

Hydroxyurea

Zahra Pakbaz, MD

Hematology Oncology

Riverside University Health System

UCR Assistant Clinical Professor of Medicine

Disclosure

- Novartis National Medical Board experts for ITP

β -Globin gene
(sixth codon)

T



GAG
(glutamic acid)



GTG
(valine)

**Hemoglobin S
solution**



Oxygenated

**Hemoglobin S
polymer**

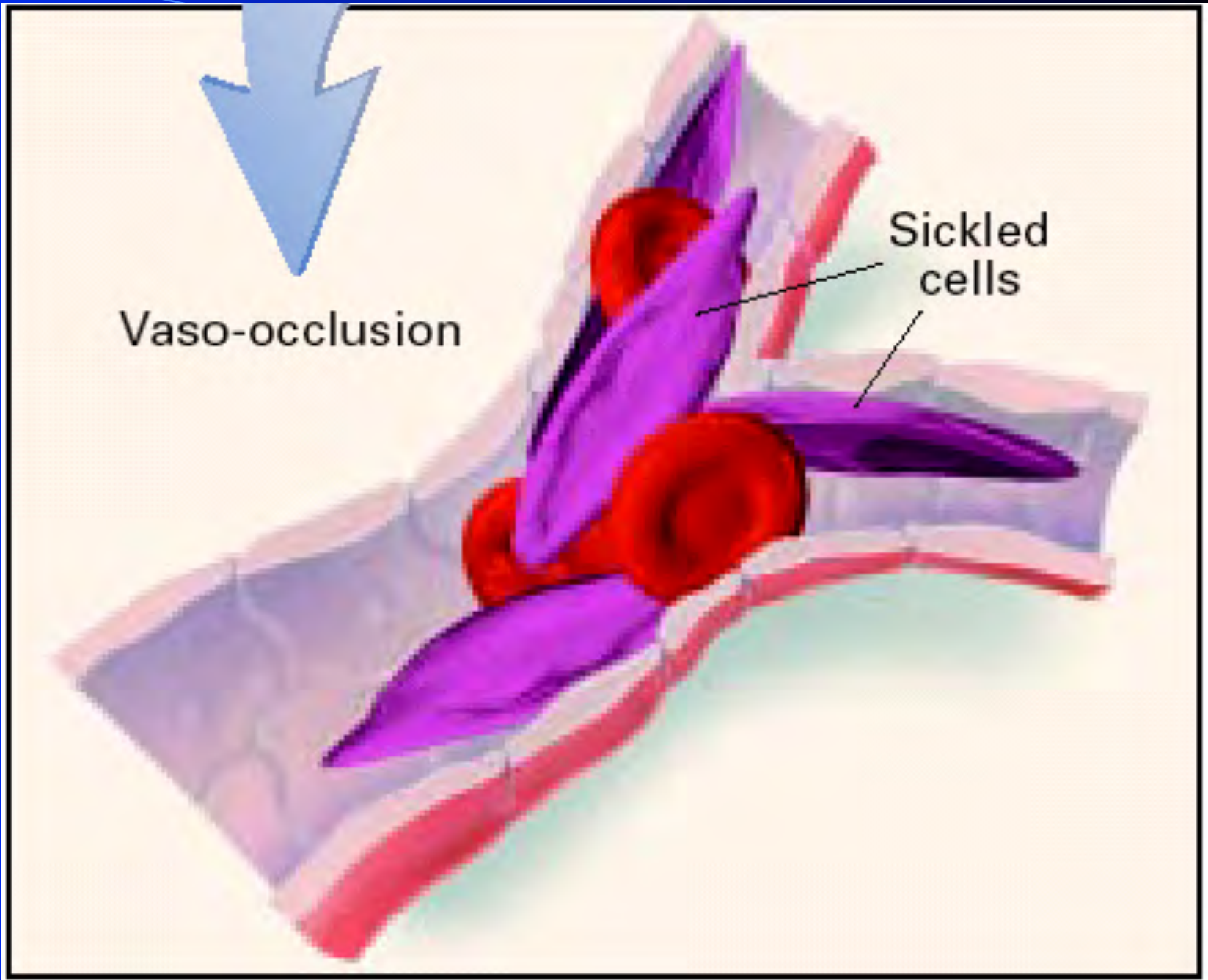


Deoxygenated

Hemoglobin S
cell



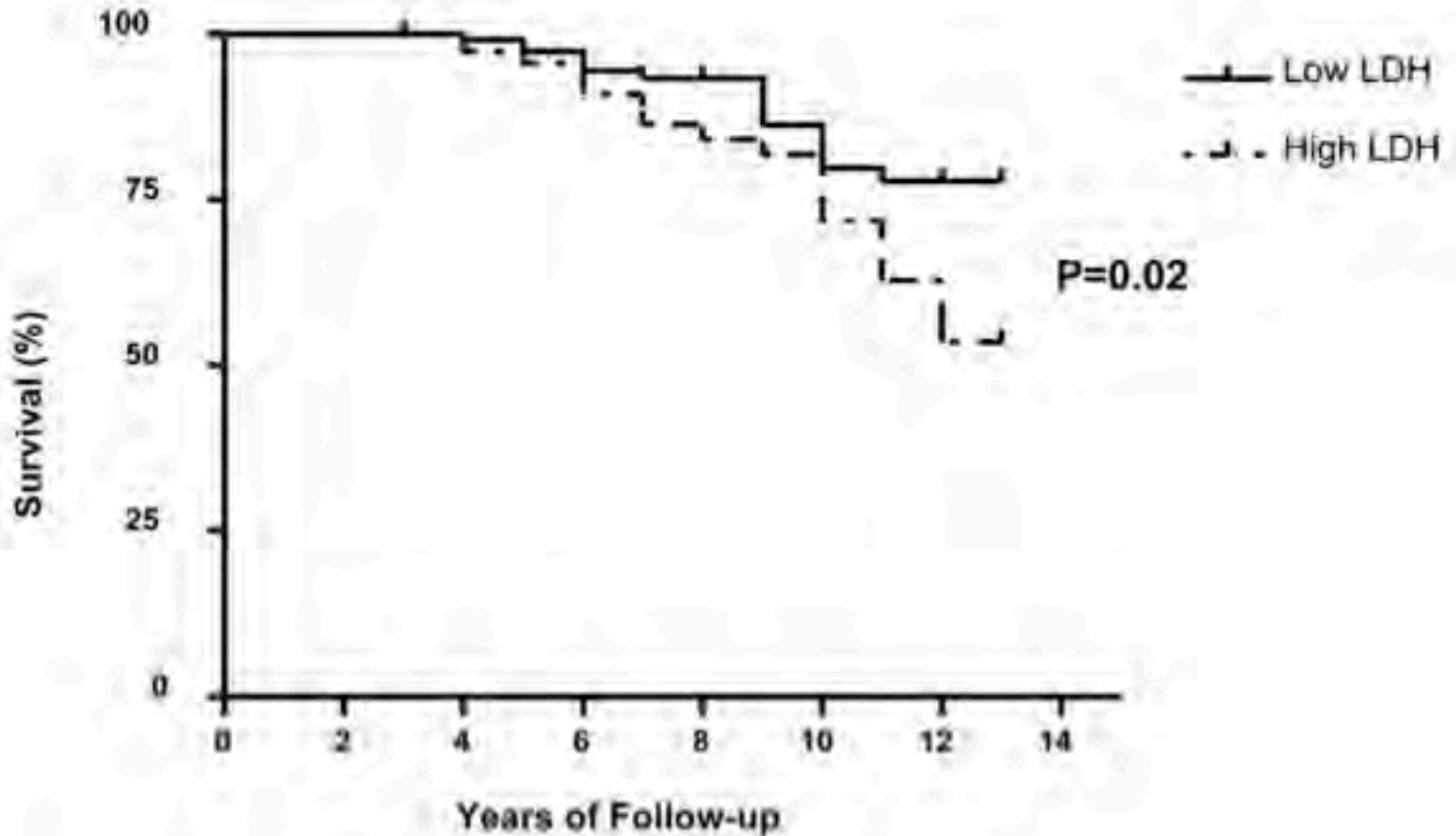
Cell
heterogeneity

