Pharmacology

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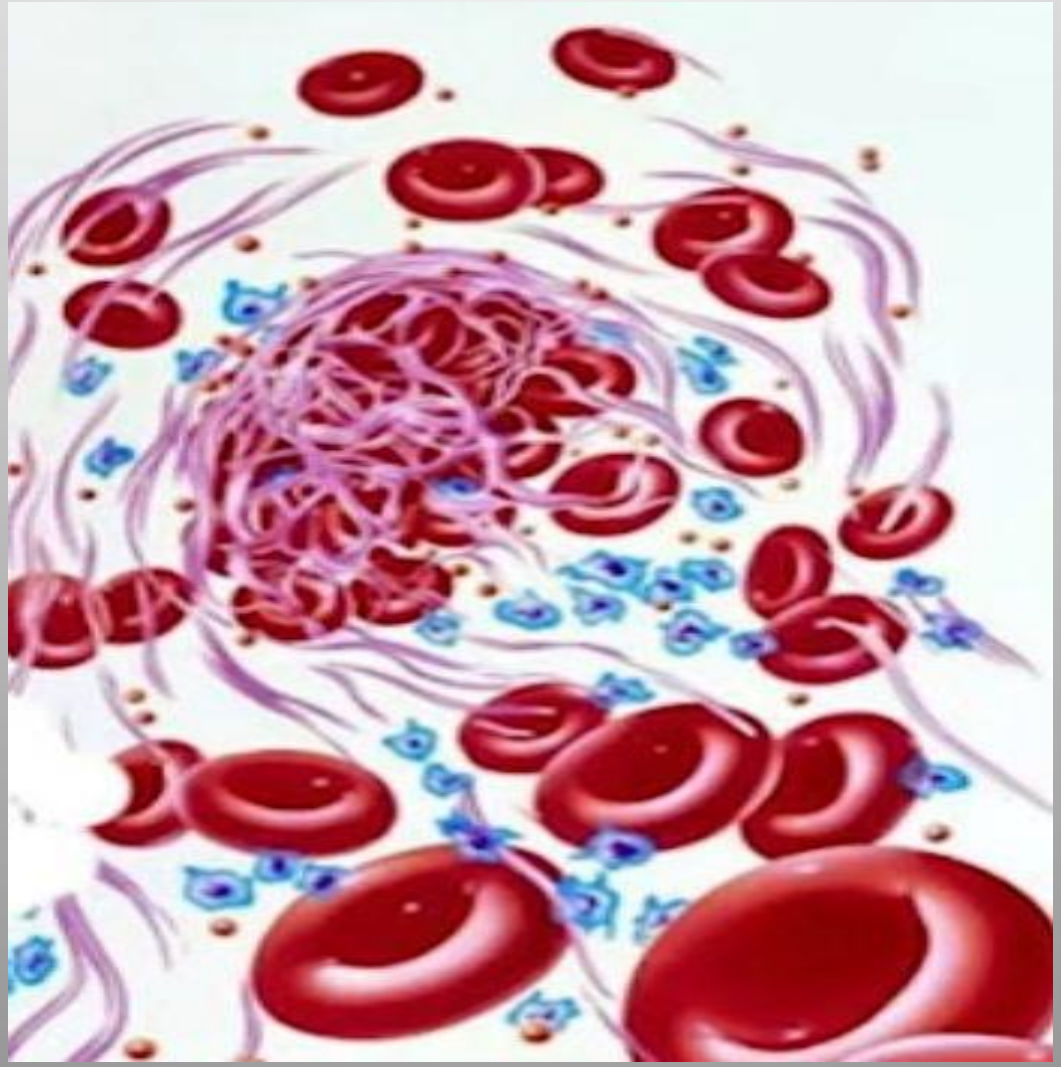
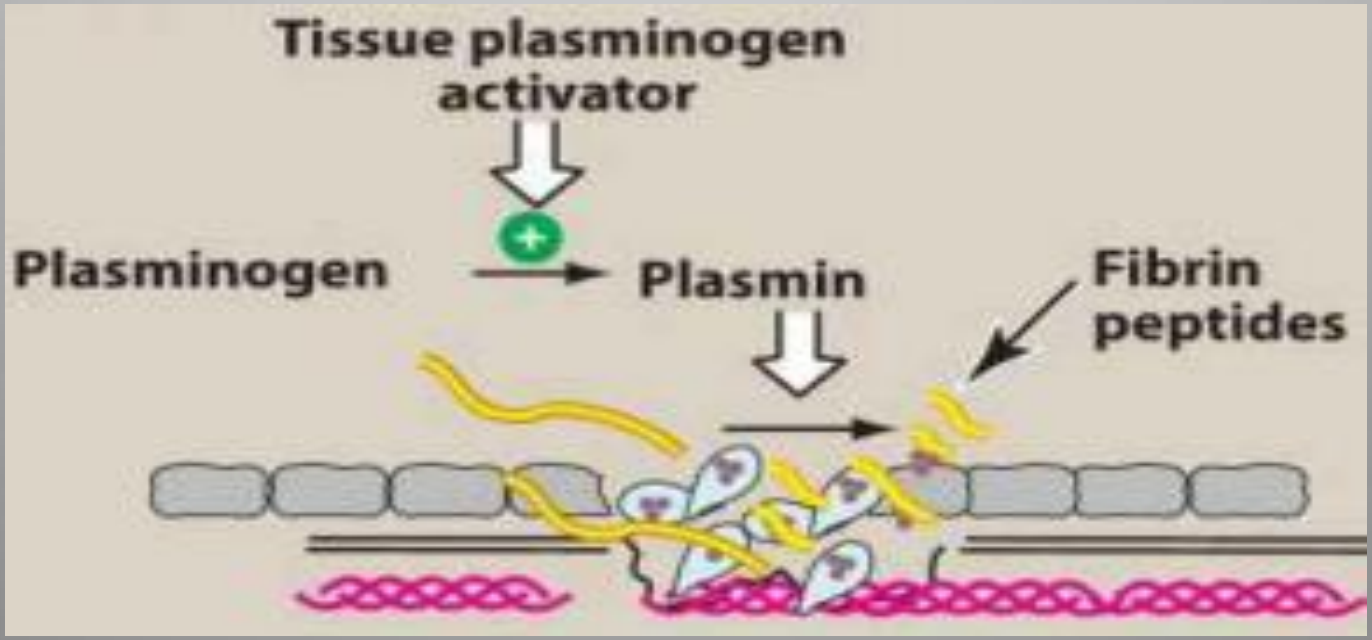
Lab.7

