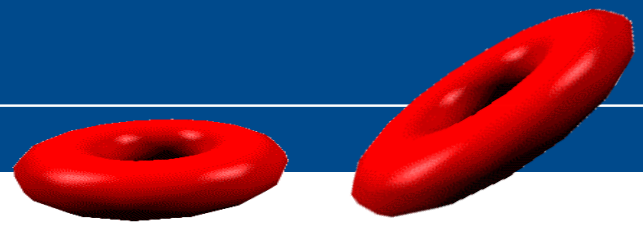

Stop the Sickle: An Update on Sickle Cell Disease

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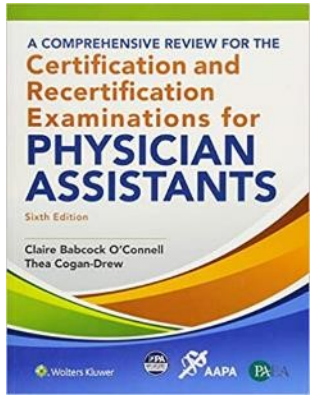
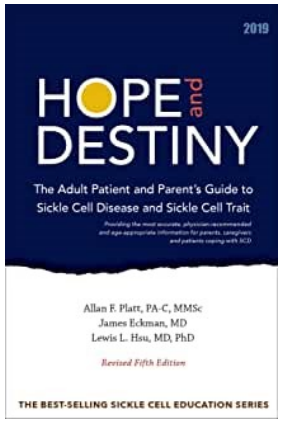
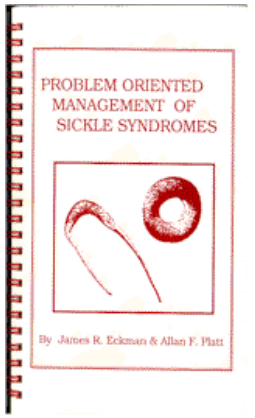
Disclosures

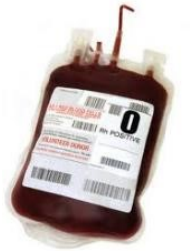


- Author of Chapter 4 – Hematology in **A Comprehensive Review for the Certification and Recertification Examinations for Physician Assistants Sixth Edition** by Claire O'Connell (Author)





- Co-Author of **Hope and Destiny 5th Edition: The Adult Patient and Parent's Guide to Sickle Cell Disease and Sickle Cell Trait** by Allan F. Platt Jr. P.A.-C. M.M.Sc., James Eckman M.D., et al. | May 12, 2019
- Sickle cell advisory board to a NIH funded project
- Webmaster of SCInfo.org website and monthly e-newsletter editor
- I do promote donating blood!!!



Objectives

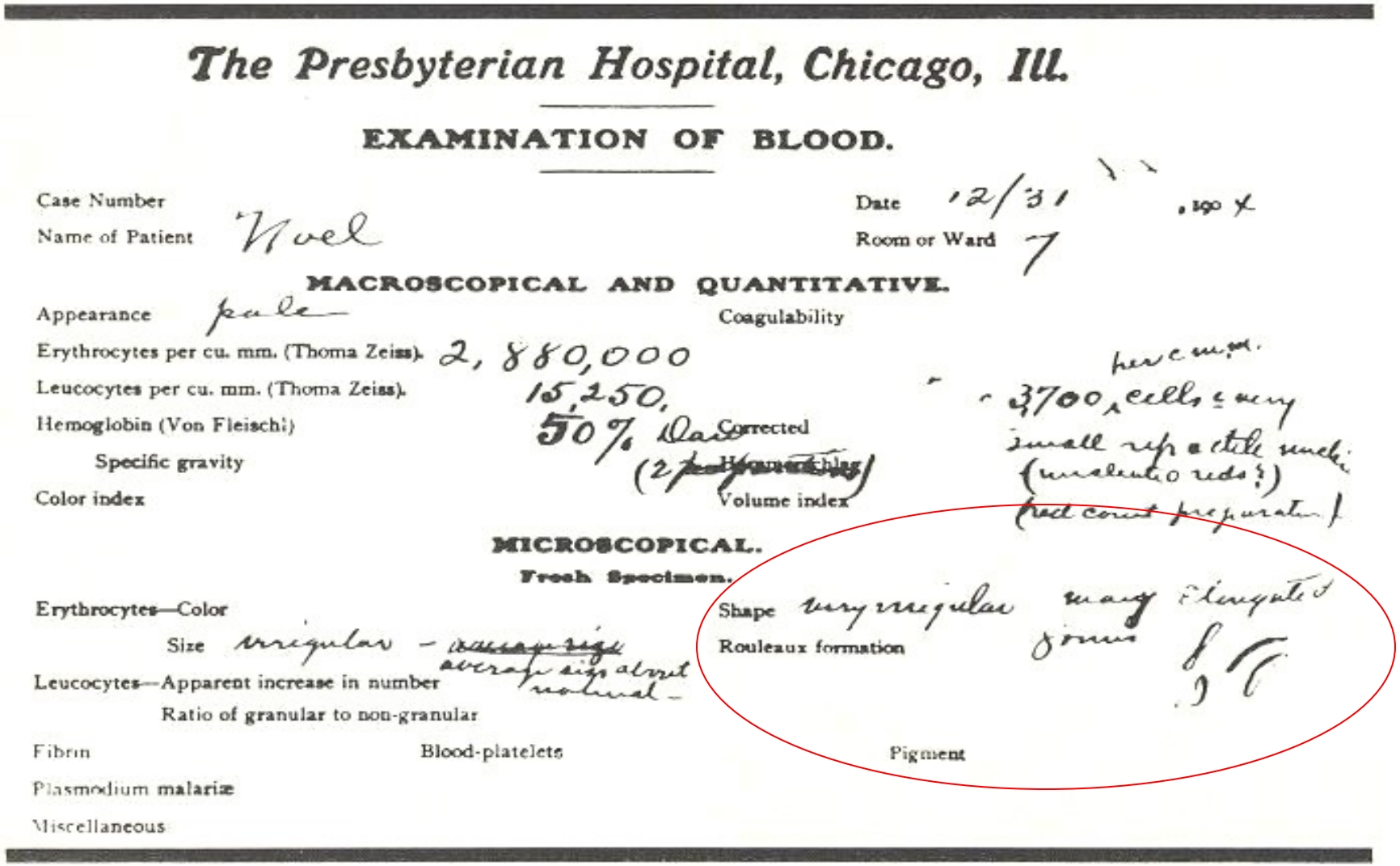
At the end of this session, participants should be able to:

- Communicate the pathophysiology of sickle cell disease
- Recognize common sickle cell complications
- Interpret common laboratory and radiologic findings in sickle cell patients
- Review the latest research and treatments for cure and prevention

Over 100 years ago….

- Ernest Irons, MD, a 27 year old intern did the patient work-up on dental student Walter Clemet Noel at Presbyterian Hospital in Chicago in 1904
- The student from Grenada was weak and dizzy with a respiratory ailment
- Reported the unusual findings to his attending James Herrick, MD
- The two doctors followed Noel for the 2 years he was a dental student.
- Irons would make house calls on Noel
- The diagnosis was unknown

Case Report



The Presbyterian Hospital, Chicago, Ill.

EXAMINATION OF BLOOD.

Case Number

Name of Patient Noel

Date 12/31 1904

Room or Ward 7

MACROSCOPICAL AND QUANTITATIVE.

Appearance pale

Coagulability

Erythrocytes per cu. mm. (Thoma Zeiss) 2,880,000

Leucocytes per cu. mm. (Thoma Zeiss) 15,250.

Hemoglobin (Von Fleischl) 50% Dale Corrected

Specific gravity

Color index

Volume index

per c.mm. 3700, cells & very small reg. actile nucle (nucleated reds?) (red count preparation)

MICROSCOPICAL.

Fresh Specimen.

Erythrocytes—Color

Size irregular – average size about normal

Shape very irregular many elongated forms

Rouleaux formation

Leucocytes—Apparent increase in number

Ratio of granular to non-granular

Fibrin

Blood-platelets

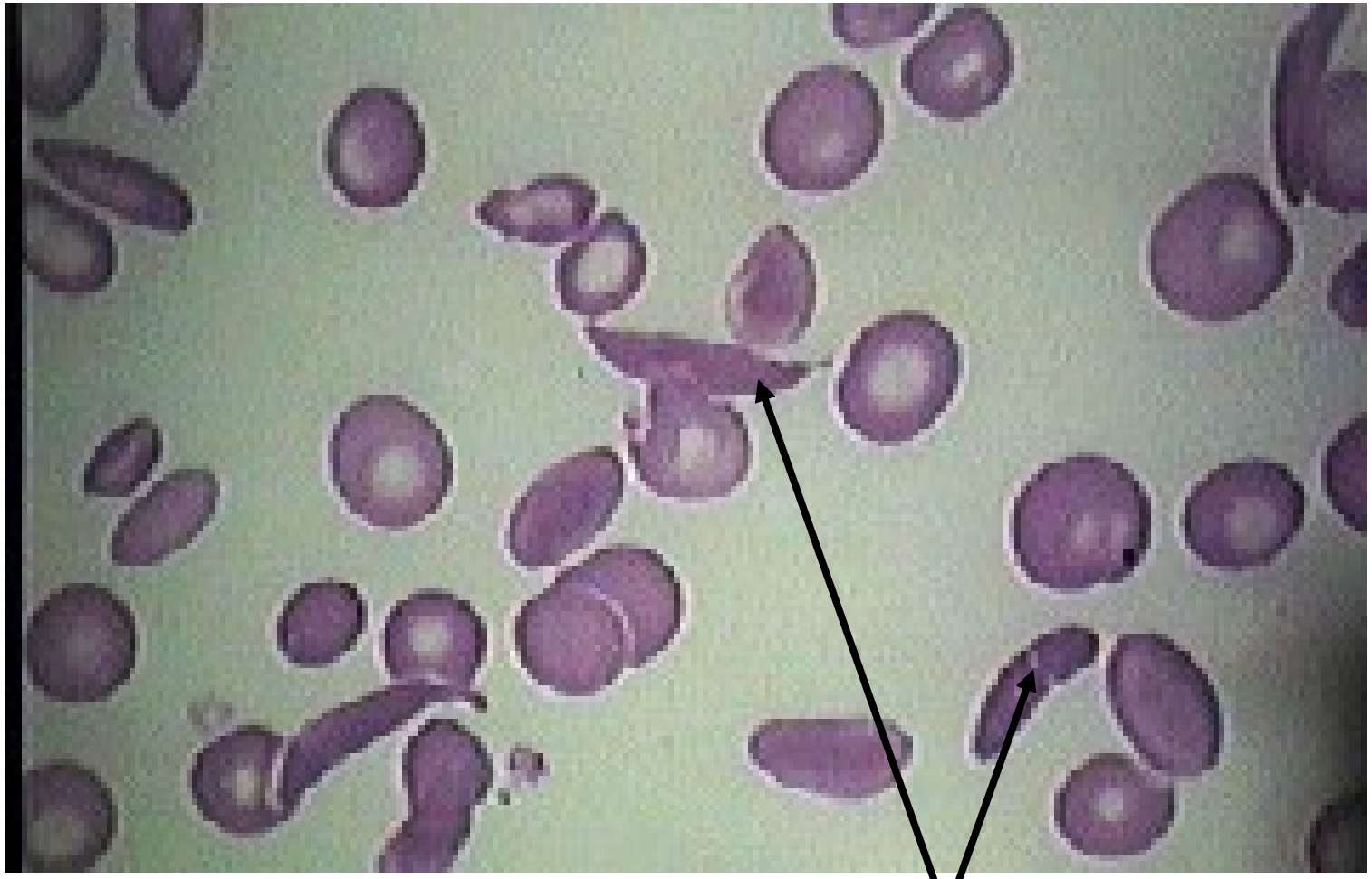
Pigment

Plasmodium malariæ

Miscellaneous

Fig 3.—Ernest Irons' blood examination report on Walter Clement Noel, Dec 31, 1904, describing and depicting the oddly shaped red blood cells.[2]

Diagnosis - Blood Smear



Herrick's Note

- Sickle shaped cells in blood

Peculiar elongated and sickle-shaped red blood corpuscles in a case of severe anemia

- *Arch Intern Med 1910; 6:512-521*

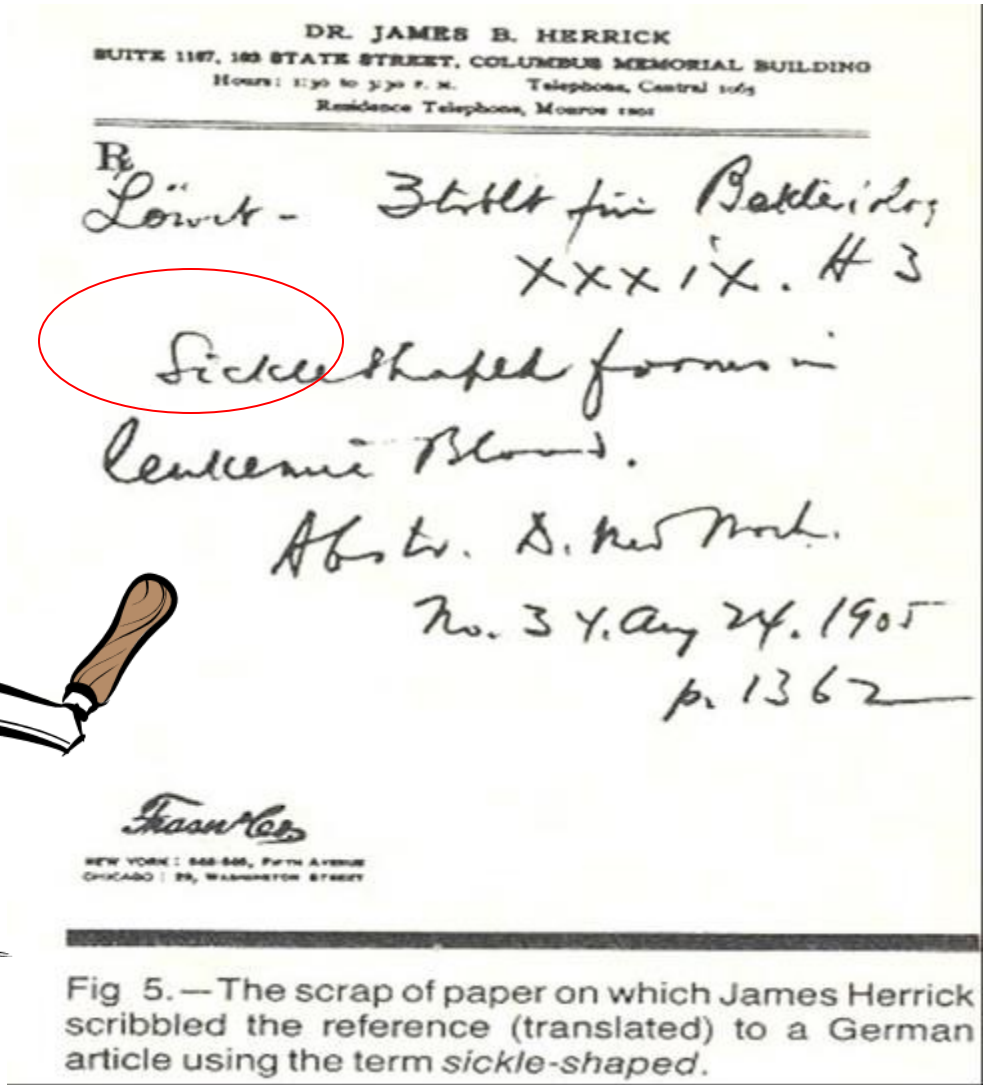


Fig 5.—The scrap of paper on which James Herrick scribbled the reference (translated) to a German article using the term *sickle-shaped*.

Time Line

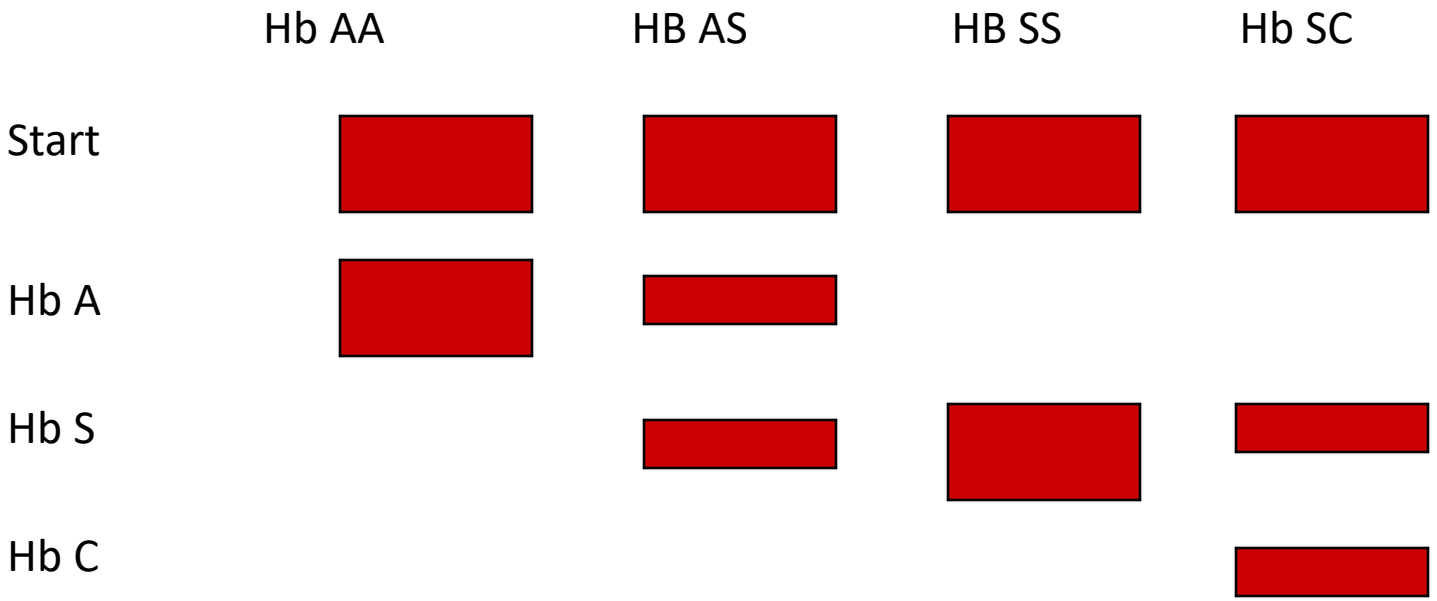
- **1927** - Hahn and Gillespie associate the sickling of red blood cells with low oxygen conditions.
- **1940** - Sherman reports that the sickling of red blood cells in the absence of oxygen is caused by a change in the hemoglobin molecule structure.
- **1948** - Watson suggests that the presence of fetal hemoglobin in the red blood cells of sickle cell newborns is the reason they do not show disease symptoms.

