Thrombolytics (Fibrinolytics)

1. Streptokinase
2. Urokinase.
3. t-PA (tissue plasminogen activator), alteplase, tenecteplase, reteplase, &.

- Both protective hemostatic thrombi & target pathogenic thromboemboli are broken down.

Circulating fibrinogen will be degraded

→ Bleeding can occur.

However, these drugs differ in their selectivity to plasminogen in clot & circulating plasminogen.

Thrombolytics (Fibrinolytics)

• **<u>Indications</u>:**

• IV for:

-Multiple pulmonary emboli

-Central deep venous thrombosis (eg, superior vena caval syndrome, ascending thrombophlebitis of iliofemoral vein).

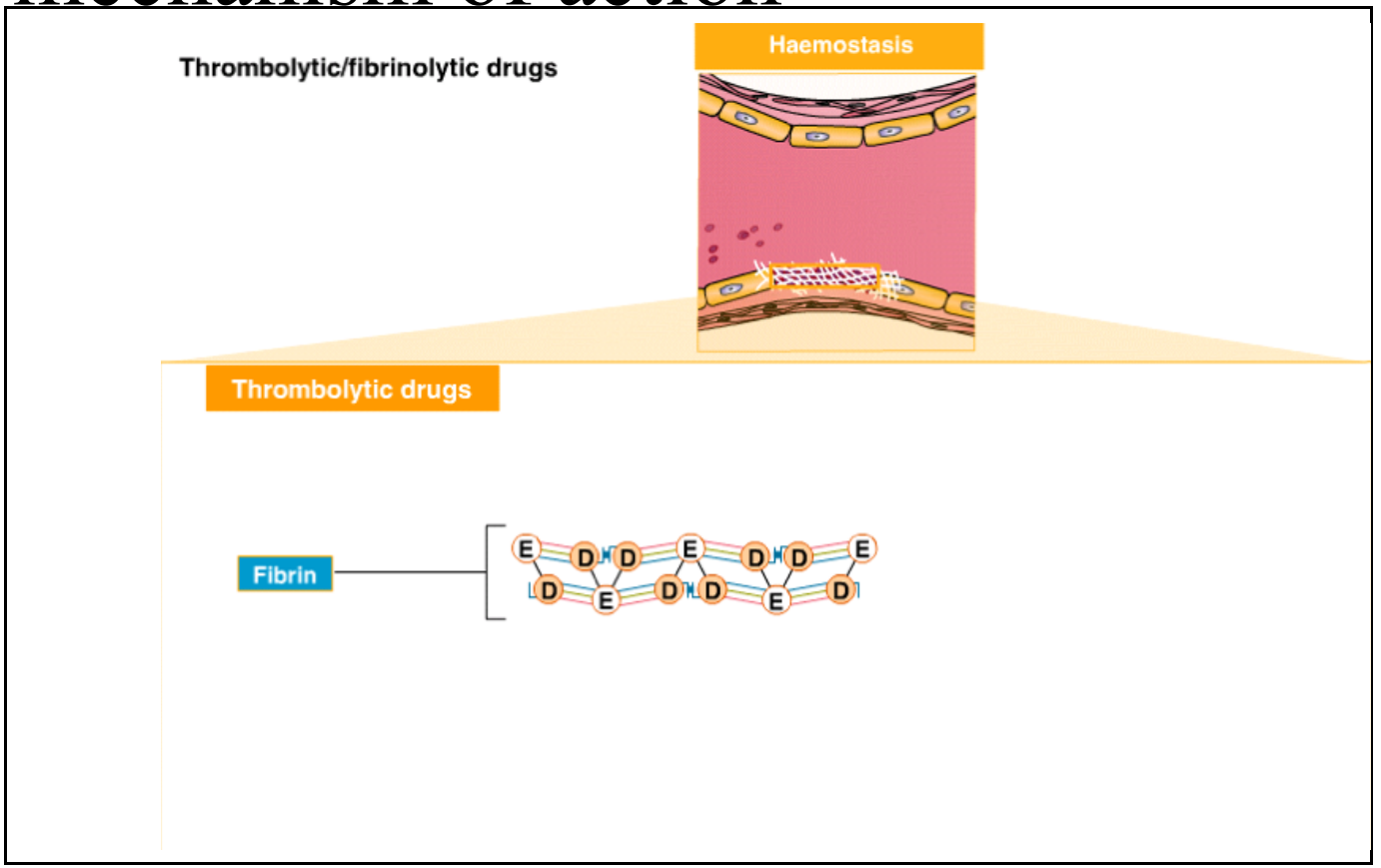
-Acute myocardial infarction

-Acute ischemic stroke: tPA should be used within 3 hours after onset of symptoms.

