Coagulopathy Case-2

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CLINICAL HISTORY

- A 42 year-old man brought to the emergency room with severe burn. Patient was rescued by firemen in a serious fire. He had been found unconscious in his house. No other family members were present at the scene.
- No other clinical information was available at the time of evaluation.

PHYSICAL EXAMINATION

- Physical examination showed 70% of the body surface area with second- and third-degree burns.

SCREENING COAGULATION LABORATORY RESULTS

- PT= 17 sec (Normal 8-14.6)
- aPTT= 49 sec (Normal 24-34.5)
- Plt= 20,000 /μL (Normal 150,000-350,000)

Differential diagnosis

- DIC -> mixing study, TT, Fibrinogen, FSP, D-dimer, blood smear review for schistocytes, clinical correlation
- Liver disease-> mixing study, clinical correlation
- SLE with lupus anticoagulant-> mixing study, dRVVT
- Other causes of factor deficiency and thrombocytopenia

DIAGNOSIS

- Disseminated Intravascular Coagulopathy

DIC

- Concurrent activation of the coagulation (thrombin) and secondary fibrinolysis (plasmin) with consumption of factors, inhibitors, platelets, and RBCs (microangiopathic hemolysis)
- The major triggering mechanism: exposure of the blood to tissue factor that initiates intense coagulation, overwhelming antithrombin and activated protein C
- Secondary to sepsis, malignancy (pancreatic cancer, APL), obstetrical complications (placental abruption, fetal demise, amniotic fluid embolism), tissue injury (esp. brain in head injury), etc.