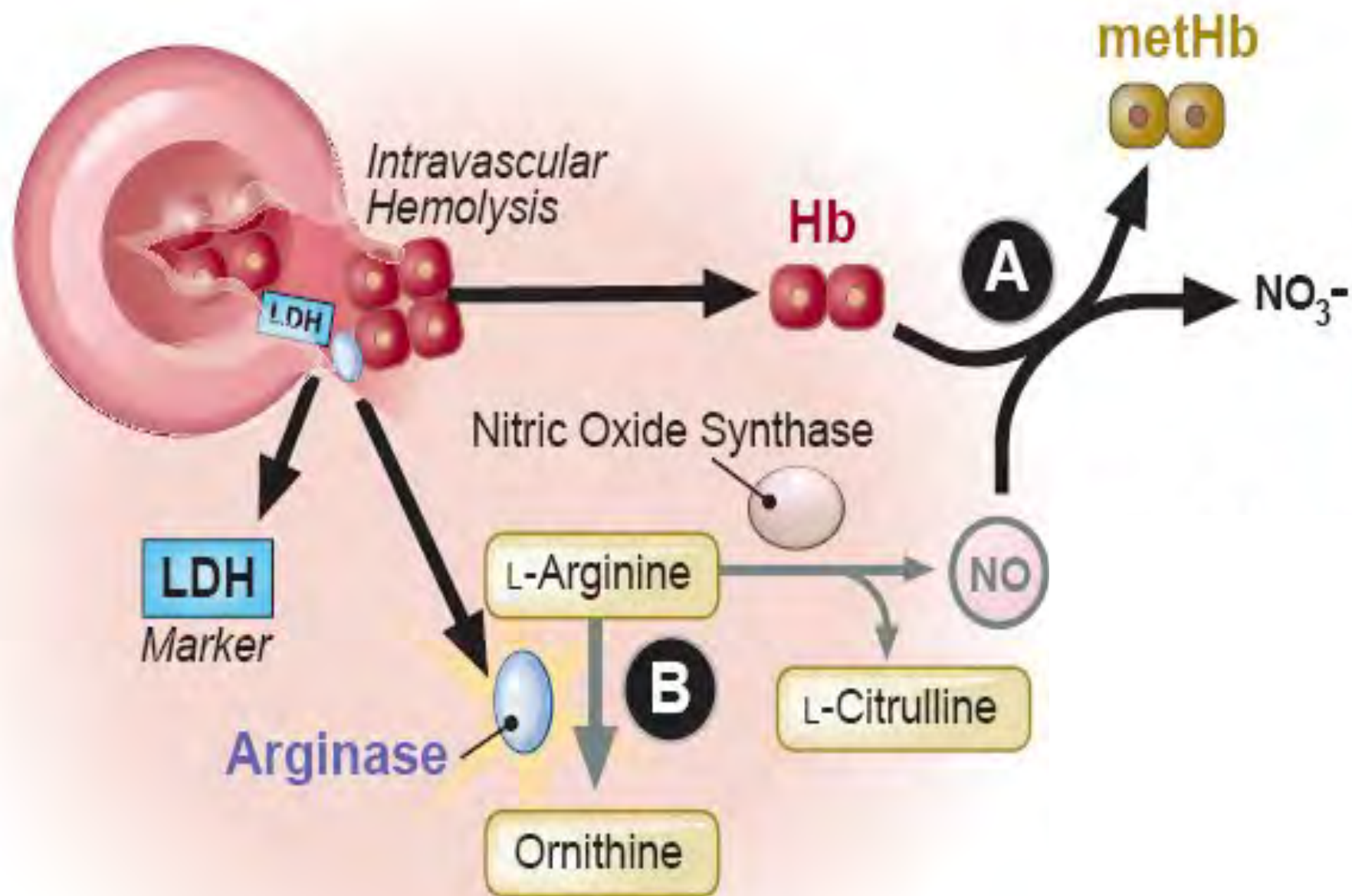


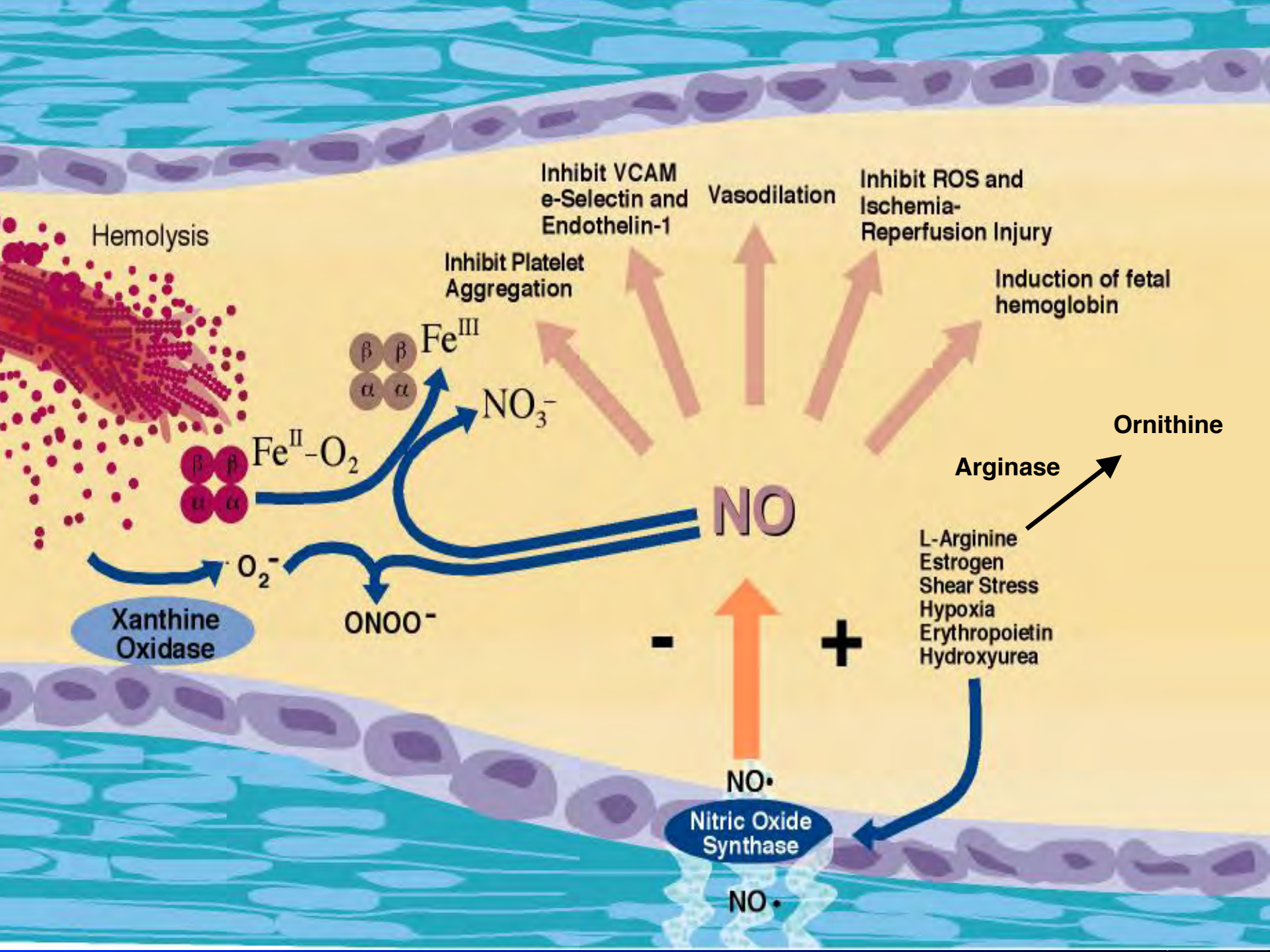
Hemolysis in SCD

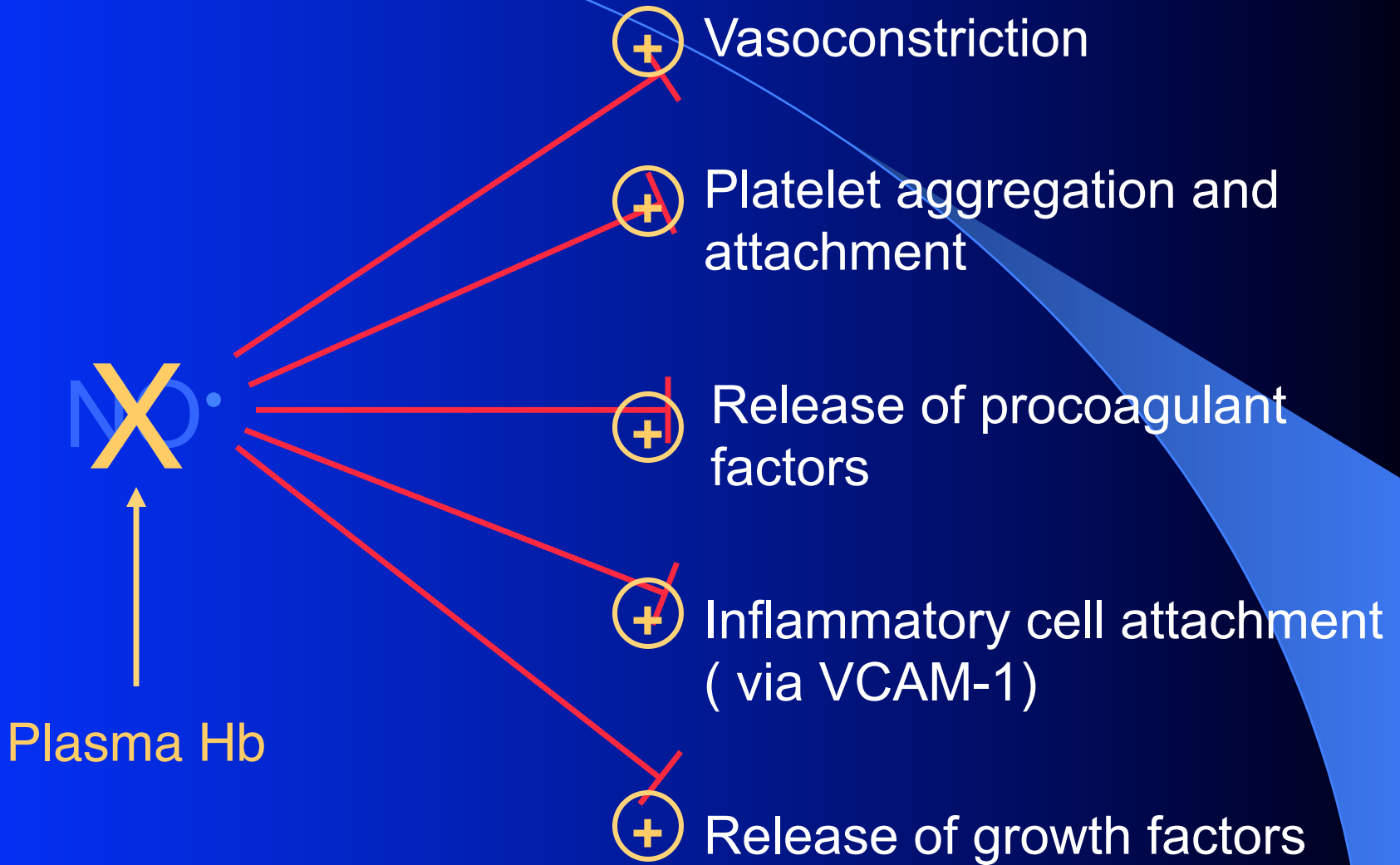
- 10% of RBCs per day hemolyze (30 g of hemoglobin)
- One third of hemolysis in SCD is intravascular and intensifies during vaso-occlusive crisis and acute chest syndrome

