Anemia in the newborn

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Normal blood counts

Age	Hbg(g/l)	MCV(fl)
1st day	170-190g/l	119
1st month	140	105
2nd-3rd m	110	95
6th m. – 2nd y	125	77
14th – 18th y	B: 150 G:140	87

Newborn

- relative polycythaemia
- macrocytosis
- reticulocytes 3%, (later up to 1%)
    - immature erythrocyte but functional, mature in 3 days
- erythrocyte: half-life 120 days

Platelets

Regardless of age:

- 140 - 400x109 / l
- Volume 7 - 11fl
- Life span 7-10 days

Anemia in the newborn

- The newborn is pale
- blood count: reduced Hbg more than 2 SD under physiologic value for that age

definition – newborn over 34 GW aged 0-28 days:

- venous Hbg below 130 g/l
- capillary Hbg under 145 g/l

Physiological anemia of the newborn

- in full-term - physiological fall between 4th to 12th week
- Hbg to 95 - 110g / l
- the cause is a decrease in EPO production due to increased saturation of O_2 in the blood

Pathophysiology

- 3 main reasons:
- increased losses – **hemorrhagic anemia**
- increased destruction of ery – **hemolytic anemia**
- insufficient creation of ery – **hypoplastic anemia**

- the development of symptoms depends on the speed of anemia progression

Hemorrhagic anemia 1

- antepartal (1/1000 births)

- placental abnormality
- abruption, praevia, traumatic AMC
- anomaly of the umbilicus
- knots, hematoma

Hemorrhagic anemia 2

Twin to twin transfusion

- only in monozygous multiple pregnancies, 13-33%
- the difference in Hbg is usually more than 50 g/l
- anemic twin - hydrops fetus
- plethoric twin - hyperviscosity syndrome

Hemorrhagic anemia 3

Intrapartum

- fetomaternal bleeding (preeclampsia, s.c.)
- S.C., especially acute
- umbilical traumatic rupture
- perinatal trauma - bleeding intracranial, visceral

Hemorrhagic anemia 4

postpartum

- birth trauma
  - Bleeding intracranial, visceral, caput succedaneum, cephalhematoma, subgaleal bleeding
- hemostasis disorders
  - congenital deficiency of coagulation factors
  - consumptive coagulopathy: DIC, sepsis

Hemorrhagic anemia 5

Hemostasis disorders

- **Deficiency K vitamin-dependent factors II, VII, IX, X**
  - vit. K administration within 6 hours after birth
  - Early form of hemorrhagic disease - bleeding in 3rd-4th. days
- **Thrombocytopenia: Immune or congenital**
- **Iatrogenic anemia**
  - Blood samples - average 0.8 - 3ml/kg/day during ICU stay

Symptoms of hemorrhagic anemia

Acute

- pallor without cyanosis or jaundice
- tachypnoea, dyspnoea
- peripheral circulatory disorder (loss of 10%)
- hypovolemic shock (loss 20-25%)
- normocytar normochromatic anemia
- reticulocytosis rises in 2-3 days

Chronic hemorrhagic anemia

- paleness without jaundice or cyanosis, unresponsive to O_2
- minimal dyspnoea
- normal CVP
- microcytary hypochrome anemia
- compensatory reticulocytosis
- hepatomegaly (extramedullary erythropoiesis)
- hydrops fetalis

Hemolytic anemia 1

- **Immune hemolysis**
  - Isoimune
  - ABO, Rh incompatibility
- **Autoimmune** - rare in newborns
- **non-immune**
  - sepsis
  - TORCH sy.

Hemolytic anemia 2

- **Congenital erythrocyte disorders**
  - membrane defects
  - enzymopathies
  - hemoglobinopathies
- **General diseases**
  - Galactosaemia
- **Nutrition deficiency**
  - Vitamin E deficiency

Hereditary spherocytosis 1

- the most common congenital hemolytic. anemia in Central Europe
- 1/5000

- integrity of the ery membrane is impaired for the mutation of some structural protein
- ankyrin, spectrin, protein 3 and 4

Hereditary spherocytosis 2

- the lipid bilayer is not anchored, forming vesicles by passing through sinuses of the spleen.
- Ery loses parts of its membrane - the surface is reduced in proportion to its volume
  - spherocyt
- it decreases its resistance and deformability in splenic sinuses
  - hemolysis

Hereditary spherocytosis 3

- anemia, jaundice, splenomegaly

3 forms:

- **light** - 30% of patients, hemolysis completely compensated by reticulocytosis, no anemia

- **moderate** - 60%, light anemia, occasionally need of RCT

- **severe** - up to 10%, severe anemia, dependence on RCT

Hereditary spherocytosis 4

- In the newborn, severe hyperbilirubinaemia with need of
  - intensive phototherapy
  - exchange transfusion

- generally normal Hbg in newborn - very quickly decreases

Hereditary spherocytosis 5

- frequent need for RCT within 6 months of life
  - The infant can not sufficiently compensate for hemolysis by increasing erythropoesis.
- cholelithiasis - 20 - 60% of patients, even before 10 years.
- transient aplastic crisis
  - Parvovirus B19 infection
  - Duration 10-14 days

