DISSEMINATED INTRAVASCULAR COAGULATION

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INTRODUCTION

- **Definition: systemic activation of blood coagulation, which results in microvascular thrombi in various organs.**

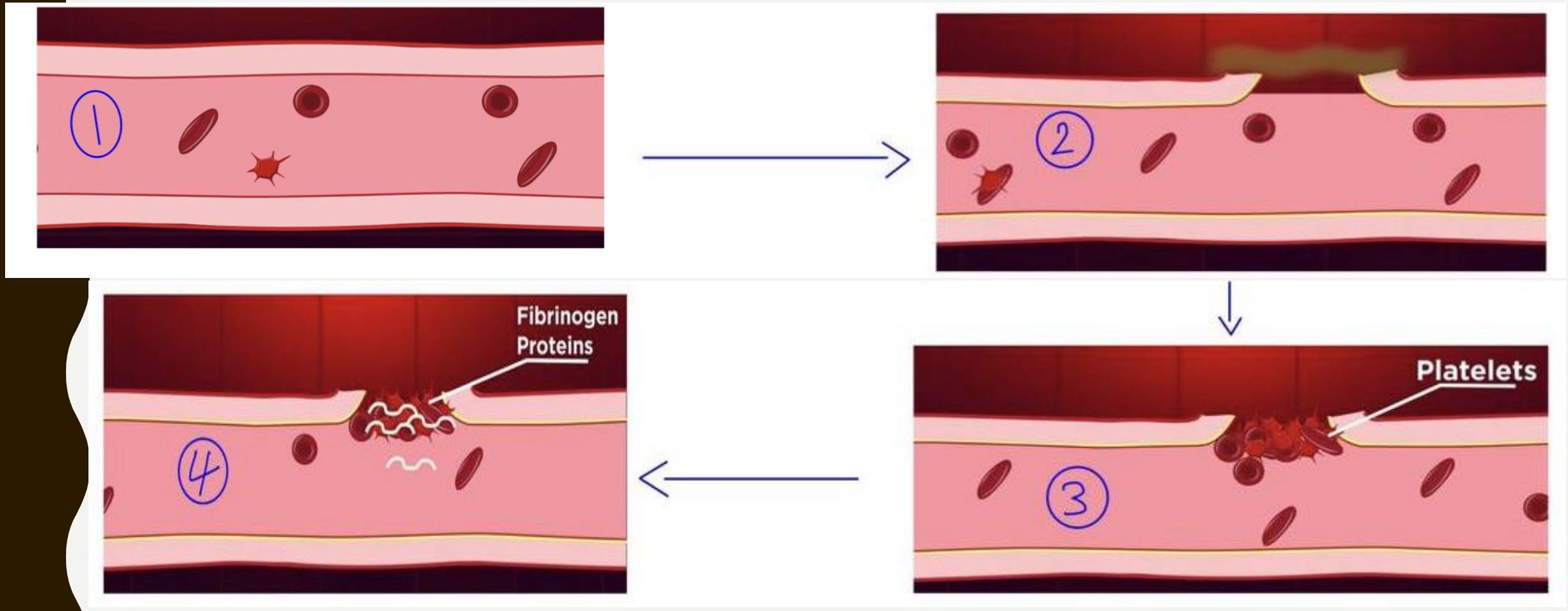
- **Consumption of coagulation proteins and platelets (from ongoing activation of coagulation) may induce severe bleeding, because most of the clotting factors have been used.**