Hemolysis is associated with higher mortality





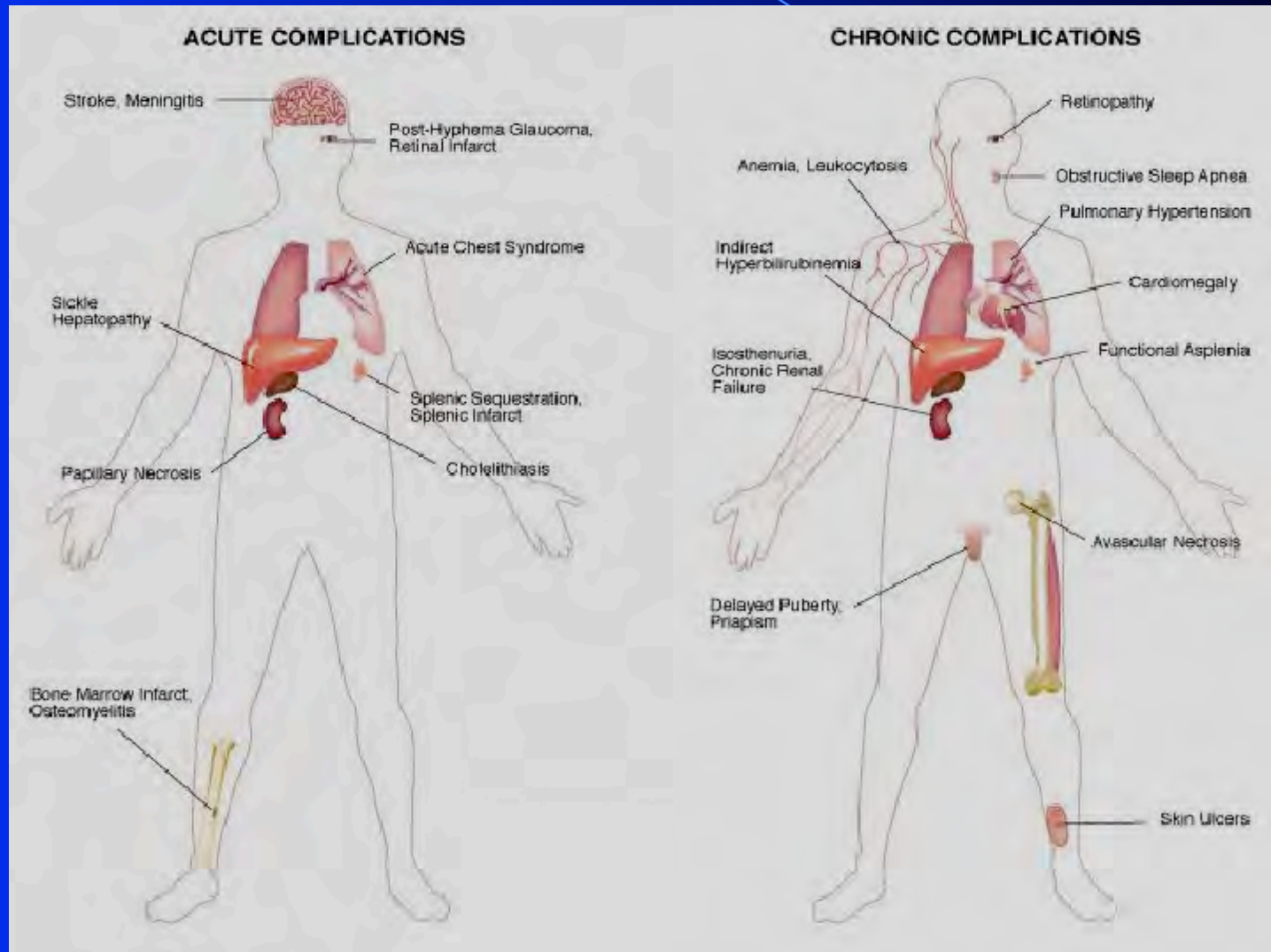




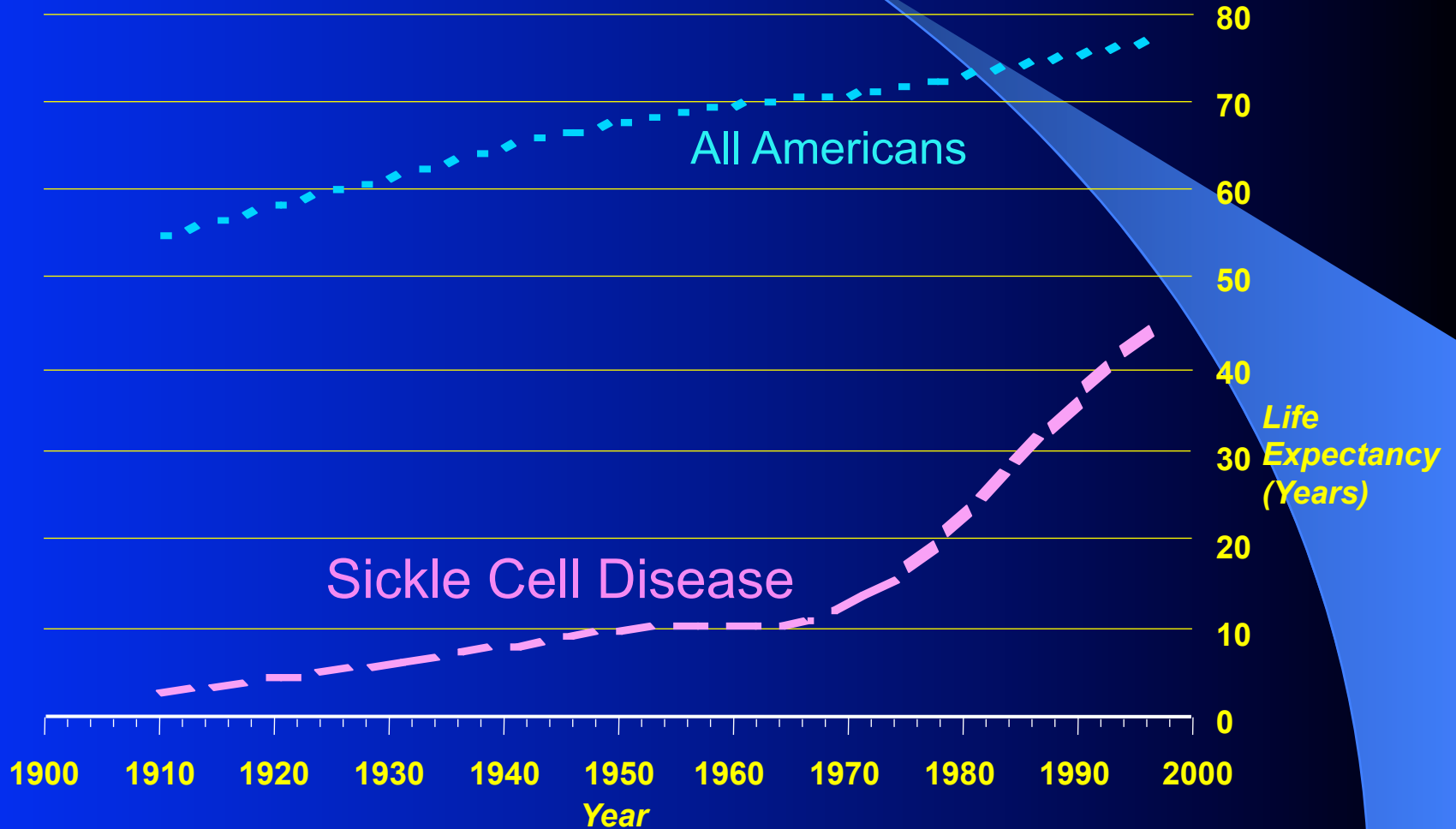
Pathophysiology of SCD

- Sickle Hb polymer formation and RBC rigidity
- RBC and WBC adhesion to activated endothelial cells
- Impaired nitric oxide bioavailability
