Symptoms and Syndromes

19 Coagulopathy and haemorrhage

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The leakage of blood from the blood vessels is referred to as **haemorrhage**. Its causes include: (*1.*) increased permeability of the vascular walls, (*2.*) pathological blood vessel condition, and (*3.*) injury to a blood vessel. • Generally, a haemorrhage may become considerably more severe in the presence of **coagulopathy**, i.e. clotting disorder. It is also quite possible for a coagulation defect to arise as a separate disorder even without existing tissue damage.

1 Coagulopathy

1.1 Forms of haemostasis

By means of the complex process of **haemostasis**, the organism seeks to protect itself spontaneously against bleeding and the corresponding loss of blood. • **Three components** are available to this end: (*1.*) blood vessels themselves (= vascular haemostasis), (*2.*) platelets and endothelial cells (= cellular haemostasis), and (*3.*) blood-clotting factors (= plasmic blood coagulation).

1. **Vascular haemostasis** comprises reflex contractions of the arteries, reinforced by the release of vasoconstrictor substances from the vessel walls (e.g. catecholamines, serotonin, thromboxane A_2).

2. The **cellular phase** of the arrest of bleeding commences as so-called **primary haemostasis,** during the course of which thrombocytes, with the aid of von Willebrand's factor, adhere to collagen fragments released from the injured vascular endothelium. The discharge of various factors from the thrombocytes then ensues. The prostaglandin-thromboxane system is directly involved in the subsequent aggregation of thrombocytes.

3. **Plasmic coagulation** is effected by a system of 15 coagulation factors. (s. p. 104) (s. tab. 5.12) So-called **secondary haemostasis** begins with the progressive activation of the plasmic coagulation system. All the coagulation factors involved are proteins and for the most part enzymatic. They are normally present in the plasma in their inactive form, and with the initiation of plasmic coagulation, they become successively activated. The clotting process (= **coagulation**) has the function of converting soluble fibrinogen into stable, insoluble fibrin. *Procoagulation and anticoagulation factors* regulate the process of coagulation.

Exogenous activation is initiated by tissue thromboplastin (= tissue factor) and the activated form of factor XII in the plasma. This complex is enlarged by ionic calcium and platelet factor 3. As a result, the activation of factors IX to IXa and X to Xa is triggered, thus forming a cross-connection between the endogenous and the exogenous system. (s. fig. 19.1)

Endogenous coagulation commences with the activation of factor XII. Factor XIIa then catalyzes the conversion of prokallikrein to kallikrein, plasminogen to plasmin and factor XI to XIa. The presence of factor XV is necessary for the activation of IX to IXa. This creates a complex comprising IXa, VIIIa, calcium and phospholipids, which then activates factor X to Xa. (s. fig. 19.1)

Depending on the causative mechanism, either the exogenous or the endogenous coagulation system is activated. These progress differently until the activation of factor X, which then allows both pathways to merge into a common final phase of coagulation. • At this point, the activation of **prothrombin II** to thrombin by the Xa/Va/calcium/phospholipid complex represents the final step of both coagulation cascades. The prothrombin complex (factors II, VII, IX and X) does not exist as such − it refers to various proteins, the synthesis of which depends on vitamin K. Soluble **fibrinogen** (I) is converted with the aid of thrombin into insoluble *fibrin*, which infiltrates and thereby solidifies the thrombocytic embolus. Thrombin simultaneously activates factor XIII to XIIIa and protein C to protein C_a. The fibrin network is further strengthened by factor XIIIa. The most effective **inhibitors** of coagulation are antithrombin III, α_2-macroglobulin, C_1-inactivator and protein C_a as well as fibrinogen-fibrin degradation products.

1.2 Fibrinolysis

The minor coagulation processes constantly taking place in the vascular system (whereby fibrin is deposited) are counteracted by simultaneous fibrinolysis. *Coagulation and fibrinolysis are thus in continuous dynamic balance.* Plasminogen is converted to plasmin by activators such as urokinase PA (isolated from urine) and tissue PA (isolated from tissue). The effect of tissue PA is strongly enhanced by the presence of fibrin. Fibrinolysis is stimulated by protein C, while plasmin activity is maintained in balance by inhibitors (e.g. α_2-antiplasmin, α_2-macroglobulin). (s. fig. 19.1)

1.3 Vasopathies

Vasopathies may arise from direct injuries to the vessel wall, but also from pathological changes in the vessel wall or in the endothelium. It can be expected that vasopathies will occur or become more severe during the course of various liver diseases or with concomitant coagulopathy.

The most common congenital vasopathy is the **Osler-Rendu-Weber disease** (*haemorrhagic telangiectasia*). It is an autosomally inherited structural defect of the blood vessels with accompanying decrease in muscular and elastic fibres in the capillaries and venules. Multiple telangiectases are most frequently found in the upper body and in the mucous membranes. Severe bleeding may occur from the nasal and pharyngeal passages as well as from the gastrointestinal tract.

The most important acquired vasopathy is the **Schoenlein-Henoch disease** (*anaphylactoid purpura*) due to toxic or allergic inflammatory blood-vessel damage accompanied by immunological reactions. Bleeding may be present in the skin, in the form of petechiae or ecchymoses, or in the gastrointestinal mucosa.

1.4 Thrombocytopathies

Thrombocytopathies may arise in the course of a liver disease and during the measures taken to treat it as well