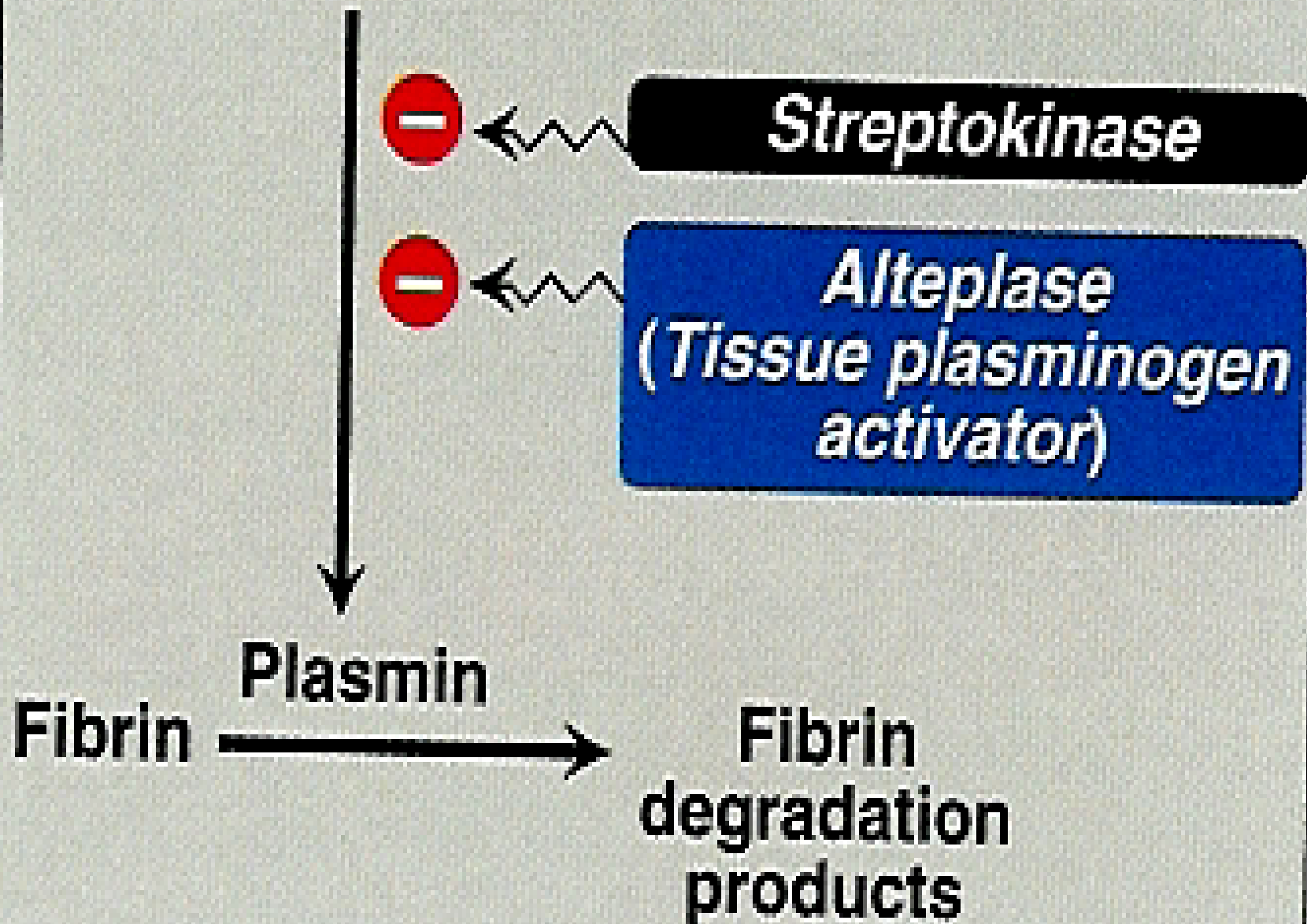


