Sickle cel disease and anesthesia

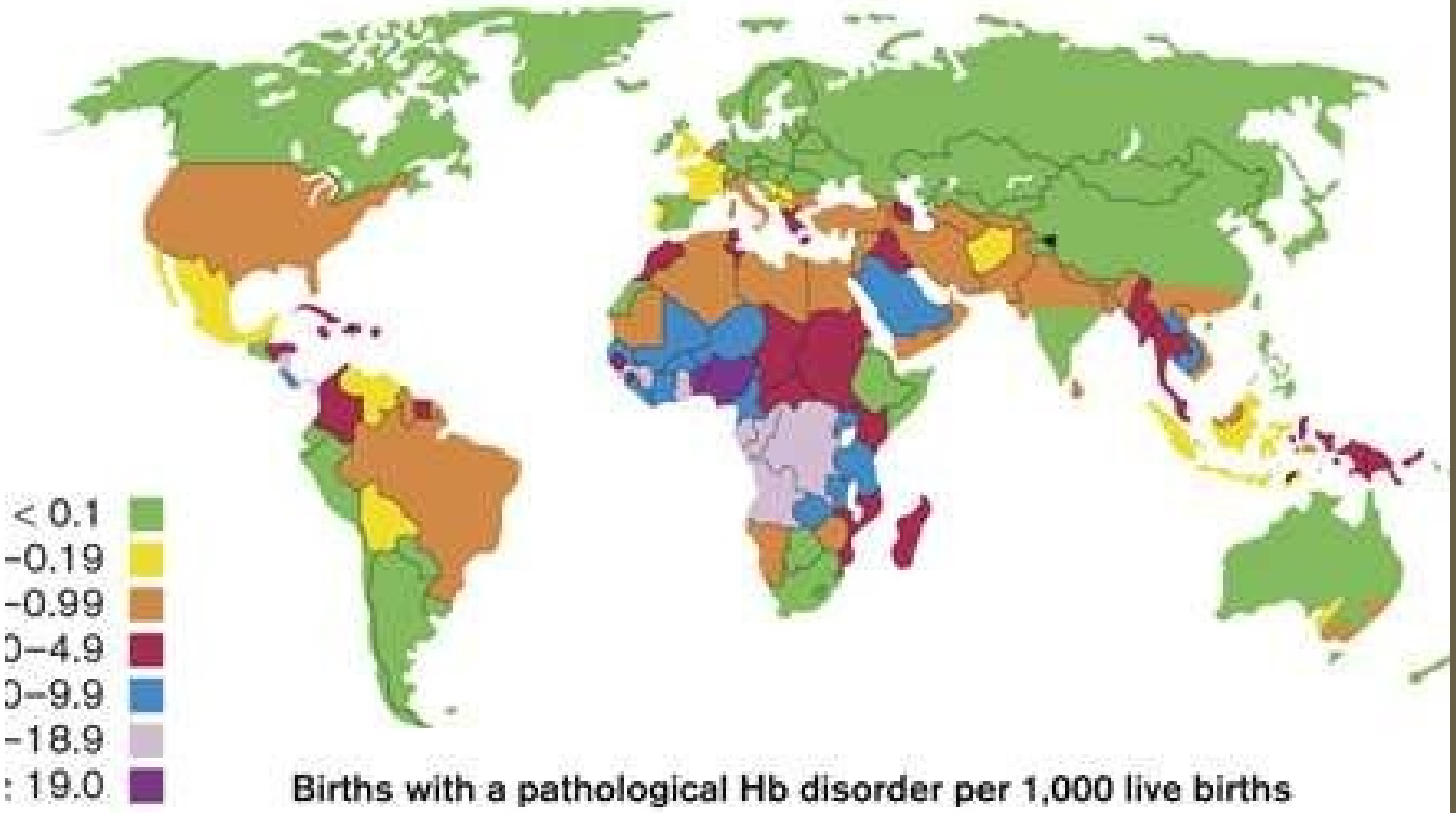
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Sickle cell disease

