Coagulopathy in Surgery Patients: Pathology/ Diagnosis/ Management

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Outline of Presentation

- Review of normal hemostasis
- Intraoperative and postoperative hemostatic defects
- Patients on Aspirin, NSAIDs
- Patients on oral anticoagulant therapy

Review of Normal Hemostasis

- Normal hemostasis requires balancing of: primary hemostasis, secondary hemostasis, and fibrinolysis

Primary Hemostasis

- Primary hemostasis is initiated by vacular injury, leading to platelet aggregation and formation of platelet plug for temporary arrest of bleeding
- ADP from injured vessel -> activates platelet, primary aggregation -> ADP, TXA_2 for secondary aggregation; phospholipids to initiate secondary hemostasis
- Attachment of platelets to collagen: vWF and GP Ib/IX

Fig 1. Platelet Plug Formation

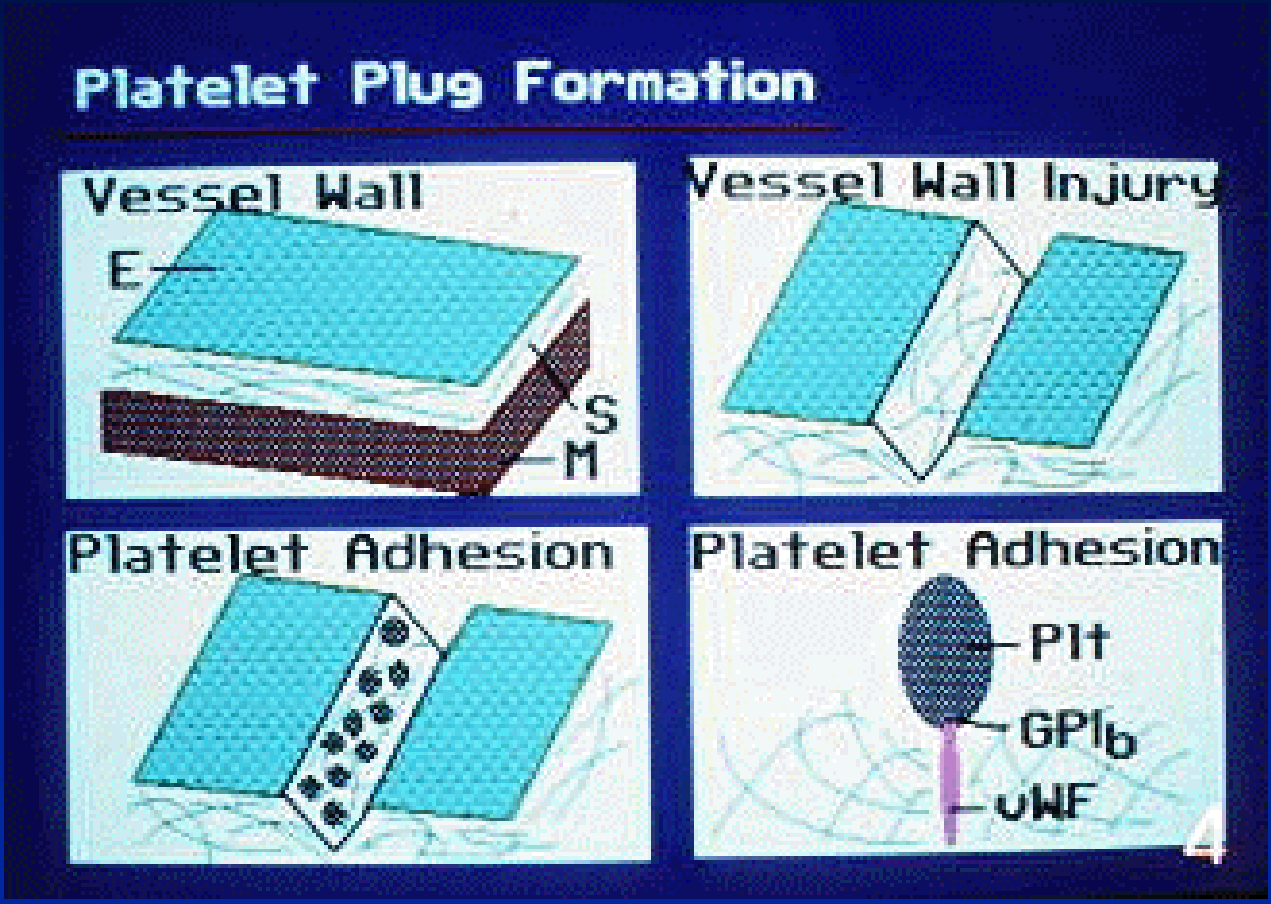
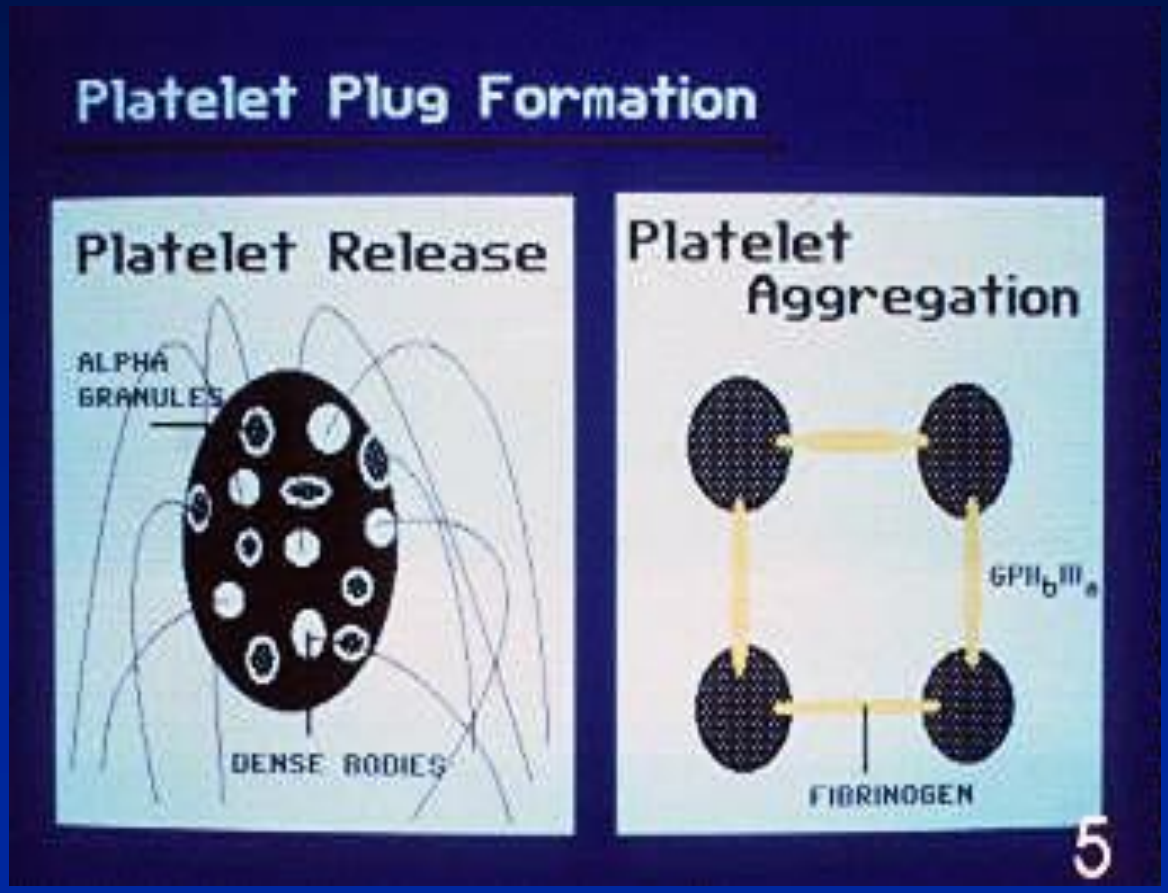