• Intra-arterially for:

-Peripheral vascular disease

Thrombolytic drugs – mechanism of action



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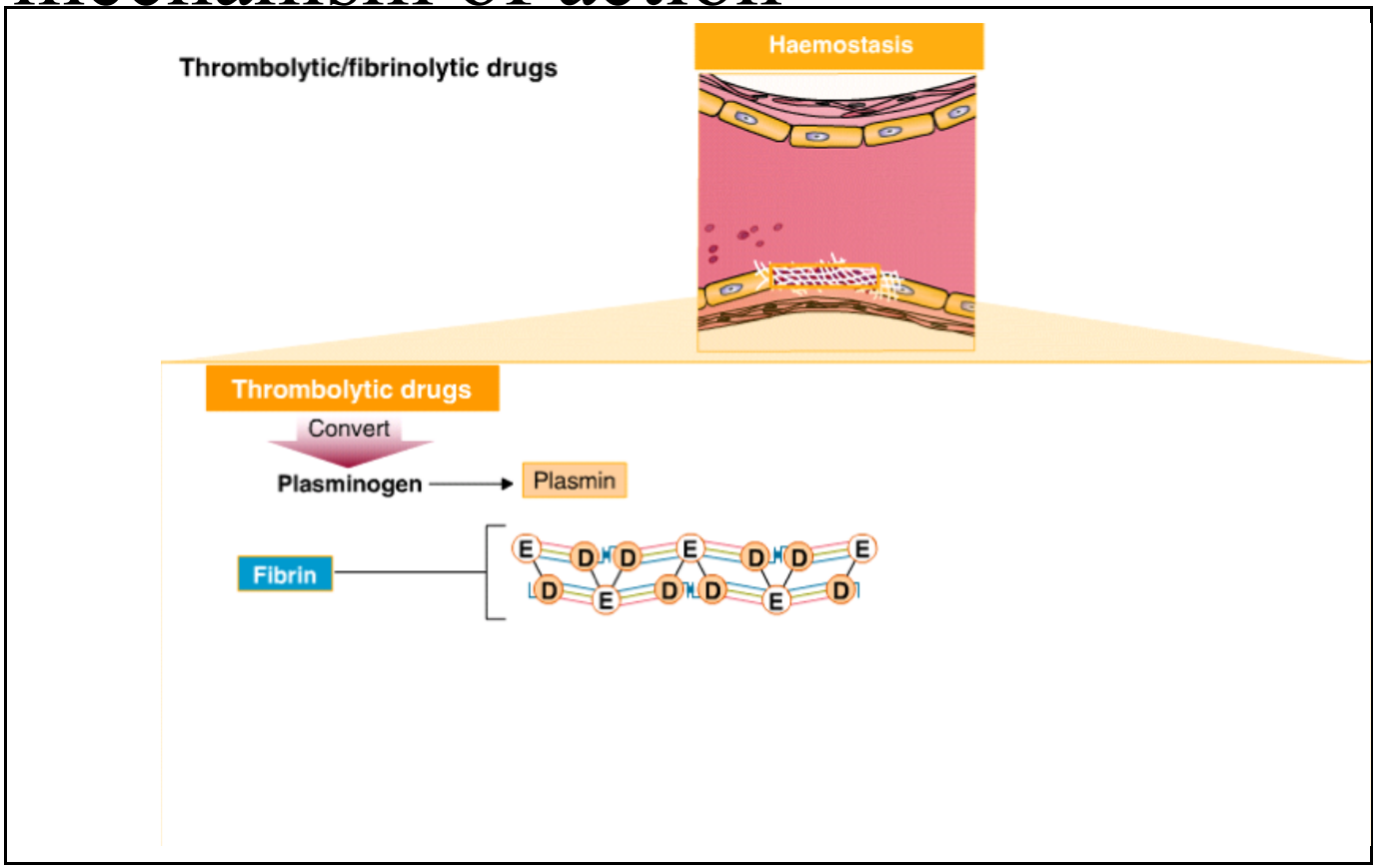