- Hereditary hemoglobinopathy, autosomal recessive
- Point mutation on chrom 11 → aberrant β globin (valine for glutamate in pos 6) → variant hemoglobin: **Hb S** (<-> HbA)
- Homozygote (HbSS) = sickle cell disease (SCD), heterozygote (HbAS) = sickle cell trait (SCT = carrier)
- Other forms: HbSC, sickle β⁰β⁺thalassemia

Epidemiology

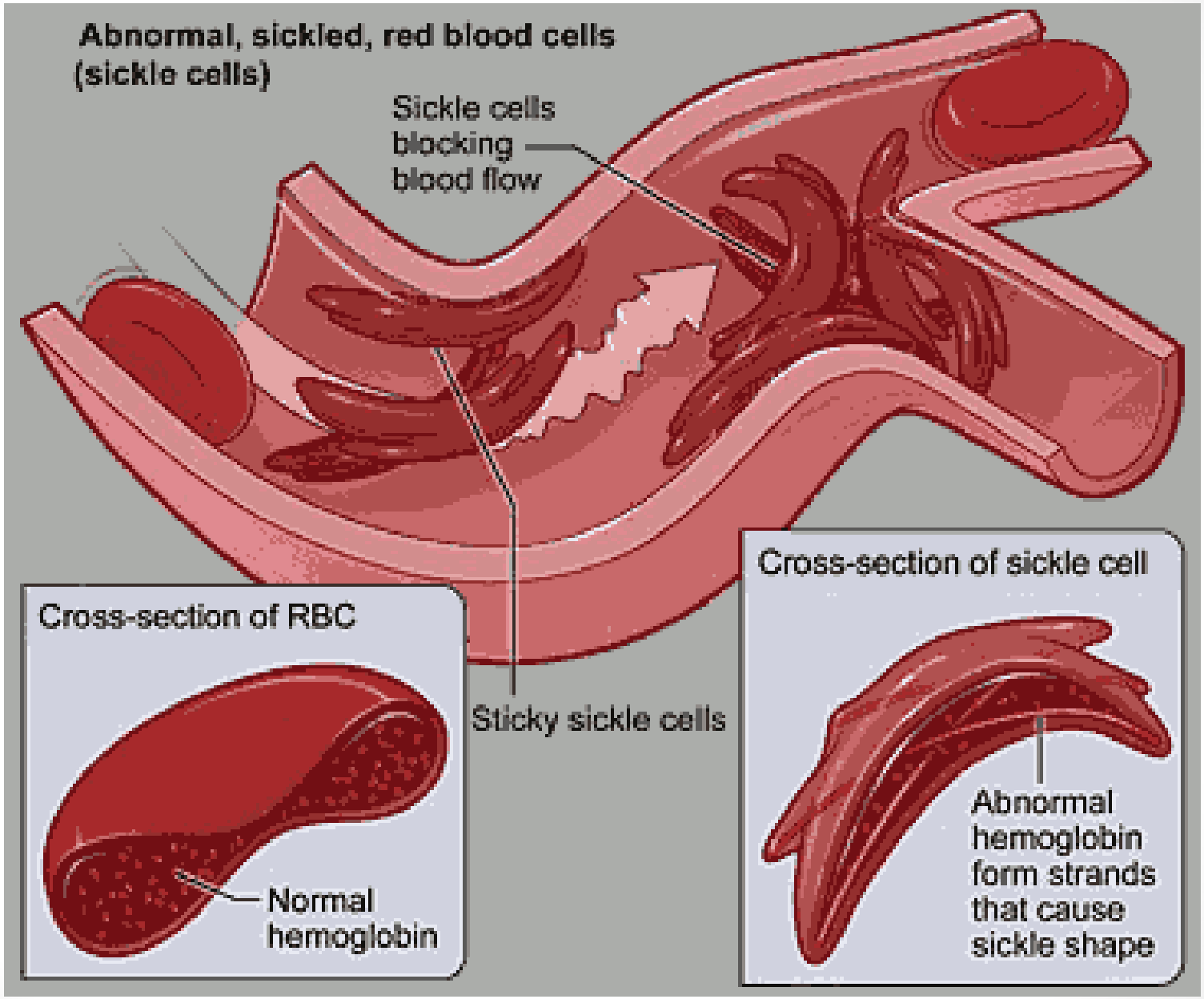
- High percentage in people from Africa (10-30%), Mediterranean Europe, Middle East, Caribbean
- In USA: 0,2% of African-Americans SCD, 8% SCT
- +/- 4 million in world
- 250,000 children are born each year



sickle hemoglobin (HbS) mutation (SCT) confers a genetic advantage against malaria so frequency is highest in areas where malaria is (or was) endemic