Hereditary spherocytosis 6

- positive family history, unconjugated hyperbilirubinemia, splenomegaly, anemia with reticulocytosis, spherocytes in peripheral blood
- **tests**: osmotic resistance, autohemolysis

- **diagnosis is problematic in newborns**:
  - spherocytes are usually lacking
  - family history may be negative in 25%

Hereditary spherocytosis 7

- splenectomy after 5 year of life (partial)
- previously completed vaccinations, pneumococcus and meningococcus
- gallbladder sonography follow - consider contemporary cholecystectomy
- after splenectomy - 2 years of PNC ATB prophylaxis.
    - at each fever, ATB must be immediately applied for high risk of sepsis

Erythrocyte metabolism

- **it determines its shape, structure and functionality**

glucose utilization:

- **90% anaerobic glycolysis** - ATP + 2,3 diphosphoglycerate
  - regulates the affinity of Hbg for oxygen

- **10% aerobic glycolysis** - pentose cycle - reduced glutathione
  - protects Hbg and membranes of erythrocyte from O_2 radicals

Enzymopathy 1

Pyruvate kinase deficiency (anaerobic glycolysis)

- lack of ATP - increased potassium loss - dehydration, stiffness - spleen sequestration
- variable severity - up to lifetime dependence on RCT
- clinical picture:
    - anemia,
    - splenomegaly,
    - severe neonatal hyperbilirubinemia,
    - cholelithiasis,
    - iron overload.

Enzymopathy 2

Glucose 6 phosphate dehydrogenase deficiency (aerobic glycolysis)

- X linked inheritance - more severe in men, Sardinia
- mostly asymptomatic, resistance to severe malaria
- serious neonatal jaundice

Glucose 6 phosphate dehydrogenase deficiency

acute hemolytic crisis

- infection, sulphonamides, antimalarials, raw beans
- within 24-72 hours: hemolysis, icterus, dark urine
- blood smear - "trickled ery" - after removing Heinz bodies in the spleen (denatured hemoglobin)

- In our country as chronic extravascular hemolysis with reticulocytosis, cholelithiasis and splenomegaly

Hemoglobinopathy

defects of hemoglobin synthesis

- a malformation of some of the globin chains - thalassemia
- synthesis of abnormal globin chains - sickle cell anemia

- fetal hemoglobin has 2 alpha and 2 gamma chains - alpha thalassemia also in fetus and newborn
- adult hemoglobin predominates after 2 months - 2 alpha and 2 beta chains

Alpha thalassemia

- deletion of 1 to 4 alpha-globin alleles

- Del. 1 allele - no clinical symptoms
- Del. 2 alleles - talasemia minor - mild anemia
- Del. 3 alleles - heavy hemolytic anemia, unstable Hbg – denatures – Heinz's body
- Del. 4 alleles - severe intrauterine anemia, fetal hydrops - death (Bart Hbg - 4 gamma strands)

Symptoms of hemolytic anemia

first symptom

- jaundice - unconjugated hyperbilirubinemia

- compensatory reticulocytosis
- pallor after 48 hours of life
- tachypnoea, hepatosplenomegaly

Hypoplastic anemia

congenital

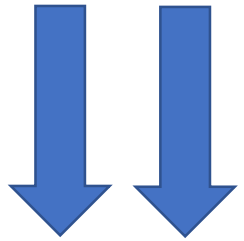
- Diamond-Blackfan sy.
- Congenital leukemia

acquired

- infections: rubella, syphilis
- aplastic crisis, aplastic anemia

Diamond-Blackfan Syndrome 1

- congenital hypoplastic anemia
- already in the newborn age
- proteosynthesis disorder on ribosomes leading to failure of highly proliferating erythropoiesis cells
- 60% of patients have one or more congenital anomalies:



Diamond-Blackfan Syndrome 2

- **craniofacial dysmorphia + small figure,**
- **neck anomaly,**
- **three-inch thumb, malformation of uropoetic tract**

- macrocytary anemia
- reduced number of red blood cells in the bone marrow
  - reticulopenia
  - elevated EPO

- Th: Corticoids

Diamond-Blackfan Syndrome 3

- 1/3 of patients - spontaneous resolution within 10 years, macrocytosis persists
- 1/3 of patients - dependent on corticosteroids, without the need for RCT
- 1/3 of patients does not respond to corticosteroids, life dependence on RCT
  - secondary hemosiderosis

- Th: bone marow transplantation

Diamond-Blackfan Syndrome 4

- as with all congenital dysfunction of the bone marrow, there is an **increased risk of malignancy**
  - leukemia
  - osteosarcoma

Symptoms of hypoplastic anemia

- dull – not significant
- start after 48 hours
- missing jaundice
- reticulocytopenia

Anemia of immaturity 1

- normochromatic, normocytar anemia of preterm babies under 32nd gestational week
- already in 3rd - 10th week of life, Hb 65 - 90g/l
- it may be completely without symptoms
- failure to thrive, of deceleration of growth rate
- a more frequent occurrence of apnoe
- reduction of activity

