Hemophilia A, Hemophilia B

Clotting-Guide
vom Labor zur Diagnose

Description:

Hemophilia A is a genetic disease characterized by a deficiency of factor VIII. In hemophilia B, factor IX is missing. Since the genes for both factors are located on the X chromosome, only men are affected by hemophilia. In women, a sufficient amount of clotting factor VIII (or IX) can be produced on the healthy X chromosome, so they have no (or only a mild) risk of bleeding. However, they can pass the mutated X-chromosome to their children. Statistically, half of the daughters of carriers are also carriers of hemophilia, depending on whether they inherit the healthy or mutated X chromosome. Likewise, half of the sons of carriers will be affected by hemophilia. Women with mutations on both X chromosomes are extremely rare. There is not always a positive family history; mutations in the factor VIII or IX genes can also occur spontaneously. Hemophilia is rare; out of 100,000 men, around 12.8 have hemophilia A and around 2.7 have hemophilia B.

The risk of bleeding in hemophiliacs depends on the severity of the factor deficiency, but also on individual characteristics and lifestyle. Typical bleeding events primarily affect the large joints and muscles (due to mechanical stress) and can occur spontaneously. If left untreated, such bleeding causes pain and progressive joint damage and even severe deformities. Severe, life-threatening bleeding can also occur after surgery or injury.

In addition to hemophilia A and B, other genetic factor deficiencies are also known, but these are not inherited on an X-chomosome and can therefore affect both sexes. Hemophilia C refers to a factor XI deficiency; factor V deficiency was previously referred to as parahemophilia. Depending on the deficient clotting factor and its residual activity, different bleeding phenotypes can occur.

Treatment options:

All hemophiliacs should receive prophylactic therapy from early childhood on to prevent bleeding. Additional treatment is required for planned operations or injuries.

The missing coagulation factor can be supplied by injecting factor concentrates, produced recombinantly or extracted from plasma. The half-life of some preparations can be significantly extended through modifications. Therefore, patients only need to inject the factor concentrate twice a week (for hemophilia A) or every 2 weeks (for hemophilia B) in order to be largely protected against bleeding.

However, up to 30% of all patients with severe hemophilia can develop alloantibodies against the coagulation factor (which is “foreign” to the patient's immune system) within the first 50 days of exposure (hemophilic with inhibitor). Such patients can no more be treated with the factor concentrate, they require bypassing therapy, e.g. recombinant activated human factor VII (Novoseven®) or activated prothrombin complex concentrates (FEIBA®) in order to achieve sufficient hemostasis. Immune tolerance induction therapy (high-dose administration of factor concentrates for several months) can be used to try to achieve immune tolerance.

Modern forms of treatment with therapeutic antibodies can also be administered subcutaneously, e.g. emicizumab (Hemlibra®) every 1-4 weeks sc.

Gene therapy for the long-term “cure” of hemophilia A and B has already been used in studies and has been approved in some cases.

The management of patients with hemophilia is complex and requires a lot of experience. Such patients should therefore, if possible, be managed in certified hemophilia treatment centers in cooperation with pediatrics, internal medicine, orthopedics and physiotherapy.

Surveillance:
Determination of factor VIII or factor IX levels with the appropriate test systems and at the appropriate time. Target areas depending on the indication (usually trough levels >50% for operations or bleeding, >5% for prophylaxis)

References:
Thomas L, Laboratory and Diagnosis, 2023, Release 5: https://www.labor-und-diagnose.de/index.html
Parameter catalog of the Clinical Institute for Laboratory Medicine, Med.Univ.Wien and AKH Vienna: https://www.akhwien.at/default.aspx?pid=3982
List of services for clinical chemistry, Univ.Klinikum Ulm: https://www.uniklinik-ulm.de/zentrale-einrichtung-klinische-chemie/leistungskatalog.html