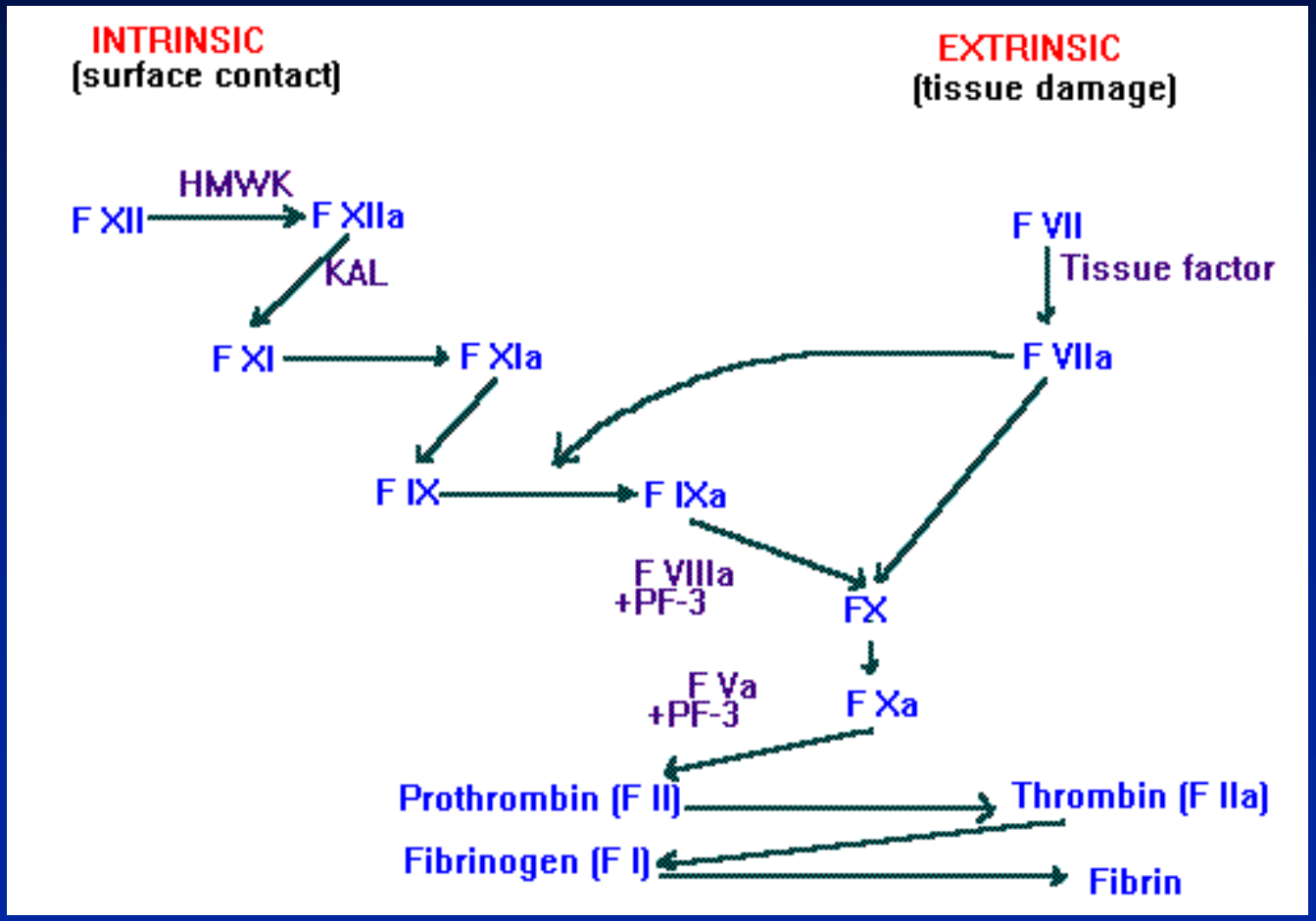
Fig 2. Platelet Plug Formation (cont'd)