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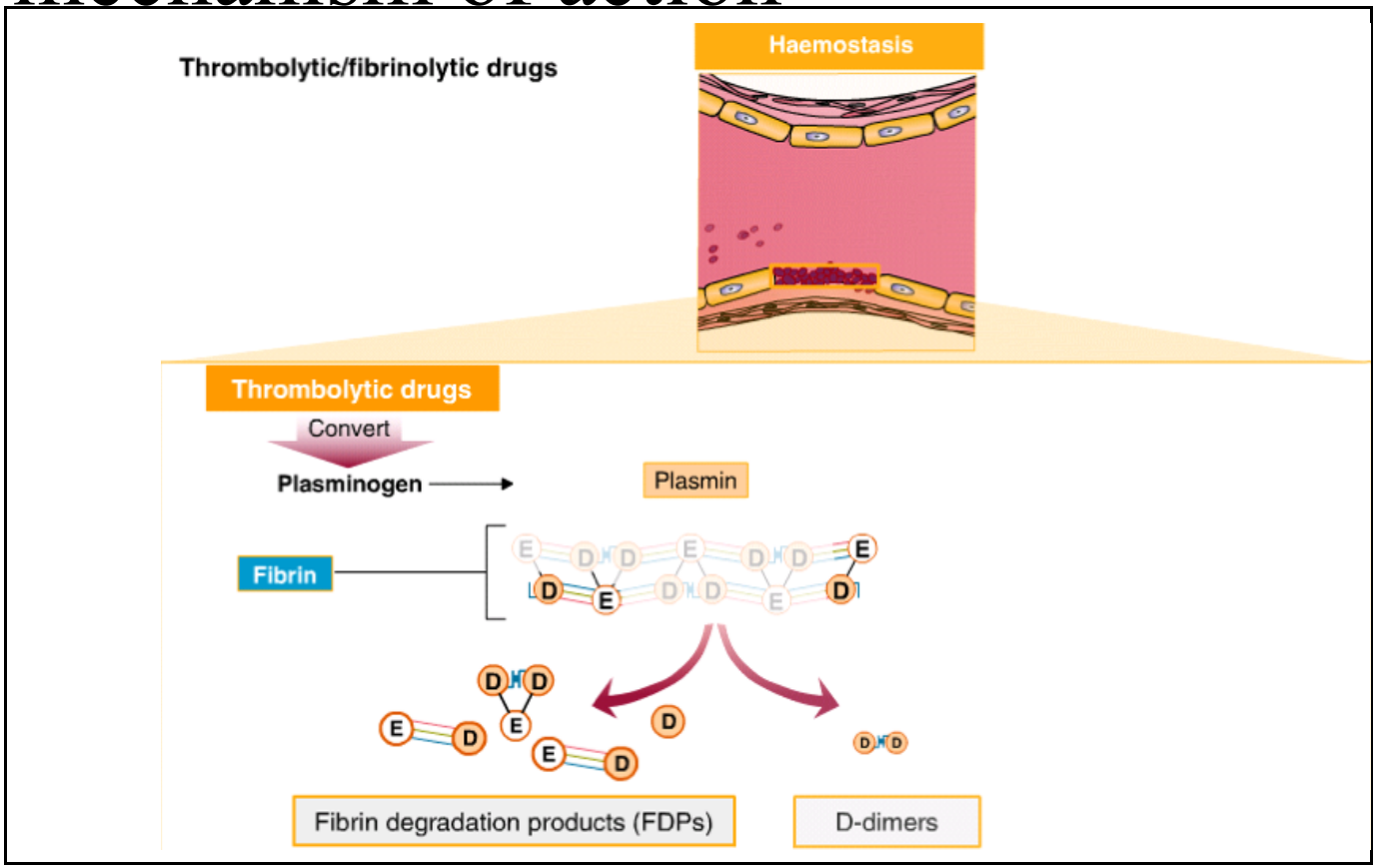

MOA:

1-Streptokinase: combines with plasminogen. The complex cleaves another plasminogen molecule to plasmin

2-Anistreplase: an acetylated streptokinase-plasminogen complex that cleaves plasminogen to plasmin

3-Urokinase: directly cleaves plasminogen to plasmin

4-t-PA: an endogenous direct activator of plasminogen. It preferentially activates plasminogen that is bound to fibrin. This, in theory, confines fibrinolysis to formed thrombi

5-Alteplase: recombinant t-PA

6-Reteplase: genetically-modified recombinant.

-Less expensive than t-PA but less fibrin-selective

7-Tenecteplase: genetically-modified recombinant t-PA long t1/2

-Slightly more fibrin-selective than t-PA

- **Streptokinase** is formed by streptococci
- **Urokinase** is a human enzyme synthesized by kidney

- As the clot dissolves, concentration of thrombin ↑ locally □ ↑ platelet aggregation & ↑ formation of new thromi
- □ Give an antiplatelet or anticoagulant to prevent thrombosis

- The earlier the thrombolytic is given the better.

- **<u>Side effects</u>:**

1) Bleeding: happens because these agents do not distinguish between the fibrin in an unwanted thrombus & fibrin in a beneficial hemostatic plug, or fibrinogen in the circulation.
2) Reperfusion arrhythmia.
3) Hypotension.

4) Hypersensitivity: with streptokinase & anistreplase (which includes streptokinase in its composition):

streptokinase is purified from culture broths of streptococci it is a foreign body & is, thus, antigenic.

Most people have had a streptococcal infection they may have circulating antibodies against streptokinase the streptokinase-antibody reaction can cause fever, hypersensitivity &/or failure of therapy (because the streptokinase molecules complexed with the antibody are pharmacologically inactive).

- Urokinase is nonantigenic because it exists normally in human urine it is used in patients hypersensitive to streptokinase.