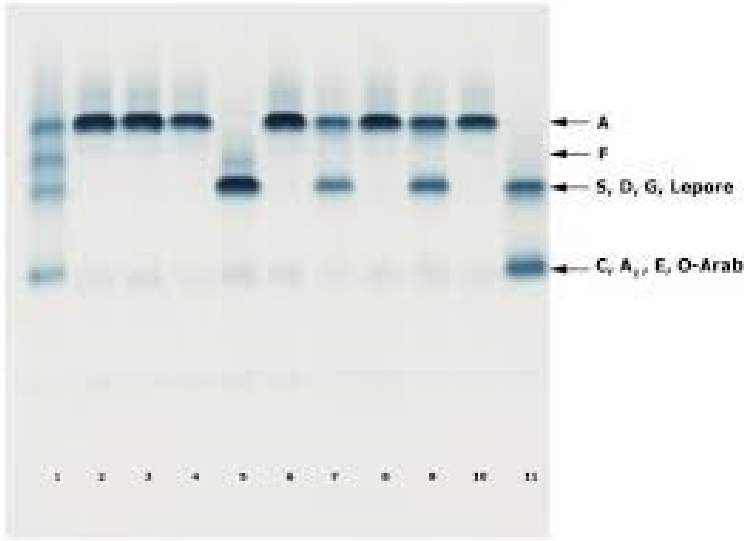
1949 - Linus Pauling

- Linus Pauling and associates publish "Sickle Cell Anemia, a Molecular Disease" in *Science.* This paper explains how protein electrophoresis was used to show that sickle cell hemoglobin differed in structure from normal hemoglobin. This was the first time that the cause of a disease was linked to a change in protein structure

Diagnosis

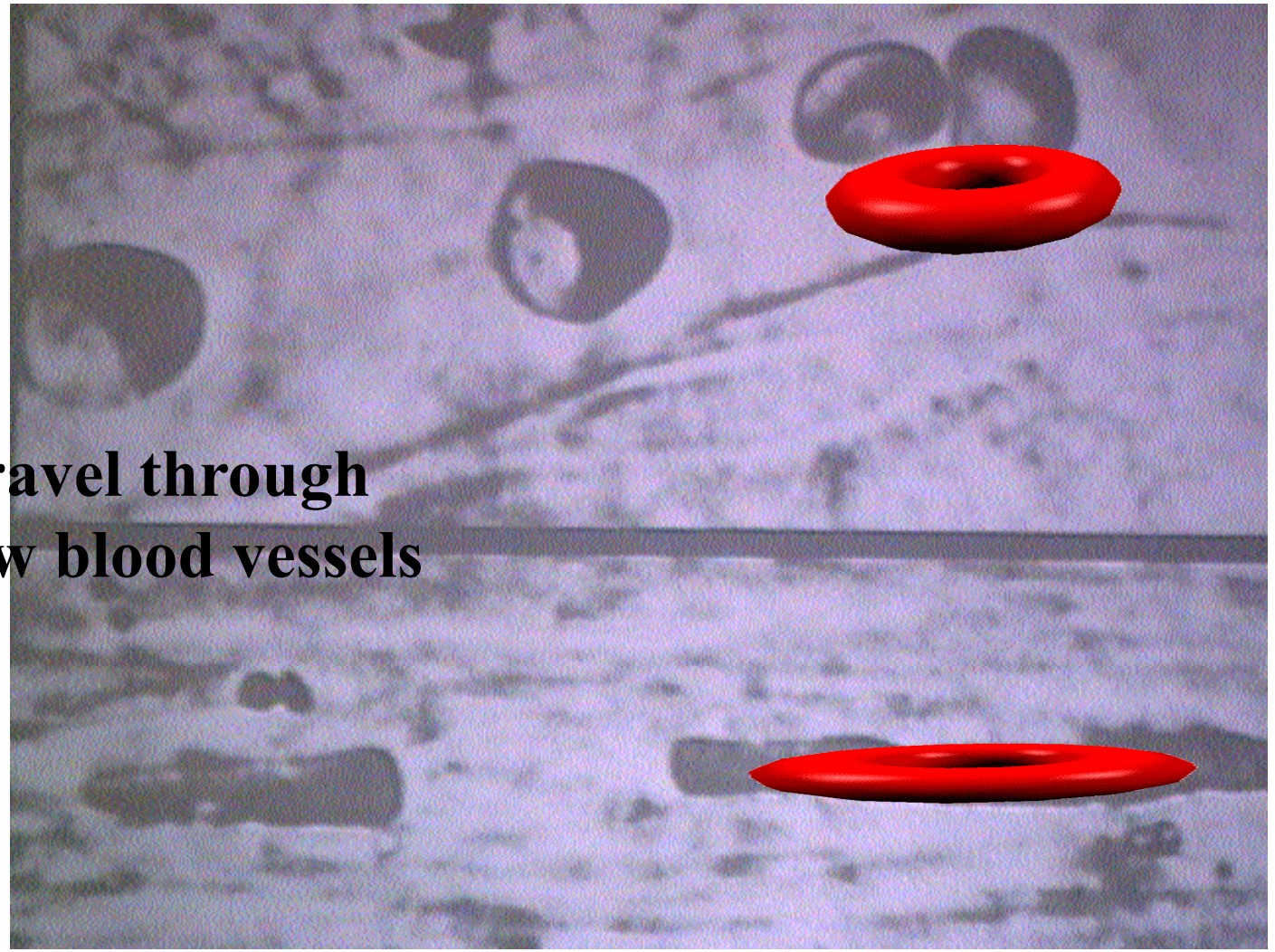
Hemoglobin Electrophoresis (also done with HPLC, IEF, and now DNA analysis)





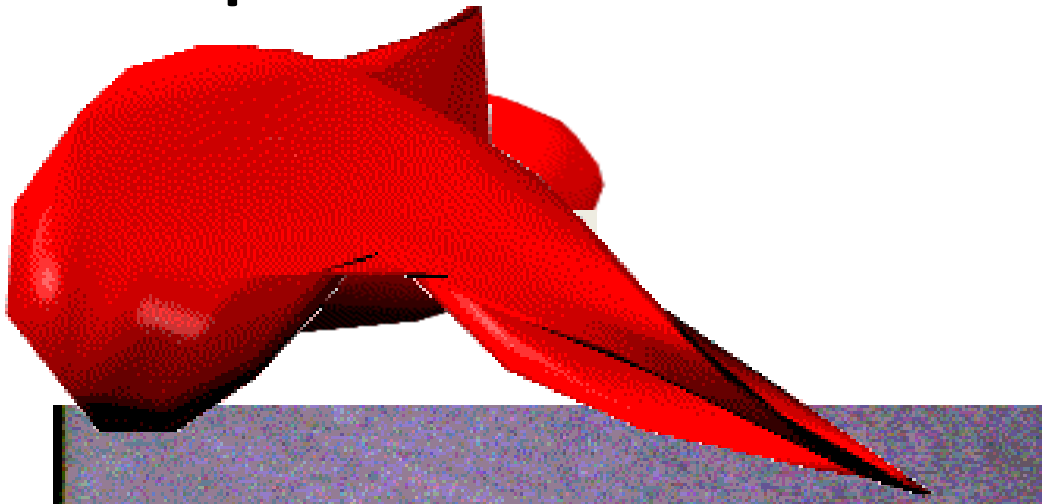
Red Blood Cells - Shape

Red cells travel through very narrow blood vessels

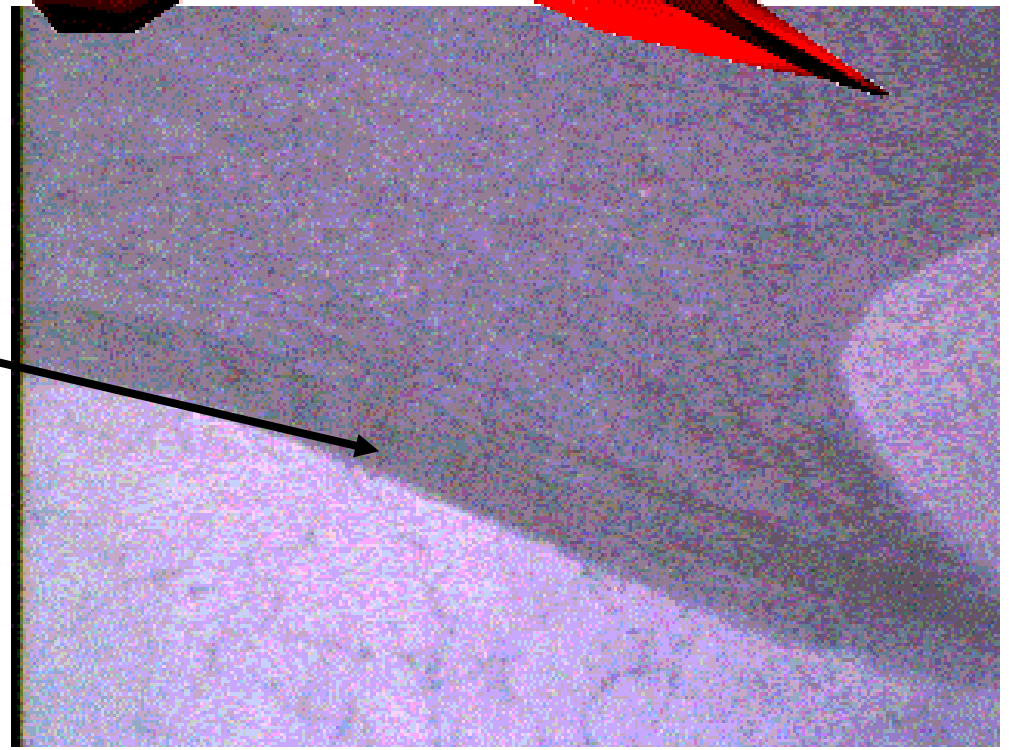


Normal Shape to Sickle

Long rods of hemoglobin form deforming the red cell



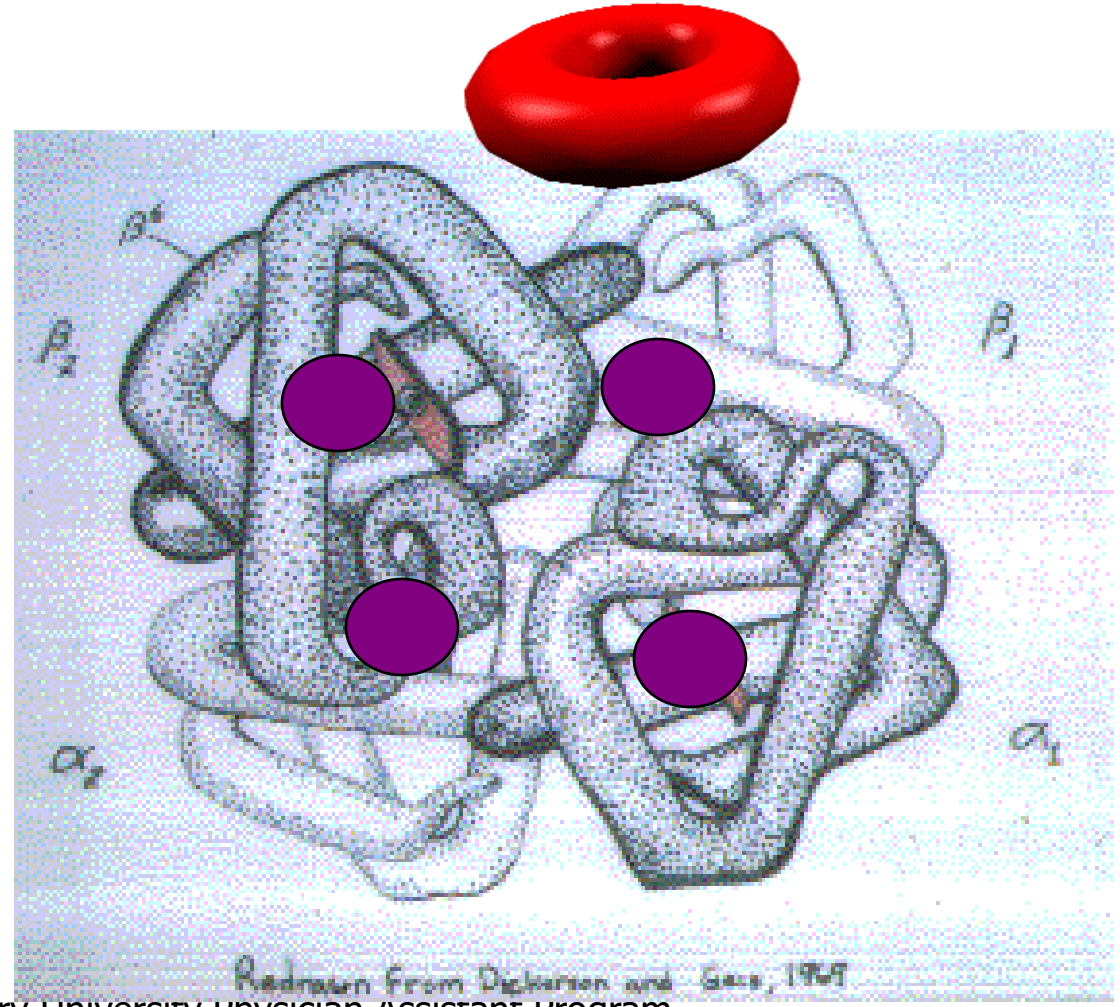
Microscope view of long rods in a sickle red blood cell



Red Blood Cells - Hemoglobin

Oxygen

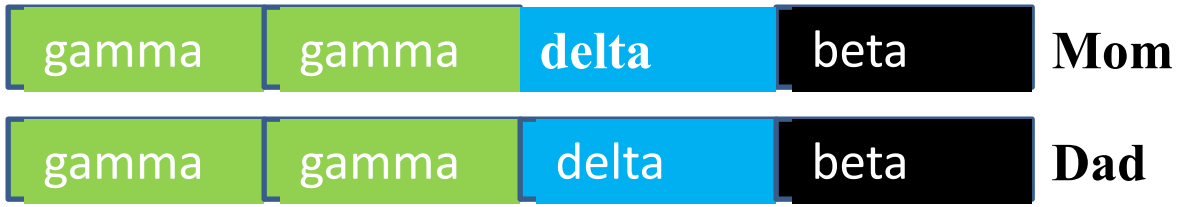
Hemoglobin, the main protein in red cells holds four oxygen molecules



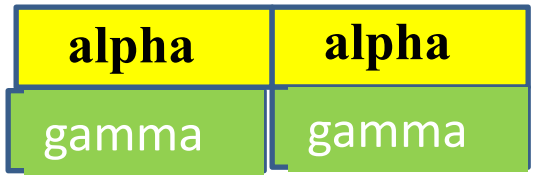
Hemoglobin FA – Biochemistry – Normal Newborn

