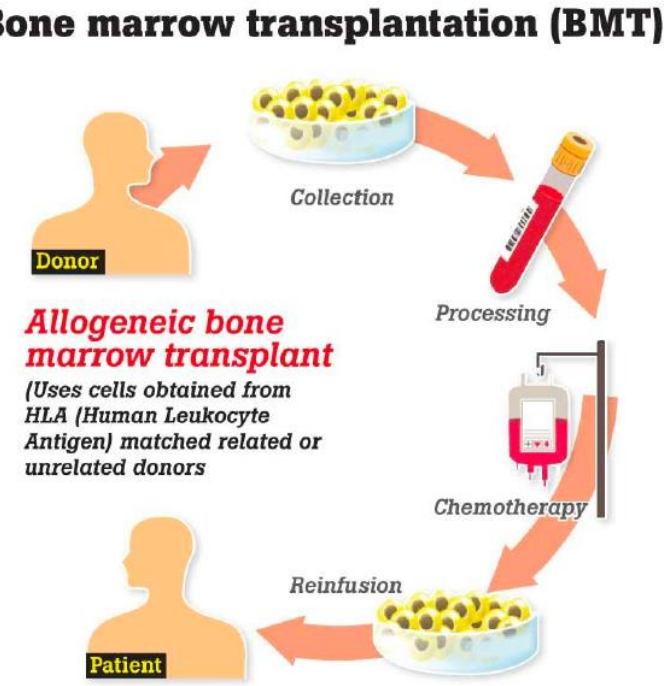
- Hydroxyurea is an orally administered drug that can improve outcomes for SCD
- Rates of pain crisis and lung complications is reduced by half
- Hemoglobin is improved
- May improve survival, reduce stroke

Three New Drugs Approved by FDA

- **L-Glutamine:** Protects Red Cells in SCD. Approved by FDA 2017
- **Voxelotor:** prevents clumping of hemoglobin. Approved by FDA 2019
- **Crizanlizumab:** blocks sticking of platelets, red blood cells, and white blood cells and lining of the blood vessel. Approved by FDA 2019
- Reduce pain, increase hemoglobin

Bone Marrow Transplant From a Genetically Matched Donor: Potentially Curative Option

- Chemotherapy to empty bone marrow and create space
- Replace with healthy donor bone marrow
- Patient is at risk of attack by donor's immune system
- Medicine for several months to suppress the immune system
- Potential cure for blood disorders such as SCD



Bone Marrow Transplant is Potentially Curative but has Risks

Risk-Benefit Paradigm for Curative Therapy for SCD

- Age
- Donor options (Less than 25% of patients have donors)
- Other treatment options

- Potential for cure
- Freedom from risk of sickle complications
- Improved survival

- Risk for death
- Treatment related complications
- Long term effects

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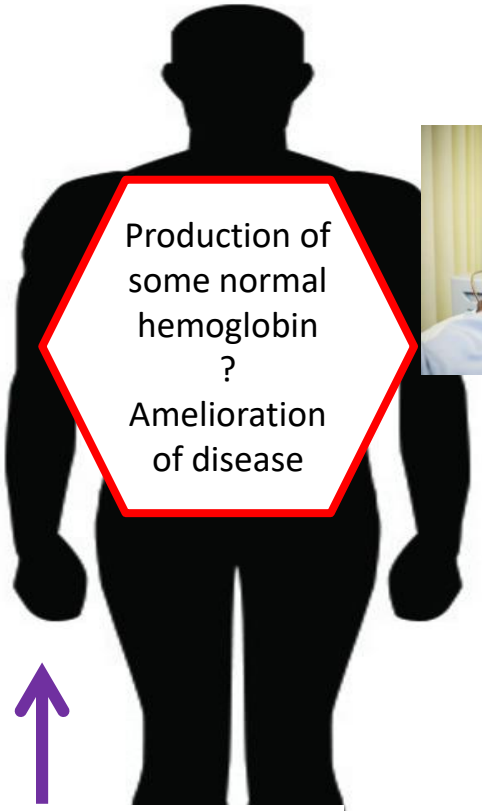
What is gene therapy?