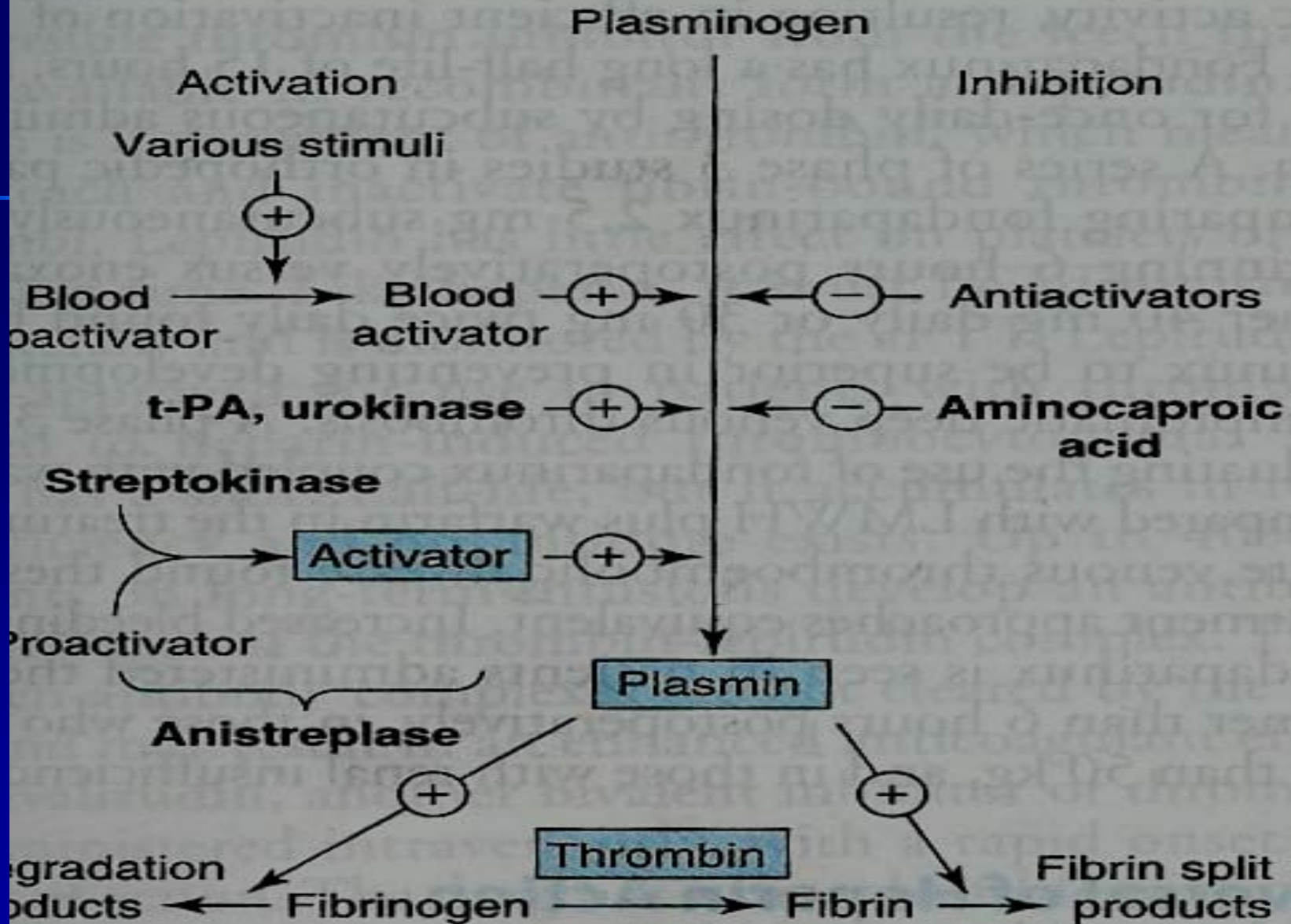
Fibrinolytic Drugs (Thrombolytic Drugs)