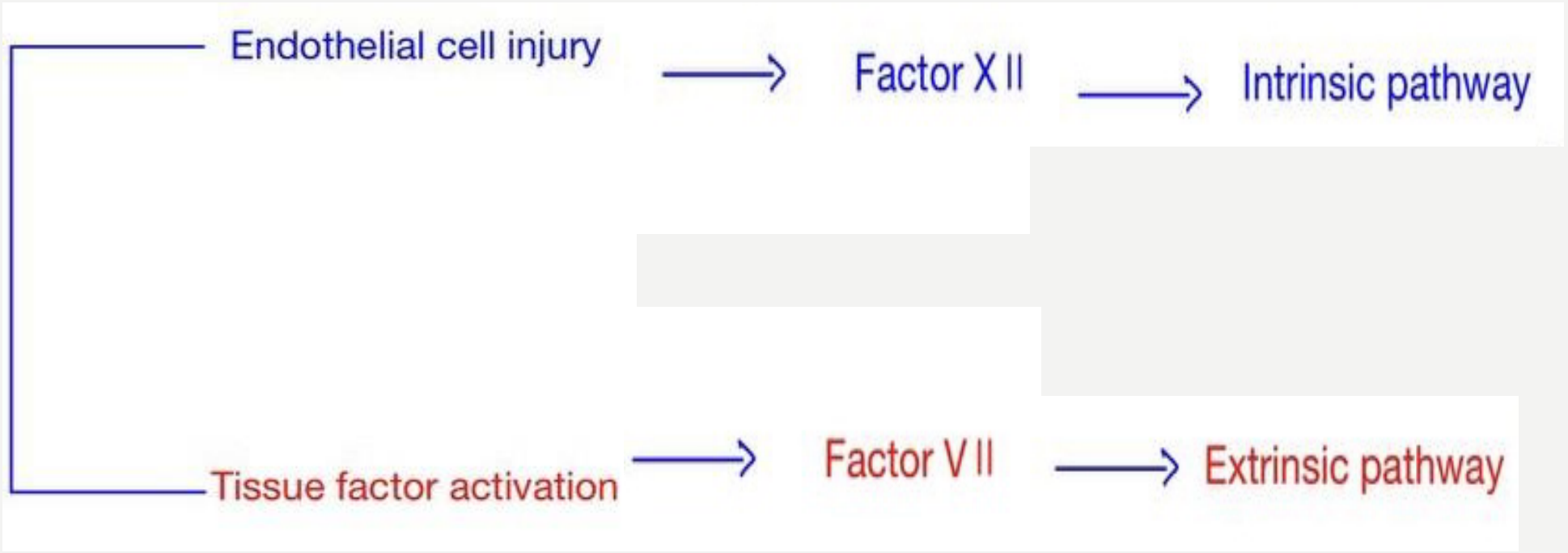
- DIC is not an independent disease, but a complication of some diseases.
- It is essentially an imbalance between the coagulation process and anticoagulation process. It is a syndrome characterized by massive activation and consumption of coagulation proteins, fibrinolytic proteins and platelets.
- The imbalance between clotting factors and the anti clotting factors lead to form microthrombi all over the body.