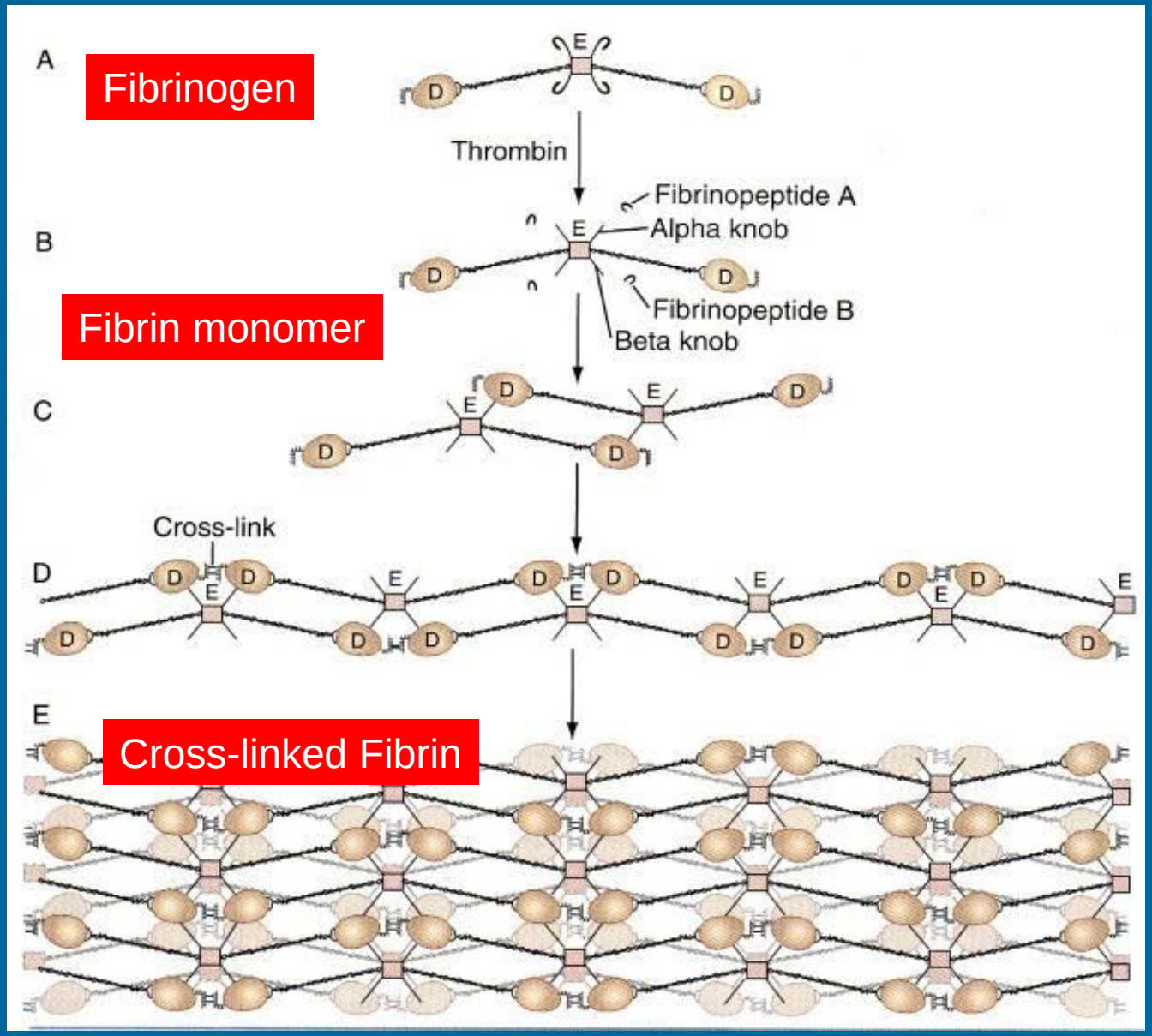
Clinical presentation

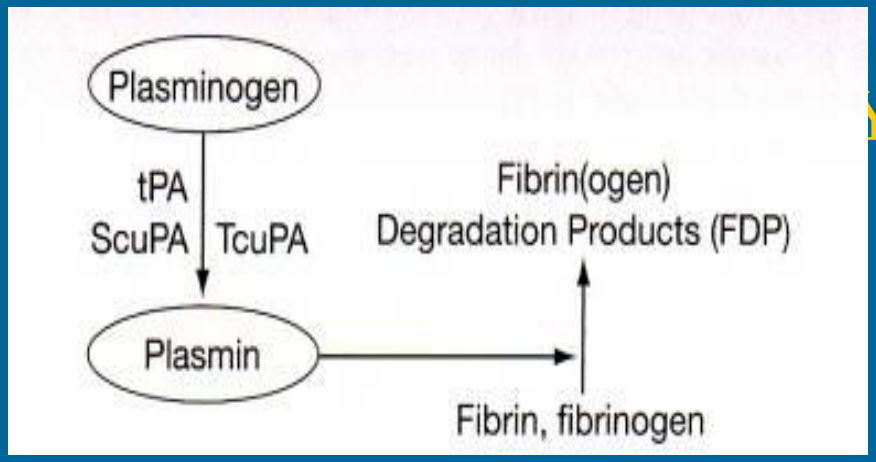
- Most frequent: bleeding due to low levels of clotting factors and platelets
- Less often: vascular thrombosis (if fibrinolytic system or protein C is impaired)

