Anesthetic Management of Sickle Cell Disease

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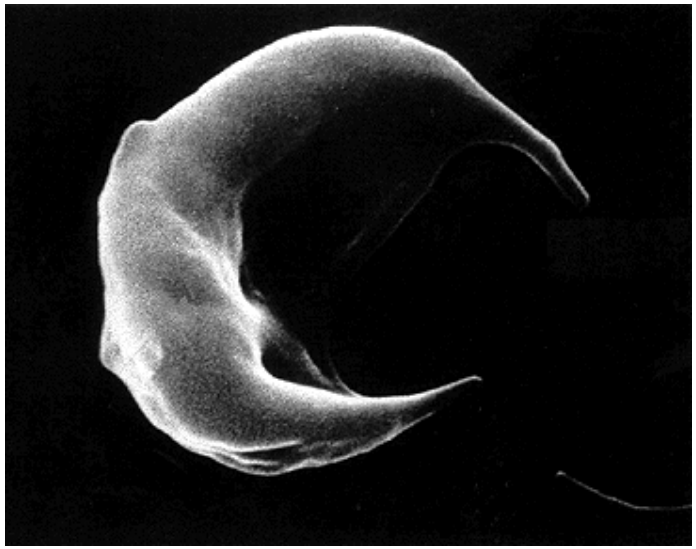
Introduction

Sickle cell disease (SCD) is a vaso-occlusive and hemolytic disorder caused by a hemoglobin (hgb) abnormality that leads to a chronic inflammatory state and progressive organ dysfunction



Genetics

- Hemoglobin structure
  - 2 Alpha subunits
  - 2 Beta subunits
  - 4 Heme complexes

- SCD is an abnormality of the beta subunit
  - Beta A is normal (i.e. AA)
  - Beta S is SCD (i.e. SS)
  - SA is the Sickle Cell Trait (SCT)

Genetics

Subunit 1	Subunit 2	
A	A	Normal
S	S	SCD
S	C	SCD Variant
S	Beta Thal	SCD Variant
S	A	Sickle Cell Trait

