

Fibrinolytic system



Fibrinolysis

- Prevents excessive fibrin deposition
- It is the body's defense against vascular occlusion.
- Fibrinolysis is essentially a localized, surface-bound phenomenon, that is catalyzed by fibrin formation i.e. 'fibrin initiates its own destruction'.

Fibrinolysis

- As well as coagulation there is a balance for dissolution of the clot .
- It also should govern that bleeding doesn't reoccur due to premature fibrinolysis.
- To ensure that fibrin deposition in excess is either prevented or rapidly removed.

Components of the Fibrinolytic system

- **Plasminogen (PLG)**
- **Plasmin**
- **Activators**
 - Endogenous
 - Exogenous
- **Inhibitors**
 - For plasmin
 - For PLG activators.

- When fibrin is formed, plasminogen is bound to the clot (Fibrin adsorbs the plasminogen from plasma).
- t-PA released from the vascular endothelium is also adsorbed on the fibrin surface and efficiently activates plasminogen to plasmin, thereby providing localized activation of fibrinolysis.

Plasminogen

- Is a plasma glycoprotein Produced by the liver.
- zymogen of the serine protease plasmin
- Plasminogen is activated by the action of specific enzymes collectively known as plasminogen activators.

Effect of plasmin

- Degradation of fibrin
 - Fibrin degradation products (FDP)s
 - D-Dimers
- Lyses factor V and VIII
- Proteolysis of fibrinogen
 - Removes small peptides

Activators

Plasminogen activators

1. Intrinsic activators

- Includes: F XIIa, XIa, kallikrein

2. Extrinsic activators:

- Almost all body tissues including vascular endothelium.

Extrinsic activators includes

1. Tissue-type plasminogen activator (t-PA)

- Has a high affinity for fibrin.
- t-PA is synthesized by endothelial cells

2. Urokinase plasminogen activator (u-PA)

- Produced by the kidney and secreted in urine and also by fibroblast-like cells in GIT.

3. Streptokinase:

- Derived from beta-haemolytic streptococci

Regulation

Regulation of fibrinolysis

- The plasmin-generating potential of plasma is sufficient to degrade completely all of the fibrinogen in the body in a very short period of time.
- It is prevented from doing so by:
 - **PLG activator inhibitors** (PAIs) most of which belong to the serine family.
 - **Inhibitors of plasmin** itself (the antiplasmins).

Inhibitors of plasminogen activation

- Plasminogen activator inhibitor-1 (PAI-1)
- Produced and secreted into the blood by endothelial cells.
- It is also present in the platelets.
- Rapidly inactivates t-PA and u-PA.

Plasminogen activator inhibitor-2(PAI-2)

- Inhibitor of tPA that is mainly produced by the placenta
- May contribute to the inhibition of fibrinolysis which occurs during pregnancy.
- It is also synthesized in monocytes and epidermal cells,
- It is not usually found in the plasma of non-pregnant subjects.

- When the amount of plasmin exceeds the amount of inhibitory agents available in plasma can the excess plasmin attack fibrinogen and other proteins.
- The fibrinolytic system is also modulated by the **protein C** pathway. It stimulates fibrinolysis activity by decreasing tPAI-1 activity.

Inhibitors of Plasmin

- A number of the broad spectrum inhibitors contribute to neutralization of plasmin.

1. α 2-Antiplasmin.

2. Alpha 2 Macroglobulin

3. Alpha 1 Antitrypsin

4. Lipoprotein A

5. Thrombin-activated fibrinolytic inhibitor

Thank you