Typical laboratry results in DIC

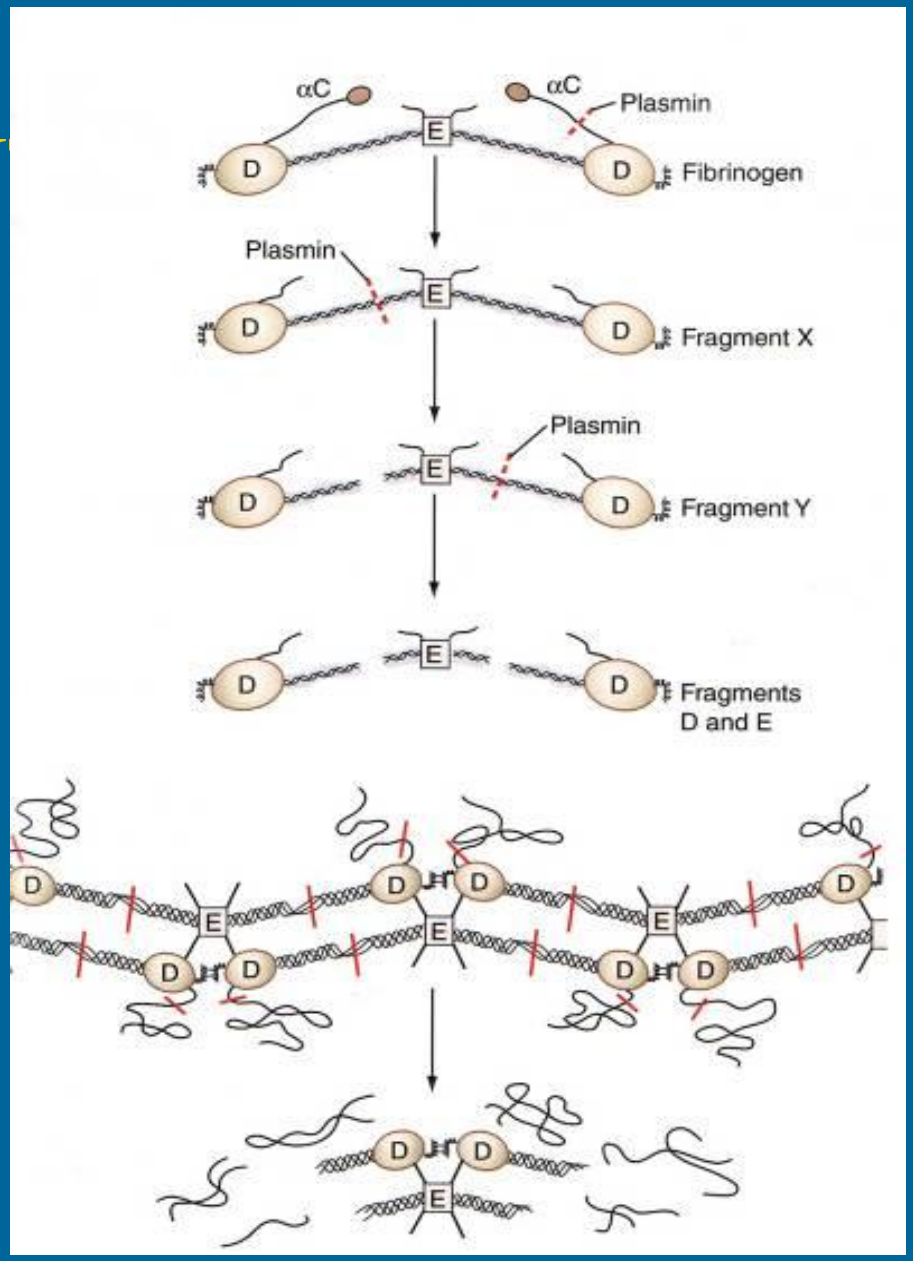
- ↑ PT & PTT, thrombocytopenia, ↓ fibrinogen, ↑ Thrombin Time, ↑ FSP/D-dimer
- Schistocytes in peripheral blood smear, ↑ LDH, ↓ haptoglobin
- Laboratory results in DIC vary greatly depending on the severity

FORMATION OF FIBRIN





D-dimer



- Activators:
  - Tissue plasminogen activator (tPA)
  - Urokinase plasminogen activator (uPA)
- Inhibitors:
  - Plasminogen activator inhibitor-1 (PAI-1)
  - α2-antiplamin