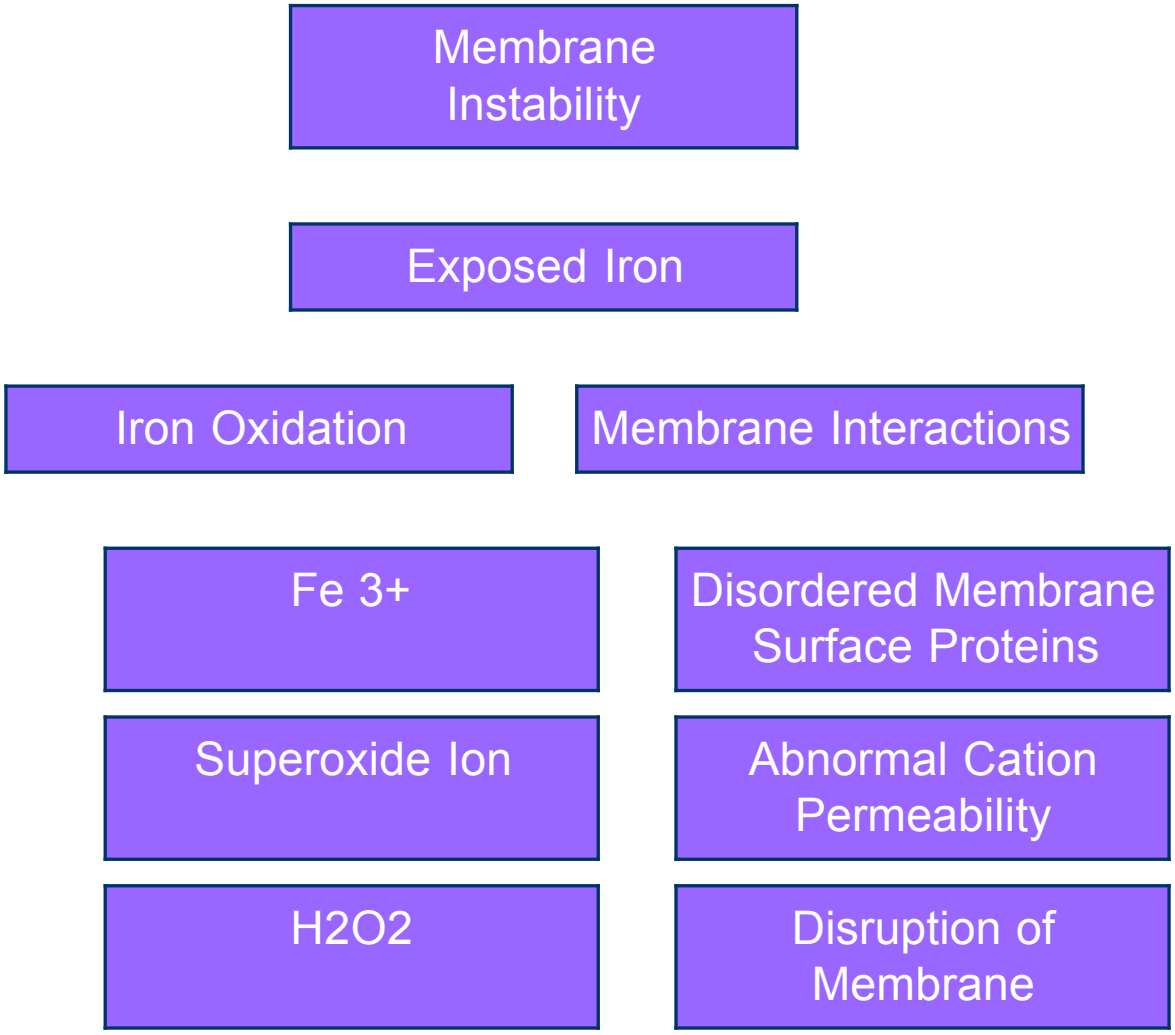
Genetics

- Marked variations in expression
  - 30% are rapidly progressive
  - 60% are less devastating
  - 10% are near normal
  - Hgb F and Alpha Thal are protective
- Not just a genetic defect
  - RBC membrane structure/function
  - RBC adhesiveness
  - Hgb scavengers and catabolism
  - Nitric Oxide generation
  - Inflammation

