Hereditary coagulopathy

Blood clotting is a process in which the gradual activation of coagulation factors produces thrombin , which converts fibrinogen to fibrin. When the balance of pro- and anti-coagulation factors is disturbed, bleeding or excessive blood clotting may occur.

Congenital bleeding conditions
Hemophilia A and B; Von Willebrand disease.

Congenital thrombophilic conditions

- Leiden mutation ; Prothrombin mutation; Antithrombin deficiency; Protein C deficiency; Protein S deficiency; Hyperhomocysteinemia; Lipoprotein (a) .

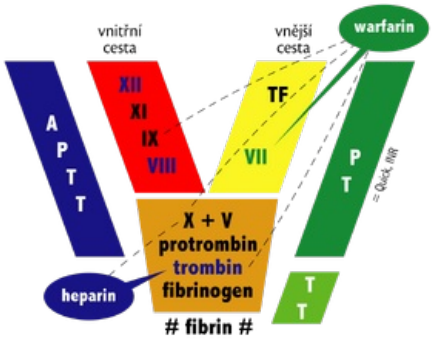
Coagulation in children

Children have a greater **tendency to bleed**. The newborn has low levels of factors II, VII, IX, X and contact factors. A healthy child reaches adult values at 3-6 months of age. Compared to adults, newborns have an increased level of von Willebrand factor and a reduced level of antithrombin, protein C and protein S, and a significantly reduced level of plasminogen.[1]

🔎 *For more information see Hemostasis, Hemocoagulation.*

Examination of coagulation and normal values in children

- Blood count;
- activated partial thromboplastin time (APTT): 28–42 s; ratio: 1–1.5 (1st day of life)...0.8–1.2 (from 1 month);
- Quick prothrombin time (PT): 11–17 s; INR: 1-1.5 (1st day of life)...0.8-1.2 (from 6 months);
- thrombin time (TT): 10–21 s;
- fibrinogen: 1.5-3.5 g/l (0-1 year)...1.54-4.5 g/l (11-16 years)...1.8-3.5 g/l (18 and over);
- antithrombin: 40-90% (neonate)...80-140% (infant-preschooler)...80-120% (18 years and older);
- D-dimers : < 500 ng/ml;
- proof of activation of the coagulation system (protamine sulfate test, ethanol gelation test).[1]

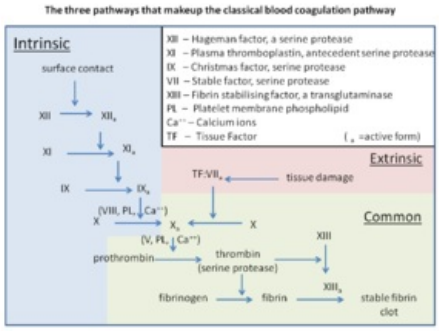


Coagulation scheme.

🔎 *For more information see Examination of blood coagulation.*

Congenital bleeding conditions

Severe bleeding on the basis of congenital coagulopathy is most often caused by hemophilia in children. There are most patients with von Willebrand's disease in the population, but a large part of them do not have significant bleeding manifestations. Other congenital coagulopathies are rare.



Classical blood coagulation pathway.

Hemophilia A and B

- Congenital deficiency of FVIII (A) and FIX (B); variously severe deficit (mild–severe);
- inheritance gonosomally recessive, X-linked; most often a newly arisen mutation;
- frequency: 1/5000 boys;
- hemophilia A is 5x more common than hemophilia B; the same clinical picture;
- **pathophysiology**: FVIII/FIX deficiency leads to impaired coagulase formation (impaired activation of FX, which is key in the conversion of fibrinogen to fibrin);
- **clinical picture**: severe bleeding according to the degree of deficiency (bleeding in case of serious injury → spontaneous bleeding in joints, muscles, bleeding even in case of minimal injury – intracranial bleeding in newborns, extensive cephalhematoma , bleeding from the navel); bleeding into the joints → synovial hypertrophy, destruction of joint cartilage, pain, limitation of mobility ("hemophilic arthropathy"); there is no excessive bleeding from small cuts and abrasions (primary hemostasis is normal);
- **laboratory examination**: prolonged APTT; other parameters in the norm; reduced level of FVIII or FIX; DNA analysis; examination of the level of vWF and the level of FVIII and FIX inhibitors;
- **therapy**: substitution of the missing factor with concentrates; in mild form of hemophilia A – desmopressin acetate; dispensary in hematology centers;
- half-life of FVIII is 8–12 hours; the half-life of FIX is 20–24 hours; frozen plasma is low in FVIII and FIX;

