POST-SAN DIEGO 2024
Novità dal Meeting della Società Americana di Ematologia

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Introduzione alla lettura «Sickle Cell Disease» (Prof. Mariane de Montalembert)

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Disclosures of Mauro Krampera

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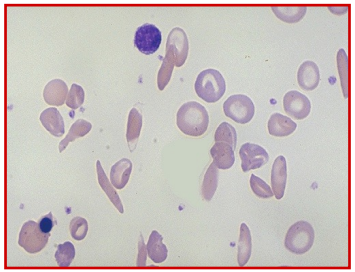
Incyte					x		
Janssen					x	x	
Novartis					x		
Otsuka					x	x	

SICKLE CELL DISEASE (SCD)

Why discussing about it?

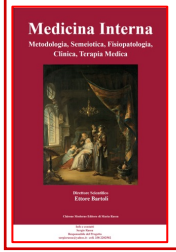


Hb electrophoresis

NORMOCHROMIC NORMOCYTIC ANEMIAS

3) HYPER-HEMOLYTIC

- **NON-IMMUNE**
  - **EXTRAGLOBULAR CAUSES (acquired)**
    - Fragmentation anemias
      - March Hemoglobinuria
      - Preeclampsia
      - TTP and HUS
      - Malaria
      - Systemic Vasculitis, etc.
  - **INTRAGLOBULAR CAUSES (congenital*)**
    - **membrane abnormalities**
      - Hereditary Spherocytosis
      - Hereditary Elliptocytosis
      - Paroxysmal Nocturnal Hemoglobinuria (PNH) *exception
    - **enzymatic abnormalities**
      - Altered glycolysis (i.e. PK deficiency)
      - Altered hexose monophosphate shunt (i.e. G-6-PD deficiency)
    - **hemoglobinopathies**
      - Unstable Hemoglobin variants
      - Sickle Cell Anemia ←
      - Methemoglobinemia (Hb M)
      - Hb variants with altered affinity for O_2



Friso S, Pizzolo F, Ferrarini I, Krampera M
Cap. VI – Ematologia
Ettore Bartoli – Medicina Interna
Chirone Moderno Editore di Maria Rassu
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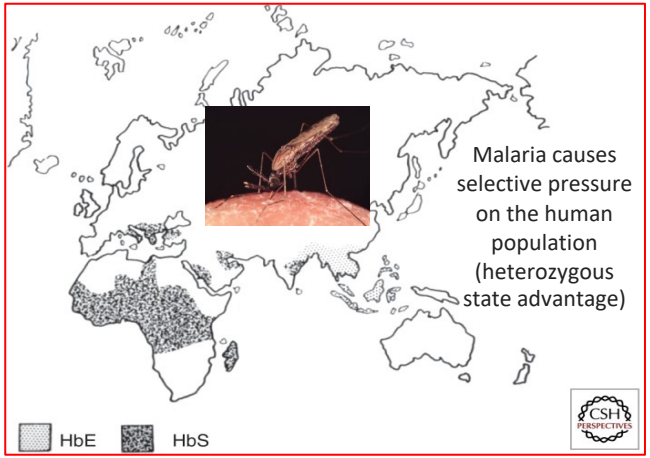
PATHOGENESIS: autosomal recessive genetic disease due to a point mutation in the beta-globin gene → GLU replacement with VAL in β^6

→ Precipitation of Hb alpha2/betaS2 tetramers at low O_2 concentration → sickle cells → obstruction of tissue microcirculation and hemocatheretic processes

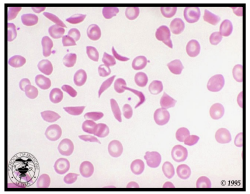


PREVALENCE WORLDWIDE: >13 million people (40.000 of them in Europe)

INCIDENCE: 300-400,000 newborns/year (+30% increase in 2050)

SICKLE CELL DISEASE (SCD)

Why discussing about it?



I. Epidemiology: Sickle Cell Trait (A/S) Incidence

A. Americans of African Descent: 1 in 12

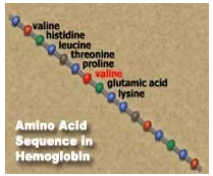
B. Also Seen in Greeks, Italians, Turks, Saudi Arabians

II. Pathophysiology

A.Normal Hemoglobin A replaced by Hemoglobin S (Hb S)

B.Substitution of Valine for glutamic acid

1.Occurs at the 6th position of the beta-chain



III.Types

A.Sickle Cell Trait (A/S)

1.No Anemia

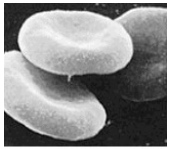
2.Hemoglobin S represents 25-40% of their Hemoglobin

3.Under normal circumstances, RBCs do not hemolyze

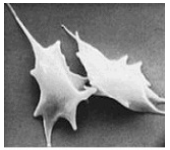
B.Sickle Cell Anemia (S/S)