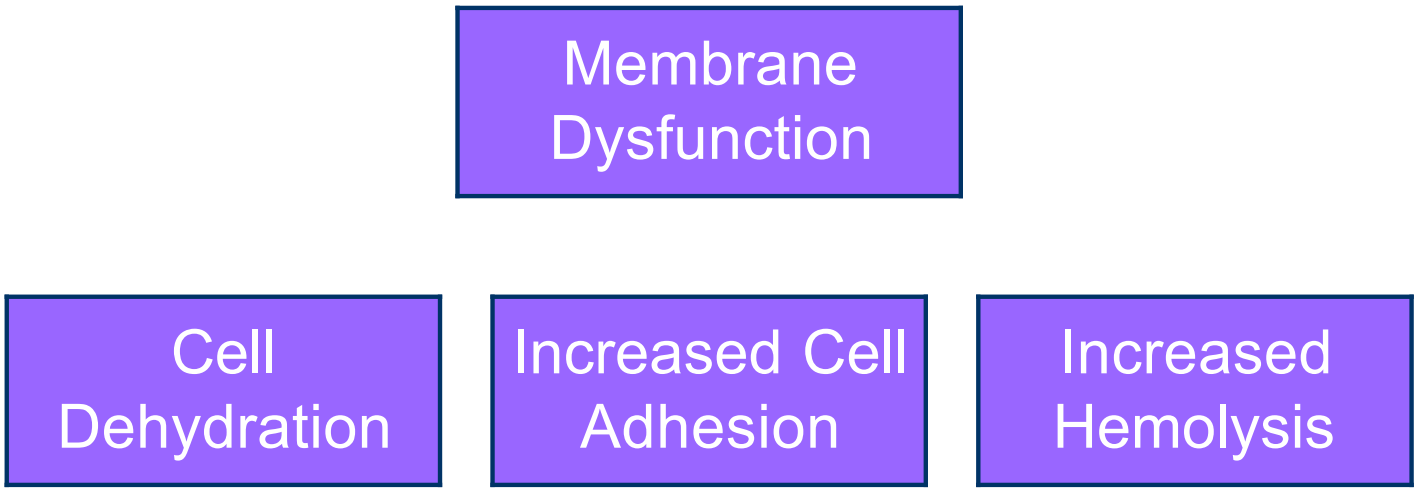
Molecular Biology & Biochemistry

- In the DNA…
  - Adenine to Thymine
- In the protein…
  - Glut Acid to Valine
- Loses a charge
  - Destabilizes
  - Decreases solubility

Molecular Biology & Biochemistry



Molecular Biology & Biochemistry



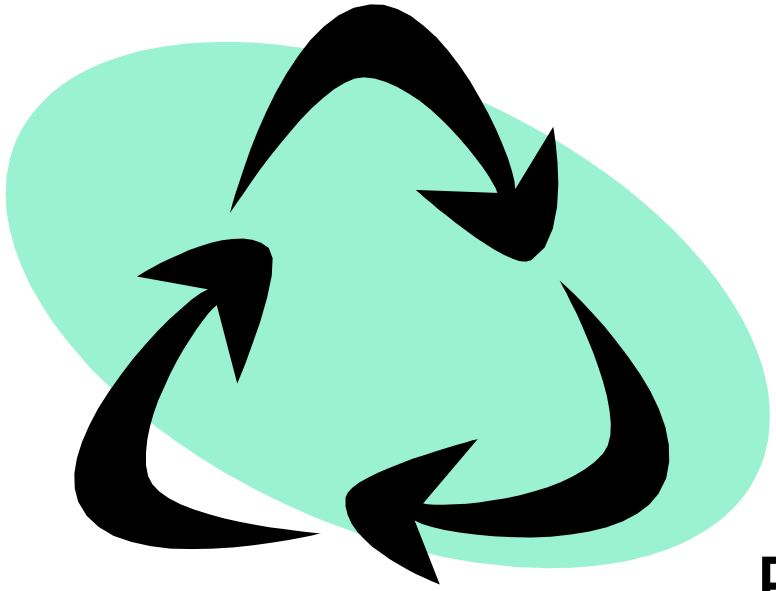
Endothelial Dysfunction

- Vascular Tone
- Fibrinolysis
- Inflammation
- Intimal Growth
- Vascular Permeability
- Lipid Transport
- Coagulation
- Vascular Architecture
- Nitric Oxide Synthesis