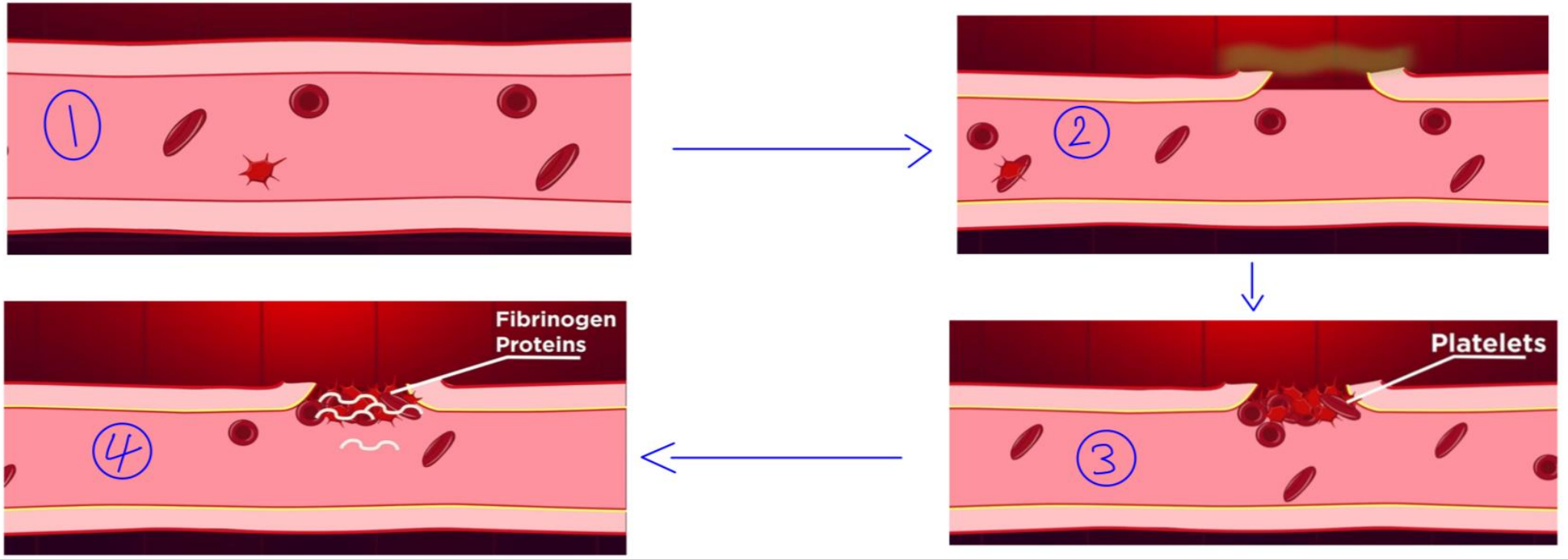
EPIDEMIOLOGY

- DIC may occur in 30-50% of patients with sepsis, and it develops in an estimated 1% of all hospitalized patients.

- DIC occurs at all ages and in all races, and no particular sex predisposition has been noted.


1
2
3
Platelets
4
Fibrinogen
Proteins


Endothelial cell injury
Factor X II
Intrinsic pathway
Tissue factor activation
Factor V II
Extrinsic pathway



Endothelial cell injury → Factor X II → Intrinsic pathway

Tissue factor activation → Factor V II → Extrinsic pathway

Factor X —Activate→ Thrombin

Fibronigen —Thrombin→ Fibrin

NORMAL HEMOSTASIS

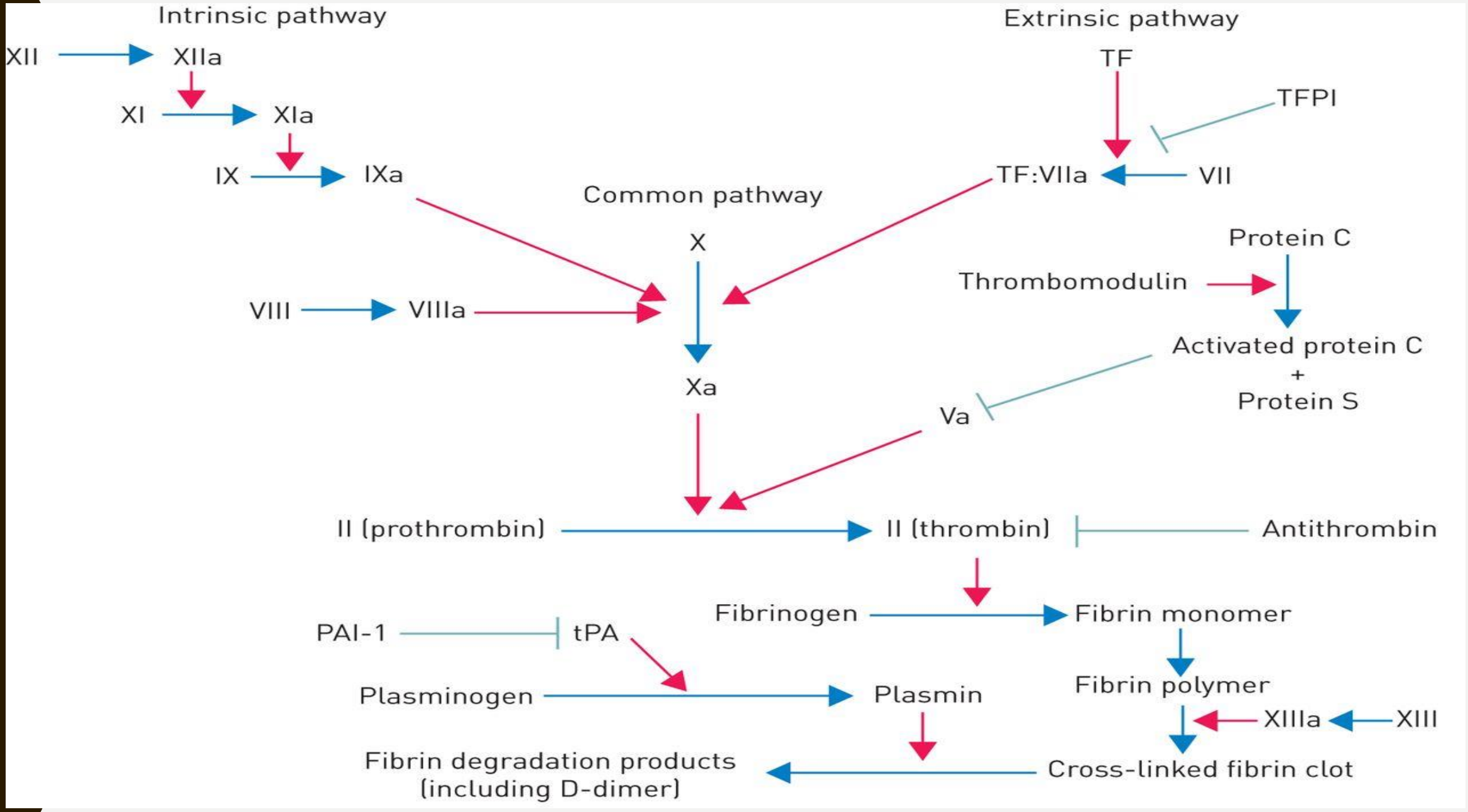
To understand DIC, it is best to first review the normal physiology of clot formation.