Pathophysiology

- HbS = unstable + less soluble
- Deoxygenation accelerated breakdown + polymerisation (gellation)
- “**sticking**” + “**sickling**”
- disruption of erythrocyte + environment (endothelium)
- Complicated process (beyond just RBC) of entire vascular milieu: **chronic vascular inflammation**
- Steady-state: 30% of RBC are sickled


Abnormal, sickled, red blood cells
(sickle cells)
Sickle cells
blocking
blood flow
Sticky sickle cells
Cross-section of RBC
Normal
hemoglobin
Cross-section of sickle cell
Abnormal
hemoglobin
form strands
that cause
sickle shape

Vasoocclusive crisis

- Hallmark of SCD: intermittent, recurrent, acute episodes of severe pain
- Acute '**triggers**' for sickling: hypoxia (sat < 85%), acidosis, intracellular dehydration, vascular stasis
- □ intricate process of vasoconstriction, leukocyte adhesion and migration, platelet activation and adhesion and coagulation
- □ **ischemia, infarction** □ **PAIN**

Clinical features

- Progressive organ damage (**chronic**) + intermittent periods of severe pain and/or pulmonary complications (**acute** crises)

Acute crisis

- Vasoocclusive crisis: acute ischemia pain
  - Bone pain, abdominal pain (>70% of patients)
  - Acute chest syndrome (ACS): pulmonary vasoocclusion and sequestration (pneumonia-like)
    - Lobar infiltrate, fever, tachypnea, chest pain
    - Mortality 2-12%, source of 25% of deaths
  - CVA (10% of children)
    - Ischemic of hemorrhagic (arterial disease)

Triggers: cold, stress (emotional and physical), alcohol

- Splenic sequestration crisis: in first 5 years of life, can lead to profound anemia and shock
- Aplastic crisis: acute suppression of normal eryhtropoiesis, linked to infections (parvovirus b19)
- Hyperhemolytic crisis: accelerated RBC death, usually secondary to infection, transfusion reaction, …

Chronic problems

- Every vascular bed in every organ is affected
- **Pulmonary**: progressive lung damage (fibrosis, vasculopathy)
- **Renal**: hyposthenuria, chronic renal failure
- **Neurological**: sequellae from (subclinical) CVAs

Table 1. Clinical Features of Sickle Cell Disease

Complication	Features
Neurological	
Pain crisis	Occurs in >70% of patients
Stroke	10% of children; subclinical microvascular occlusion in ≈20%. Cause of >20% deaths.
Proliferative retinopathy	50% of SC adults; rare in SS homozygotes
Peripheral neuropathy	Unusual complication
Chronic pain syndrome	A small subset of patients
Pulmonary	
Acute Chest Syndrome	Occurs in 40% of patients; mortality rate of 1.1% for children and 4.8% for adults.
Airway hyperreactivity	35% of children
Restrictive lung disease	10–15% of patients
Genitourinary	
Hyposthenuria	Nocturnal enuresis not a sensitive predictor
Chronic renal insufficiency	Present in 5–20% of adults
Urinary tract infection	Increased incidence; may trigger ACS
Priapism	10–40% of men
Pregnancy	Probable increased incidence of obstetrical complications, increased incidence of VOC
Gastrointestinal	
Cholelithiasis	Up to 70% of adults
Liver disease	Viral hepatitis from transfusion in up to 10% of adults. Liver failure <2%.
Dyspepsia	Mucosal ischemia, rather than increased acid production, is thought to be the cause. Reflux is not a complication of SCD.
Hematological	
Hemolytic anemia	Typical baseline hemoglobin levels are 6–9 g/dl in SS disease, higher in SC disease and Arab phenotype.
Acute aplastic anemia	Parvovirus B19 infections trigger acute severe exacerbations of anemia
Splenic enlargement/fibrosis	Less affected: SC disease, Arab haplotype
Orthopedic	
Osteonecrosis	Up to 50% of adults
Osteomyelitits	Salmonella and *Staphlococcus aureus* are commonest pathogens.
Dactylitis	Early onset is a marker of disease severity
Vascular	
Leg ulcers	20% of SS adults; rare in SC disease
Immunological	
Immune dysfunction	Increased susceptibility to infections
Erythrocyte auto/alloimmunization	Increased incidence of transfusion
Hemolytic transfusion reactions	Alloimmunization

ACS = acute chest syndrome; SCD = sickle cell disease; SS = patients homozygous for hemoglobin S; VOC = vasoocclusive crisis.