Nitric Oxide Dysfunction

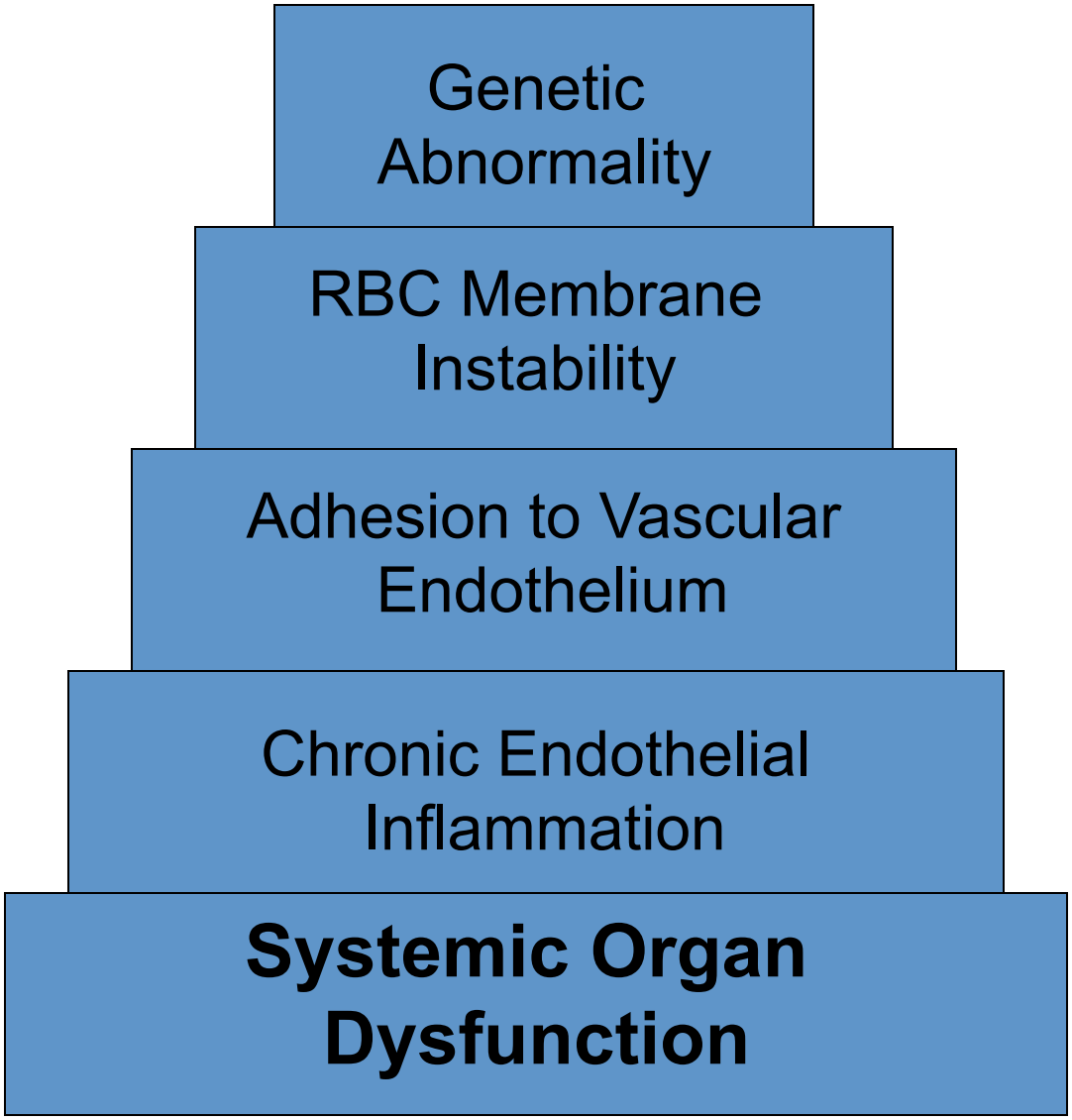
- Vasoconstriction
- Leukocyte Adhesion
- Hemoglobin polymerization
- Platelet Aggregation
- Vascular Wall Remodeling

Hgb
Polymerization



NO
Dysfunction

Endothelial
Inflammation
and Destruction


Genetic Abnormality
RBC Membrane Instability
Adhesion to Vascular Endothelium
Chronic Endothelial Inflammation
Systemic Organ Dysfunction

Molecular Biology & Biochemistry

TAKE HOME POINT

The clinical effects of SCD are only *partially* related to the immediate structure of the RBC

Widespread biochemical changes associated with SCD are responsible for systemic dysfunction

Clinical Manifestations

- Neurologic
  - Pain Crisis
  - Stroke
  - Retinopathy
  - Peripheral Neuropathy
  - Chronic Pain
- Pulmonary
  - Acute Chest Syndrome
  - Airway Hyperreactivity
  - Restrictive Lung Disease
- Genitourinary
  - Chronic Renal insufficiency
  - UTIs
  - Priapism
- Gastrointestinal
  - Cholelithiasis
  - Liver Disease
  - Dyspepsia
- Haematologic
  - Hemolytic Anemia
  - Aplastic Anemia
- Orthopaedics
  - Osteonecrosis
  - Osteomyelitis
- Immunologic
  - Immune Dysfunction

Vaso-Occlusion

Hallmark of SCD: Intermittent, recurrent acute episodes of severe pain thought to be caused by acute ischemia.