It starts with transient vasoconstriction to limit the blood flow to the injured area.

it is a localized process that results in a primary platelet plug through platelet adhesion and aggregation followed by a secondary fibrin clot through the activation of the coagulation cascade, which occurs in a series of enzymatic steps that lead to the formation of thrombin. Thrombin then converts soluble fibrinogen to an insoluble clot of fibrin polymers, which forms a mesh that incorporates the previously formed platelet plug as well as RBCs, if present. this secondary hemostasis coagulation cascade thought to be initiated either through tissue factor (TF) release into the bloodstream, which activates factor VII and then the extrinsic system, or through disruption of the endothelium exposing collagen and the subendothelium directly to blood. This results in platelet aggregation, which in thought to activate factor XII in vivo and subsequently the rest of the intrinsic (contact) cascade.

- ONCE A FIBRIN CLOT IS PRODUCED, IT IS STABILIZED BY COVALENT CROSS-LINKING THROUGH THE ACTIONS OF FACTOR XIII. THE LAST STEP OF THE HEALING PROCESS IS FOR BLOOD CLOTS TO BE REORGANIZED AND RESORBED BY FIBRINOLYSIS SO THAT UNIMPEDED BLOOD FLOW THROUGH THE ORIGINALLY DAMAGED VESSEL CAN BE REESTABLISHED..

The body initiate pathway to breakdown the clot →fibrinolytic pathway is activated in DIC ,Stimulation of endothelial cells by cytokines causes the release of tissue plasminogen activator from endothelial cells. Both tissue plasminogen activator and plasminogen attach to fibrin polymers, and plasmin (generated by tPA cleavage of plasminogen) cleaves fibrin into D-dimers and other fibrin degradation products. DIC can, therefore, cause both thrombosis and bleeding (if the consumption of platelets and/or coagulation factors is excessive).