Diagnosis

- **Screening-test**: rapid solubility test
  - Negative: no HbS present
  - Positive: Hb electrophoresis to determine type of hemoglobinopathy

Anesthetic management

Preoperative assessment

- SCD has high incidence of perioperative complications (<-> SCT) (as high as 50%)
- Risk of perioperative SCD complications and organ dysfunction
- Predictors for complications
  - Type of surgery (high risk for eg sectio, d&c)
  - Pattern of acute exacerbations
  - Increased age
  - Pregnancy
  - Pre-existing infection
- Presence and degree of organ damage (lung, kidney, brain)

Preoperative investigations

- History and examination (recent SCD events)
- Hematocrit (typical baseline-Hb for SCD 6-9 g/dl)
- Plasma ureum/creatinine, urine dipstick
- Chest Rx
- Pulse oximetry
- Others as indicated (blood crossmatch, lung function tests, aBGW, ECG, neurological imaging)

Prophylactic transfusion

- **Controversial**, lots of opinions-studies
- Transfusion goal? Hb of 10 g/dl (Hct 30%) and/or HbS < 30%
- Aggressive vs conservative transfusion: equal benefit, more complications with aggressive
- Risk of transfusion: high incidence of alloimmunization (30%)
- Low risk: no benefit; moderate/high risk: possible benefit (vs. transfusion-risk)
- **individual assessment**: risk of patient, risk of procedure, benefit/risk of transfusion

Intraoperative management

- Avoid
  - Hypoxia: adequate oxygenation, no benefit hyperoxygenation
  - Dehydration: adequate hydration according to renal pathology
  - Hypothermia: normothermia
  - Acidosis: standard anesthesia care, HCO3 alkalinization not effective
  - Stress: anxiolytica, adequate analgesia

Anesthetic technique

- Regional anesthesia
  - Early studies indicated more complications with regional anesthesia (however most were obstetrics and sicker patients)
  - Other studies: no adverse effect
  - Succesfull in treating VOC pain, controlling pain unresponsive to opioids, with better oxygenation of affected tissues
- definitely place for LRA (optimal pain control, better oxygenation, rheology of affected area, less opioid use); as combination with GA or LRA alone

Tourniquet

- Not absolutely contraindicated
- Cases where it’s used without any problem, however it does create possible ‘sickling environment’
- Prior to inflation carefull and fully exsanguination to prevent stasis
- Balance risk of tourniquet vs risk of surgery without

Postoperative management

- Basic supportive care
  - Adequate analgesia
  - Supplemental oxygen
  - Adequate hydration
  - Early mobilization
- Vasoocclusive pain crisis
  - Analgesia (LRA, opioids, adjuvants)
  - Psychological support
  - Plasma transfusion ?

- Acute chest syndrome (+/- 3 days post surgery)
  - Oxygen
  - Bronchodilators, incentive spirometry
  - Analgesia
  - Antibiotics
  - Transfusion if necessary
  - Steroids, NO
  - Mechanical ventilation

Treatment

- Mean age of death with SCD: 42 men, 48 women
- Folate supplementation
- Immunization, antibiotics
- Hydroxyurea
- ACE-inhibitors
- Cure= bone marrow transplant
- Future
  - iNO
  - Genetic treatment

Conclusion

- SCD = chronic inflammatory vascular disease = systemic disease
- Significant perioperative morbidity and mortality
- STANDARD GOOD ANESTHETIC CARE
  - Observation and vigilance
  - Avoid triggers (hypoxia, hypoperfusion, acidosis, hypothermia)
  - Case to case management
  - Recognize and treat complications

- **Literature**
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