Acute exacerbation of a chronically derranged endothelial environment

Involves vasoconstriction, leukocyte adhesion, platelet activation, and coagulation, not just sickled cells.

Acute Painful Episodes

- Risk Factors
  - High Hgb Levels
  - Low Hgb F
- Precipitating Factors
  - Cold
  - Dehydration
  - Infection
  - Stress
  - Menses
  - Alcohol
  - Obstructive Sleep Apnea

Acute Painful Episodes

- Associated Symptoms
  - Fever
  - Swelling
  - Diaphoresis
  - Tenderness
  - Hypertension
  - Tachypnea
  - Nausea / Vomitting
- Affected Areas
  - Lumbar Spine >
  - Abdomen >
  - Femoral Shaft >
  - Knee

Pulmonary Complications

- Pulmonary Disorders
  - Airway Hyperreactivity
  - Pulmonary Fibrosis
  - Upper Airway Obstruction
  - Acute Chest Syndrome
- Pulmonary Mechanics
  - ↓ Vital Capacity
  - ↓ Total Lung Capacity
  - ↓ Diffusing Capacity
  - Pulmonary Hypertension

Pulmonary Complications

- ↓ O2 Delivery
  - Lung Disease
  - VQ Mismatch
  - Vascular Damage
  - ↓ NO Transport
  - Abnormal Vasculature
- Compensation
  - ↑ Minute Vent
  - ↑ Stroke Volume
  - ↑ DPG
  - ↑ Nitric Oxide Production

Acute Chest Syndrome (ACS)

- New pulmonary infiltrate
- Chest pain
- Temperature > 38.5 C
- Tachypnea, wheezing, or cough

Acute Chest Syndrome (ACS)

- Etiology
  - Unknown - 50%
  - Pulmonary infarction - 16%
  - Fat embolism - 9%
  - Pneumonia - 20%
  - Mixed infections - 4%
  - Other pathogens - 1%

Acute Chest Syndrome (ACS)