Chromosome 16

Chromosome 11



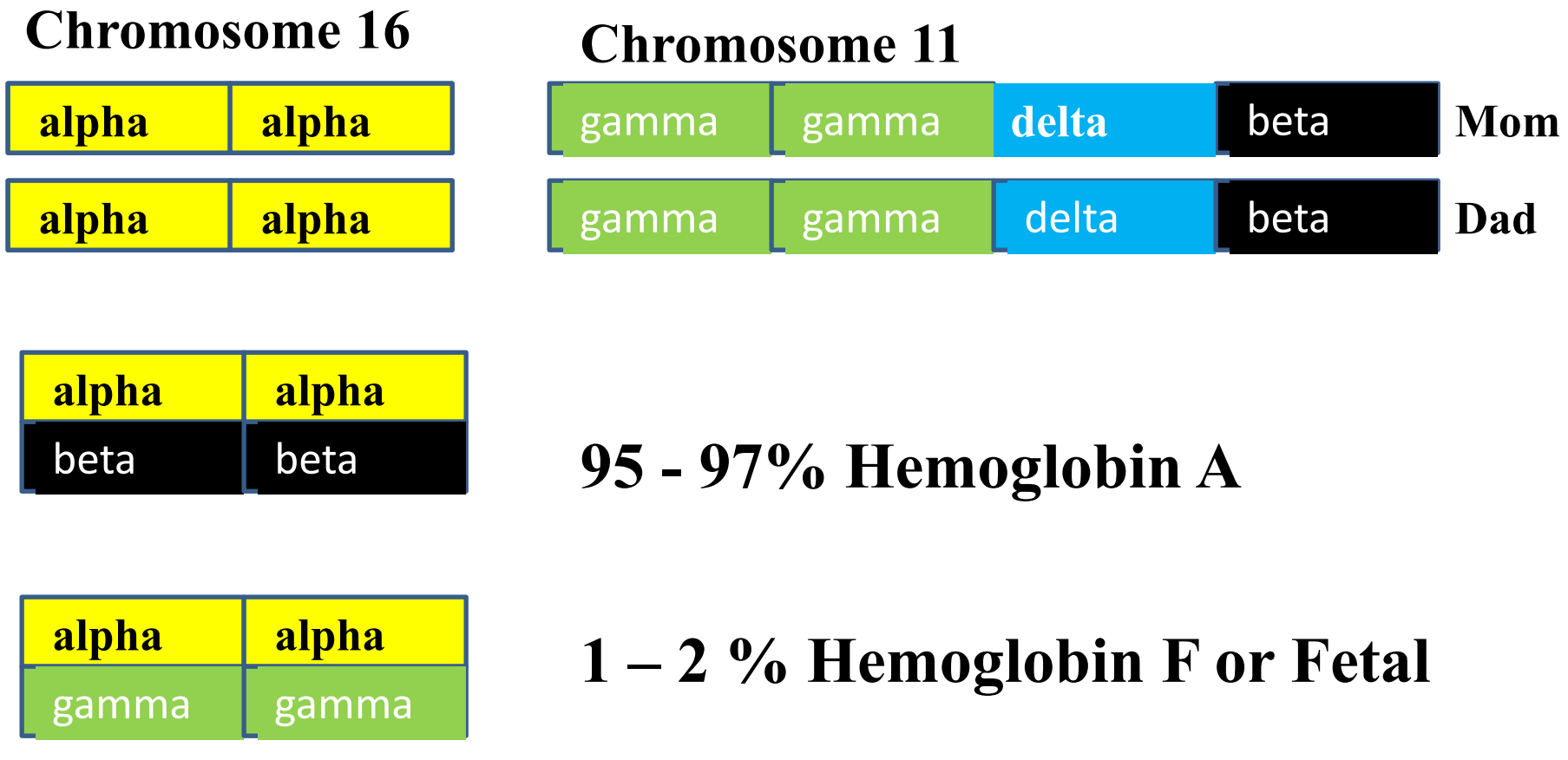
50 – 20 % Hemoglobin A



Hb F (newborn): 50% to 80%
(6 months): 8%
(over 6 months): 1% to 2%

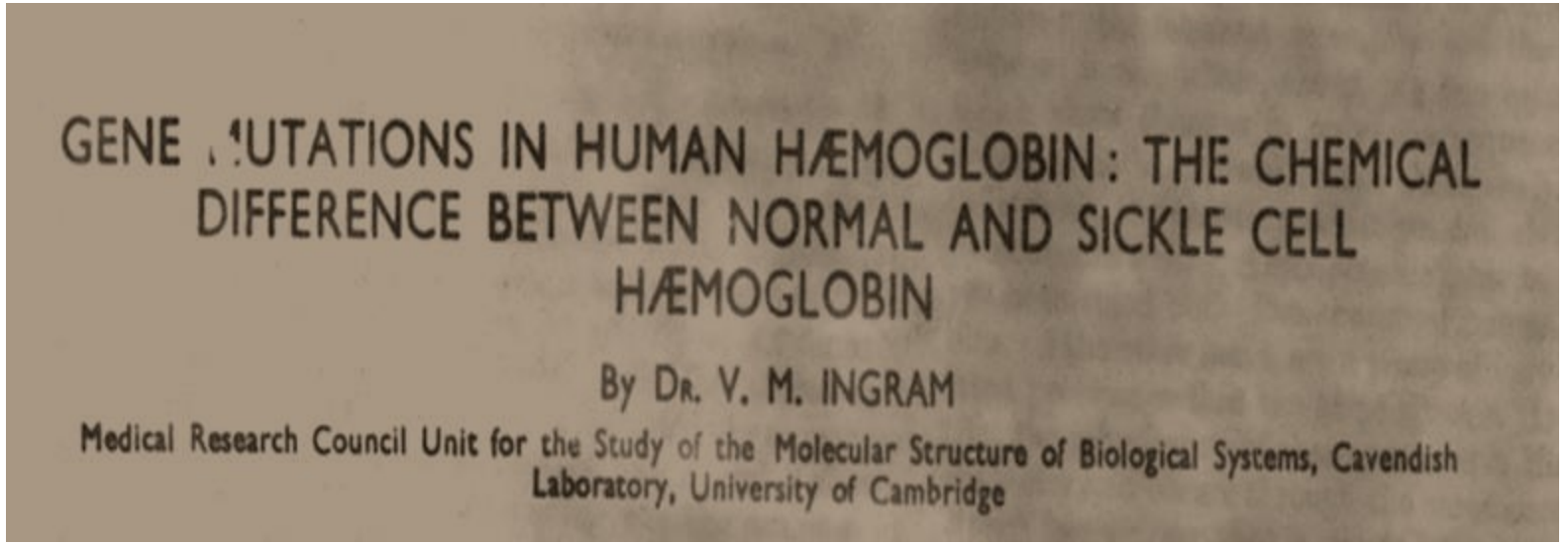
2% Hemoglobin A2

Hemoglobin A – Biochemistry – Normal Adult



1956 - Dr V.M.Ingram

- Vernon Ingram and J.A. Hunt sequence hemoglobin and discover that the change of a single amino acid in the protein sequence is the cause of sickle cell anemia.

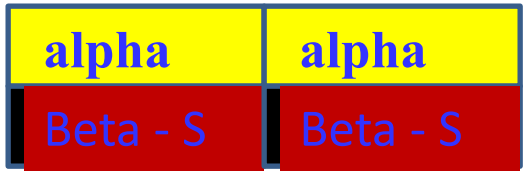


GENE MUTATIONS IN HUMAN HÆMOGLOBIN: THE CHEMICAL DIFFERENCE BETWEEN NORMAL AND SICKLE CELL HÆMOGLOBIN

By Dr. V. M. INGRAM

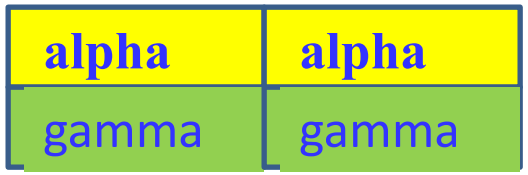
Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems, Cavendish Laboratory, University of Cambridge

Hemoglobin – Biochemistry – Sickle Trait



47% Hemoglobin S

50% Hemoglobin A

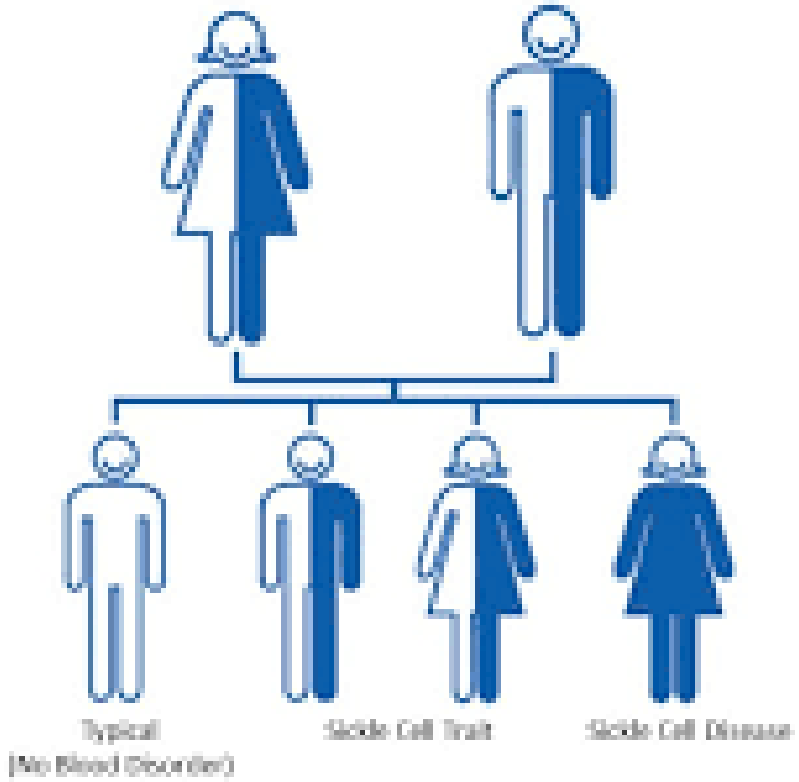


1% Hemoglobin F or Fetal

% Hemoglobin A2

Genetics

- Autosomal recessive inheritance



Types of Sickle Cell Disease

Hb SS

Hb SC

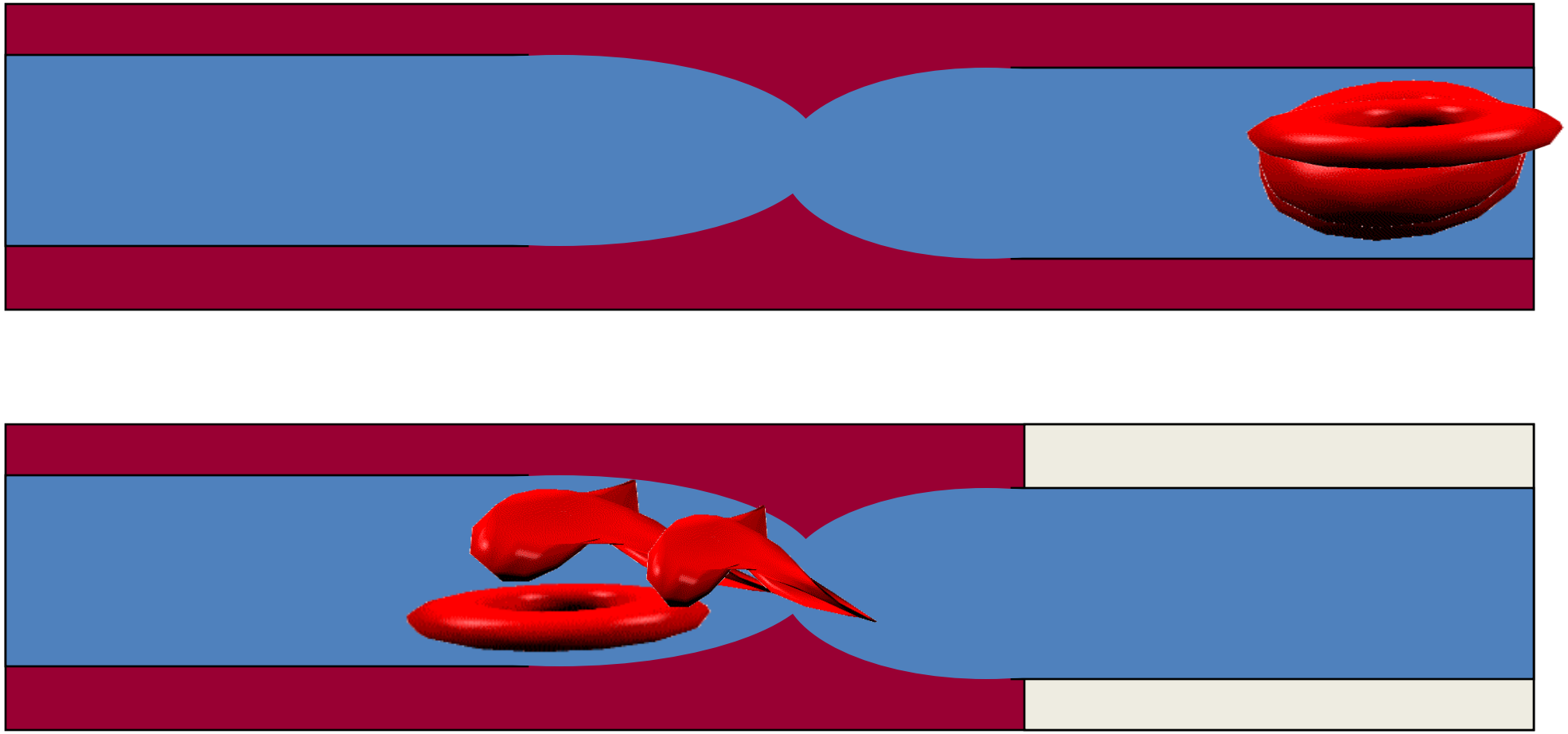
Hb S beta 0 Thalassemia

Hb S beta + Thalassemia

Hb SS with persistent Fetal Hemoglobin

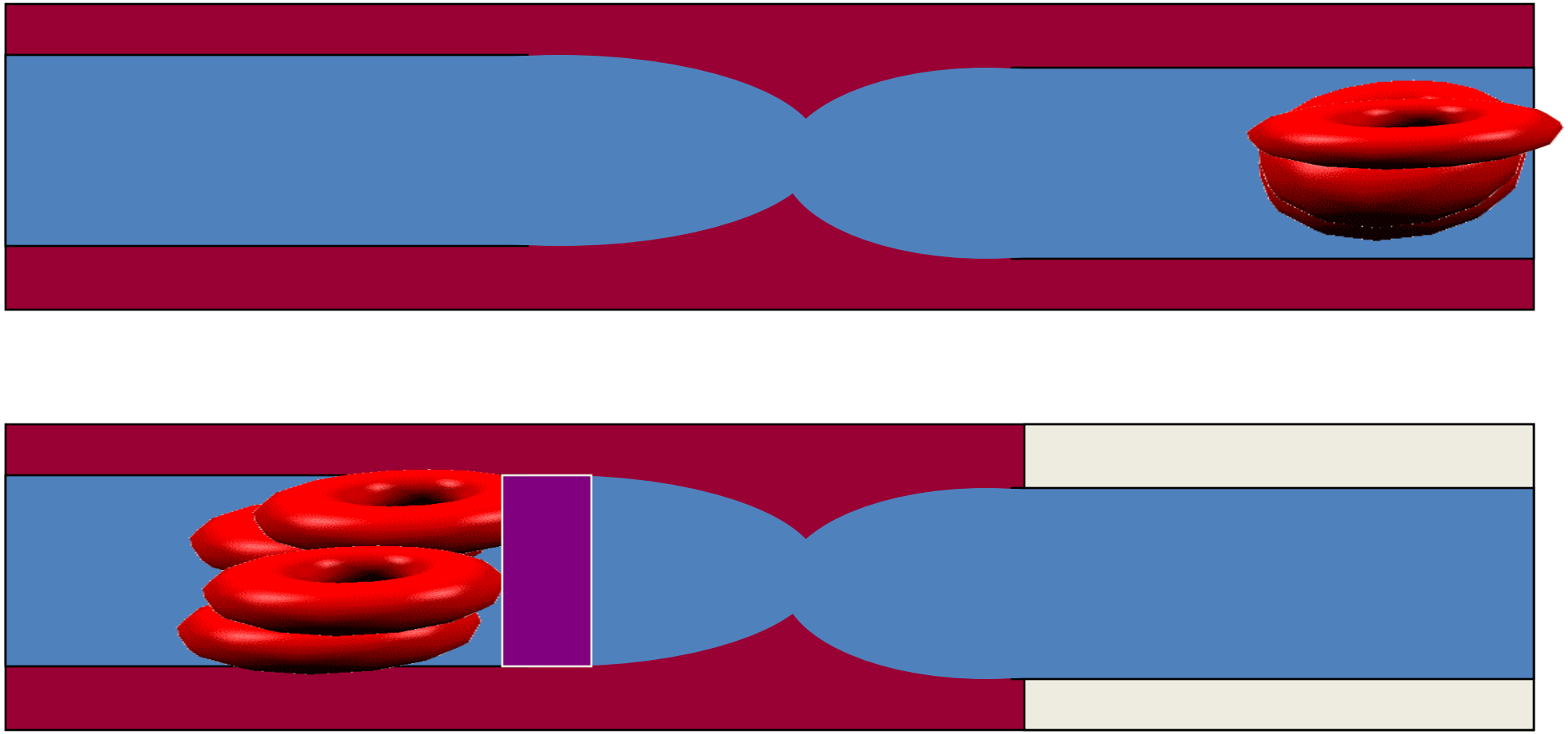
Hb SD, SO-arab, SE

Normal vs. Sickle red cells



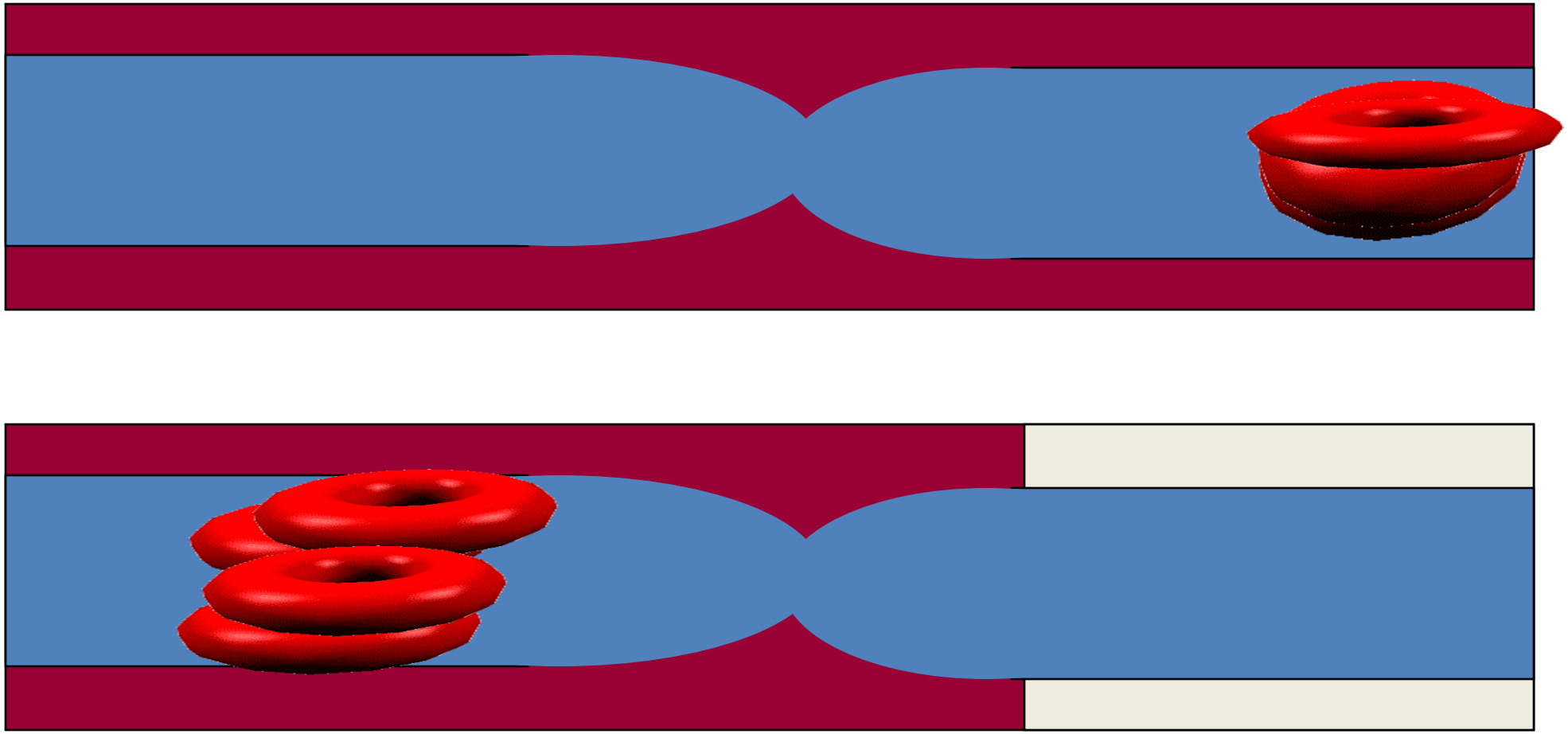
If no oxygen, then pain and damage occurs