Thrombolytic Drugs

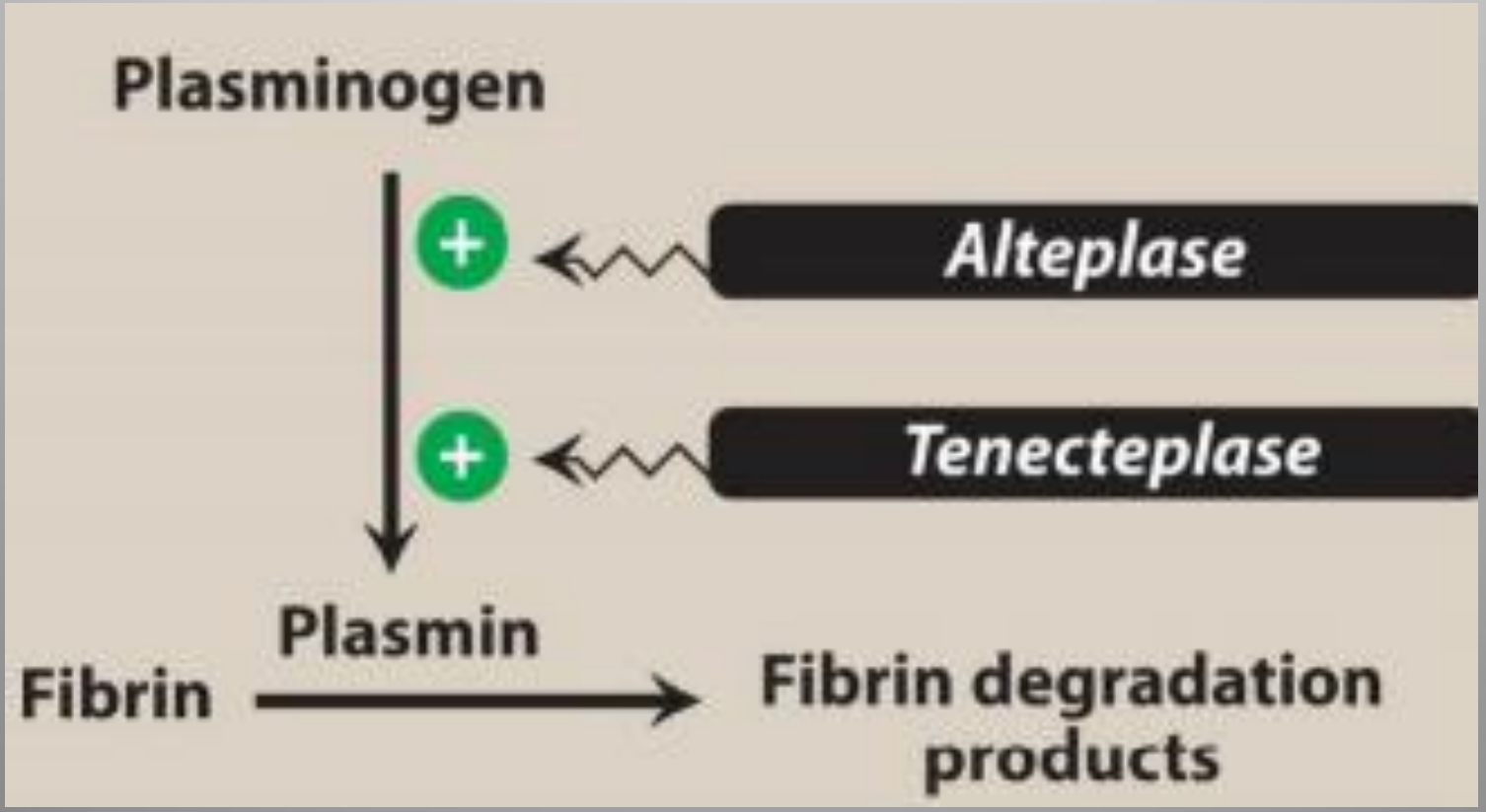


Fibrinolysis:

During clot formation, the fibrinolytic pathway is locally activated. Plasminogen is enzymatically processed to plasmin (fibrinolysin) by plasminogen activators in the tissue. Plasmin limits the growth of the clot and dissolves the fibrin network as wounds heal.