1.Initially infant's RBCs mainly contain fetal Hb F

2.Within months the abnormal Hb S replaces the Hb F



Normal Red Blood Cells



Sickled Red Blood Cells

Severe illness compromising the quality of life

IV. Precipitating Factors for acute crises

A.Preceded by infection 25% of the time

B.Cold Weather due to reflex vasospasm

C.Dehydration in warm weather

V. Symptoms: Acute Vaso-Occlusive Episode

A.Child under age 18 years

B.Recurrent painful crises

C.Sudden onset pain in abdomen, chest, back and joints

VI. Lab: Sickle Cell Crisis

A.Profound Anemia

B.Reticulocyte Count <1%

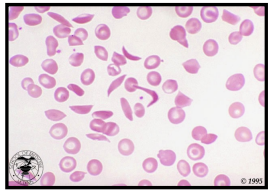
VII. Course

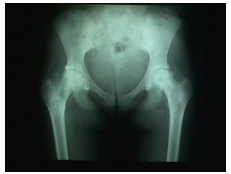
A.Acute Crisis usually resolves spontaneously 7-10 days

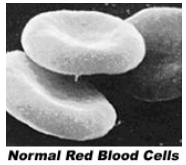
Sickle Cell Disease (SCD)

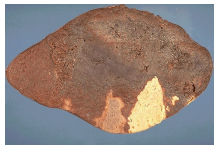
VIII. Complications

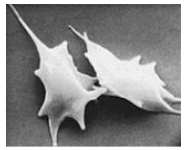
- A. Hematuria in Sickle Cell Anemia
  - 1.Most common Sickle Cell Anemia complication
- B. Priapism in Sickle Cell Anemia
- C. Cerebrovascular Accident in Sickle Cell Anemia
- D. Avascular Necrosis of Femoral Head
- E. Splenic Sequestration and Infarct
  - 1.See Asplenic
- F. Chronic organ damage
  - 1. Lung
  - 2. Kidney (Chronic Renal Failure)
  - 3 .Liver
  - 4. Skin (Chronic skin ulcers)
- G. Congestive Heart Failure
- H. Eye complications
  - 1. Proliferative retinopathy
  - 2. Retinal Infarcts
  - 3. Retinal Detachment
  - 4. Vitreous Hemorrhage
- I. Jaundice (Unconjugated Hyperbilirubinemia)
- L. Cholelithiasis











IX. Management

- A.Blood Transfusions (up to erythro-exchange)
- B.Nutritional Supplements
  - 1. Folic Acid 1 mg/day
- C.Prophylactic Antibiotics
  - 1. See Asplenic
  - 2. Penicillin V 150 mg bid up to age 3
- D.Pain control for acute crisis
  - 1. Requires aggressive Narcotic Analgesia
  - 2. Consider Patient Controlled Analgesia (PCA Pump)
  - 3. Morphine is preferred over Meperidine (Seizure risk)
- E.Intravenous fluids
- F.Immunizations (In addition to standard CDC)
  - 1. See Asplenic
  - 2. Haemophilus influenzae B Vaccine
  - 3. Pneumococcal Vaccine
  - 4. Hepatitis B Vaccine
- G.Hydroxyurea
  - 1. Increases production of fetal Hemoglobin
  - 2 .Indicated for 3 or more crises per year, over age 18

Severe illness compromising the quality of life

H. Gene therapy ?

Sickle Cell Disease (SCD) still remains a major high-impact health problem in developing countries

ASH 2024 San Diego: >500 abstracts concerning Sickle Cell Disease (SCD)

Prof. Mariane de Montalembert, MD, PhD

- **MD degree** and **PhD in Ethics** at the Paris Descartes Medical School;
- **Specialization** in Pediatrics, Statistics (option clinical research), Red cell diseases (hemoglobinopathies in children), and Transfusion.
- **Paediatrician** at the Necker-Enfants Malades Hòpital in Paris, France since 1985;
- **Responsible** for the Centre for Haemoglobinopathies in Necker-Enfants Malades Hòpital since 1994 (Therapeutic Education Unit for 700 children and families);
- **Responsible** for the French Register of Sickle Cell Disease children treated with hydroxyurea;
- **P.I.** of several researches in clinical pediatrics about Sickle Cell Disease and Thalassaemia;
- **Member** of the French Society of Pediatrics, chairing the Ethic Committee for more than 10 years;
- **Member** of the **French Society of Hematology**, the European Reference Network in rare Haematological Diseases (**EuroBloodNet**), the European Hematology Association (**EHA**), and the American Society of Hematology (**ASH**);
- **Member** of the EHA Board (2020-2024) and **Member** of the Blood Editorial Board (2021-2024);
- **Member** of the Cochrane Commission since 2014.
- **Coordinator** of the EHA Topic in Focus group on hemoglobinopathies since 2023;
- **Teaching activity** for the European School of Hematology (**ESH**) and **online course in French** covering the care of adults and children with sickle cell disease (70 hours) and offering validated training in therapeutic education (40 hours). Around **300 healthcare professionals** from France, Africa and the French West Indies have taken this course and graduated from the University of Paris.

Current affiliation: Department of General Pediatrics and Pediatric Infectious Diseases, Sickle Cell Center, Necker-Enfants Malades Hospital, Assistance Publique – Hôpitaux de Paris (AP-HP), Université Paris Cité, Paris, France, and Laboratory of Excellence GR-Ex, Paris, France.

Prof. Mariane de Montalembert

Lecture on «Sickle Cell Disease»