Clotting system is too active



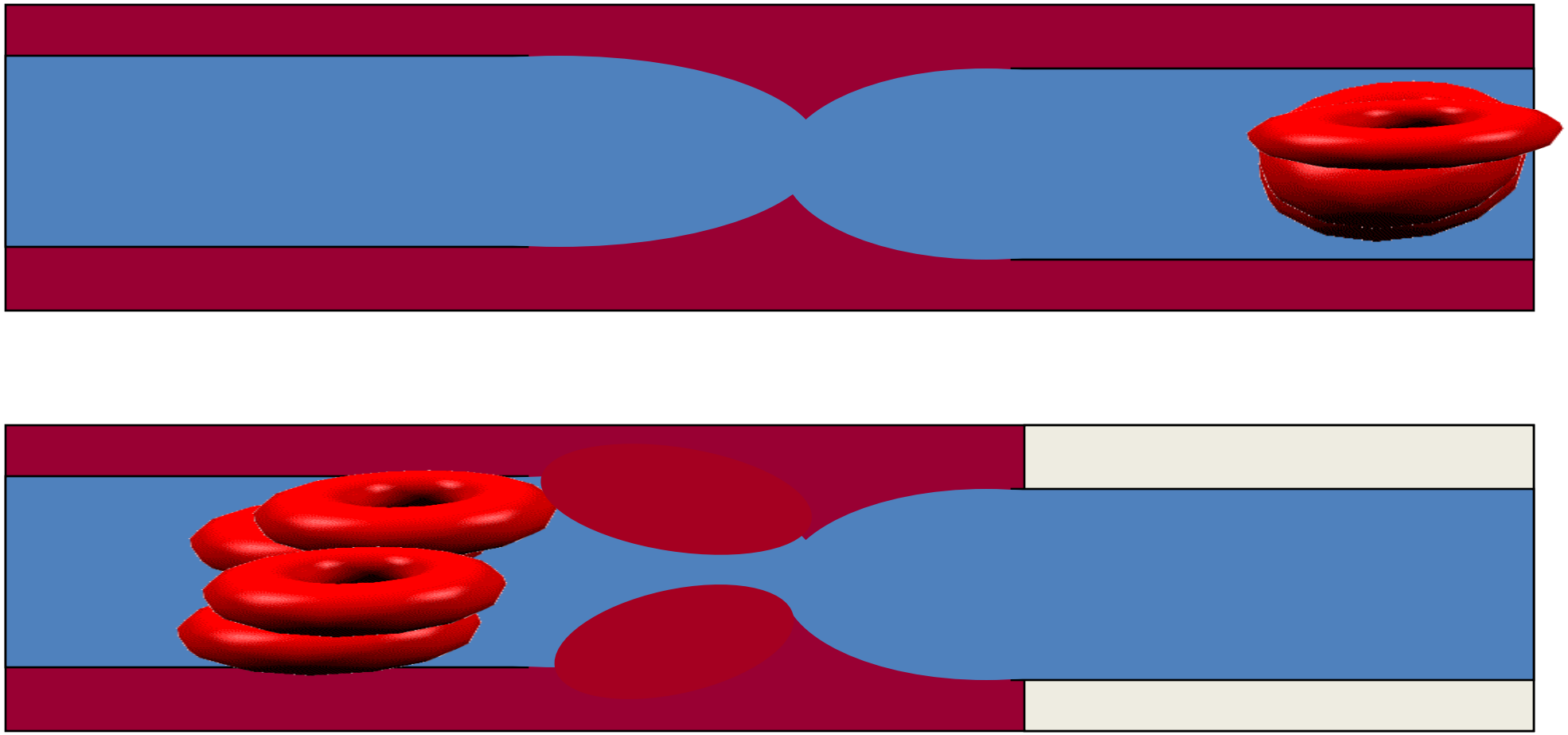
Fibrin clot blocks blood flow, then pain and damage occurs

Sickle red cells are stickier



Sticky red cells block blood flow, then pain and damage occurs

Low levels of Nitric Oxide (NO)

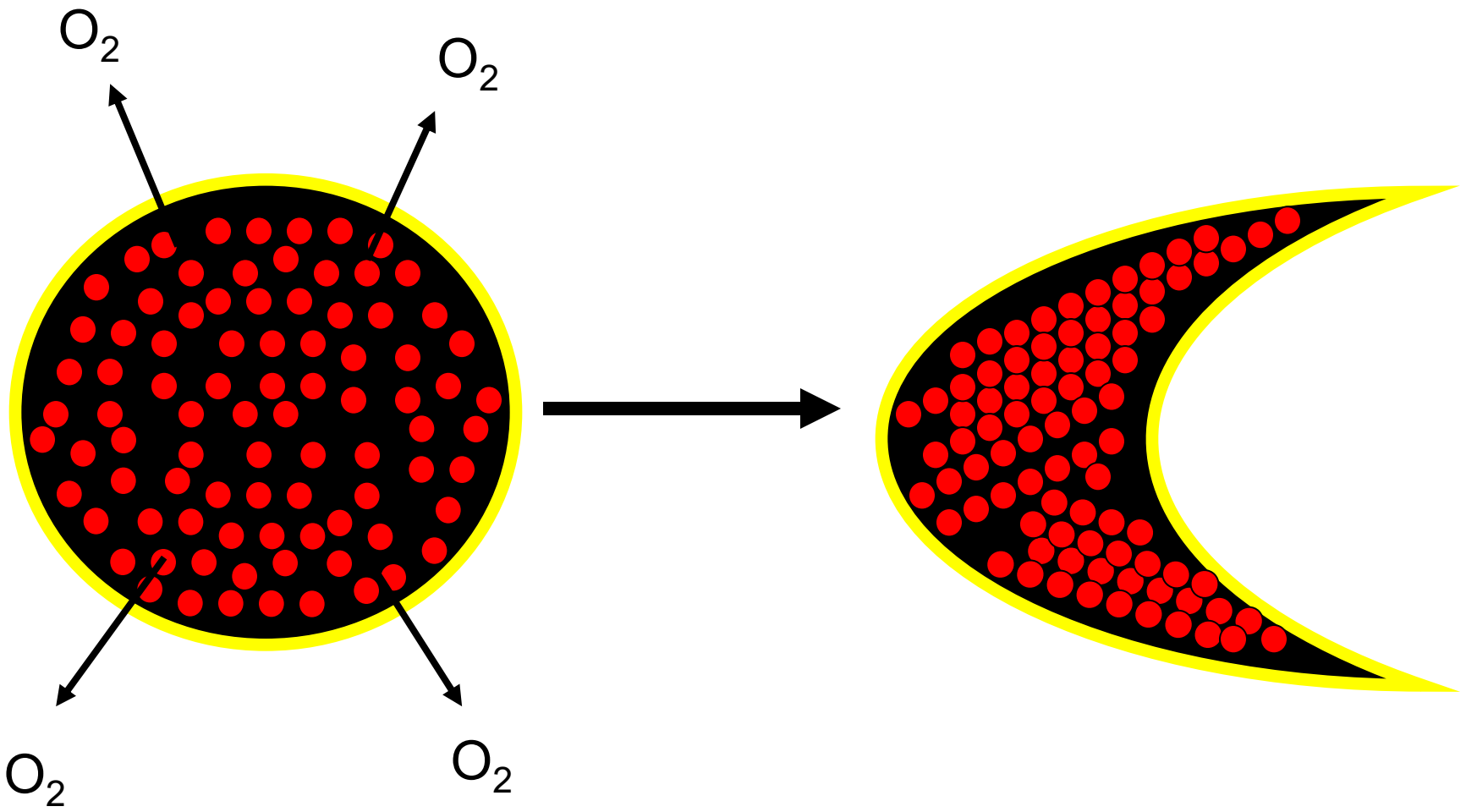


Vasoconstriction blocks blood flow, then pain and damage occurs

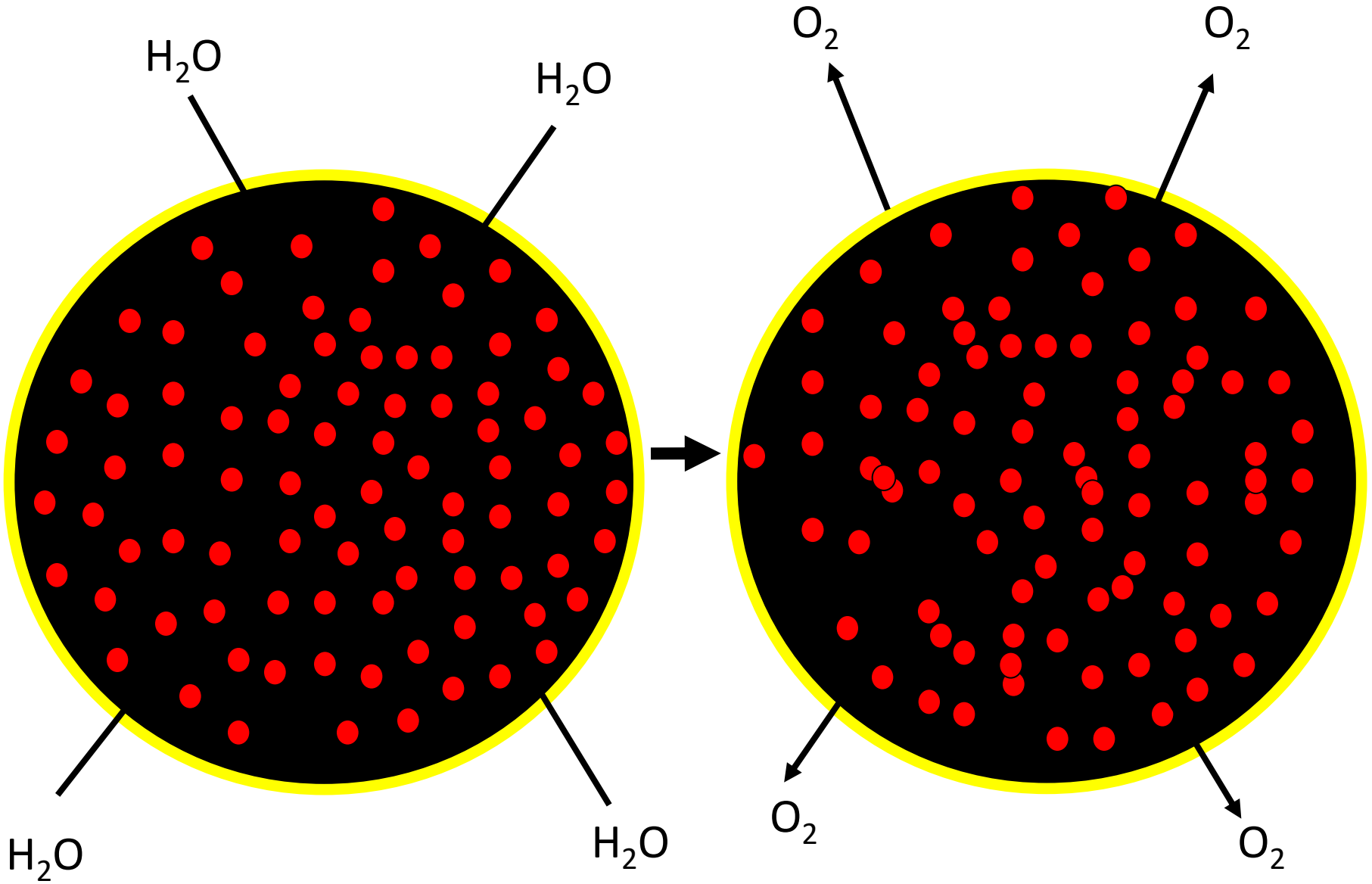
SICKLE BIOCHEMISTRY

- **Deoxygenation**
- **Intracellular hemoglobin concentration**
- **pH (Amount of Acid in the blood)**
- **Temperature**

SICKLING - Hb CRYSTALS



HYDRATION

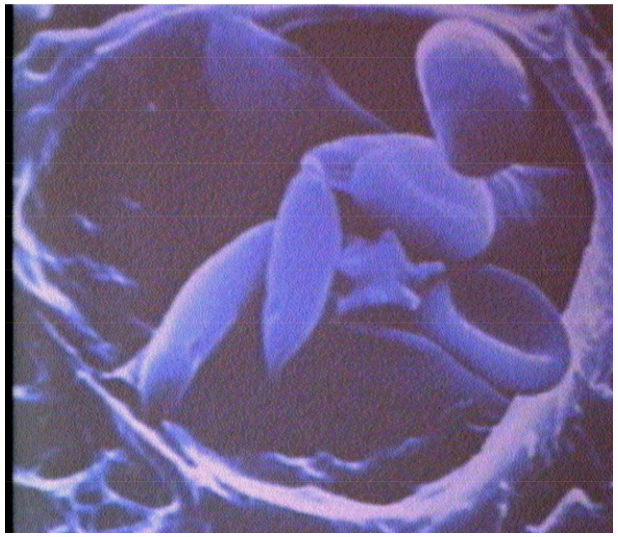


Sickle Cell Disease Complications

- Sickle cells become trapped and destroyed in the spleen causing Splenic Sequestration
- Anemia - hemolysis
- Pain episodes acute and chronic
- Gall Stones
- Strokes or aneurysms
- Kidney failure
- Pneumonia or Chest Syndrome
- Increased Infections
- Bone infarctions - AVN
- Retinopathy
- Priapism
- Iron Overload if transfused

ABC's of Managing Acute Sickle Cell Pain

- A - Assessment of the pain
  - LOCATES, Typical pain?
- B – Believe the patient's level of pain
- C – Complications or cause of pain
- D – Drugs and distraction
  - Pain Medication - WHO ladder
- E – Environment, rest in quiet
- F - Fluids – Hypotonic - D5W
  - Fixed dosing – NO PRN dosing



Acute or Chronic Pain

- Acute pain – hours to weeks
  - Sickle cell related or other cause
  - Treat the source and the pain level
  - Start with short acting analgesics progress to longer acting
- Chronic Pain – Over 6 months
  - Bone infarction, AVN…
  - Long acting safe NSAIDS
  - Long acting Opiates
- Both pain syndromes combined
  - Keep baseline treatment and add acute analgesics

Where is the Pain

- **Atypical pain should prompt a search for complications or non-sickle cell source**
- Head pain – Meningitis, Hemorrhage, Stroke, Infarction
- Chest Pain – Acute Chest, PE, Pneumonia
- Abdominal – RUQ gall stones, Hepatic sequestration LUQ-spenic sequestration
- Back – Renal infarction, Salmonella Osteo
- Fever – sepsis, pyelo, osteo, pneumonia
- Multi-organ – Multi organ system failure

Work-up

- History – causes of increased sickling (dehydration, infection) – fever, N/V/D, head ache, Abd pain, Chest pain, cough, urinary freq/urgency, dysuria, hematuria
- PE – Gen, HEENT, Chest, Abdomen, Extremity
- Lab- CBC/Retic, UA, Complete Metabolic Profile CMP
- Consider Type and cross if symptomatic anemia or complication
- CXR if cough, dyspnea, pain. Bone films if focal bone pain and tenderness. CT for head and abdominal pain