 - New mechanism investigated by the NHLBI Vascular Therapeutics Section and others

Complications of SCD



Increases in Life Expectancies of Patients with Sickle Cell Disease





U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute



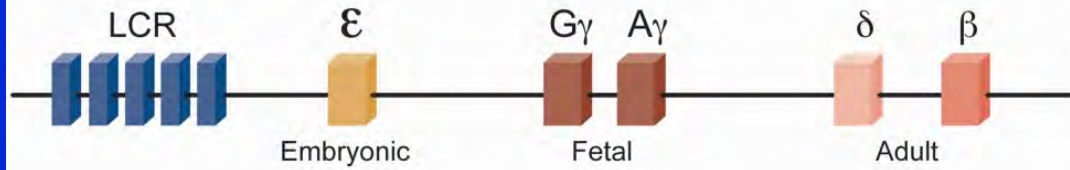
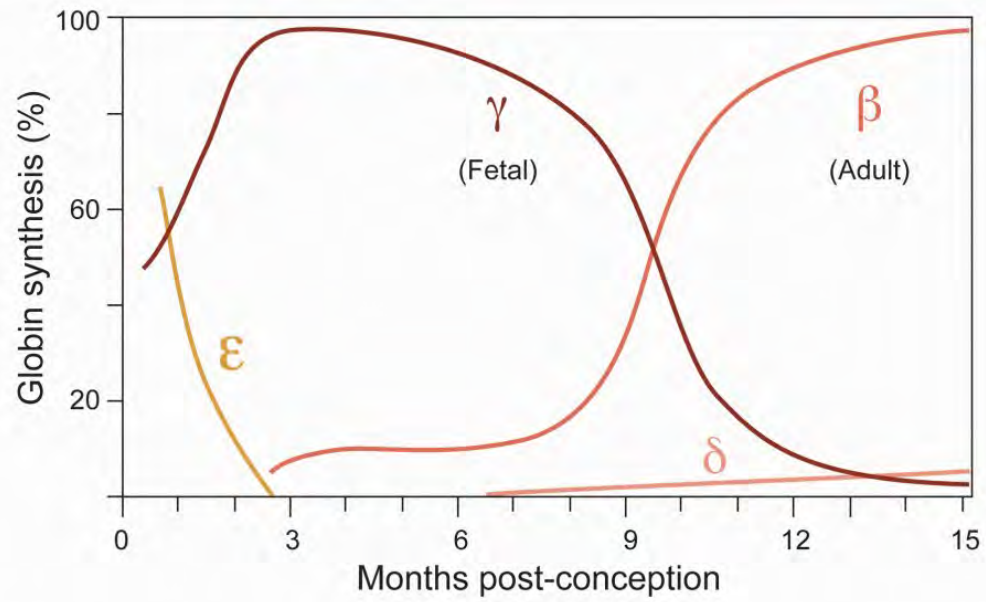
Evidence-Based Management of Sickle Cell Disease

