

# Development of hematopoiesis

- Yolk sac – extraembryonic production of primitive nuclear erythroblasts from 16.-20. day, production of embryonic hemoglobin (Gower 1, Gower 1 and Portland 1)
- Hepatolienal period – from 6. week in the liver, from 12. week in spleen, production of fetal hemoglobin HbF (it has higher affinity to oxygen), except erythroblasts also production of thrombocytes and granulocytes, lymphocytes from 6. week in thymus
- Bone marrow period – from 20.week – production of all three blood lines, production of adult types of hemoglobin Hb A and HB A2
- Erythropoiesis is stimulated by erythropoietin, production of EPO firstly in the liver, from 30. week in kidneys

# Status and changes at birth

- Values of hemoglobin first day of life – 145-220 g/l, then decrease, at the same time retreat of physiologic macrocytosis (MCV 95-121 fl) in newborns (premature newborns)
- In newborns - dominance of HbF (60-95%), then gradual decrease, at the end of first year approximately 1%, shortly after the 1. year they reach adult values – HbA 97%, HbA2 1,5-3,2%, HbF not more than 0,5%
- Values of leukocytes 1. day of life –  $9,0 - 30,0 \times 10^9/l$ , then decrease
  - in neonates up to day 5 neutrophil predominance, from day 5 to 5 years lymphocyte predominance, then granulocytes predominance again
- Values of thrombocytes are of adult values immediately after birth

# Erythropoiesis of newborn

- Causes of physiologic anemia of newborns
  - decrease of the erythropoietin level because of increased oxygen tension, which is related to spontaneous ventilation and closure of ductus arteriosus
  - Shortened erythrocyte survival with HbF, physiological hyperbilirubinemia
- The lowest values of hemoglobin in healthy mature newborn between 2.-3.month (the lower limit of normal value is 90g/l), decrease of Hb in premature newborns is earlier and deeper
- In case of Rh or ABO incompatibility – hemolytic anemia with unconjugated hyperbilirubinemia – if escalated, risk of kernicterus

# Development of coagulation parameters

- Thrombocytes start to appear in embryo from 11. week of gestation, in 30. week they are at adult values
- Production of coagulation parameters starts at 10.-11. week of gestation
- In mature newborn:
  - Lower values of vit. K dependent coagulation factors ( F II, VII, IX, X)
  - Lower values of F XI and XII too
  - F I, V, VIII and XIII are at adult values, vWF is increased
  - Low values of inhibitors of coagulation (Antithrombin, protein C and S), plasminogen
- > **newborns are in danger of bleeding as well as thrombotic complications**

# Hematooncology in pediatry

- Most common diseases: acute leukemias (app. 30% tumors in children) – 80% ALL, 15 AML, CML, MDS rarely
- Metastatic tumors of children age: neuroblastoma, Ewing sarkoma, rhabdomyosarkoma, meduloblastoma, Hodgkins lymphoma

# Hemorrhagic diathesis in children

- ITP – idiopathic thrombocytopenic purpura (mostly children from 2 to 4 years), above 10 years mostly chronic form of ITP, in 1 year old children often in combination with autoimmune disease, often positive anamnesis of viral infection before development of ITP (2-3 weeks before first signs) – development of bleeding complications from full health - petechias, hematomas, mucous and GIT bleeding, CNS bleeding (to 1%)
- NATP (neonatal alloimmune thrombocytopenia) – decrease of thrombocyte count because of autoimmune reaction – mother's immune system destroys thrombocytes of its own fetus – reaction to father's antigens, this can be caused by fetomaternal transfusion or bleeding during birth - connected with abnormally increased risk of bleeding when compared with ITP !
- Thrombotic thrombocytopenic purpura in children – rarely
- - mostly hemolytic-uremic syndrome or other types of microangiopathic autoimmune hemolytic anemias

# Hemorrhagic diathesis in children

- Signs of hemophilia – in case of severe forms in newborns by bleeding from umbilical cord or CNS bleeding, otherwise during teeth growth, often in case of first motoric activity of children, after trauma and during operations
- vWD
- Coagulopathies (such as DIC, etc...) have similar pathophysiology when compared with adults, but children have smaller amount of blood, so we have to manage these conditions quickly as we have not much time. Not only search for diagnosis, but treat it immediately.