FDP vs. D-DIMER

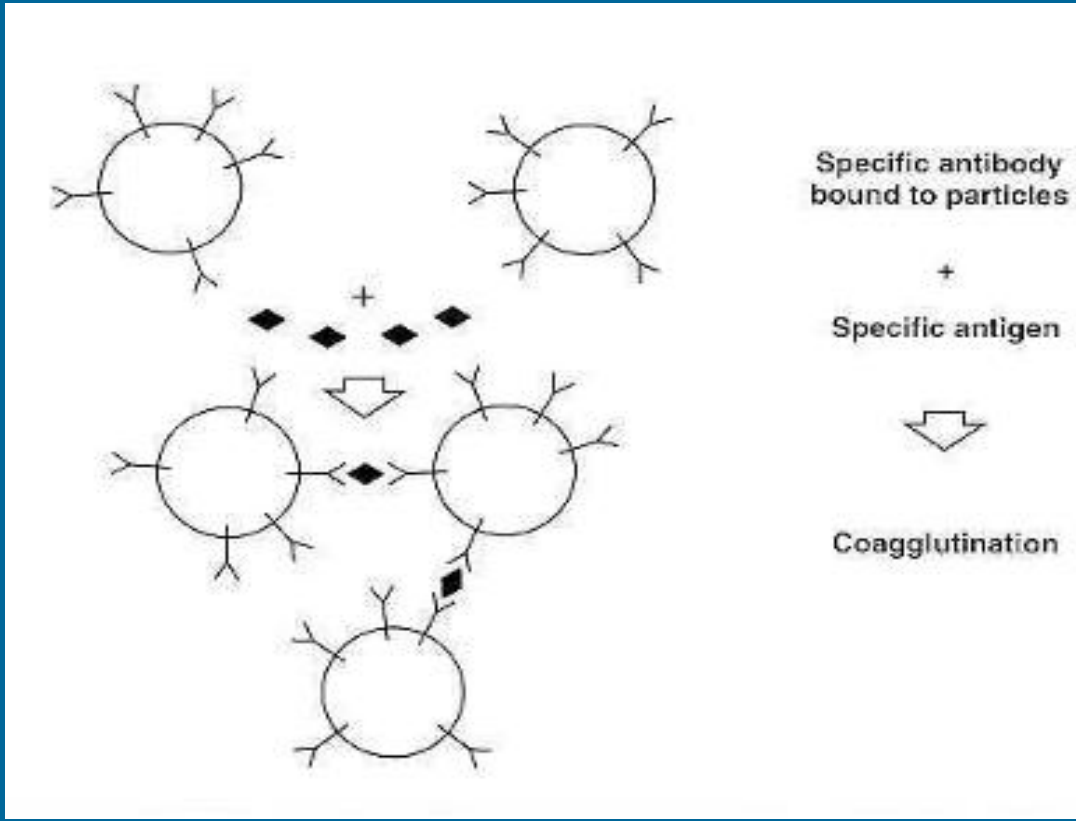
- Fibrin is formed as the end result of coagulation cascade activation
- Fibrinolysis causes cleavage of fibrinogen, fibrin, and fibrin clot, yields FSP (FDP)
- Only cleavage of fibrin clot (crosslinked fibrin) yields D-dimer -> D-dimer is more specific for DIC

Testing: FSP and D-dimer

- Semi-quantitative FSP
- Qualitative D-dimer
- Semi-quantitative D-dimer
- Quantitative D-dimer

SEMI-QUANTITATIVE FSP

- The first test developed (in the early 70's)
- Latex agglutination, FSP antibodies are bound on latex beads, if sample contains FSP, agglutination can be detected



SEMI-QUANTITATIVE FSP

- Semi-quantitation:
  - Serial dilution of sample (1: 20 through 1:640)
  - A positive result at 1:20 corresponds to 20 μg/mL of fibrinogen equivalent units (FEU)

SEMI-QUANTITATIVE FSP

- Early generation FSP polyclonal antibodies cross-react with fibrinogen
  - Must use serum or plasma in tubes with bovine thrombin (consumes fibrinogen)
- Current FSP monoclonal antibodies do not cross react with fibrinogen
  - Can use plasma or serum
  - False-positive result with rheumatoid factor
- Clinical application: DIC, hyperfibrinolysis

QUALITATIVE D-DIMER

- Monoclonal antibodies directed against D-dimer domain
  - More specific for in-vivo fibrin clot formation
- Manual latex agglutination technique (as for FSP), plasma or serum sample:
  - Cut-off value: 0.5 μg/mL FEU
  - Semi-quantitative format: dilutions 1:2 through 1:16
- Abnormal result in DIC
- Normal result in primary fibrinolysis
- False-positive result by rheumatoid factor

QUANTITATIVE D-DIMER

- Automated ELISA, immuno-turbidimetry
- Increased in DIC (>0.66 μg/mL)

- Quantitative D-dimer also has high negative predictive value for venous thromboembolism (VTE including DVT, PE):
  - <0.4 μg/mL, VTE can be ruled out
  - Very sensitive but not specific: high Negative Predictive Value / low Positive Predictive Value

DIC: Treatment:

- Treat underlying conditions
- Blood components (RBC, platelet concentrate, cryo, FFP)