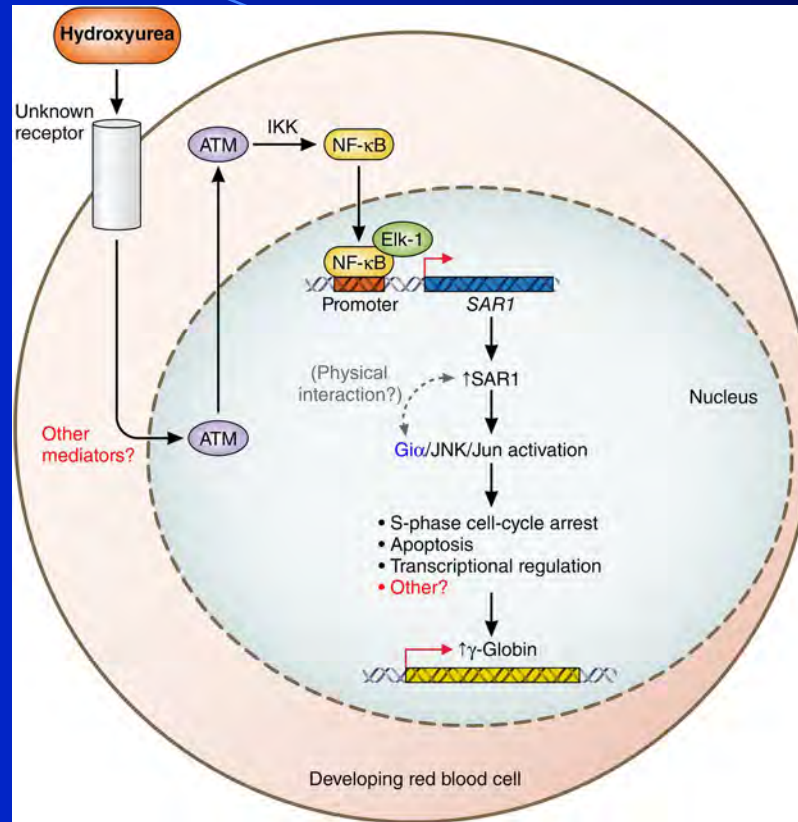
<http://www.nhlbi.nih.gov/guidelines>

Expert Panel Report, 2014

Efficacy of Hydroxyurea

- 44% reduction in pain hospitalization
- 40% reduction in mortality rate
- Decreased acute chest syndrome
- Decreased transfusion requirements





Delivering nitric oxide

Hydroxyurea Indication

- 3 or more painful crisis in one year
- Pain interfering with daily activities and QoL
- In CKD on EPO, add hydroxyurea to improve anemia
- SB⁺ and SC w/ pain interfering daily activities and QoL
- H/o severe or recurrent ACS
- Severe symptomatic anemia interfering with QoL
- Infants 9 month or older regardless of severity of disease

Hydroxyurea

- Start low, titrate to maximum tolerated dose
- 15mg/kg/d (10 if renal insufficiency)
- Maximum dose 35mg/kg/d
- Check CBC q 2wks
- Increase by 5mg/kg/d if:
 - ANC > 2500 cells/mm³
 - PLT > 95000 cells/mm³
 - Hb > 5.3 g/dl and retic count > 95000 /mm³

Hydroxyurea

- Stop if
 - ANC < 2000 cell/ul
 - PLT < 80,000
 - Hb < 4.5
 - Retic count < 80,000 when hb < 9g/dl
- Resume after 1-2 wks when counts recover
- Reduce dose by 2.5 mg/kg/d
- Try to increase again

Hydroxyurea and Sperm Counts

- 91% of sickle cell men have baseline sperm abnormality
 - Mostly forward motility and morphology
- Lower spermatozoa on hydroxyurea

Thank you!

Questions?

z.pakbaz@ruhealth.org