Platelets

Platelet appearance

Mammalian platelets appear on stained blood films as pale blue granular fragments which are usually considerably smaller than the red cells. They are anuclear. Because of their size they are often overlooked, but it is good practice to assess platelet numbers and morphology routinely on blood smears. Platelets may be seen on several of the colour plates. Avian and reptilian platelets are much larger than mammalian platelets, though still smaller than the red cells, and they are true cells with nuclei

Platelet production (megakaryocytopoiesis)

Like erythropoiesis, this occurs in the bone marrow. From stem cell differentiation to platelet production takes about 3 days. It appears that the megakaryocytes remain in the bone marrow to shed platelets and do not normally enter the circulation.

Circulating platelets

The numbers in circulation vary slightly with species, but are generally around 200 – 400 × 10^9/l. The main exceptions are the horse, where the lower limit of normal is about 90 × 10^9/l, and the goat where numbers as low as 50 × 10^9/l are often found. About half as many again (one-third of the total platelet mass) are stored in the spleen, with constant dynamic exchange between circulating and stored platelets. In splenectomized animals the circulating platelet numbers increase by 50% because the total body stock of platelets remains the same and they are then all in circulation. Platelets survive for about 10 days.

Platelet function

(1) Normal running maintenance of the endothelium. Platelets are essential to maintain capillary endothelial integrity, and it appears that they are constantly being incorporated into the endothelium itself to perform this function. In cases of severe thrombocytopenia (platelet count under 20 × 10^9/l) the endothelium becomes weak and red cells may actually escape through the walls of intact uninjured capillaries. Petechiation, ecchymoses and even spontaneous haemorrhage then result.

(2) Repair of damaged endothelium. It is in this situation that the platelets function as an integral part of the clotting process.

(a) An injury to the endothelium exposes underlying collagen and a single layer of platelets sticks to this (platelets do not normally stick to intact blood vessels).

(b) Upon exposure of platelets to the collagen fibres of the vessel wall, serotonin, histamines and adenosine diphosphate (ADP) are released into the ambient fluid (`platelet release'). The adenosine diphosphate (ADP) causes adherence of the second platelet layer to the first and aggregation of a platelet plug.

(c) The plug retracts to form a mechanically strong patch which seals the hole. In time this is replaced by normal endothelium.

Platelet abnormalities

Thrombocytosis

(Increase in platelet numbers, i.e. platelet count greater than 500×10^9/l)

(1) Reactive. In haemorrhagic cases the consumption of platelets soon leads to an increase in circulating numbers via a feedback effect. Young platelets which are often very large are usually seen on a blood smear.

(2) Splenectomy. In splenectomized patients there is a redistribution into the circulation of the platelet mass normally stored in the spleen.

(3) Megakaryocytic leukaemia.

(4) Drug induced. Vincristine increases platelet shedding from the megakaryocytes and may be used therapeutically for this purpose.

Thrombocytopenia

(Decrease in platelet numbers, i.e. platelet count less than about 200×10^9/l in most species)

(1) Functional. In the early stages of a haemorrhagic condition when demand is great but bone marrow production has not yet responded, a low platelet count will be seen.

(2) Disseminated intravascular coagulation (DIC) or consumption coagulopathy. This is a serious condition which is frequently fatal, and affected animals are invariably obviously systemically ill. The platelets are all used up in massive abnormal intravascular clotting so that few are left in peripheral blood , this may result in secondary haemorrhage. The intravascular coagulation is due to the release of tissue thromboplastin into the circulation and can be brought on by a number of triggering factors. The condition is fortunately quite rare in animals, but it may be associated with such things as persistent septicaemia, incompatible blood transfusion, certain viral infections such as infectious canine hepatitis (ICH), neoplasia, obstetric complications and heat stroke. Treatment is by i/v administration of heparin, in addition to vigorous therapy directed at the underlying disease condition.

(3) Exposure to ionizing radiation.

(4) Drugs, such as chemotherapeutic agents, chloramphenicol, sulfadiazine, estrogen.

(5) Lymphosarcoma, in cases where the bone marrow is so severely infiltrated by neoplastic cells that everything else is crowded out.

(6) Infection e.g. Anaplasma, and other bacterial and viral infections .

Clotting mechanism

Blood coagulation appears as a simple action namely the conversion of a liquid into a solid state. Complicated reactions of various factors functioning in a normal sequence are required to produce clotting.

1- The extrinsic route

- Tissue damage releases a substance, tissue thromboplastin, or factor III, which combines with Ca^{2+} ions and factor VII, plus tissue phospholipids and enzymes from tissue damage, to activate Factor X.
- Factor X is the beginning of the common pathway.

2- The intrinsic route

- Cascade involves factor XII and platelet phospholipids activating Factor XI, which with Ca^{2+} activates factor IX, factor IX combines with factor VIII, Ca^{2+} and platelet phospholipids to activate factor X

- Endothelial release of factor XII -platelet aggregation - changes in the platelet structure.

3- The final common pathway

- Factor X, factor V and phospholipids from the cell membranes of damaged tissue and from platelets together form **prothrombin activator**.
- Prothrombin activator, and Ca^{2+}, convert prothrombin to thrombin
- Thrombin, in the presence of Ca^{2+} and Factor XIII is an enzyme, which converts fibrinogen to fibrin and the clot forms.

The coagulation system which culminates in the formation of a clot in response to a damaged blood vessel must be reversed and the clot removed. This is accomplished by a fibrinolytic enzyme system consisting of the inactive precursor plasminogen (profibrinolysin) and the active component plasmin (fibrinolysin).

Plasmin is a proteolytic enzyme that is active at a neutral pH and is capable of digesting fibrin into a number of soluble fragments. It also has the capacity to digest fibrinogen and to attack a number of other coagulation factors. For protective purposes body fluids contain large amounts of antiplasmin.

<u>Laboratory tests for coagulation</u>:

1. Coagulation time.
2. Bleeding time.
3. Platelet counting and evaluation.
4. Fibrinogen test.
5. One-stage prothrombin test.

<u>Tests for measuring intrinsic system factors</u>:

1. Partial thromboplastin time.
2. Prothrombin consumption.

3. Thromboplastin generation test (TGT).