

Haemophilia A and B

Transmission of haemophilia

The human cell possesses a double set of chromosomes one of which is contributed by the father's germ cell and the other by the mother's germ cell. A chromosome pair is defined as a sex chromosome pair whereby females have two X chromosomes (homozygous), whilst males have one X and one Y chromosome (heterozygous).

The genes for the coagulation factors VIII and IX are located on the X chromosome. For this reason, it is almost always the male offspring who are affected by the disease because they are heterozygous in terms of their sex chromosomes (XY). Female offspring almost always have a healthy X chromosome and can therefore compensate for a defective allele on their second X chromosome. In this case they are known as carriers. The figures summarise the two classic patterns of transmission.

Fig. 1: Pattern of transmission with a haemophilia allele in the mother

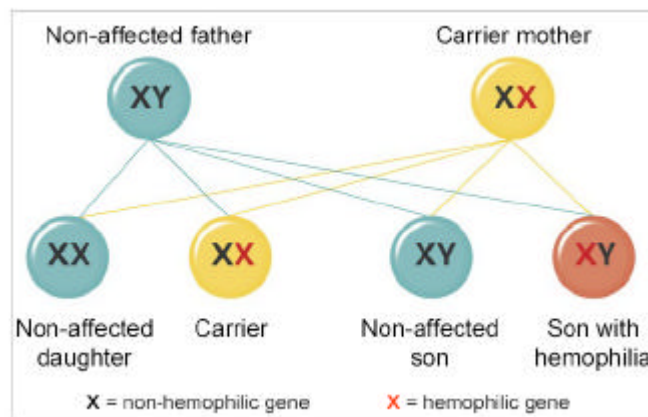
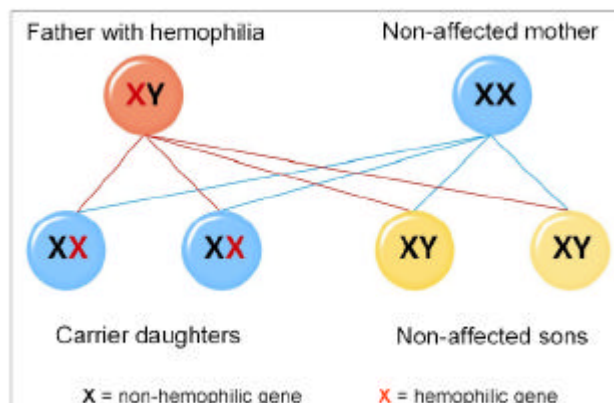


Fig. 2: Pattern of transmission with a haemophilia allele in the father



About 70 percent of haemophilia is passed on according to this pattern of inheritance. The remaining 30 percent of all cases of haemophilia are new mutations.

Severity of haemophilia A and B

The severity of the haemophilia is dependent on the quantity of residual factor in the bloodstream. This is expressed as a percentage of the *normal activity (100 percent)* or as a quantity in International Units (IU) per millilitre (ml) of blood. Within the normal range, activity values range between 50 and 150 percent.

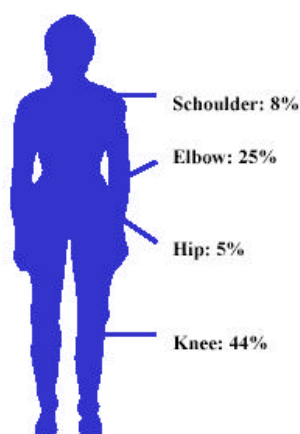
Table 1: Severity of haemophilia A and B

Severity of haemophilia	Residual activity of FVIII/FIX (%)	I.U. per ml plasma	Severity of bleedings
severe	< 1	< 0.01	regular joint and muscle bleedings (to some extent spontaneous bleedings without clear reason)
moderate	1 - 5	0.01 – 0.05	Bleedings after surgery, trauma or tooth extractions
mild	5 - 30	0.05 – 0.3	rare bleedings after surgery or severe trauma

Manifestation of bleeding in haemophilia A and B

Patients with haemophilia A and B are frequently affected by bleeding into the muscles and joints. Spontaneous bleeding can occur without a clear cause – especially in severe haemophilia. If bleeding into a joint recurs there is a danger of irreversible joint damage with impaired mobility in consequence.

Fig. 3: Frequency of bleeding into a joint in haemophiliacs



Treatment options for haemophilia A and B

For many patients with mild haemophilia A treatment is possible with the synthetic hormone desmopressin (DDAVP, Minirin[®]). This substance leads to the release of factor VIII from its storage compartments. Bleeds in all other patients must be treated by intravenous replacement of the appropriate coagulation factors VIII or IX. Today, virus-inactivated plasma-derived and recombinant products are used for this purpose (see also: C. Kasper: Registry of Clotting Factor Concentrates 2006; www.wfh.org).

With regard to the type of treatment, one can distinguish between prophylactic treatment and on demand treatment. Prophylaxis with coagulation factor is often used in growing children with severe haemophilia and serves to protect them from joint damage due to recurrent bleeding into the joint. On demand treatment in the event of bleeding is often used in adults instead of prophylaxis. In countries with limited economic resources, prophylaxis tends to be rather rare. The dosage of factor concentrates depends on the localisation and severity of the bleeding.