Lab Pearls

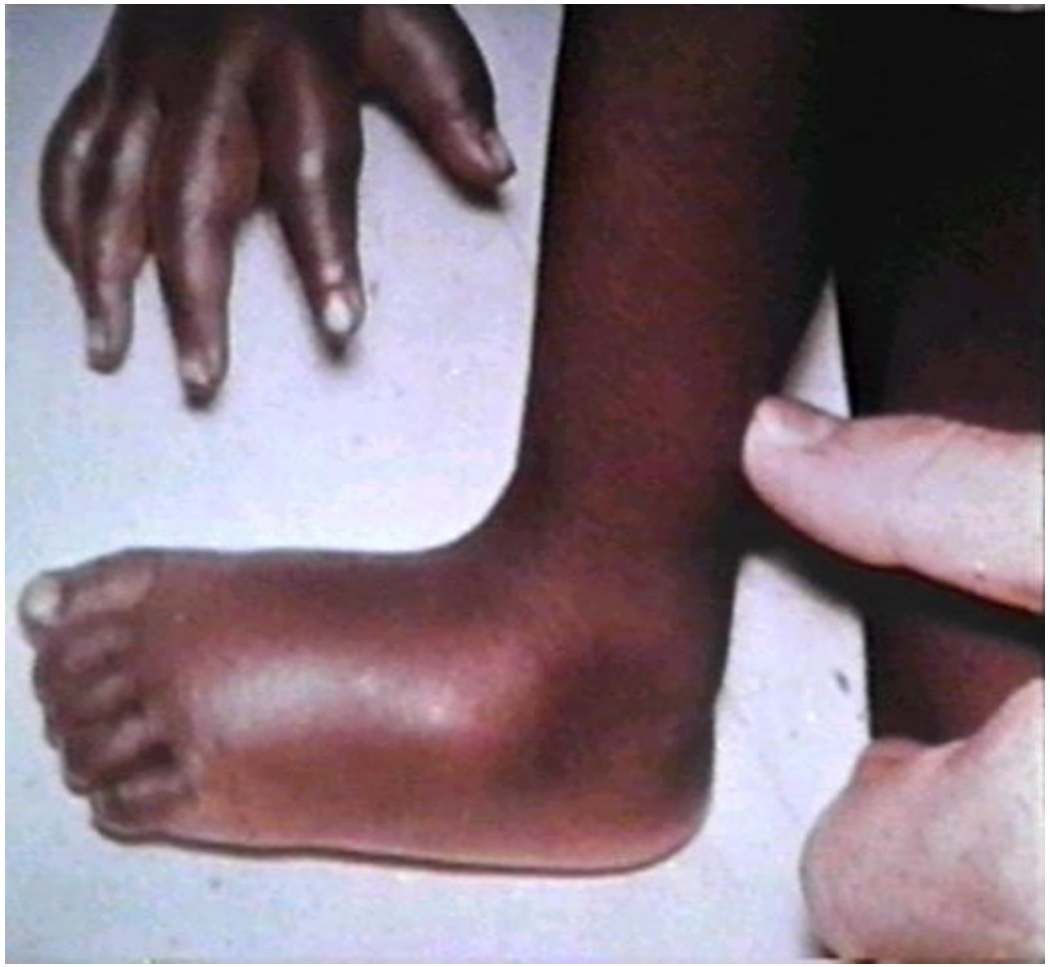
- Each patient has their own normal
  - Don’t treat the number - check the patient’s presentation
  - Usually Hct/Hb are low, WBC , Retics and Platelets are elevated
  - WBC >20K or left shift needs investigation
  - Indirect bilirubin and LDH are normally elevated with hemolysis
  - Direct bilirubin, Alk Phos, AST,ALT elevations should prompt Hepatic/GB work-up
  - LDH and high indirect bilirubin are normal in chronic hemolysis

Who to Admit

- Pain that is not manageable at home or after 8 hours of aggressive pain management
- Complications – Pneumonia, stroke, TIA, Chest syndrome, priapism, pregnancy, pyelo, osteo, multiorgan system failure, falling Hb/Hct, High WBC (20,000) Left shifts, fever…

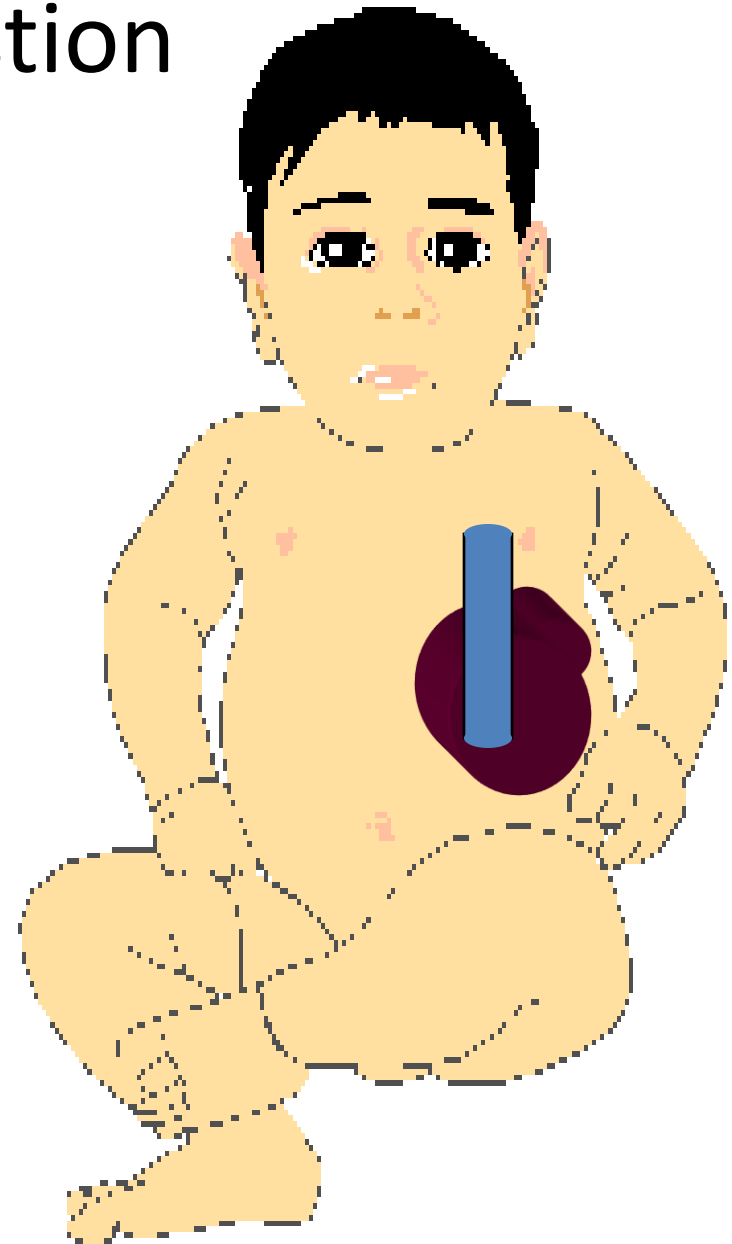
Hand Foot Syndrome - Dactylitis

- Ages six months - two years. May be first presentation to ER
- This is treated with fluids and pain medication.
- Consider osteomyelitis



Abdominal Pain - Splenic Sequestion

- Sudden trapping of blood within the spleen
- May be associated with fever, pain, and respiratory symptoms.
- Circulatory collapse and death can occur in less than thirty minutes.
- Gall stones in children and teens - cholecystitis

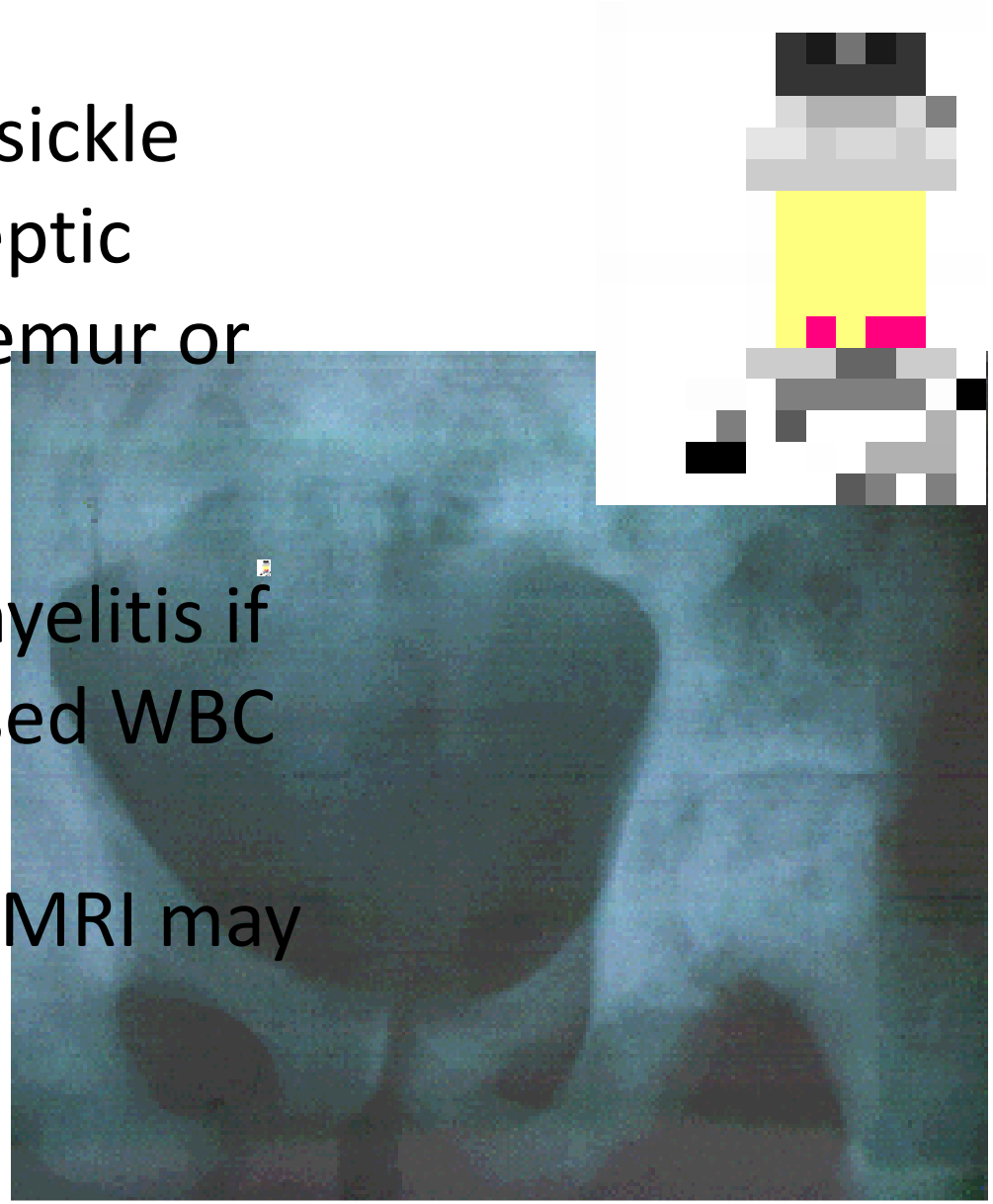


Focal Bone Pain

Bone infarction, sickle arthritis, and aseptic necrosis of the femur or humerus.

Consider osteomyelitis if febrile or increased WBC

Xray, bone scan, MRI may help

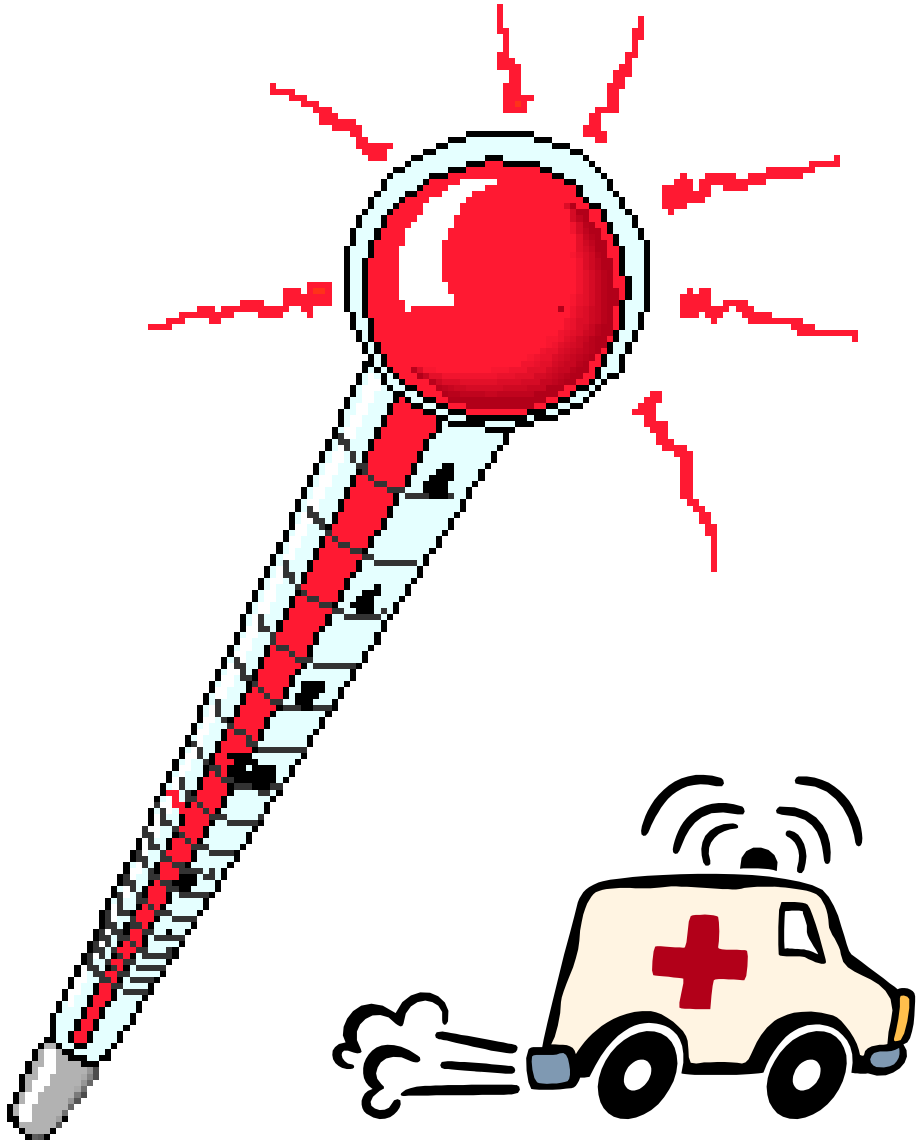


Fever

<u>Fever indicates Sepsis until proven other wise</u>

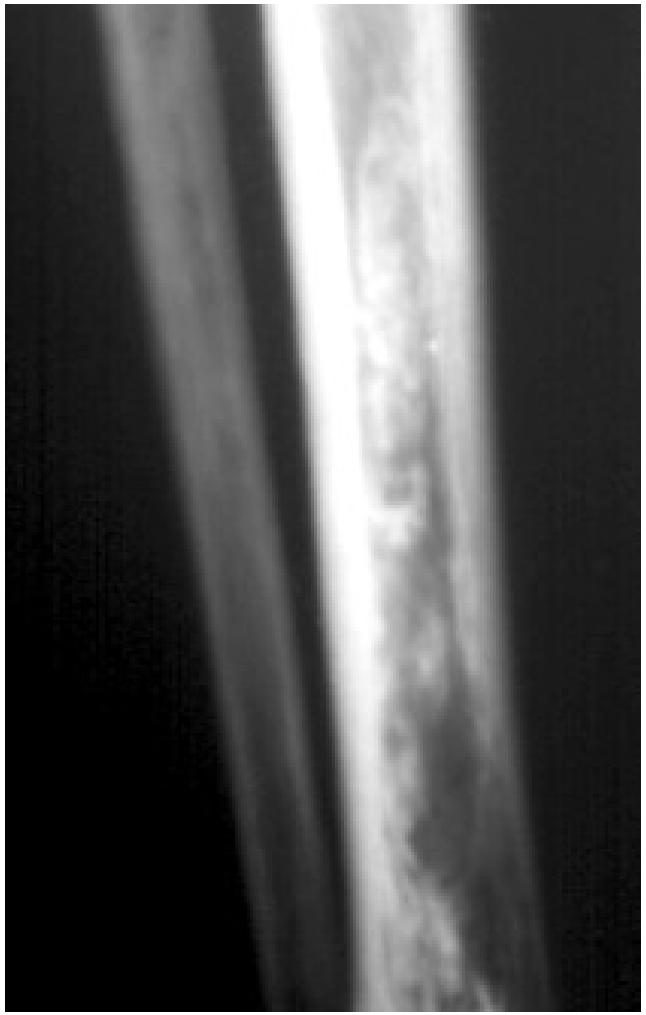
Do cultures then treat with antibiotics covering pneumococci

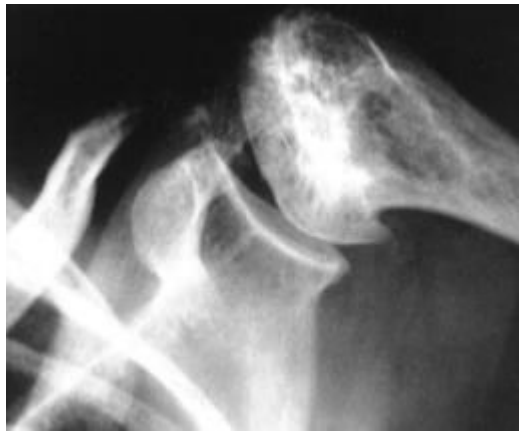
Remember that the most common pain medications mask a fever (NSAIDS, acentaminphen)

