凝血系統

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- *凝血系統主要部份* =

  1.血管壁　2.血清蛋白(血液凝固及溶解因子)　3.血小板

(I)血管內皮

- *具抗凝血作用:*

  -抗凝血素 (如 **GAG, TFP, thrombomodulin, EPCR)**

  -血栓溶解素 (如 **tPA, uPA, plasminogen**受體, **PA**受體)

  -抗血小板 (如 **prostacyclin, nitric oxide, carbon monoxide, ADPase)**

- ***具凝血作用:***

  -凝血素 (如 tissue factors, 凝血因子受體, fibrin)

  -抗血栓溶解素 (如 PAI, TAFI)

  -激活血小板 (如 vWF, PAI)

- ***控制血管張力:***

  -血管擴張如 nitric oxide, carbon monoxide, prostacyclin, ADPase

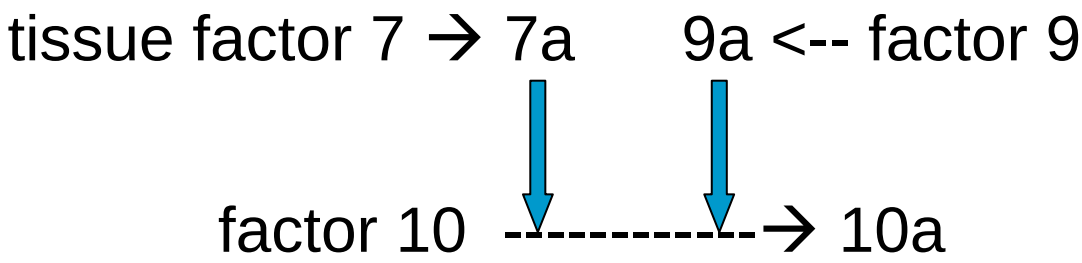
  -血管收縮如 PAI, endothelin 1

(II)凝血

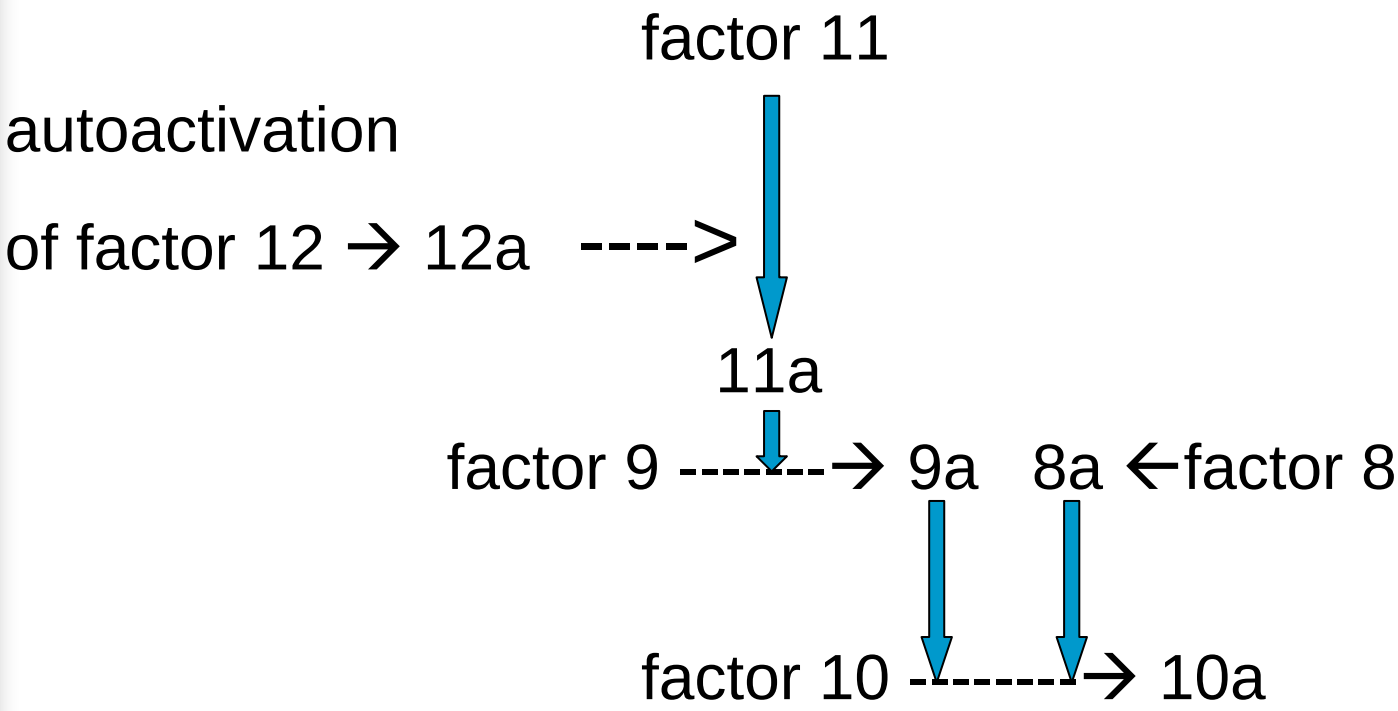
(1)凝血機轉 (Coagulation cascade):-

- 外部 (tissue factor)路徑 (引起體內in vivo凝血):

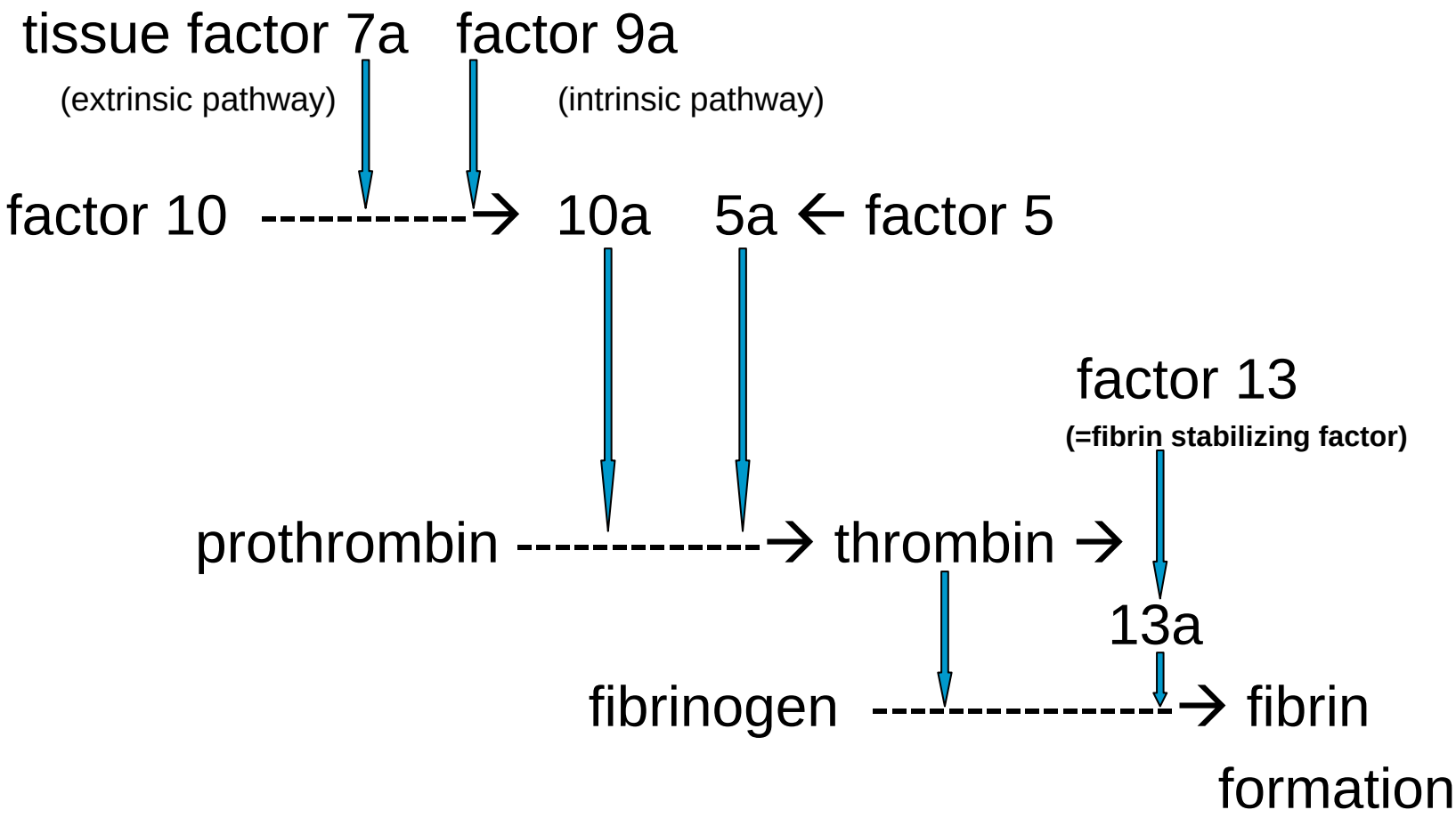
-血管損傷 →激活血管內皮細胞及白血球引起第十凝血因子活化:



- ***內部(血管壁接觸引起 in vitro凝血)路徑:***



共同凝血路徑:


tissue factor 7a
factor 9a
(extrinsic pathway)
(intrinsic pathway)
factor 10
10a
5a
factor 5
factor 13
(=fibrin stabilizing factor)
prothrombin
thrombin
13a
fibrinogen
fibrin
formation

(2)抗凝血作用:-

- 內生性抗血小板素如：endothelial PGI2, nitric oxide, carbon monoxide, ADPase

- Antithrombin =血清主要抗thrombin及其他凝血因子
  -中和thrombin及其他活化凝血因子

- Protein C-protein S-thrombomodulin系統:
  -結合及移除thrombin及其他凝血因子

(3)血栓溶解系統:-

Plasminogen activators eg. tPA, uPA

↓

Plasma plasminogen --→ plasmin

↓

fibrin ----------→ fibrin degradation products

(eg. D-dimer, potent anticoagulant and antiplatelet actions)

(4)血栓溶解抑制素:-

- Plasminogen activator inhibitor (PAI)
- Antiplasmin (抑制 plasmin)
- Thrombin-activatable fibrinolysis inhibitor (TAFI)

(III)血小板

(1)血小板黏著(Adhesion):-

- 血管內皮損傷 →內皮抗血小板功能不良 →血小板黏著內皮損傷處(**von Willebrand factor vWF激活血小板受體 = glycoprotein Ib;及 collagen receptors GPIa/IIa = integrin)**

(2)血小板激活(Activation):-

- 因爲: 血清內泌素如 **epinephrine, thrombin;**
- 激活引起分泌: **ADP, ATP, serotonin, adhesive proteins (eg. fibrinogen, vWF, fibronectin), growth factors (eg. platelet-derived growth factor, transforming growth factor), procoagulants (platelet factors 4 and 5), platelet activation and vasoconstriction TXA2 (= major cyclooxygenase, blocked by aspirin)**

(3)血小板集結(Aggregation):-

- Fibrinogen或 vWF結合 GPIIb/IIIa血小板受體 → 激活血小板 integrins →血小板擴散，集結，血凝塊 →血小板填塞(platelet plug)(凝血系統 fibrin加強穩定)

"Thrombin paradox"

- Thrombin可以:
  1. ***促進凝血***,於血管內皮損傷處激活凝血因子及血小板集結
  2. ***防止凝血***,正常無發炎血管內皮激活內生性抗凝血素以釋出 protein C, tPA, PGI2及 nitric oxide.

抗凝血藥物

(1) **Heparin:-** = 快速抗凝血作用.
-結合 antithrombin及 thrombin以抑制thrombin.

(2) **Warfarin (coumadin):-** =抑制維生素K (=抗prothrombin及凝血因子 7,9,10之輔因子)

(3) **Thrombin inhibitors:-** 如. hirudin, argatroban

(4) **血栓溶解劑 thrombolytic (fibrinolytic) drugs:-** 如 streptokinase, urokinase, tPA

- 激活 plasminogen → plasmin (分解 fibrin)

(5) ***抗血小板藥物：-*** -

Aspirin –減少 cyclooxygenase抑制 TXA2 (=血小板集結及血管收縮介體).

Clopidogrel (Plavix) –抑制 P2Y12 ADP receptor (以抑制血小板激活及集結)

(6) ***Phosphodiesterase inhibitors***:-

Dipyridamole –抑制 phosphodiesterase →激活 PGI2 合成 (血小板抑制作用)

Cilostazol –抑制 phosphodesterase;及血管擴張作用

(7) ***Glycoprotein IIb/IIIa antagonists***:-

如 abciximab, eptifibatide, tirofiban (Aggrastat)

- 抑制血小板 GPIIb/IIa receptors (= fibrinogen及 vWF結合處)以抑制血小板活化及集結.