Secondary Hemostasis

- Secondary hemostasis involves clotting factors, cacium, and phospholoipids -> forming a fibrin clot to stabilize the platelet plug
- Coagulation cascade: activated clotting factor + calcium + phospholipid + procoagulant clotting factor -> procoagulant clotting factor becomes activated

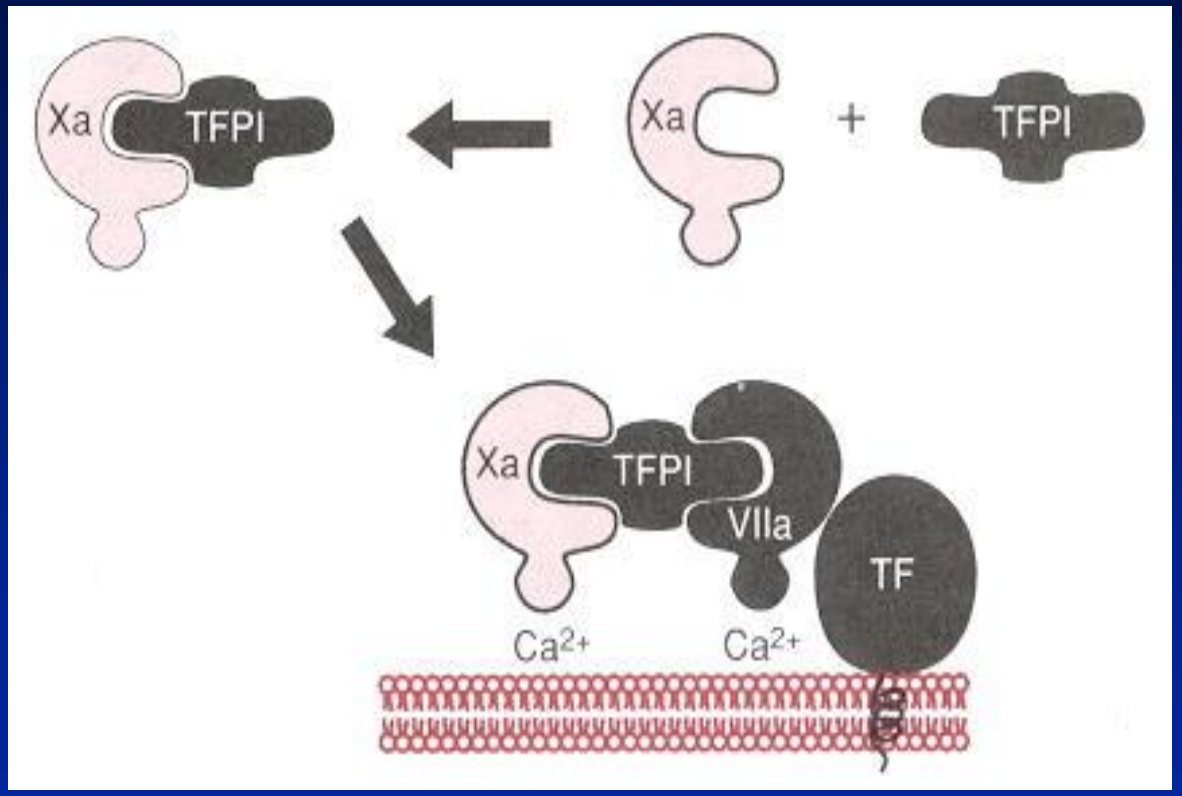
Fig 3. Intrinsic and Extrinsic Systems of Coagulation



Tissue Factor Pathway Inhibitor

- Inhibition of factor VIIa by tissue factor pathway inhibitor (TFPI)
- In this model, the binding of TFPI to factor Xa results in a conformational change in the TFPI that facilitates the inhibition of factor VIIa, which is complexed to tissue factor (TF).