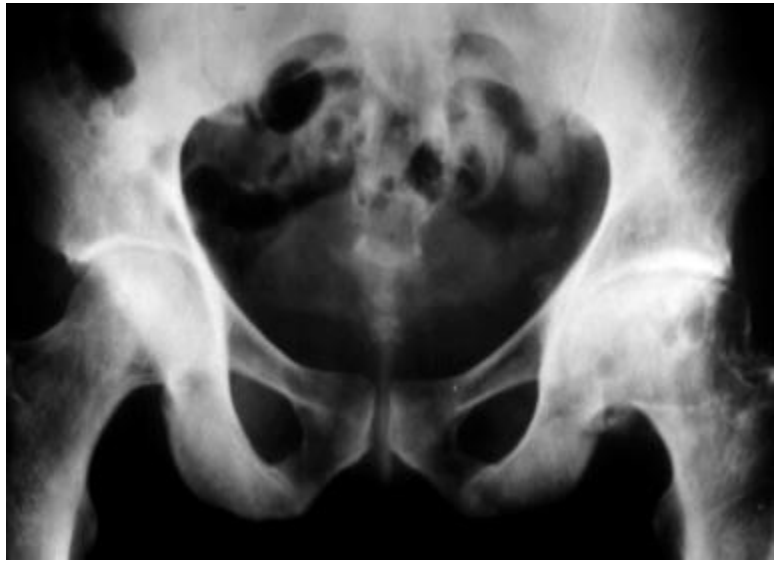


MIXED PAIN SYNDROMES

Severe Acute and Chronic Pain







Chest Pain - Acute Chest Syndrome

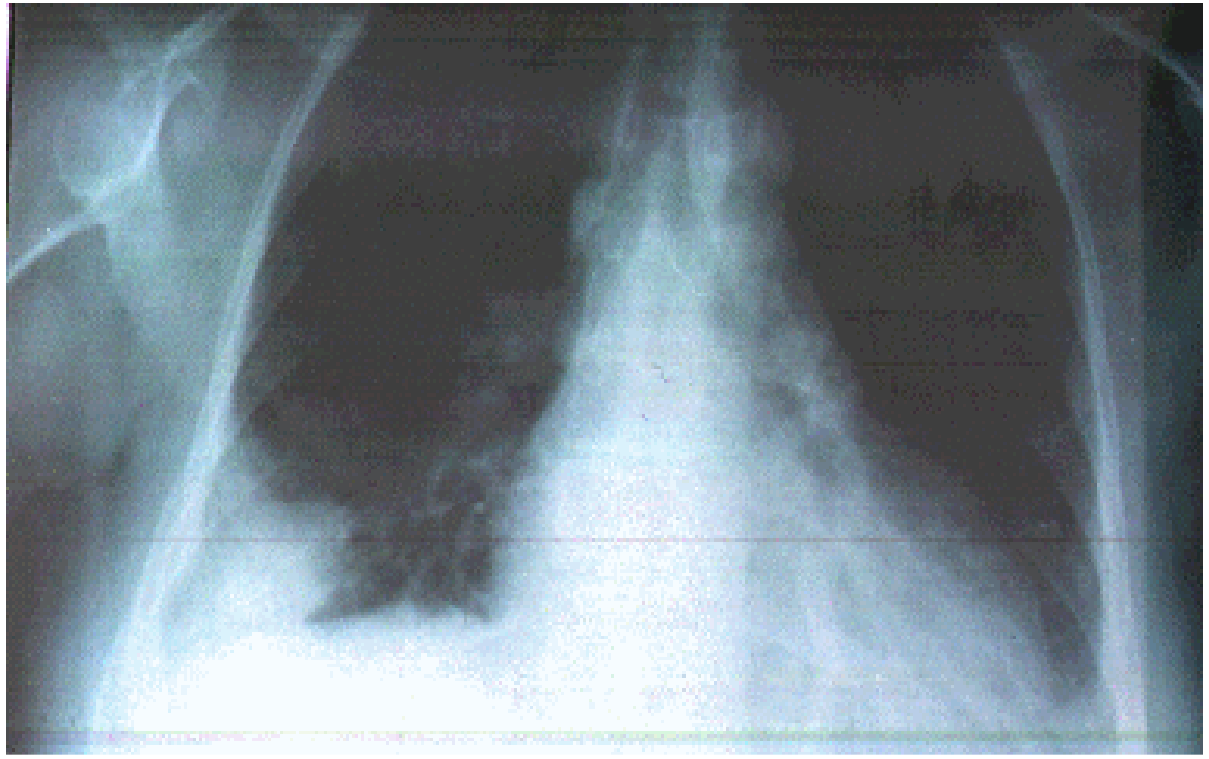
Chest pain

Infiltrate

Dyspna and Hypoxia

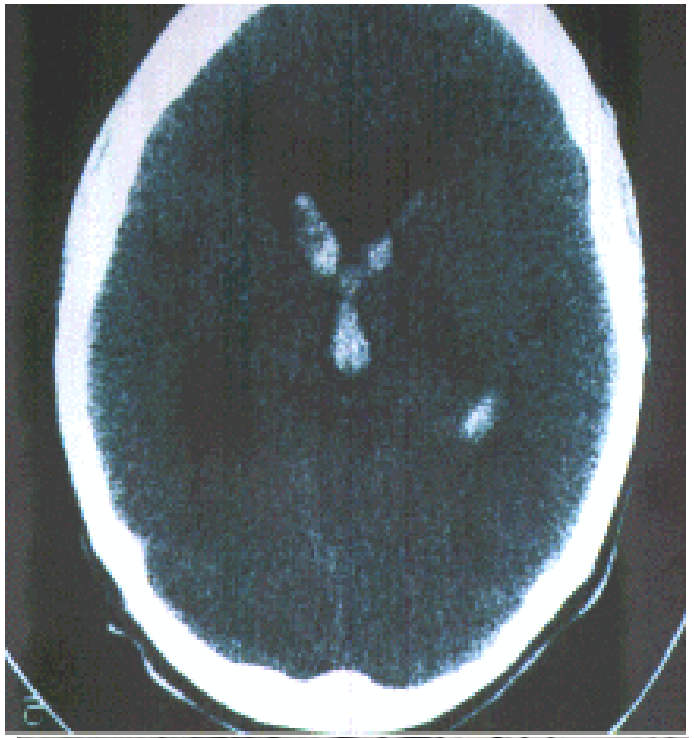
Treat with O^2, Transfusions and antibiotics

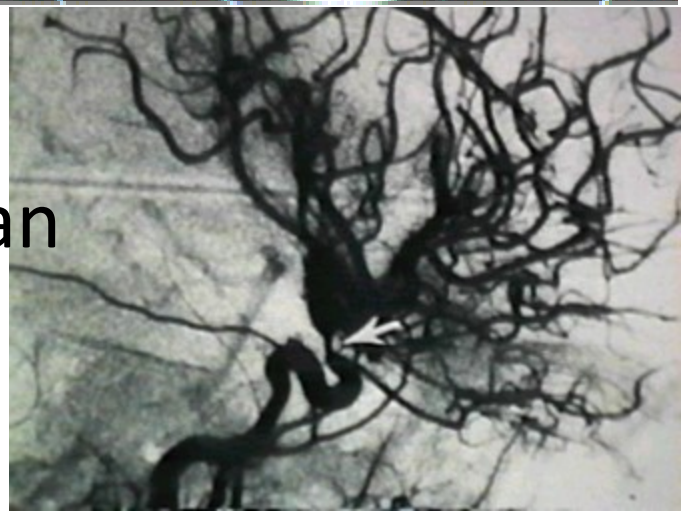
Prevent with incentive spirometry and pre-op transfusion to Hb 10



Headache
Strokes vs Meningitis

- Children have blocked flow
- Adults have aneurysms
- Presents with headache, weakness,
- Numbness, speech problems
- Fever or Increased WBC – Meningitis
- Trans Cranial Doppler (TCD) screening can identify kids at risk
- Transfusion for life or BMT





Frequent pain events

- Worse disease, highest mortality
- Needs Case Management Plan
- Consider referral for **Hydroxurea** therapy
  - Reduces episodes by 50%
  - Reduces admits by 50%
  - Reduces need for blood by 50%
  - Prolongs life

Advances in Sickle Cell Disease

- 1972 - Congress passes the National Sickle Cell Anemia Control Act
- The NHLBI establishes Comprehensive Sickle Cell Centers for research
- 1980 - First statewide newborn screening program is implemented
- 1986 - PROPS shows that prophylactic administration of penicillin to children prevents death from pneumococcal infection

1984 - Bone Marrow Transplant

- 1984 First sickle cell cure by BMT
- 6.5% of SCD patient eligible
- 1% of SCD patients have a HLA match
- 276 BMTs done by 2009 in children/teens
  - Survival 91%- 97%, Graft failure 7% - 10%
- 2008 Reduced intensity transplant works
- 2009 Trial with unrelated stem cells

Krishnamurti L, Kharbanda S, Biernacki MA, Zhang W, Baker KS, Wagner JE, WuCJ. Stable long-term donor engraftment following reduced-intensity hematopoietic cell
transplantation for sickle cell disease.Biol Blood Marrow Transplant. 2008 Nov;14(11):1270-8

Blood and marrow transplantation for sickle cell disease: overcoming barriers to success.Source:Current opinion in oncology [1040-8746] Bolaos-Meade yr:2009 vol:21 iss:2 pg:158 -61

1984 - Hydroxyurea

- 1984 Hydroxyurea found to increase Fetal hemoglobin in sickle cell patients
- 1991 Multicenter Study of Hydroxyurea in Sickle Cell Anemia (MSH) stopped early 1995 because of benefits – reduced crisis, admits, transfusions all by 50%
- 2003 Hydrea prolongs life
- 2008 Consensus Statement from the NIH – Not used enough

- http://consensus.nih.gov/2008/statement_sicklecell.htm
- Steinberg MH, Barton F, Castro O, Pegelow CH, Ballas SK, Kutlar A, Orringer E, Bellevue R, Olivieri N, Eckman J, Varma M, Ramirez G, Adler B, Smith W, Carlos T, Ataga K, DeCastro L, Bigelow C, Saunthararajah Y, Telfer M, Vichinsky E, Claster S, Shurin S, Bridges K, Waclawiw M, Bonds D, Terrin M. Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia: risks and benefits up to 9 years of treatment. JAMA. 2003 Apr 2;289(13):1645-51.

1987 - Newborn Screening

- 1987 the NIH held a consensus development conference on Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies.
  - "every child should be screened for hemoglobinopathies to prevent the potentially fatal complications of sickle cell disease during infancy."
  - 14 states are doing newborn screening for sickle cell

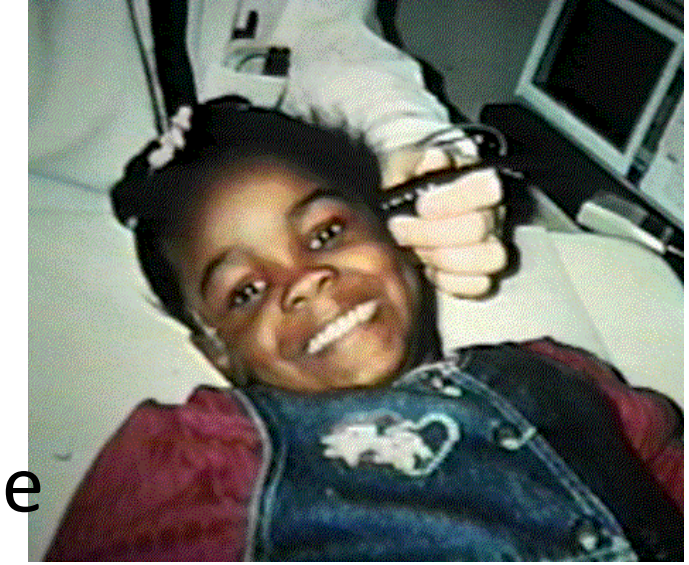
- *2002 44 states did Hb screening*
- *Now in 2009 all 50 states are screening for hemoglobinopathies http://genes-r-us.uthscsa.edu/nbsdisorders.pdf*

1995 –Transfusion Guide

- In surgical settings, simple transfusions to increase hemoglobin (Hb) levels to 10 g/dL are as good as or safer than aggressive transfusions to reduce sickle hemoglobin (Hb S) levels to below 30 percent.
- Transfusions to maintain a hematocrit of more than 36 percent do not reduce complications of pregnancy.

Vichinsky EP, Haberkern CM, Neumayr L, et al. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. The Preoperative Transfusion in Sickle Cell Disease Study Group. *N Engl J Med* 1995;333:206-13.

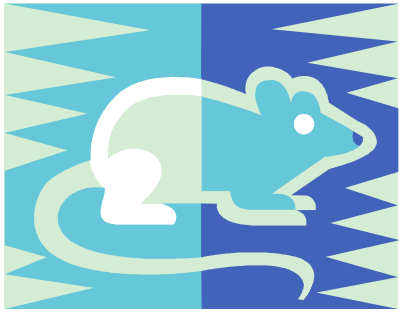
1997 - STOP Study



- 1997 The Stroke Prevention Trial in Sickle Cell Anemia (STOP) demonstrated that periodic transfusions could prevent first time stroke insusceptible children.
- Trans Cranial Doppler Ultrasound (TCD) screening is effective
- All SCD patients 24 months of age should be screened - should be repeated every 6-12 months during early childhood.

1997 - Sickle cell mouse

- 1997 investigators inserted the human gene responsible for sickle cell disease into mice, thereby creating transgenic models of the human disease.
- 2008 - **Gene Therapy Corrects Sickle Cell Disease In Laboratory Study** ScienceDaily Dec. 4, 2008
- Using a harmless virus to insert a corrective gene into mouse blood cells, scientists at St. Jude Children's Research Hospital have alleviated sickle cell disease pathology. In their studies, the researchers found that the treated mice showed essentially no difference from normal mice.

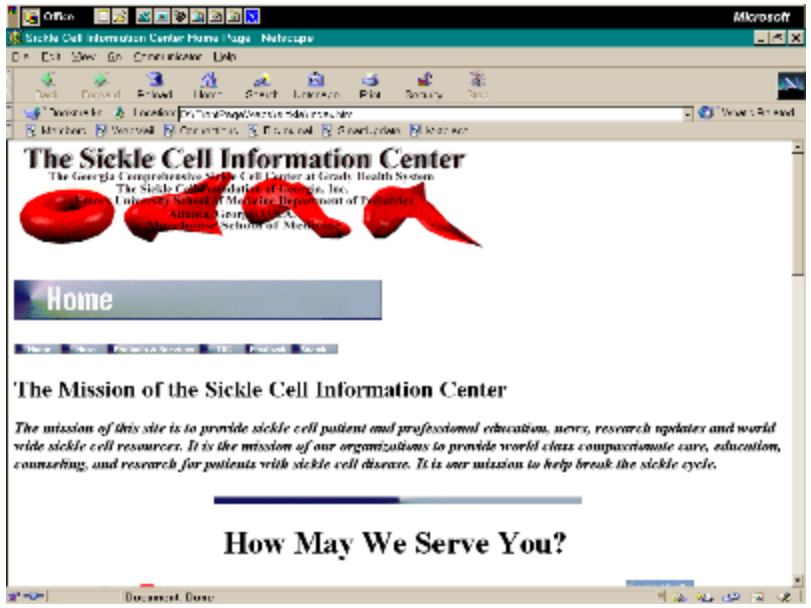


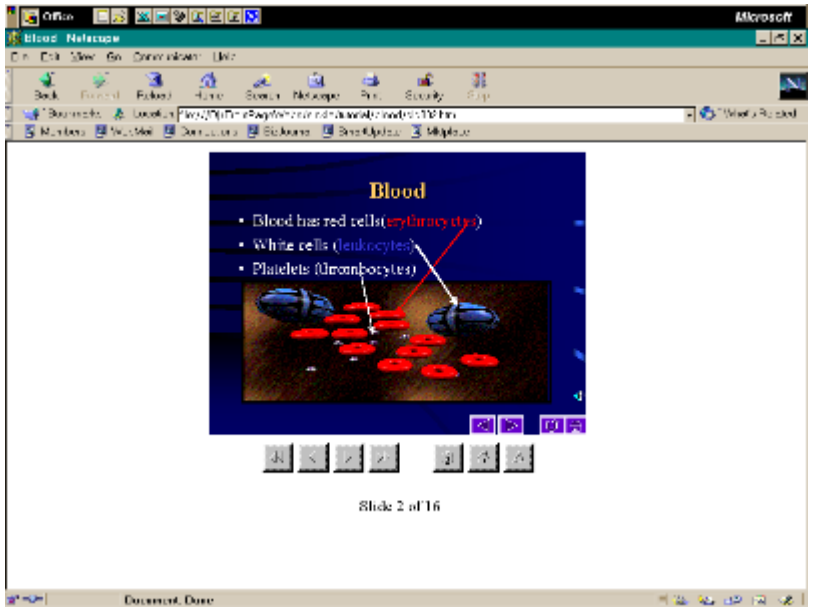
1998 - Unrelated Stem Cell Transplant

- **1998: First Unrelated Stem Cell Transplant:** Doctors at the AFLAC Cancer Center of Egleston Children's Hospital at Emory University in Atlanta perform an unrelated donor cord blood stem transplant on Keone Penn, a 12-year-old with sickle cell anemia. He did develop GVHD.
- Clinical Trial underway now

1998 - SCInfo.org

- **World Wide Web Site - The Sickle Cell Information Center**
  - **http://www.SCInfo.org**
  - **Information for providers, patients, teachers, employers, administrators**
  - **Monthly E-mail Newsletter aplatt@emory.edu**
  - **Clinical guidelines published**





2000 - Acute Chest Syndrome

- 2000 A multicenter group at 30 sites reported that acute chest syndrome is commonly precipitated by fat embolism and infection, especially community-acquired pneumonia. Adult patients with neurologic symptoms frequently developed respiratory failure. Aggressive treatment with transfusions and broncho dilators improved oxygenation and allowed most patients to recover.
- Incentive Spirometer use prevents this (1995 NEJM)

Incentive spirometry to prevent acute pulmonary complications in sickle cell diseases.
Bellet PS, Kalinyak KA, Shukla R, Gelfand MJ, Rucknagel DL.
N Engl J Med. 1995 Sep 14;333(11):699-703.

2000 - Prevnar

- 2000 – pneumococcal conjugate vaccine (PCV) Prevnar is released for immunization
- Pneumoccal infections went from1.7 infections per 100 person-years (1995-2000) to 0.5 infections per 100 person-years (2001-2002), which represents a 68% reduction.
- This has saved lives!!!
- 2010 - New Prevnar

Effectiveness of the 7-valent pneumococcal conjugate vaccine in children with sickle cell disease in the first decade of life.
Adamkiewicz TV, Silk BJ, Howgate J, Baughman W, Strayhorn G, Sullivan K, Farley MM. Pediatrics. 2008 Mar;121(3):562-9.

