Haemoglobinopthies in Obstetric ICU

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Inherited Hemoglobinopathies – Three groups

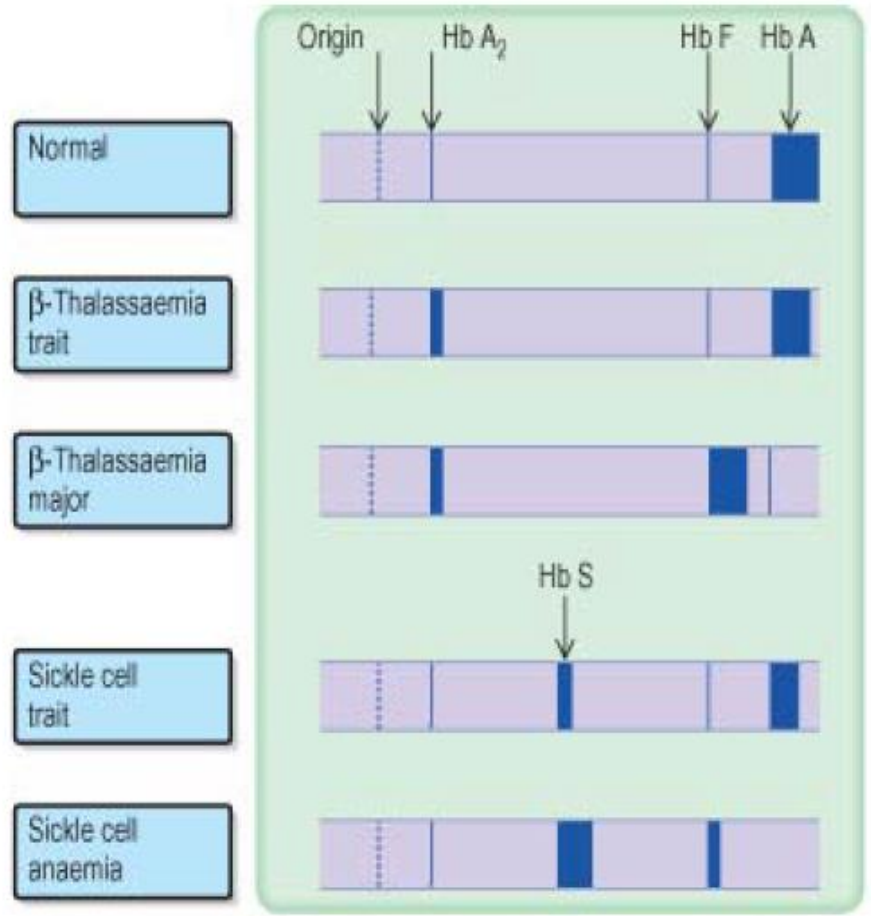
Structural haemoglobin variants

Thalassemia syndromes - reduced rate of synthesis of globin chains

condition in which fetal hemoglobin synthesis persists beyond the neonatal period - hereditary persistence of fetal hemoglobin

Screening tests for haemoglobinopathies

- Haemoglobin electrophoresis
- High-performance liquid chromatography (HPLC) – HbF , Hb A2
- Detection of other variant HbS



Screening

- Late carrier detection can lead to adverse outcomes in offspring.
- Ideally, haemoglobinopathy screening would occur preconception or in the first 10 weeks of gestation in high-risk couples to enable completion of laboratory assays, genetic counselling and DNA testing, with the option of pregnancy termination before 12 weeks gestation where acceptable.

Complications of thalassemia in pregnancy

- Thalassemia in combination with gestational anemia (secondary to increased fluid compartment of the body) account partly for different complications of the thalassemic pregnancy, such as:
  - fetal intrauterine growth restriction (IUGR) and
  - preterm labor.
- Most centres transfuse pregnant women aiming to maintain hemoglobin at the preconception goal (10 g/dL) to ensure appropriate fetal growth.
- Despite following this approach, IUGR may be present, suggesting the role of other fetoplacental and maternal factors, while transfusion-acquired red-cell antibodies should be checked prior to pregnancy.