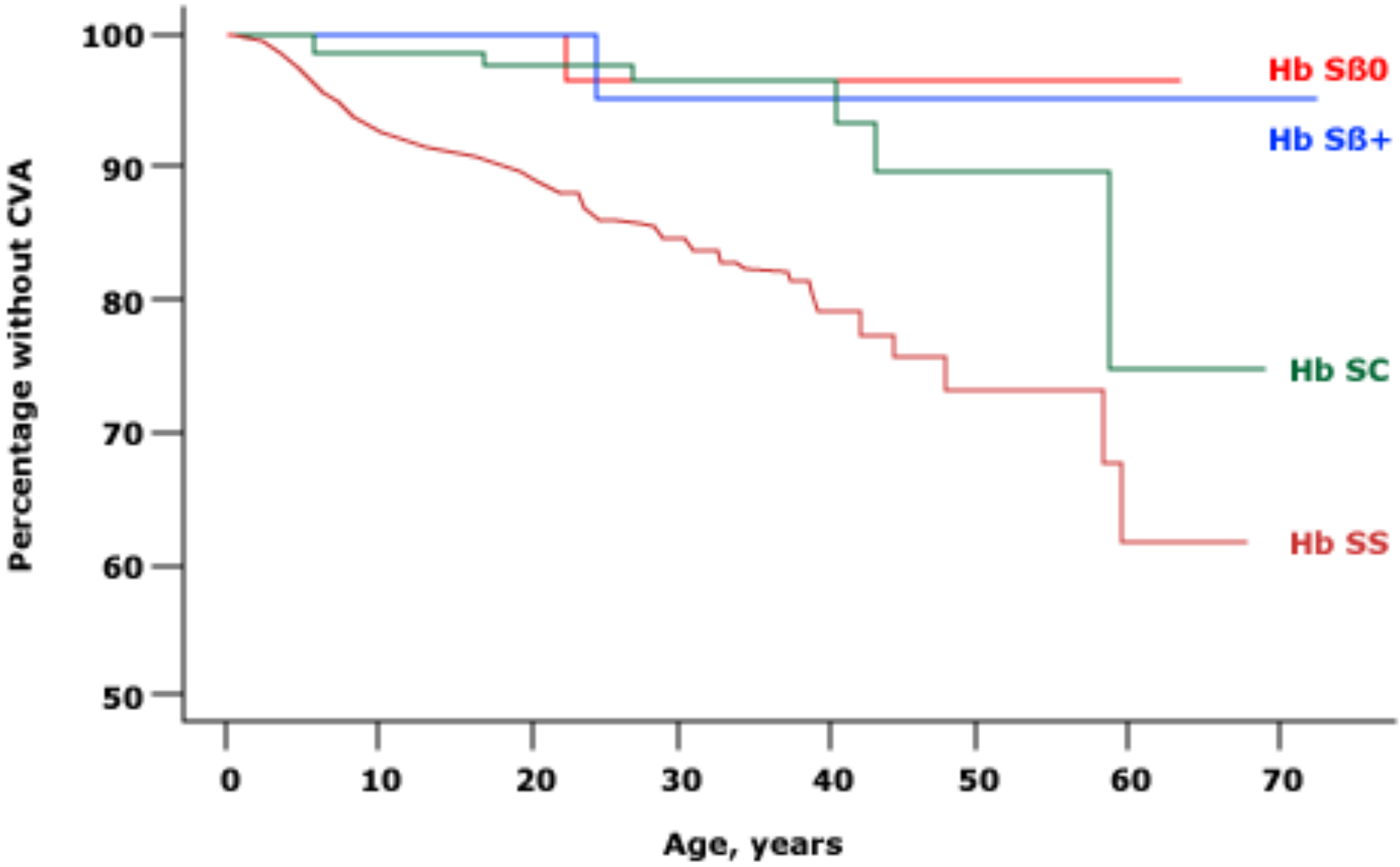
- Fever
- Cough
- Tachypnea
- Chest Pain
- Shortness of breath
- Arm and Leg Pain
- Abdominal Pain
- Rib and Sternal Pain
- Wheezing

Acute Chest Syndrome (ACS)

- Outcomes
  - 13% Mechanical Ventilation
  - 11% Neurologic Events
  - 3% Death

Neurologic Complications

- Transient Ischemic Attacks
- Stroke
- Spinal Cord Infarction
- Intracerebral Hemmorhage
- Vestibular Dysfunction
- Sensory Hearing Loss
- Cognitive Impairment


Percentage without CVA
100
90
80
70
60
50
0
10
20
30
40
50
60
70
Age, years
Hb Sß0
Hb Sß+
Hb SC
Hb SS

Cerebral Vascular Accidents

- Infarctive Stroke Risk
  - Prior TIAs
  - Low steady state Hgb
  - Elevated systolic blood pressure
  - High rate of ACS or an episode within 2 wks
- Haemorrhagic Stroke Risks
  - Low steady state Hgb
  - High steady state leukocyte count

Cerebral Vascular Accidents

- Prevention
  - Chronic transfusion program
  - Goal Hgb S < 30%
  - Reduces risk by 92%

Renal Complications

- Manifestations
  - Painless hematuria
  - Renal infarction
  - Renal colic
  - Nephrogenic diabetes insipidus
  - Focal glomerulosclerosis
  - Renal medullary carcinoma

Renal Complications

- Pathophysiology
  - High blood pressure
  - Increased GFR
  - Decreased concentrating ability

Preoperative Care

- Risk Assessment
- Laboratory Work
- Prophylactic Transfusion

Risk Assessment

- Predictors of Postoperative Complications
  - Type of surgical procedure
  - Increased age
  - Recent complications
  - Hospitalizations within last year
  - Temporal clustering of ACS
  - Abnormal Xray
  - Pregnancy
  - Infection
  - Haplotype

Risk Assessment

- D and C - 19%
- C-Section - 17%
- Hysterectomy - 17%
- Cholecystectomy - 8%
- Splenectomy - 8%
- Orthopaedic - 3%