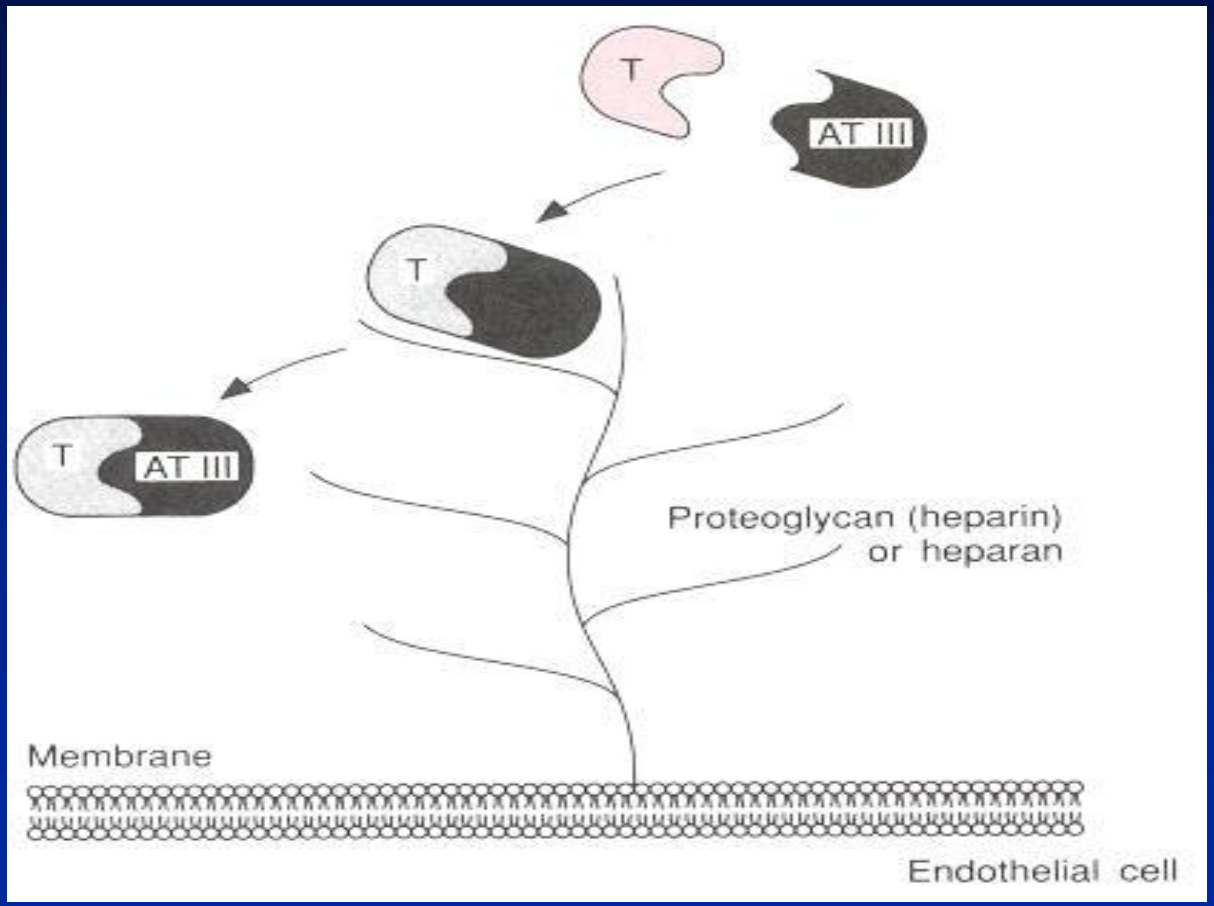
Fig 4. Tissue Factor Pathway Inhibitor



Antithrombin III

- Thrombin inhibition by AT III in the presence of heparan molecules on the endothelial cell surface
- The binding of AT III to the heparan results in a conformational change in the AT III that results in rapid inactivation of thrombin. Both thrombin and antithrombin bind to the heparan. After complex formation with AT III, the complex rapidly dissociates from the heparan