Thalassemia - postpartum stage Complications

- Thalassaemic patients have a chronic hypercoagulable state, with an increased incidence of thromboembolic episodes.
- The mechanisms for this include:
  - the presence of abnormal red cells that shed prothombotic microvesicles,
  - a variety of changes in platelet function,
  - elevated levels of endothelial adhesion proteins,
  - elevated levels of plasma coagulation factors, and
  - low plasma levels of the natural anticoagulants, protein C and protein S and heparin co-factor II.
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Venous thromboembolism in thalassemia

- Those who have had a splenectomy have a further increase in their risk of thrombosis
- Venous thromboembolism is more frequent in patients with associated organ dysfunction such as diabetes, cardiopulmonary abnormalities, hypothyroidism, and liver function anomalies.
- Many of these effects can be partially abrogated by hypertransfusion which will suppress endogenous red cell production.
- Thus unless there is a history of venous thromboembolism or additional risk factors such as antiphospholid syndrome, heparin thromboprophylaxis is not routinely used during pregnancy in women with thalassaemia major, although it is routine practice to recommend subcutaneous heparin for 6 weeks post delivery.

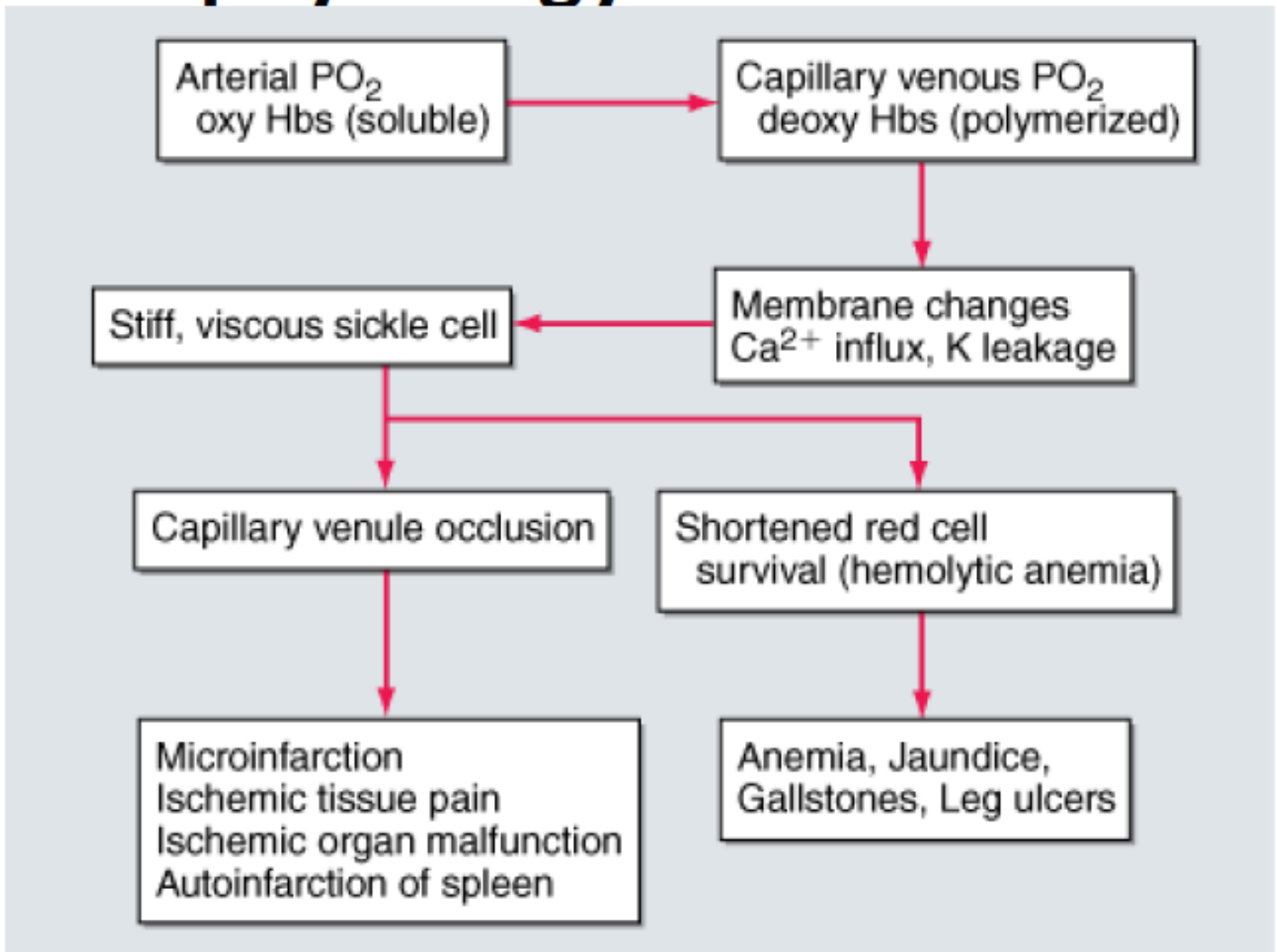
Thromboprophylaxis

- Low- molecular-weight heparin prophylaxis should be administered in hospital followed by a 7-day post discharge regimen after vaginal delivery or a 6-week regimen after CS