Mechanism of Action

Act directly or indirectly to convert plasminogen to plasmin within the thrombus thus hydrolyzes fibrin → lysis of the thrombus

Plasminogen





- 1. Streptokinase.**
- 2. Anistreplase.**
- 3. Urokinase**
- 4. Tissue plasminogen activators (t -PA).**

- Should be given as soon as possible.**
- Fibrinolytics are given intravenously.**
- Bleeding can occur (Systemic fibrinolysis).**

Uses

1. **Acute myocardial infarction.**
2. **Acute thrombotic stroke.**
3. **Peripheral artery occlusion.**
4. **Pulmonary embolism.**
5. **Deep venous thrombosis.**

Contraindications

Pregnancy

Cerebrovascular disease

Uncontrolled hypertension.

Peptic ulcer

Streptokinase

Is a protein (not enzyme) synthesized by B-hemolytic streptococci.

Mechanism of Action

- **Acts indirectly by forming plasminogen-streptokinase complex which converts inactive plasminogen into active plasmin.**
- **It is the least expensive.**
- **T 1/2 = half an hour.**
- **I.V. Infusion (250,000U then 100,000U/h for 24-72 h).**

Side effects

1. **Antigenicity** Fever, allergic reaction.

2. Hypotension.

3. Not used in patients with streptococcal infections.

**** 1 year at least must elapse before its use again (its action is blocked by antistreptococcal antibodies that appears 4 days or more after the initial dose).

Anistreplase (APSAC)

- **Anisoylated plasminogen-Streptokinase activator complex**
- **Is a complex of purified human plasminogen + bacterial streptokinase that rendered inactive by introducing anisoyl group at its active site.**
- **Upon administration, anisoyl group is hydrolyzed liberating streptokinase-plasminogen complex.**

Advantages

- 1. Longer duration of action (4 - 6 hours).**
- 2. Given as a bolus I.V. (30 U over 3 - 5 min.).**
- 3. More thrombolytic activity.**
- 4. Greater clot selectivity.**

Disadvantages

(less than streptokinase alone).

- 1. Expensive.**
- 2. Antigenic.**
- 3. Systemic lysis.**
- 4. Allergic reactions.**

Urokinase

Human enzyme synthesized by the kidney, obtained from either urine or cultures of human embryonic kidney cells.

- acts directly converting plasminogen to active plasmin.

- **Dose** 300,000U then 300,000U/h for 12h.

Disadvantages

- 1. Expensive.**
- 2. Systemic lysis.**

Advantages

- 1. Not antigenic.**
- 2. No Hypotension.**

Tissue Plasminogen Activators (t - PA)

Alteplase

- **Alteplase** (Single Chain).
- **Reteplase** (Deleted Form).
- **Tenecteplase**
- **All are recombinant human t - PA.**
- **Synthesis by recombinant DNA technology.**

Advantages

1. **Clot specific (fibrin specific).**
 - **activate fibrin-bound plasminogen rather than free plasminogen in blood.**

2. **No systemic fibrinolysis.**
3. **No hypotension.**
4. **Non-antigenic (Can be used in patients with antistreptococcal antibodies).**

Alteplase

very short half life (5 min.)

(60 mg i.v. bolus + 40 mg infusion over 2 h).

Retepase (two I.V. bolus of 10 U).

Antiplasmin (Antifibrinolytics)

**inhibit plasminogen activation and thus
inhibit fibrinolysis and promote clot stabilization.**

Tranexamic Acid.

Aminocaproic Acid

Aprotinin.

Aminocaproic Acid & tranexamic acid

- **Synthetic**
- **It competitively inhibits plasminogen activation**
- **Given orally**
- **Intravascular thrombosis**

Aprotonin

It acts by blocking plasmin.

Uses

Can be taken orally or I.V.

- 1. Adjunctive therapy in hemophilia.**
- 2. Antidote for Fibrinolytics.**