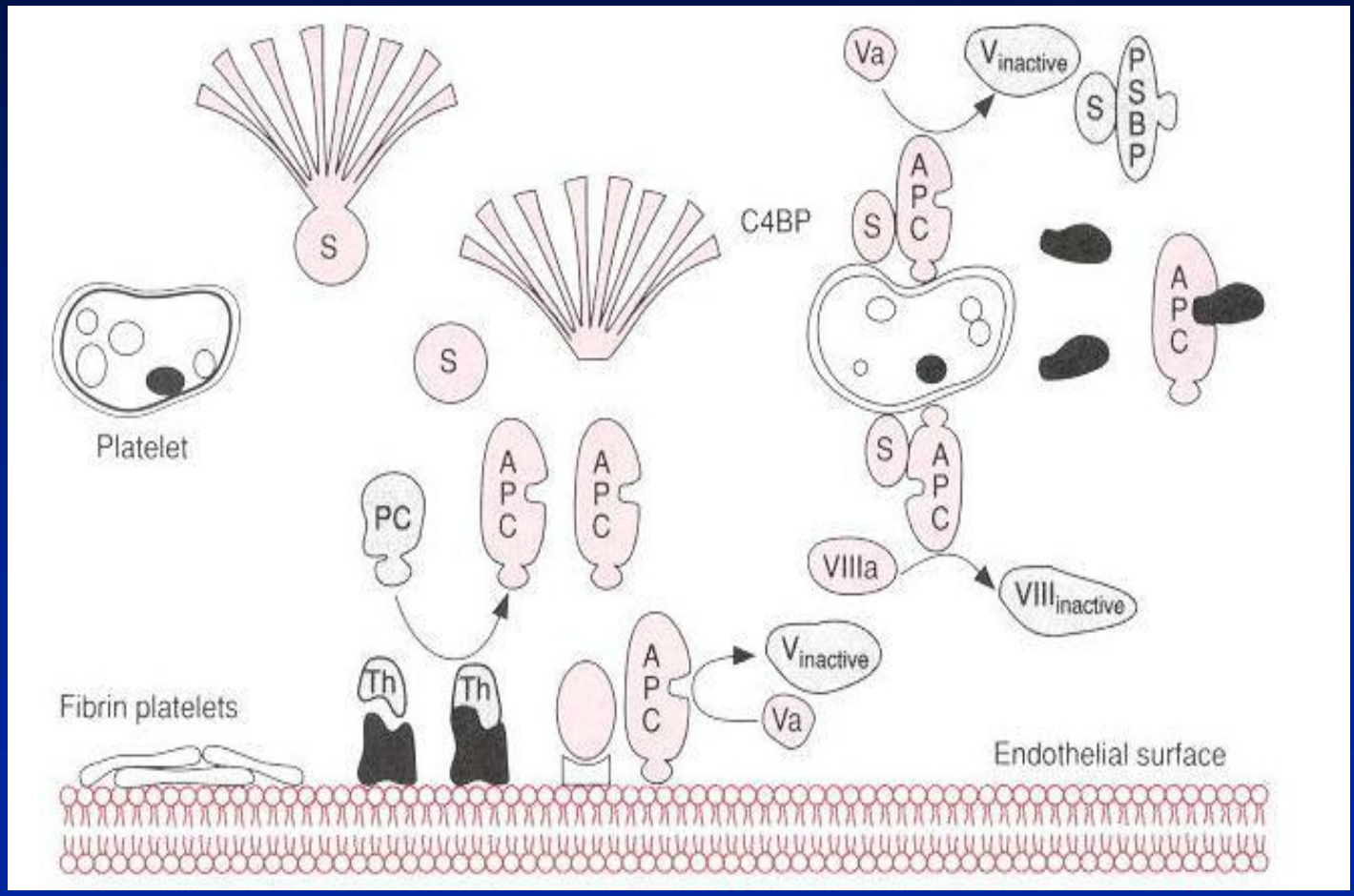
Fig 5. Antithrombin III



Proteins C and S

- On the endothelial cells in the capillaries, thrombin binds to thrombomodulin. The thrombin/thrombomodulin complex rapidly converts protein C (PC) to activated protein C (APC)
- The APC subsequently functions as an anticoagulant by enzymatically degrading clotting factors Va and VIIIa on membrane surfaces. Protein S (PS) is required as a co-factor for these inhibitory steps to occur.

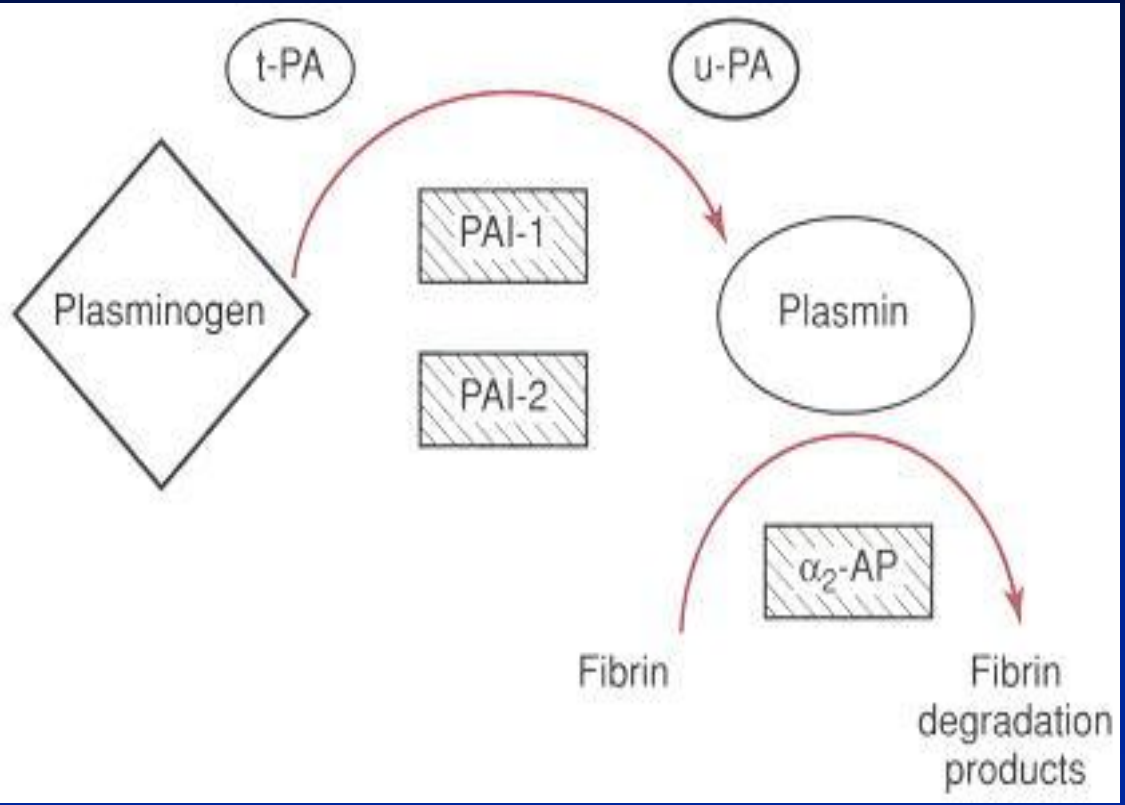
Fig 6. Proteins C and S



Fibrinolysis

- Fibrinolysis prevents clot formation from complete intravascular thrombosis
- Fibrinolysis is initiated through the intrinsic and extrinsic pathways of coagulation