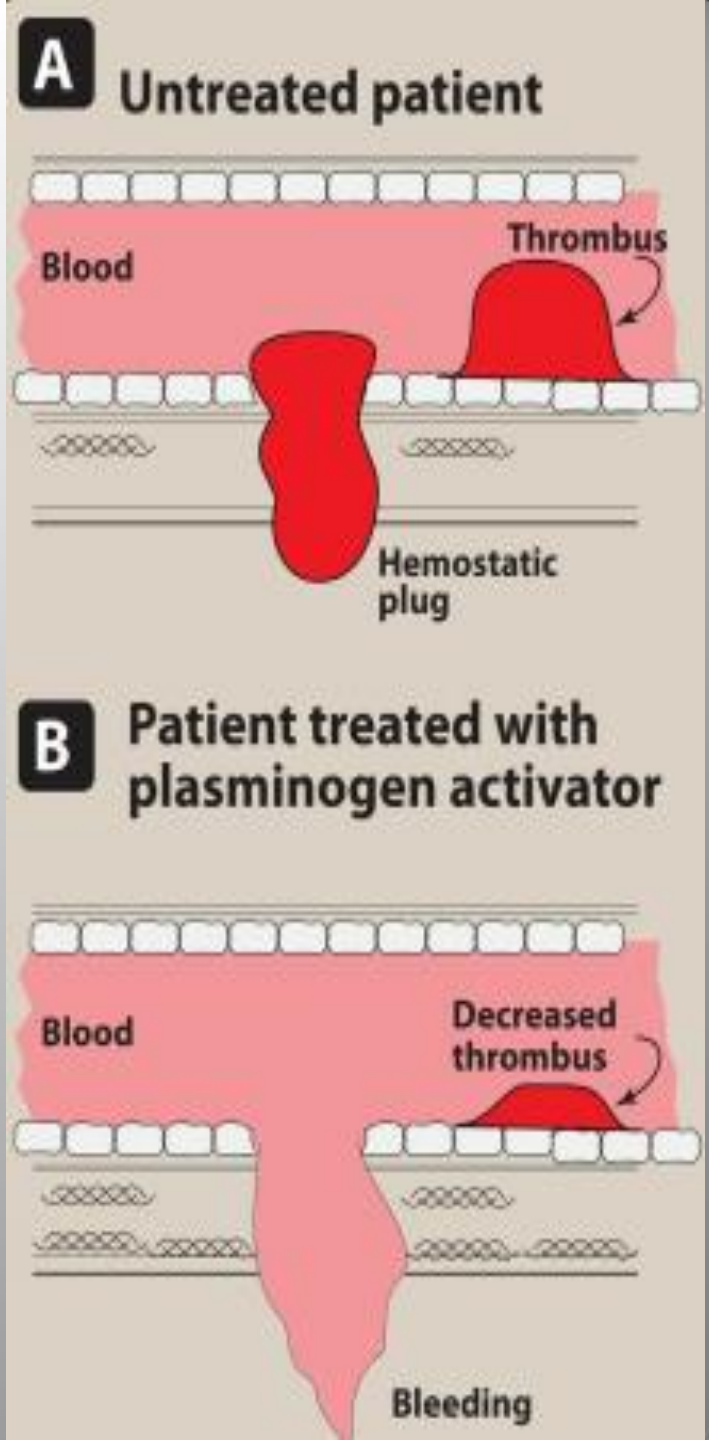


- The thrombolytic agents act either directly or indirectly to convert plasminogen to plasmin, which, in turn, cleaves fibrin, thus lysing thrombi.



- Clot dissolution and reperfusion occur with a higher frequency when therapy is initiated early after clot formation because clots become more resistant to lysis as they age. Unfortunately, increased local thrombi may occur as the clot dissolves, leading to enhanced platelet aggregation and thrombosis.
- Strategies to prevent this include administration of antiplatelet drugs, such as aspirin, or antithrombotics such as heparin.

Thrombolytic agents do not distinguish between the fibrin of an unwanted thrombus and the fibrin of a beneficial hemostatic plug. Thus, hemorrhage is a major adverse effect. For example, a previously unsuspected lesion, such as a gastric ulcer, may hemorrhage following injection of a thrombolytic agent.



- Originally used for the treatment of DVT and serious PE, thrombolytic drugs are currently used less frequently because of tendency to cause serious bleeding. For MI, intracoronary delivery of the drugs is the most reliable in terms of achieving recanalization. Thrombolytic therapy is more effective if they are administered within 6–12 h of onset of symptoms. Thrombolytic agents are usually administered intravenously. Thrombolytic agents are helpful in restoring catheter and shunt function, by lysing clots causing occlusions. They are also used to dissolve clots that result in strokes.

- These drugs are contraindicated in pregnancy and in patients with healing wounds, a history of cerebrovascular accident, brain tumor, head trauma, intracranial bleeding, and metastatic cancer.

- The antidote for the fibrinolytics is aminocaproic acid, a plasmin antagonist.

Alteplase , *reteplase* and *tenecteplase*

Alteplase (formerly known as tissue plasminogen activator or tPA) is originally derived from cultured human melanoma cells. It is now obtained as a product of recombinant DNA technology.

Tenecteplase is recombinant tPA with a longer half-life and greater binding affinity for fibrin than alteplase.

Alteplase has a low affinity for free plasminogen in the plasma, but it rapidly activates plasminogen that is bound to fibrin in a thrombus or a hemostatic plug. Thus, alteplase is said to be “fibrin selective” at low doses.

Alteplase is approved for the treatment of MI, massive PE, and acute ischemic stroke. Tenecteplase is approved only for use in acute MI.

Alteplase has a very short half-life (5 to 30 minutes), and therefore, a portion of the total dose is injected intravenously as a bolus, and the remaining drug is administered over 1 to 3 hours, depending on the indication.

Tenecteplase has a longer half-life and, therefore, may be administered as an intravenous bolus. Alteplase may cause angioedema, and there may be an increased risk of this effect when combined with angiotensin-converting enzyme (ACE) inhibitors.

THANK YOU