SCD in pregnancy

- The term sickle cell disease (SCD) or disorder refers to a group of conditions caused:
  - by the autosomal recessive inheritance of the ‘sickle’ gene which is a result of a point mutation on the gene encoding the B-globin chain in haemoglobin to produce sickle haemoglobin (HbS).
- SCD includes:
  - homozygous HbS disease (HbSS or sickle cell anaemia)
  - compound heterozygotes combining HbS with other abnormal haemoglobins such as HbC causing HbSC disease
  - HbS with B-thalassaemia causing HbSBþthalassaemia disease or HbSB0thalassaemia disease and with other rarer haemoglobins such as HbD, and HbO-Arab

Pathophysiology of sickle cell crisis



Pregnancy with SCD – High risk

- Pregnancy in women with SCD has long been identified as high risk with medical and pregnancy related risks being more common compared to women without SCD.

Sickle Cell Trait in Labour

- Blood to be obtained for full blood count (CBC) and cross-match of 4 units of blood
- Ensure good hydration and oxygenation during labour and postpartum to prevent sickle cell crisis

- Request cord blood, neonatal haemoglobinopathy screening of the newborn
- Monitor for sickle cell crisis or infection

Indications for Blood Transfusion in Sickle Cell Disease during Pregnancy and the Postpartum Period

- Exchange transfusion - the aim is to reduce haemoglobin HbS to 30% or less, followed by top up ''Hyper-transfusion'' to maintain sickle cell disease haemoglobin (Hb S) at 50% or less.

Management of Sickle Cell Crisis

- In the event of a sickle cell crisis the following should be adhered to:
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    - Rehydrate with IV saline, unless the patient has an adequate oral intake (4 litres/24 hours + IV for an average adult) and maintain a fluid chart
    - Monitor oxygen saturation levels (pO2) with pulse oxymetry and with arterial blood gases when indicated by symptoms and signs of anoxia as in chest infection and/or chest syndrome (sickling in the lungs)
    - urgent red cell exchange
    - Do not transfuse without discussion with a Haematology Consultant unless the haemoglobin (Hb) <6g/dl or more than 2 - 3g/dl below usual level

Management of crises…

- Cross match three units of blood for emergency use (Sickle cell disease patients frequently have red cell antibodies and are difficult to cross match)
- Ensure good hydration and oxygenation during labour and postpartum
- Request cord blood/neonatal haemoglobinopathy screen of the newborn.

- Patients with SCD should be considered for low-dose aspirin 75 mg once daily from 12 weeks of gestation in an effort to reduce the risk of developing pre-eclampsia
- Patients with SCD should be considered for prophylactic low-molecular-weight heparin during antenatal hospital admissions.

Roles for transfusion in SCD and pregnancy

- continuation of a transfusion programme for those managed that way prior to pregnancy
- consideration of prophylactic transfusions in those with severe disease prior to pregnancy
- those with a twin pregnancy (with an expected higher complication rate)
- Those who need an emergency transfusion for the management of an acute severe crisis usually go on to have regular transfusions for the rest of the pregnancy

Possible complications of blood transfusions

- Formation of atypical red cell antibodies
- Transmission of infection
- Iron overload
- Paradoxically, blood transfusion may provoke an acute sickling episode, or a hyperhaemolysis syndrome.

Key message

Haemoglobinopthy in pregnancy is high risk	Detection of Haemoglobinopathies in pregnancy may be challenging	Role of transfusion- to maintain Hb between 8-9g/dl	Need to maintain optimum Hct and HbS concentration in HbSS
Risks of transfusion - Development of alloantibodies, TTI	Role of antibody screening and extended red cell phenotype matched blood for transfusion	Measures for prevention of Sickle cell crises	Role of antenatal screening and prenatal diagnosis