Fig 7. The Fibrinolytic System



Differential Diagnosis of Perioperative Bleeding Diatheses

- Medications
- Renal and hepatic diseases
- Unrecognized congenital defects in hemostasis

Medications

- Urgent nature of emergency surgery may fail to detect the use of certain drugs
- Aspirin irreversibily inactivates platelets
- Other NSAIDs: transient effect (1-2 days)
- Antibiotics can: (1) impair platelet function; (2) prolong PT
- Coumadin: prevents synthesis of functional factors II, VII, IX, X

Medication (cont'd)

- Hemostatic tests:
  - Aspirin, NSAID, antibiotics: increased BT, normal Plt, [abnormal platelet aggregation]
  - Coumadin: increased PT & PTT,
  PT & PTT corrected with 1:1 mixing,
  [decreased factors II, VII, IX, X]
- Treatment:
  Aspirin-> platelets
  Coumadin-> (1) vitamin K;
  (2) fresh frozen plasma

Renal and Hepatic Diseases

- Uremic patient: platelet dysfunction
  Hemostatic tests:
  prolonged Bleeding Time, [abnormal platelet aggregation]
- Hepatic disease: loss of clotting factors and inhibitors, causing a generalized hemostatic failure mimicking DIC
  Hemostatic tests: abnormal PT, PTT, thrombin time, fibrinogen, FSP

Renal and Hepatic Diseases (cont'd)

- Treatment:
  (1) Uremic patient-> 1-desamino-8-D-arginine vasopressin (DDAVP), cryoprecipitate
  (2) Hepatic failure-> fresh frozen plasma, cryoprecipitate

Unrecognized Congenital Defects in Hemostasis

- Routine screenning (H/P, lab tests) can miss some mild inherited defects (factor VIII, IX, vWF, etc)
- Mild defects present with subclinical manifestations, normal coagulation screen tests (PT, PTT)
- Patients bleed with surgery
- Diagnostic tests: specific factor assays (pre-op sample)-> factor replacement treatment