Intrinsic pathway
XII
XIIa
XI
XIa
IX
IXa
VIII
VIIIa
Extrinsic pathway
TF
TFPI
TF:VIIa
VII
Common pathway
X
Xa
Protein C
Thrombomodulin
Activated protein C
+
Protein S
Va
II (prothrombin)
II (thrombin)
Antithrombin
Fibrinogen
Fibrin monomer
PAI-1
tPA
Plasminogen
Plasmin
Fibrin polymer
XIIIa
XIII
Fibrin degradation products
(including D-dimer)
Cross-linked fibrin clot

PREDISPOSING FACTORS

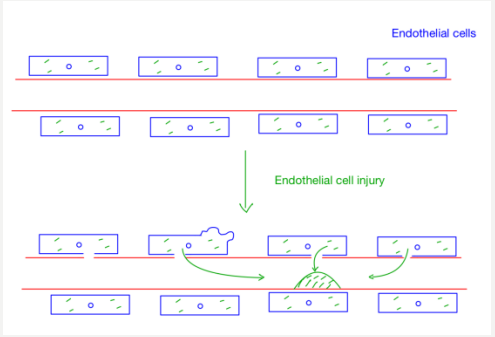
- Complications of obstetrics (abruptio placentae, saline-induced therapeutic abortion, retained dead fetus ,): Placental tissue enters or is exposed to the maternal circulation.

- Infection, particularly with gram-negative organisms [tissue factor (cell surface protein) get activated by antigens , which activate blood coagulation].

- Blood transfusion reaction

- Cancer (leukaemia , adenocarcinomas in the prostate, lung, breast or pancreas) .

- Endothelial cell injury .



PATHOGENESIS

- Some medical condition release procoagulants that tips the scale in favor of clot formation.
- Release of procoagulants, (tissue factors, bacterial components, enzymes/major endothelial injury) → excessive activation of coagulation cascade → thrombosis of small/medium blood vessels → activation of fibrinolysis to resolve clots → fibrin degradation products released into circulation → interfere with platelet aggregation, clot formation
- Depletion of platelets, fibrin, coagulation factors → consumption coagulopathy
- Acquired, paradoxical process of thrombosis, bleeding

Acute vs Chronic

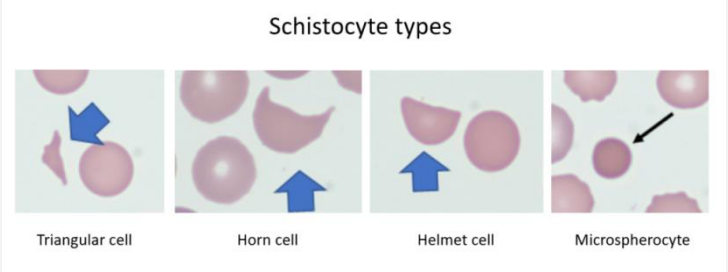
- Acute DIC : excess thrombin is generated to such a high degree in a short time that it overcomes the large amounts of natural anticoagulants normally present in the plasma, an explosive generation of blood clots (consumptive coagulopathy) → **Bleeding** into the subcutaneous tissues, skin, and mucous membranes occurs, because we had consumed the clotting factors .

- In chronic DIC, the process is the same, but it is less explosive. Usually there is time for compensatory responses to take place, which diminish the likelihood of bleeding but give rise to a **hypercoagulable state**. These changes in the blood can be detected by testing the coagulation system.

- Slowly evolving DIC primarily causes venous thromboembolic manifestations (deep venous thrombosis, pulmonary embolism), although occasionally cardiac valve vegetations occur; abnormal bleeding is uncommon.

- Severe, rapidly evolving DIC, in contrast, causes thrombocytopenia, depletion of plasma coagulation factors and fibrinogen, and bleeding. Bleeding into organs, along with microvascular thromboses, may cause dysfunction and failure in multiple organs.

- Delayed dissolution of fibrin polymers by fibrinolysis may result in the mechanical disruption of RBCs, producing schistocytes and mild intravascular hemolysis



SIGNS & SYMPTOMS

1- **Circulatory signs**

Signs of diffuse or localized thrombosis

Signs of spontaneous and life-threatening hemorrhage

2- **Cardiovascular signs**

- **Hypotension**
- **Tachycardia**

3- **Gastrointestinal signs**

- **Hematemesis (**vomiting blood**)**
- **Hematochezia (**fresh blood per-rectum**)**