Preoperative Labs

- Routine
  - Hemoglobin
  - BUN / Creatinine
  - Urine Dipstick
  - Chest X-ray
- Consider
  - Crossmatch
  - Pulmonary Function Tests
  - Arterial Blood Gases
  - Electrocardiogram
  - Liver Function Tests
  - Neurologic Imaging

Preoperative Transfusions

- Prevention of Complications
- Correction Anemia
- Replacement of Losses

Preoperative Transfusions

Griffith 1993	Not needed in minor procedures
Koshy 1995	Decreased complications in low risk, nothing in moderate risk
Vichinsky 1995	Exchange transfusion does not dec SCD complications but inc transfusion related complications
Haberkern 1997	Similar complications between aggressive and non-aggressive transfusions
Vichinsky 1999	Similar complications except an increase in ACS in aggressive and no transfusions

Preoperative Transfusions

- Complications
  - Red Cell Alloimmunization
  - Stroke
  - Pain Crisis
  - Acute Pulmonary Deterioration
  - Infection (Hepatitis C / HIV)
  - Increases Postop Orthopaedic Infections

Preoperative Transfusions

	Hct of 30%	Hgb S <30%
Low Risk	NOT indicated	NOT indicated
Moderate Risk	May be beneficial	NOT indicated
High Risk	May be beneficial	Questionable indication
ACS	Reduces hypoxemia	Reduces hypoxemia
Pain Crisis	NOT indicated	NOT indicated

Intraoperative Care

- Oxygenation
- Hydration
- Temperature
- Acid Base Status
- Anesthetic Technique

Oxygenation

"No clinical data in the anesthetic and surgical literature to demostrate that hypoxia precipitates perioperative sickle events."

No need to

- Avoid preoperative meds
- Use intraoperative hyperoxia
- Use prolonged posto supplemental O2

Hydration

"…there are no conclusive clinical data to support prophylactic modification of standard fluid management to prevent perioperative sickle events."

Thermoregulation

"Maintenance of normothermia is…the basis of care for SCD patients, as it is for the general patient population."

Acid Base Status

“ It seems unlikely that minor fluctuations in acid-base status are the primary trigger of complications.”

Technique

"…regional anesthesia does not appear to be contraindicated in SCD…"

General Intraoperative Care

“ We do not advocate therapeutic nihilism… we encourage adherence to these basic standards of anesthetic care.”

Specific Procedures

- Orthopaedics
  - Tourniquets are okay!
  - Fat embolism may cause ACS

Specific Procedures

- Neurosurgery
  - Mannitol and urea are okay
  - Limited evidence on hypotension
  - Hypocarbia (25-30) appears okay

Specific Procedures

- Cardiac
  - No increase in hemolysis with mechanical valves
  - Hypothermia w/o transfusion has been performed
  - No concerns with cross clamping and low flow states

Postoperative Care

- Basic Care
- Acute Chest Syndrome
- Pain Crisis

Basic Postoperative Care

- Focus on lung function
  - Early mobilization
  - Pulmonary toilet
  - Supplemental O2
  - Analgesia

Acute Painful Episodes

- Primary Treatments
  - Opiates / PCA
  - Ketorolac
  - Epidural
  - Steroids
- Other Possibilities
  - FFP
  - Inhaled Nitric Oxide
  - Anticoagulation
  - Poloxamer 188

Acute Chest Syndrome

- Treatment
  - Correct dehydration
  - Acetaminophen
  - Incentive spirometry
  - O2 support
  - Bronchodialators
  - Transfusions
  - Exchange transfusion
  - Pain Control
- Antibiotics
  - Cefotaxime
  - Cefuroxime
  - Clindamycin
  - Azithromycin
  - Erythromycin
  - Vancomycin

Conclusion

- SCD is a chronic inflammatory disease, not simply a disease of RBC morphology
- Careful attention must be paid to the preoperative risks and potential postoperative complications
- Fundamental to the care of a patient with SCD are the basic principles used in any safe anesthetic