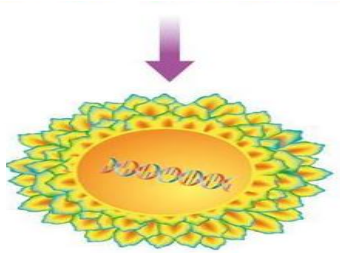
- An experimental technique
- Uses genes to treat or prevent disease.
- May allow doctors to treat a disorder by inserting or altering a gene in a patient's cells
- Adding a healthy gene
- Replacing a mutated gene with a healthy copy of the gene.
- Inactivating, or "knocking out," a mutated gene
- Inactivating a normal gene to activate a silent gene

Gene Therapy by Adding a Healthy Gene or Modifying a Gene

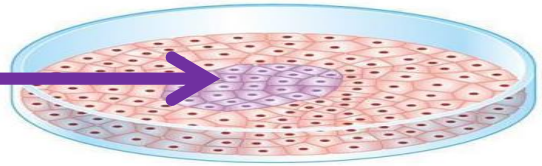


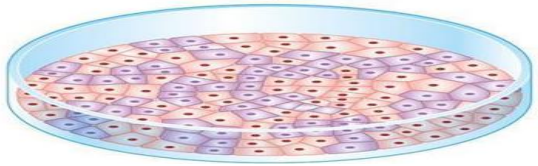
Normal beta globin gene synthesized in the lab

Blood making cells collected from patient



Lenti virus vector inserts gene into blood making cells OR Gene is modified





Patient receives high dose chemotherapy to to create marrow space

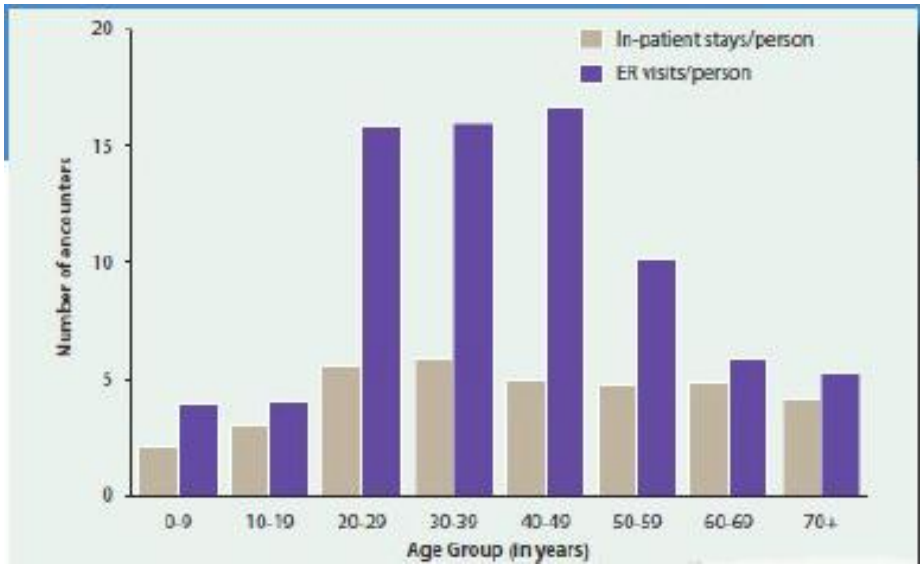
Blood making cells containing normal gene are infused into the patient

SCD Clinical and Research Strengths in Georgia

- Georgia has SCD programs with a large number of patients
- Community based organizations in GA are active in supporting patients
- Large number of research projects funded by NIH, CDC, HRSA, PCORI
- Numerous clinical trials, observational studies
- Largest experience with bone marrow transplantation
- Several ongoing gene therapy studies

Limited Access to Quality Care

- 94% of patients in GA had Emergency department or hospital visit
- Hospital visits increase with age
- Children ~ Four ED visits. Impacts school & activities
- Adults ~ >15 visits,
- Adults have barriers in access to insurance, quality care
- Behavioral health not supported



Hydroxyurea is Underutilized: Health Disparity

- CHOA is leading efforts to improve poor HU utilization nationally
- Only 38% of patients meeting clinical criteria received a prescription for hydroxyurea.
- One 77% of children received polysaccharide pneumococcal vaccine at age 2 years
- Only 23% of these toddlers received screening with Doppler ultrasound for detecting stroke risk at age 2 years

Limited Investment in Quality Care and Research

- Investment in SCD research is lower than in other genetic diseases
- Federal funding and philanthropic giving for Cystic fibrosis is more than for SCD though there are 3 times as many individuals living with SCD
- Most patients are on Medicaid, with limited access to care
- There is a lack of support for comprehensive care, case management , chronic pain, mental health and complementary medicine
- Lack of comprehensive and specialist care for adults with SCD

SUMMARY

- SCD is a major public health problem in Georgia
- Advances in care have provided patients many treatment options
- Several medications (Hydroxyurea, L-Glutamine , Voxeletor and Crizanlizumab) are FDA approved for SCD
- Bone marrow transplantation and Gene Therapy offer a curative option to selected patients
- Challenges remain in access to quality care, resources and research funding

Suggested Legislative Priorities that May Help Patients with Sickle Cell

- Explore ways to improve access to SCD treatment.
- Expand behavioral and mental health services across the state.
- Support sickle cell testing and counseling in the community.