4- **Genitourinary signs**

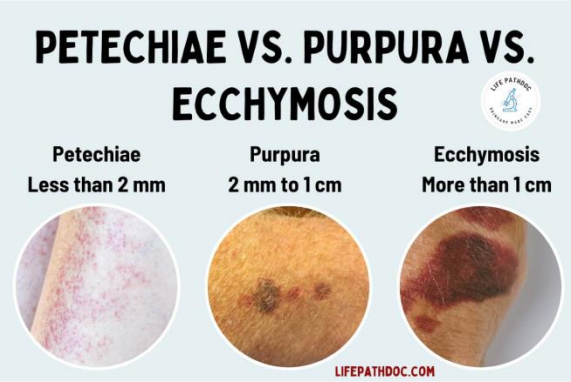
- **Hematuria**
- **Menorrhagia (**heavy menstrual bleeding**)**
- **Uterine hemorrhage**

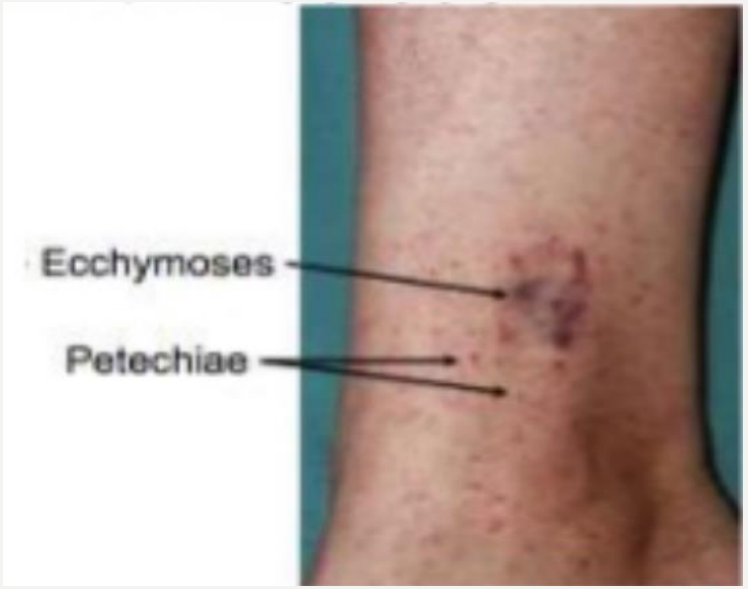
5- **Dermatologic signs**

--Ecchymosis (bruises**)**

--Purpura (red or purple discolored spots on the skin that do not blanch on applying pressure**)**

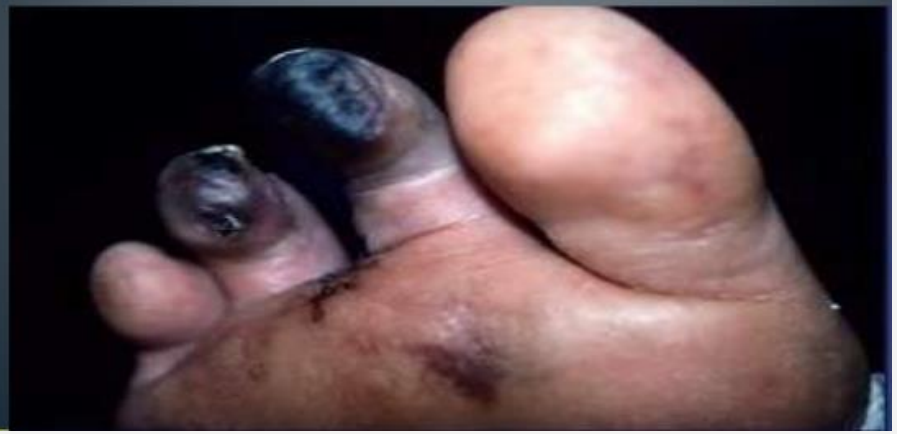
- Bleeding from mucosal sites **-Petechiae**