2005 - Exjade

- 2005 - The FDA approved Exjade (deferasirox) an oral iron chelator for the treatment of iron overload.
- Iron overload is common with multiple transfusions
- Infusions of Desferoxamine with a pump was alternative

Trait vs.. Disease

8 –10% in US Blacks have Hb S trait (3.5 million individuals)

Majority have no symptoms

Hematuria is most common symptom

Under extreme hypoxia, heat, dehydration or altitude change:

- Splenic sequestration
- Pain events
- Sudden Death

2007 - Sickle Cell Trait

- 2007 National Athletic Trainers Association Consensus Statement: Sickle Cell and the Athlete
  - 13 football player deaths
  - Basketball and distance running
- 2008-09 NCAA Sports Medicine Handbook
- Exclude from serial sprints and performance tests. Stop is cramps, trouble breathing, weakness. Train over time but Do not push past endurance
- Testing for all college athletes?
- CDC Toolkit http://www.cdc.gov/ncbddd/sicklecell/toolkit.html

2009

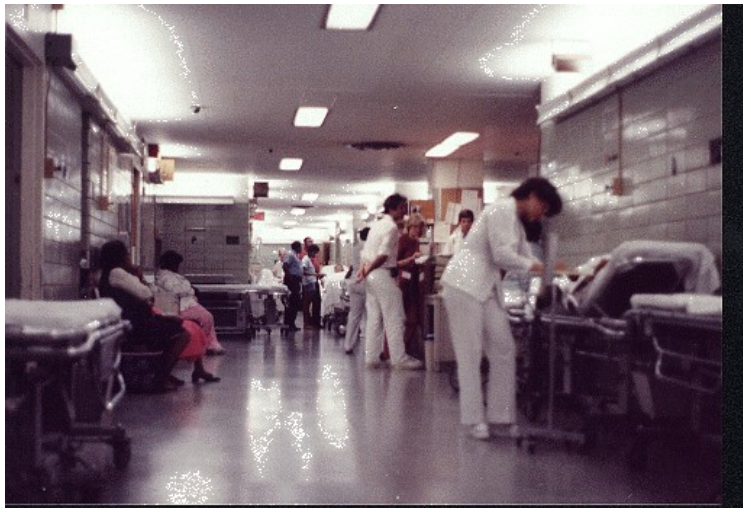
- Stem cell research ban reversal - March 9, 2009
- June 19, 2009 The First Sickle Cell Disease World Day at the United Nations
- December – NEJM reports 10 SCD adults received a partial bone marrow transplant with 90% success

1984 First 24 hr Sickle Cell Center – Atlanta, GA

- 24 Hour Urgent Care
- Comprehensive Primary Care PA-MD teams
- Model of Cost Effective Disease Management
- Education
- Research
- Now Day Centers in US - S. FL, Chicago, Boston, Baltimore …

Why Start a Center in Atlanta?

- Prior to 1984 all patients seen in the ER
- Erratic care, no continuity, poor pain management
- Many hospitalizations, Many ER visits, Many patient complaints
- Long waits for care
- No comprehensive care
- High cost of care

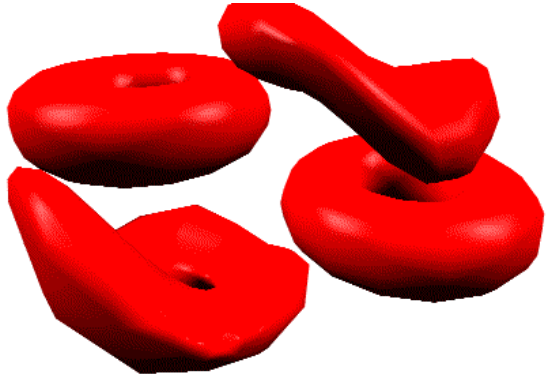


•24 hour dedicated Sickle Cell Center

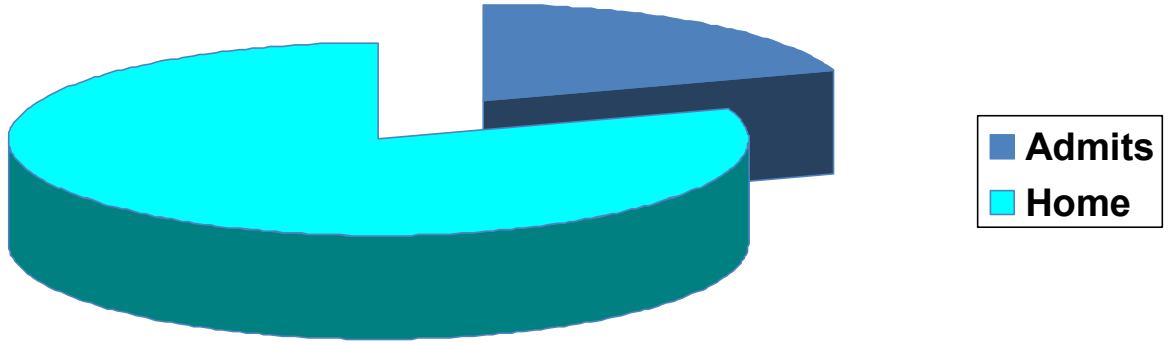
- Step wise - multimodal approach with parenteral agents and pain assessment
- Evaluate to determine cause of pain
- Bed rest, quiet environment
- Hydration: IV D5W or oral
- Analgesics
  - NSAIAs - Ketorolac
  - Agonist Narcotics - Morphine
  - Agonist-Antagonist - Nalbuphine
  - Adjuvants - Hydroxyzine

10 year data 1991 - 2001

- 20,968 pain episodes
- 1,076 patients over 15 years old
  - Average age 36.8 years old
  - oldest patient 82
- 51% male, 49% female visits
- Pain Assessment using VAS
- Admission if:
  - Complication: Fever, infiltrate, hct…
  - Return within 48 hours
  - Pain not manageable after 8 hours



8 Hour Treatment - 20,968 episodes over 10 years

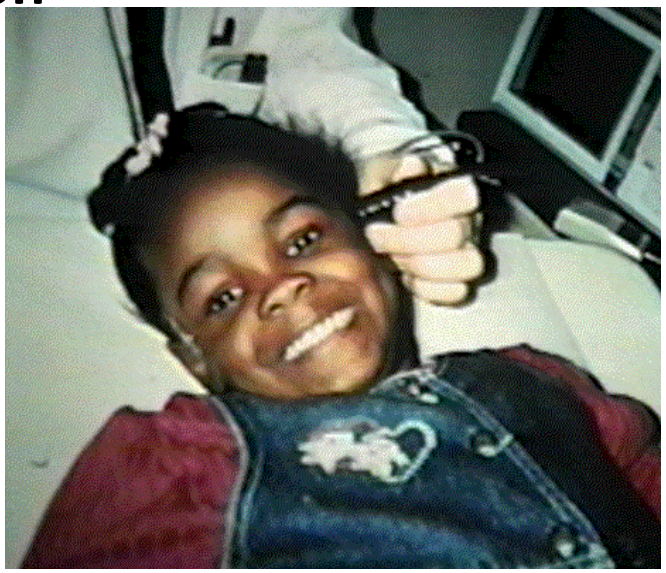


20% Admitted, 80% went home

3988 Admissions + 52 Left AMA + 92 Critical Care

Comprehensive Primary Care

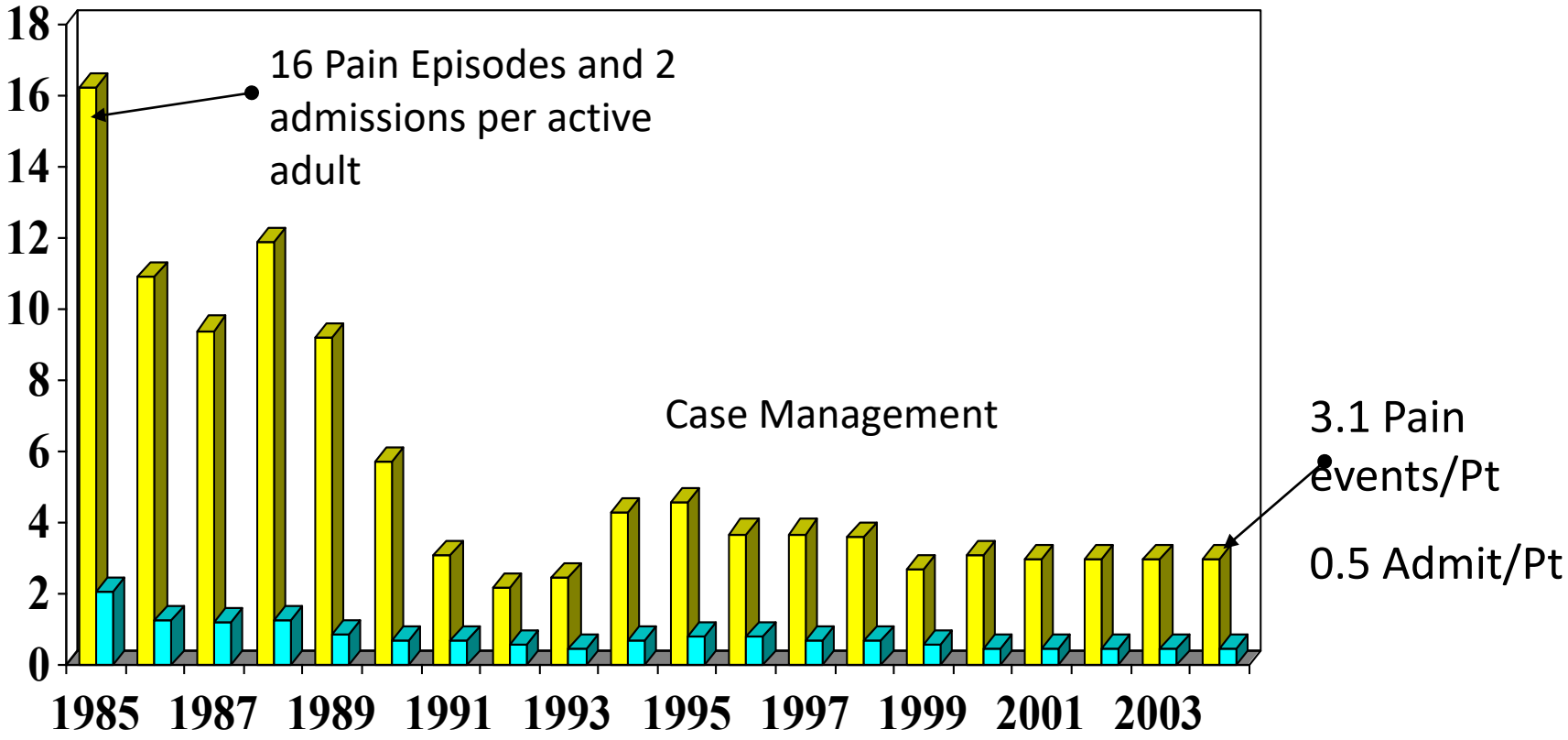
- **Pediatric Team (MD, PA, RN, SW, Psychology)**
  - **Outpatient, Inpatient, Case Management**
  - **Child psychology – testing, intervention**
- **Adult Team (MD, PA, RN, SW, CNS)**
  - **Outpatient, Inpatient, Case Management**
  - **CNS Psychiatry for intervention**
- **Hydrea Monitoring**
- **Leg Ulcer Care**
- **Stroke Prevention, TCD**
- **Transfusion Therapy**



Center Benefits

- **Patient Satisfaction increased**
- **Admissions and ED visits per person decreased saving $16 million/yr costs for $3 million investment**
- **Medical Home model providing primary care**
- **ED care and Grant income cover preventive care**
- **Reduced risk management by expert care, excellent documentation and tracking**
- **Better staff and patient attitudes**
- **Research foundation for more grants**
- **Better patient and medical staff education**

Pain Crisis Episodes and Admissions per Active Adult



Race and Sickle Cell

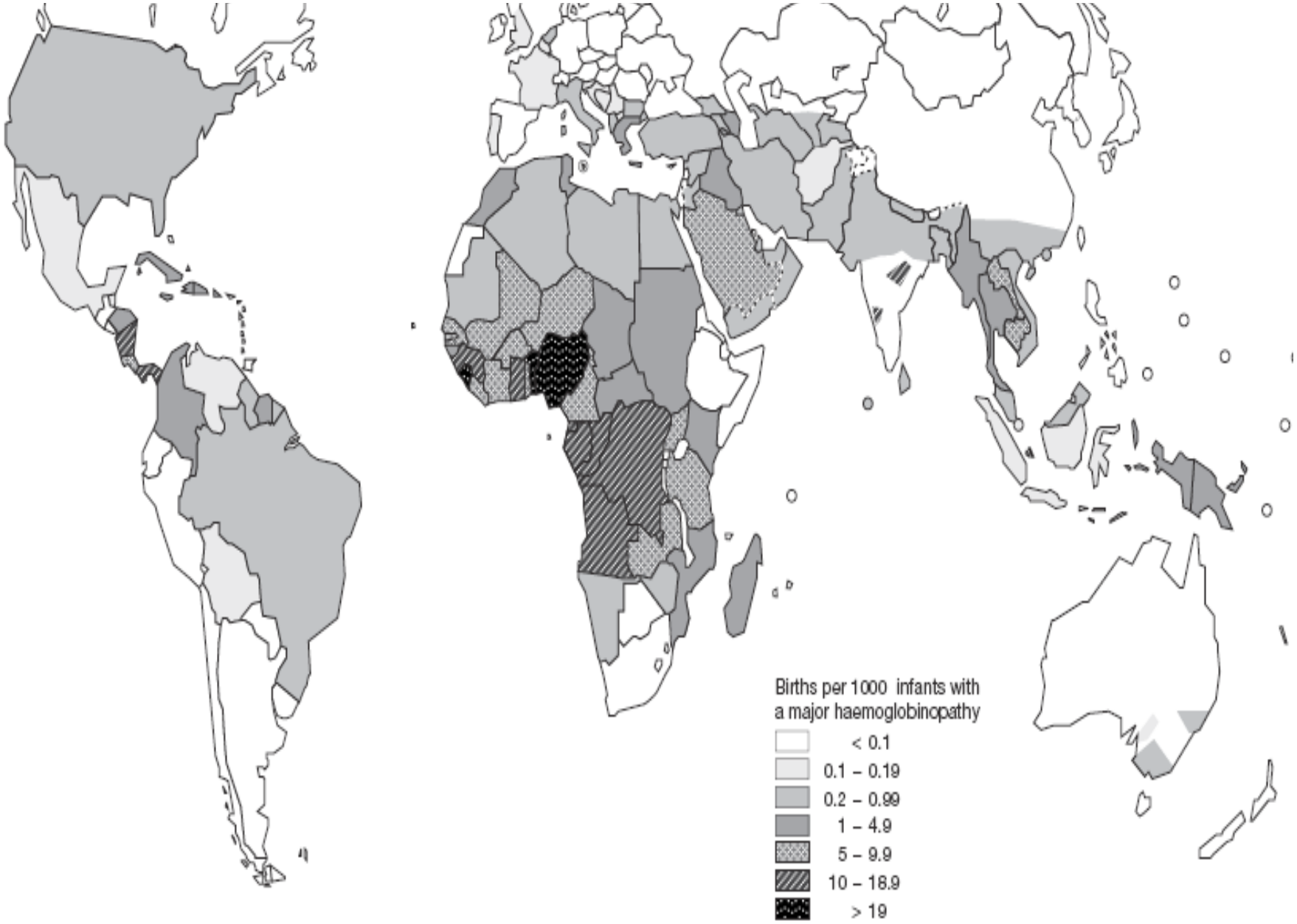
Sickle Cell in USA

- SCD affects approximately 100,000 and SC trait 3 million Americans.
- SCD occurs among about 1 out of every 365 Black or African-American births.
- SCD occurs among about 1 out of every 16,300 Hispanic-American births.
- About 1 in 13 Black or African-American babies is born with sickle cell trait (SCT).

https://www.cdc.gov/ncbddd/sicklecell/data.html

Incidence of Sickle Cell Disease and Thalassemia World wide

http://www.who.int/genomics/public/geneticdiseases/en/index2.html#SCA

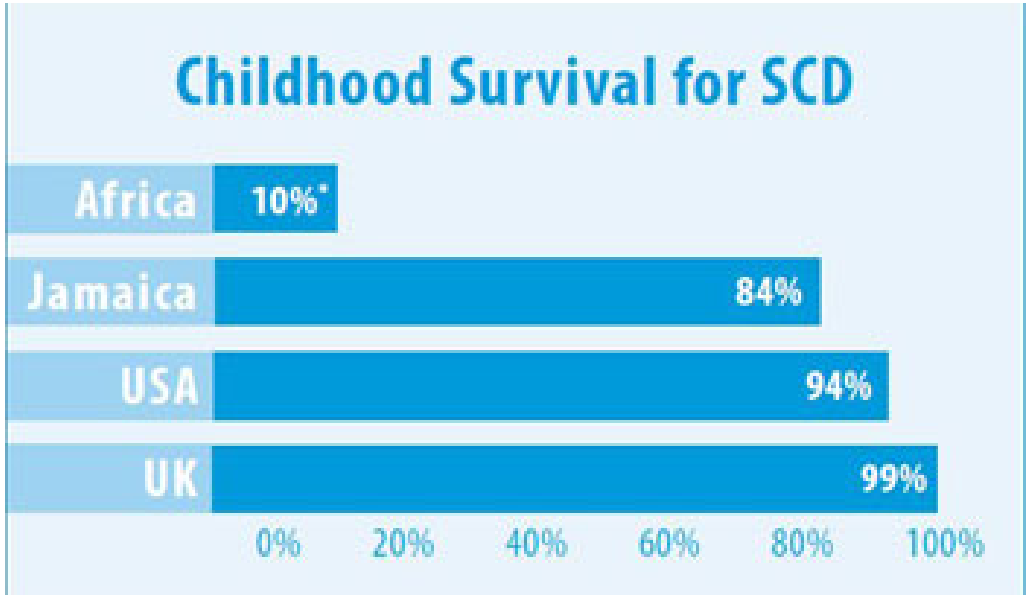


Global Burden

Burden of Sickle Cell Disease	
COUNTRY	SICKLE CELL BIRTHS/YEAR
Nigeria	91,011
Dem. Rep. Congo	39,743
Tanzania	11,877
Uganda	10,877
Angola	9,017
Cameroon	7,172
Zambia	6,039
Ghana	5,815
Guinea	5,402
Niger	5,310
Sub-Saharan Africa Total	242,187
Worldwide Total	305,773

