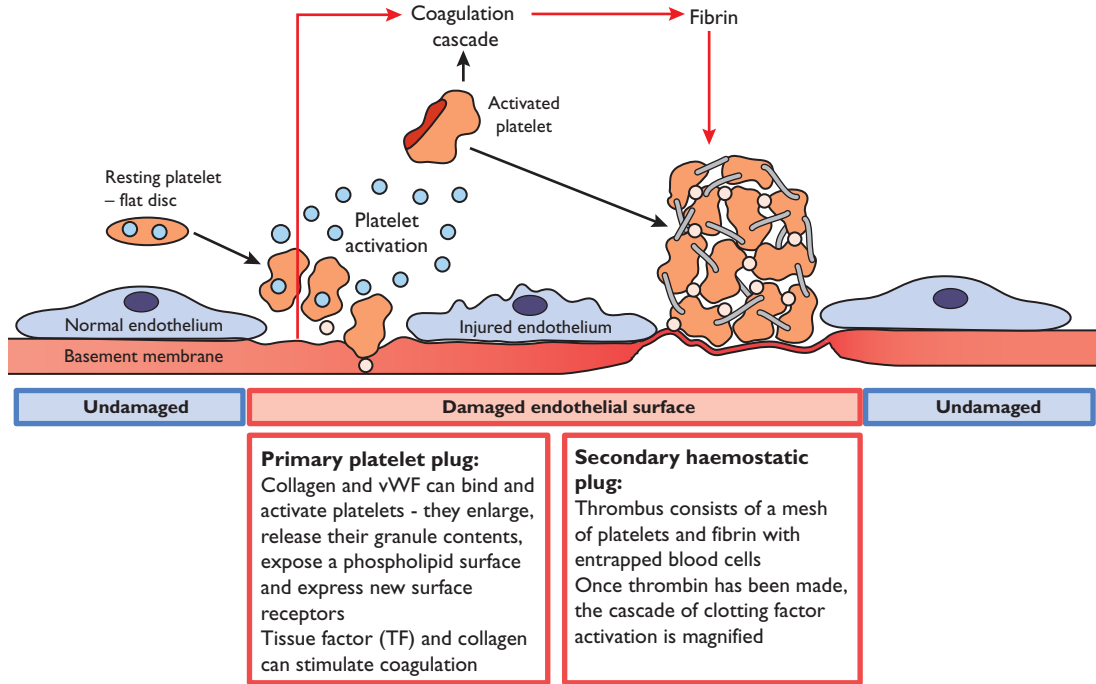


Figure 7.2 Platelet adhesion, activation and aggregation. Platelet aggregates ('primary platelet plugs') can plug small breaches in the endothelium, but serious tears require the addition of a fibrin mesh (generated by the coagulation cascade) to stabilize the platelets and form thrombus while healing takes place



Their role in thrombosis can be divided into three phases (Fig. 7.2):

- adhesion of platelets to vessel wall
- secretion of granules
- aggregation of platelets with platelets.

When the endothelium is damaged and collagen is exposed, the first event is **adhesion** of platelets. This is achieved via platelet surface membrane receptors:

- **gp Ia**, which binds to collagen
- **gp Ib**, which binds to von Willebrand's factor (vWF)
- **gp IIb/IIIa**, which binds to fibrinogen and vWF.

Following adhesion, the platelets release the contents of their granules. There are three main types of granules, the alpha granules, dense granules and lysosomes. The most important secretory products are calcium, which is needed for the coagulation pathway, and adenosine diphosphate (ADP) and thromboxane (TxA₂) which induce platelet aggregation. **Platelet aggregation** involves the gpIIb/IIIa receptor complex mentioned above. This is expressed after activation and is most important in binding fibrinogen which acts as a bridge to the adjacent platelet (Fig. 7.3). Not surprisingly,

there are 'loops' in this process to amplify the reaction. Most importantly, activated platelets express membrane phospholipid (formerly known as platelet factor 3), which stimulates the intrinsic pathway of the coagulation cascade (see below) resulting in the production of thrombin. **Thrombin** acts to stimulate platelets and so enhances the reaction.

The platelet has another important facet to its character; it has mechanical properties. An unstimulated platelet has a disc shape maintained by microtubules and actin and myosin filaments at the periphery. On activation, the platelet is transformed into a sphere with long pseudopods which spread over the damaged surface and then, after aggregation, the internal filaments slide so that the platelet plug contracts to stabilize and anchor it.

The most common cause of defective platelet function is aspirin therapy due to inhibition of cyclooxygenase resulting in impaired thromboxane A₂ synthesis. After a single dose of aspirin, the defect lasts 7–10 days, ie. the life of the platelet.

Coagulation components

The components and pathway involved in coagulation are shown in Fig. 7.3.