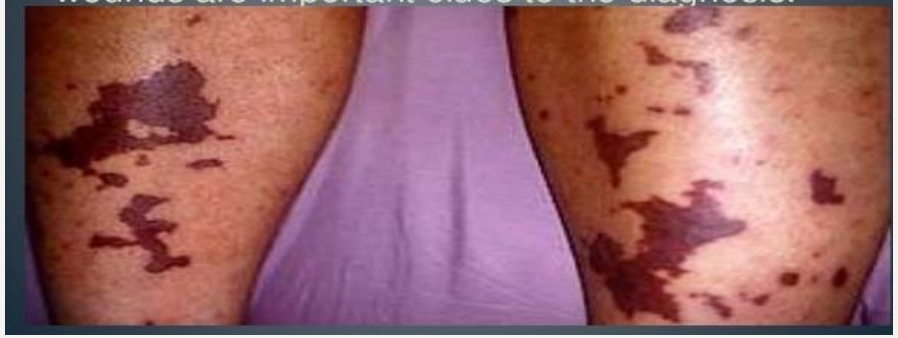
Thrombosis

- It is most commonly manifested by digital ischemia and gangrene, renal cortical necrosis and hemorrhagic adrenal infarction may occur.



Bleeding :84%~95%

- It may occur at any site, but spontaneous bleeding and oozing at venipuncture sites or wounds are important clues to the diagnosis.



COMPLICATION

- **DIC can cause complications, especially when it isn't treated properly. Complications can occur from both the excessive clotting that happens in the early stages of the condition and the absence of clotting factors in the later stages. Complications include:**

1. **blood clots that cause a lack of oxygen to limbs and organs thus causing necrosis.**
2. **Stroke.**
3. **excessive bleeding that may lead to death.**
4. **Acute kidney injury.**
5. **Change in mental status due to if either thrombi or hemorrhage to areas of the brain arise.**

7. Respiratory dysfunction leading to dyspnea and hemoptysis.
8. Hepatic dysfunction.
9. Cardiac tamponade.
10. Hemothorax.
11. Intracerebral hematoma.

HISTORY

- a recent history of severe infections or trauma as well as hepatic failure, obstetric complications, and malignancy.
- A remote history of deep vein or arterial thromboses may also be suggestive of DIC.
- experience bleeding from multiple sites including gingiva, areas of trauma or surgery, the vagina, the rectum, or through devices such as urinary catheters.

- Symptoms of hematuria, oliguria, and anuria may be seen if concomitant renal failure from DIC results.
- dyspnea and hemoptysis if pulmonary hemorrhage or pulmonary embolism is occurring.
- A patient could also experience chest pain if arterial occlusion of a coronary artery develops