Fig 8. Thromboxane Pathway

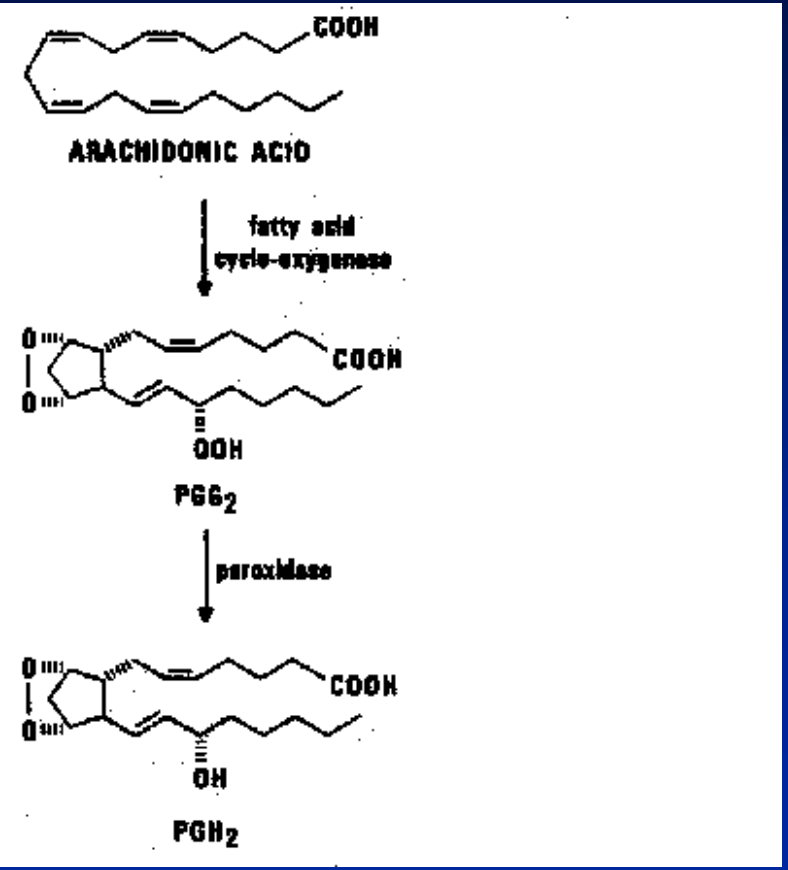
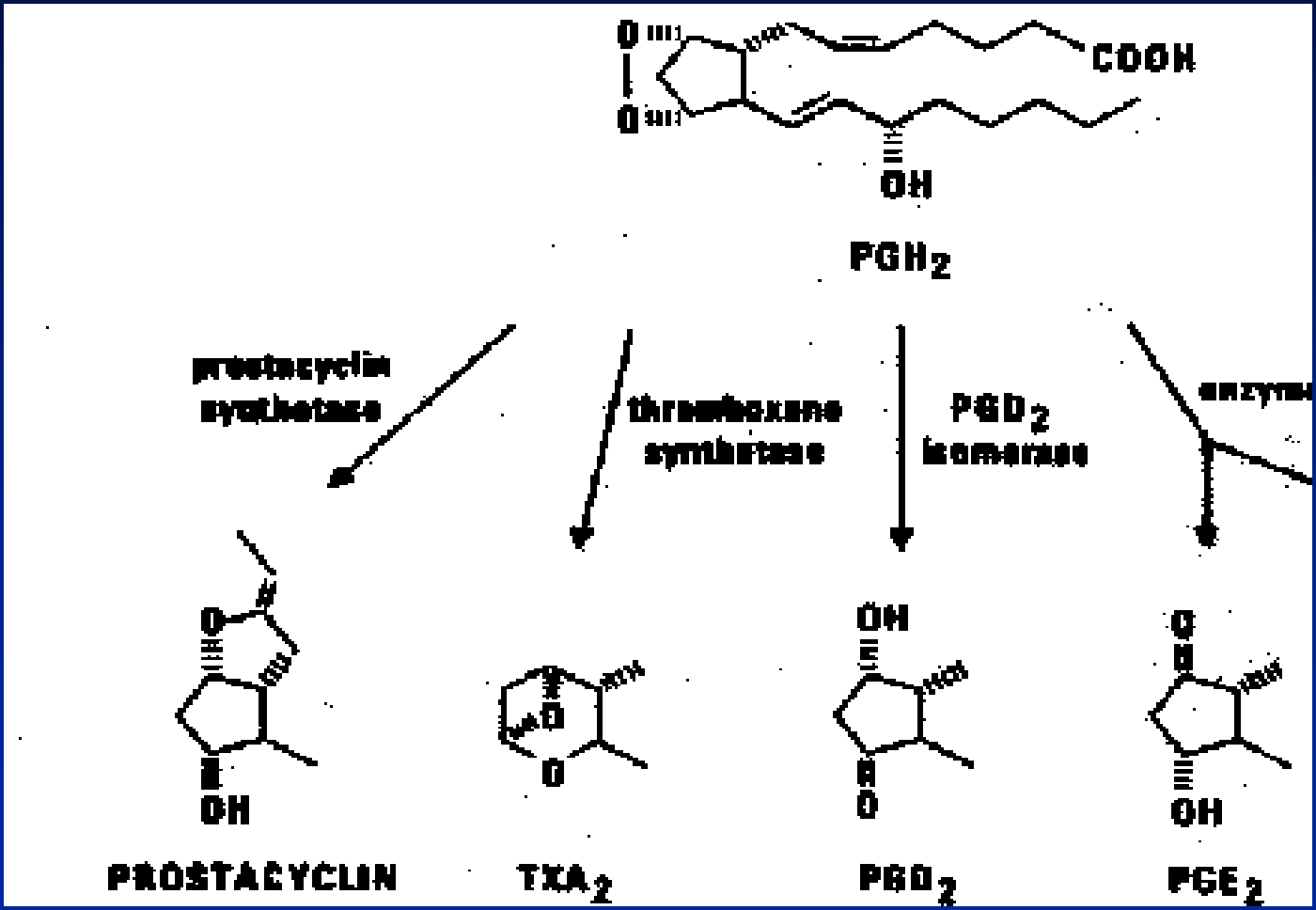


Fig 9. Thromboxane Pathway (cont'd)



Patient on Aspirin, NSAIDs

- Asprin inhibits cyclooxygenase-> permanently disable platelets
- Other NSAIDs temporarily disable platelets
- To prepare for surgery
  Patients on Aspirin-> take off Aspirin, wait for 5-7 days
  Patients on other NSAIDs-> take off NSAIDs, wait for 2 days

Patients on Oral Anticoagulant

- Coumadin as vitamin K antagonist
- Vitamin is needed for production of functional factors II, VII, IX, X
- Monitor of coumadin treatment by international normalized ratio (INR)
  $INR = (PT_{pt} / PT_{mean})^{ISI}$
- Therapeutic range of INR: 2-3

Patients on Oral Anticoagulant (cont'd)

- To prepare for surgery:
  - Stop coumadin
  - Vitamin K can normalize PT in 12 hours
  - For emergency surgery: fresh frozen plasma