- **complications**: development of an inhibitor against FVIII or FIX as a result of substitution treatment;
- do not use acetylsalicylic acid and nonsteroidal antirheumatic drugs.[1][2]

🔎 *For more information see Hemophilia.*

Von Willebrand disease

- The most common congenital bleeding disorder (1-3% of the population); the acquired form also rarely occurs;
- deficiency or dysfunction of the von Willebrand factor (vWF) - i.e. quantitative or qualitative disorder;
- **pathophysiology**: vWF is formed in vascular endothelium and megakaryocytes; vWF is a glycoprotein that binds to glycoprotein Ib and IIb/IIIa of blood platelets, thereby stimulating their aggregation and adhesion to the damaged vessel wall; vWF is a carrier and stabilizer of FVIII;
- **clinical picture**: variable bleeding manifestations; often asymptomatic; the most common manifestations are epistaxis, noticeable formation of hematomas , bleeding after an injury in the mouth; heavy menstrual bleeding;
- **laboratory examination**: APTT prolonged and normal; examination of the level of FVIII and vWF, its antigen (vWF Ag) and functional activity (vWF RCo), examination of ristocetin-induced platelet aggregation (RIPA) and analysis of vWF multimers; genetic tests;
- **therapy**: mild forms do not require treatment; severe bleeding – antifibrinolytics, desmopressin acetate (increases the level of FVIII/vWF), substitution with plasma concentrate; dispensary in hematology centers.[1]
  🔎 *For more information see Von Willebrand disease.*

Congenital thrombophilic conditions

Virchow's triad contributes to thrombosis: 1. damage to the vascular endothelium, 2. slowing of blood flow, 3. imbalance in the blood clotting system.

Leiden mutation

- The most common congenital thrombophilic condition (5% of carriers in our population);
- Leiden mutation in factor V gene → resistance to activated protein C;
- AD inheritance; carriers are mostly asymptomatic (they will not experience any thrombosis in their lifetime);
- Significantly increased risk of thrombosis in carriers using hormonal contraception.[1]
  🔎 *For more information see Leiden mutation.*

Prothrombin mutation

- FII; in children, a higher frequency of thrombosis in the CNS area.

Antithrombin deficiency

- Tendency to the development of venous thrombosis, already in adolescents and in young adulthood; homozygous form incompatible with life.

Protein C deficiency

- Heterozygotes – venous thrombosis in childhood; homozygotes – purpura fulminans; treatment: protein C concentrate.

Protein S deficiency

- Venous and arterial thrombosis.

Hyperhomocysteinemia

- Venous thrombosis and CNS thrombosis.

Lipoprotein (a)

- High levels of lipoprotein (a) - a moderate risk factor for venous thrombosis and ischemic stroke.[1]

Links

Related Articles

- Disorders of hemostasis : Bleeding conditions (pediatrics) • Hemorrhagic diatheses (pathology) • Acquired coagulopathy • Thrombocytopathy
- Hemostasis • Haemocoagulation • Examination of blood coagulation • Examination of bleeding

Reference

1. LEBL, J – JANDA, J – POHUNEK, P. *Klinická pediatrie.* 1. edition. Galén, 2012. 698 pp. pp. 556–561. ISBN 978-80-7262-772-1.
2. MUNTAU, Ania Carolina. *Pediatrie.* 4. edition. Praha : Grada, 2009. pp. 254-256. ISBN 978-80-247-2525-3.