Anemia of immaturity 2

- tachypnea
- tachycardia
- heart murmur
- severe anemia
    - hypoxia
        - metabolic acidosis

Anemia of immaturity 3

etiology: lack of erythropoetin

- in case of premature babies, it is produced in the liver
  - is less sensitive to hypoxia than kidney
- premature birth does not accelerate EPO creation
- the relationship between the degree of immaturity and the severity of anemia

Anemia of immaturity 4

- less red blood cells at birth, shortened ERY-Hbf survival
- rapid growth - high demands
- alimentary Causes (Fe)
- frequent blood withdrawals
    - 1ml for 1kg baby = 70ml for 70kg adult

Diagnostics 1

- **blood count**
- **Hbg**
- **Blood type, Rh factor**

- **Coombs testing** - positive for auto / isoimmune hemolysis
  - direct
  - indirect

Diagnostics 2

MCV - mean red blood cell volume

- **Microcytes**
  - sideropenia, thalassemia
- **Normocytes**
  - acute hemorrhage, feto-maternal transfusion, isoimmunization
- **Macrocytes**
  - Diamond - Blackfan sy.
  - Vitamin B12 or folic acid deficiency

Diagnostics 3

Reticulocytes

- **normal**
  - acute nlood Loss
- **reduced**
  - hypoplastic anemia
- **increased**
  - hemolytic anemia

Diagnostics 4

Blood smear

Spherocyte: congenital spherocytosis, ABO incompatibility

Pyknocyte: Glucose 6 phosphate dehydrogenase deficiency

Eliptocyte: heredit. eliptocytosis

Schistocyte: consumption coagulopathy

Diagnostics 5

- Apt test, Kleihauer-Betke test , flow cytometry
  - detection of Hbf in the mother during fetal-maternal transfusion

- serum ferritin
  - soluble intracellular Fe supply
  - acute phase reactant - falsely elevated in inflammation, always be investigated with CRP

Diagnostics 5

- soluble transferin receptor
- Fe, transferin
- inflammatory parameters
  - Blood count, CRP, Pct
- serology of TORCH

Diagnostics 6

- bilirubin
- hemocoagulation, occult bleeding
- ultrasound - abdomen, brain
- genetics
- bone marrow sample

Diagnostics 7

- sufficient placental transfusion
  - delayed umbilical cord clamping of 60-240s
- restriction of iatrogenic blood loss
- timely and sufficient supplementation of Fe
  - Ferritin below 300ug / l
- recombinant EPO

Therapy

- red cell transfusion masses - 20 ml / kg
- acute indication - extensive blood loss with the need for immediate replacement
  - transfusion of 0 Rh negative blood crossed with umbilical cord blood
- anemia of immaturity - gradual anemization
- RCT indication based on Htk, Hbg, presence of compensatory reticulocytosis, postnatal age and cardiorespiratory status

Red cell transfusion

- blood resuspension, erythrocyte solution, where the plasma is replaced by an electrolytes
- Htk 55 - 65%, ideally up to 5 days old
- deleukotyzated - reduced risk of transmission of infection
- irradiated - for the risk of graft versus host reaction
  - especially in relational transfusions
- until 1st year of life - CMV negative transfusion
- Kell negative - all children (especially girls) and women of fertile age

RCT risk

- infections: CMV - 30 - 70% seropositive donors
- haemolysis: passively transferred by IGG from mother
- hyperkalaemia: at TREM 20ml/kg for 2-3 hours = low risk
- hypocalcemia: citrate
- hypothermia, hypervolemia
- creation of O_2 radicals

EPO 1

- growth factor responsible for fetal and neonatal erythropoiesis

Synthesis:

- fetus and premature newborn
  - liver
- full-term newborn
  - kidney

EPO 2

Controversial views:

- according to the study, it does not reduce the risk of early RCT until the 3rd week
- reduces the risk of late RCTs after the 3rd week

CONS:

- significantly increases risk of retinopathy

EPO 3

PROS:

- protective effect in brain ischemia
- reduces the risk of BPD
- unclear protective effect on NEC

Fe

- fast growing and dividing cells - hormone secretion, synt. DNA and collagen
- O_2 Carrier, oxygenation and hydroxylation catalysator
- coenzyme of the respiratory chain
- immunity - neutrophyles function
- growth and development of CNS and mental abilities

Deficiency of Fe

Reduced Ferritin

- full term newborn - in 4-6.m.
  - 1 mg / kg / day

- immature - in the 2nd month.
  - 2-4-6mg / kg / day

- supplementation ends with normalization of ferritin and Hbg

Fe supplementation

Maltofer - Fe_3 + as ferric hydroxide

- it is actively absorbed after binding to ferritin and then transported with transferrin
- advantage - less undesirable GIT symptoms than Fe 2+ (Aktiferin)
- administered together with vit. C - improves absorption

Nutritional Supplements

Folic acid

- reducing to tetrahydrofolate - coenzymes for the synthesis of purine and pyrimidine nucleotides
- deficiency affects mainly rapidly dividing cells
- supplementation ends at 40 gestatuional wek

Vitamin B_{12} - only for a proven deficiency