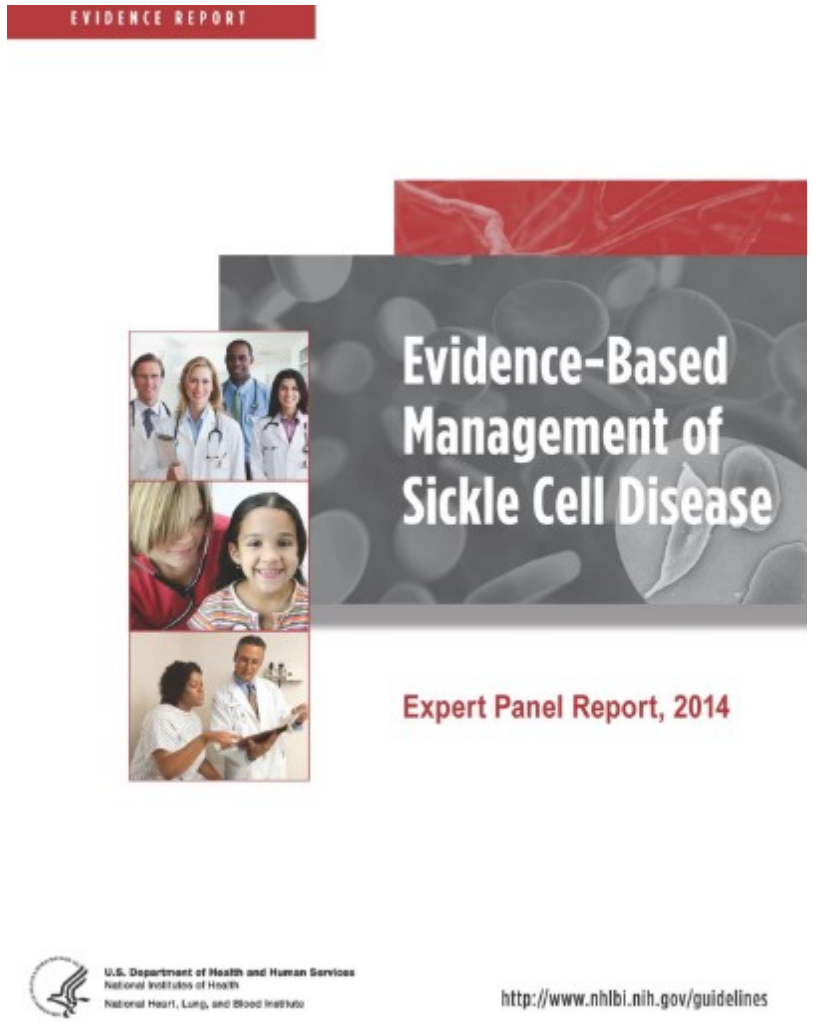
http://www.fic.nih.gov/News/GlobalHealthMatters/november-december-2014/Pages/sickle-cell-disease.aspx

100 million people across the globe live with SC trait



Management Guidelines - 2014

- **Free guide book as PDF** http://scinfo.org/2015/09/30/nih-evidence-report-evidence-based-management-of-sickle-cell-disease/
- **American Society of Hematology (ASH) Pocket Guides for Sickle Cell Disease** http://scinfo.org/2015/11/25/health-care-provider-guidelines-web-resources/



2017 Endari or L-glutamine oral powder

- FDA approved 7/17 for sickle cell 5 years old and older
- fewer hospital visits for pain,
- fewer hospitalizations for sickle cell
- fewer days in the hospital
- fewer occurrences of acute chest syndrome

Genetic cure 2017

http://www.nejm.org/doi/full/10.1056/NEJMoa1609677?query=featured_home

12 year old boy with Hb SS in Paris, France
Now 2 years out
No symptoms

2019 60 Minutes
https://www.cbsnews.com/news/could-gene-therapy-cure-sickle-cell-anemia-60-minutes/

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ORIGINAL ARTICLE

Gene Therapy in a Patient with Sickle Cell Disease

Jean-Antoine Ribeil, M.D., Ph.D., Salima Hacein-Bey-Abina, Pharm.D., Ph.D., Emmanuel Payen, Ph.D., Alessandra Magnani, M.D., Ph.D., Michaela Semeraro, M.D., Ph.D., Elisa Magrin, Ph.D., Laure Caccavelli, Ph.D., Benedicte Neven, M.D., Ph.D., Philippe Bourget, Pharm.D., Ph.D., Wassim El Nemer, Ph.D., Pablo Bartolucci, M.D., Ph.D., Leslie Weber, M.Sc., Hervé Puy, M.D., Ph.D., Jean-François Meritet, Ph.D., David Grevent, M.D., Yves Beuzard, M.D., Stany Chrétien, Ph.D., Thibaud Lefebvre, M.D., Robert W. Ross, M.D., Olivier Negre, Ph.D., Gabor Veres, Ph.D., Laura Sandler, M.P.H., Sandeep Soni, M.D., Mariane de Montalembert, M.D., Ph.D., Stéphane Blanche, M.D., Philippe Leboulch, M.D., and Marina Cavazzana, M.D., Ph.D.

N Engl J Med 2017; 376:848-855 | March 2, 2017 | DOI: 10.1056/NEJMoa1609677

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Sickle cell disease results from a homozygous missense mutation in the β-globin gene that causes polymerization of hemoglobin S. Gene therapy for patients with this disorder is complicated by the complex cellular abnormalities and challenges in achieving effective, persistent inhibition

MEDIA IN THIS ARTICLE

FIGURE 1

2019 FDA approves 2 new Preventive Drugs

- Crizanlizumab, a P-selectin inhibitor, was approved by the FDA in November 2019 – Blocks red cell adhesion, IV infusion monthly.
- Voxelotor is a daily oral hemoglobin S (HbS) polymerization inhibitor increasing the affinity of Hb for oxygen, Can be used with Hydrea.

Need for Adult Care

Blood Adv (2020) 4 (16): 3804–3813. https://doi.org/10.1182/bloodadvances.2020001743

Building access to care in adult sickle cell disease: defining models of care, essential components, and economic aspects

Julie Kanter,[1] Wally R. Smith,[2] Payal C. Desai,[3] Marsha Treadwell,[4] Biree Andemariam,[5] Jane Little,[6] Diane Nugent,[7,8] Susan Claster,[7,9] Deepa G. Manwani,[10] Judith Baker,[7] John J. Strouse,[11,12] Ifeyinwa Osunkwo,[13] Rosalyn W. Stewart,[14] Allison King,[15] Lisa M. Shook,[16,17] John D. Roberts,[18] and Sophie Lanzkron[19]

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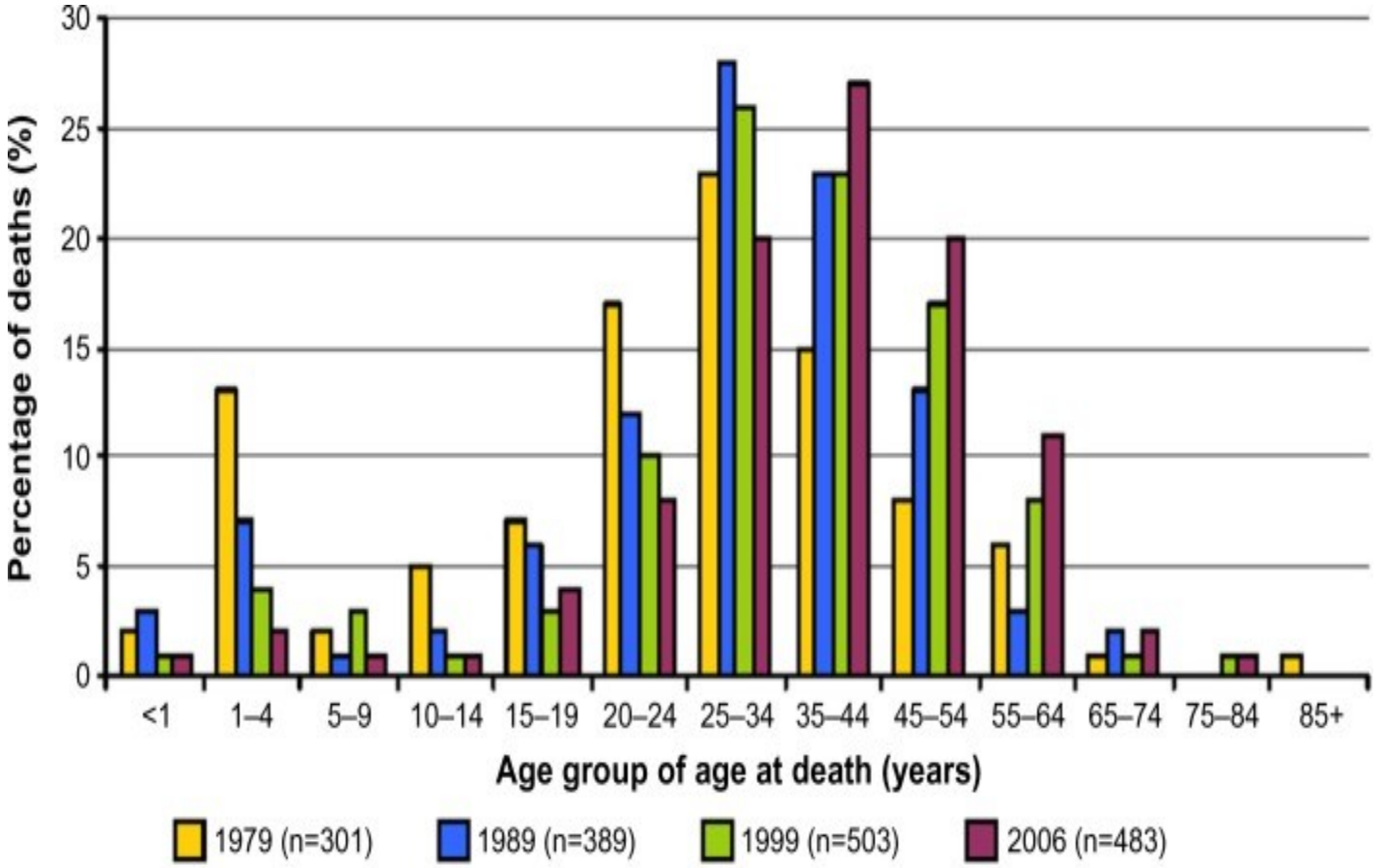
Key Points

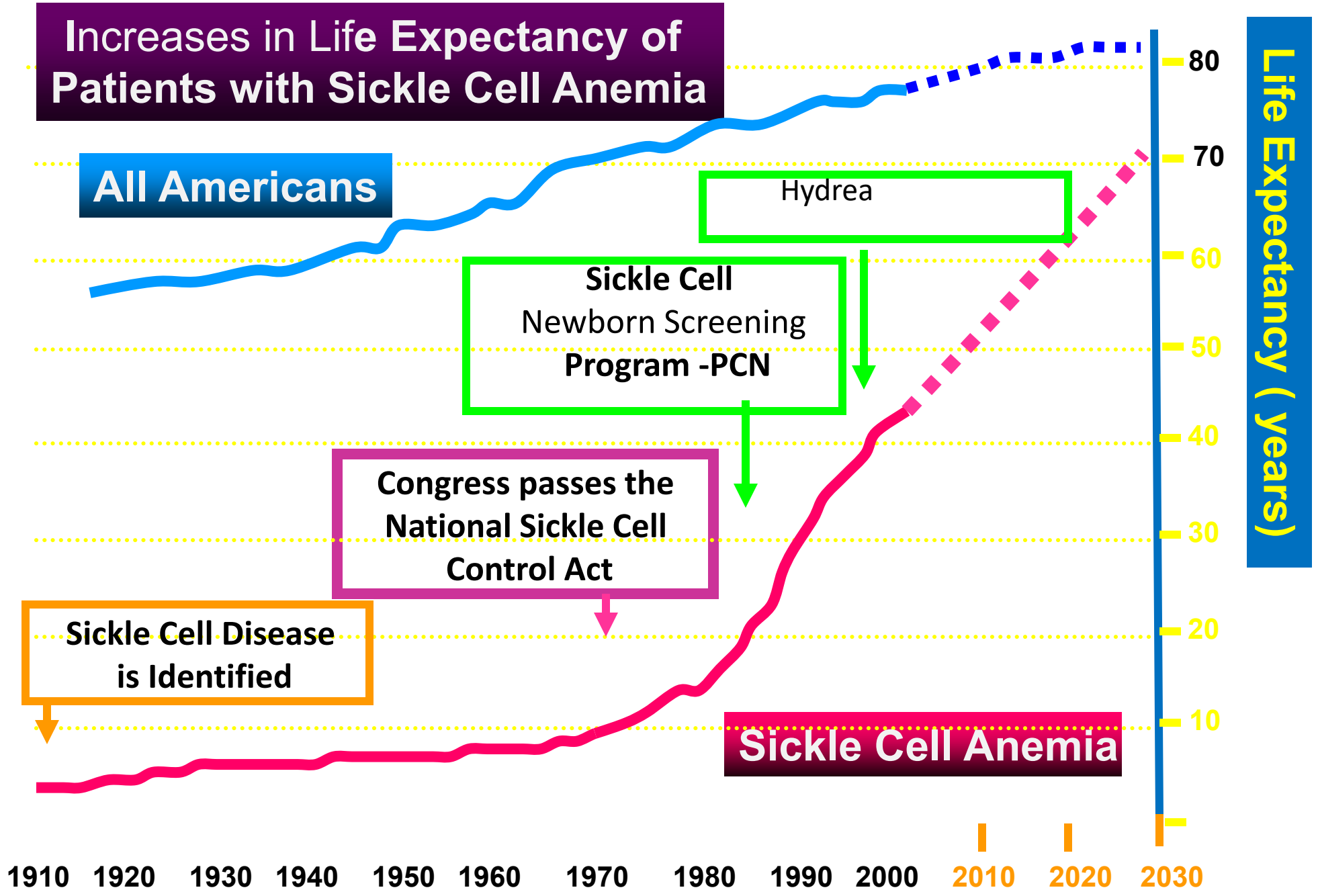
- This article defines elements of adult sickle cell centers to facilitate

Sickle cell disease (SCD) is the most common inherited blood disorder in the United States. It is a medically and socially complex, multisystem illness that affects individuals throughout the lifespan. Given improvements in care, most children with SCD survive into adulthood. However, access to adult sickle cell care is poor in many parts of the United States, resulting in

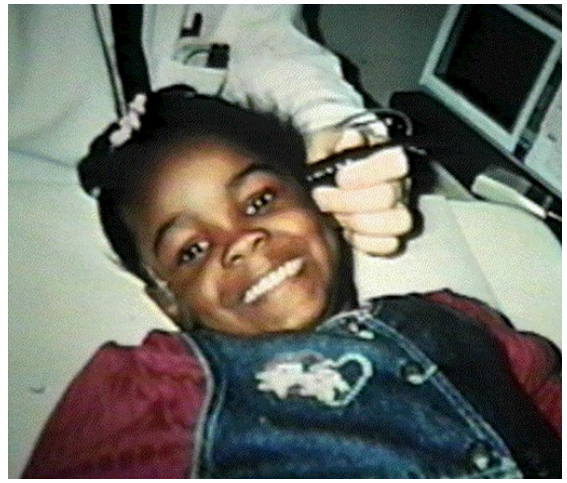
Life expectancy 1979 - 2006



J Blood Med. 2015; 6: 229–238.
Published online 2015 Jul 10. doi: 10.2147/JBM.S60515


Increases in Life Expectancy of Patients with Sickle Cell Anemia
All Americans
Hydrea
Sickle Cell Newborn Screening Program -PCN
Congress passes the National Sickle Cell Control Act
Sickle Cell Disease is Identified
Sickle Cell Anemia
Life Expectancy (years)
80
70
60
50
40
30
20
10
1910
1920
1930
1940
1950
1960
1970
1980
1990
2000
2010
2020
2030

Take Home Points



- Have patient referred to a sickle cell center
- Daily low dose Penicillin –birth -6yo
- TCD screen to prevent strokes with chronic monthly transfusion
- Hydroxyurea (Hydrea) prolongs life, prevents pain and complications by half also adding oral Glutamine (Endari) as an antioxidant can help reduce episodes
- Prevent crisis and complications by decreasing infections, dehydration,and temperature change
- New November 2019 - Crizanlizumab, a P-selectin inhibitor, Blocks red cell/platelet/endothelium adhesion, IV infusion monthly.
- Voxelotor is a daily oral hemoglobin S (HbS) polymerization inhibitor increasing the affinity of Hb for oxygen, Can be used with Hydrea.
- Curative Options – BMT, gene therapy, But risk and cost.
- Pain management – R/O other causes and then Hydration D5W, Oxygen if hypoxic, treat cause, good pain management by believing your patient

Resources

- **CDC:** https://www.cdc.gov/ncbddd/sicklecell/index.html
- SCInfo website: www.SCInfo.org
- Movie Spilled Milk https://www.spilledmilkmovie.com/watch.html
- **ASH Sickle Cell Guidelines** https://www.hematology.org/education/clinicians/guidelines-and-quality-care/clinical-practice-guidelines/sickle-cell-disease-guidelines
- **NIH Sickle Cell Guidelines** https://www.nhlbi.nih.gov/health-topics/evidence-based-management-sickle-cell-disease
- **Trust Guidelines and Policies on the Management of sickle cell disease and thalassaemia** at https://www.stgeorges.nhs.uk/service/diagnostic-services/haematology/sickle-cell-disease/trust-guidelines-and-policies-on-the-management-of-sickle-cell-disease-and-thalassaemia/
- **Medscape – Sickle Cell** https://emedicine.medscape.com/article/205926-overview
- **STATPearls– Sickle Cell -** https://www.ncbi.nlm.nih.gov/books/NBK482164/
- **The International Association of Sickle Cell Nurses and Professional Associates (IASCNAPA)** https://www.iascnapa.org/
- **Gene Thereapy** https://www.thegenehome.com/ A review of gene therapy for patients and providers
- **NIH Genetics Home Reference Sickle Cell Information** https://ghr.nlm.nih.gov/condition/sickle-cell-disease