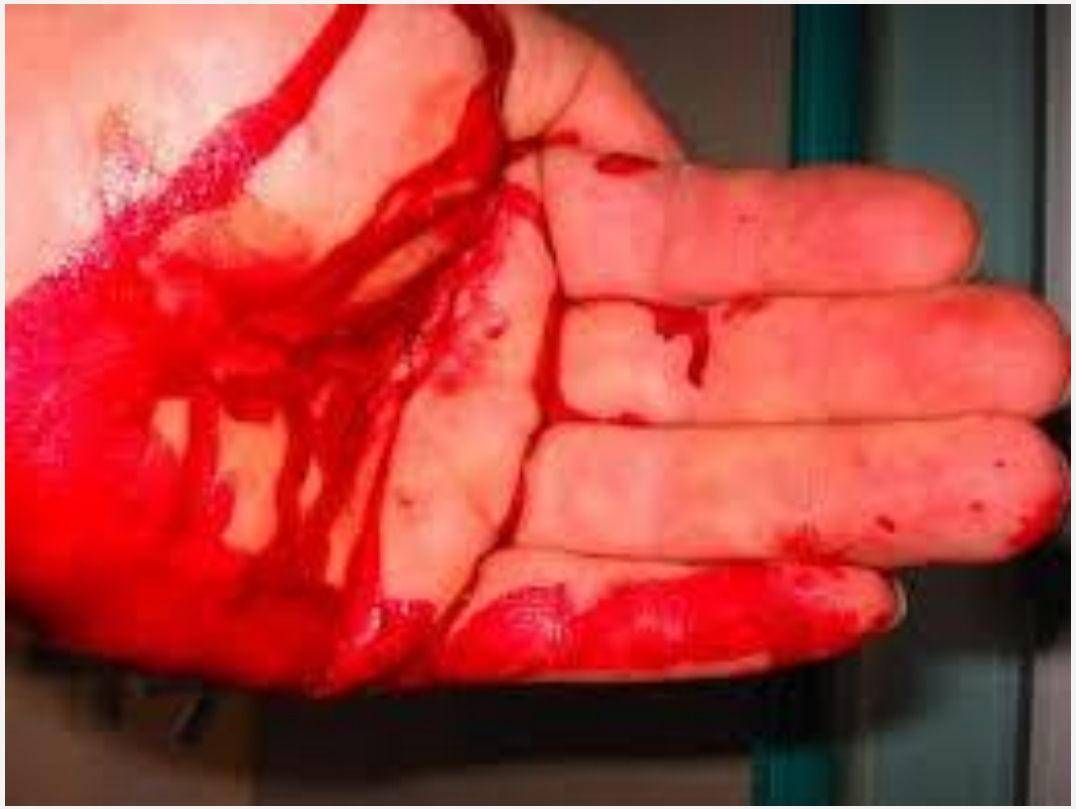
PHYSICAL EXAMINATION

- obvious bleeding, or frank hemorrhage in various areas of the body may be noted by inspection.
- Skin lesions including ecchymosis, hematomas.
- jaundice from liver failure.

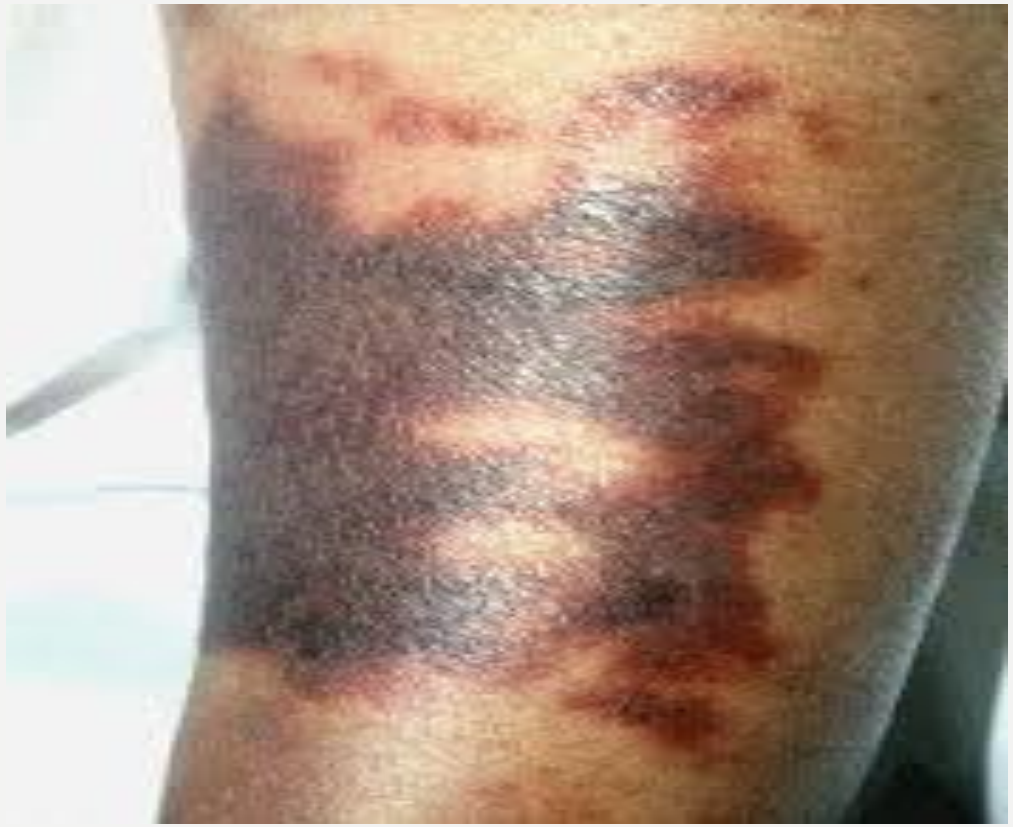
necrosis, and gangrene may also arise.

- Excessive coagulation may lead to widespread purpura, petechiae, and cyanosis.

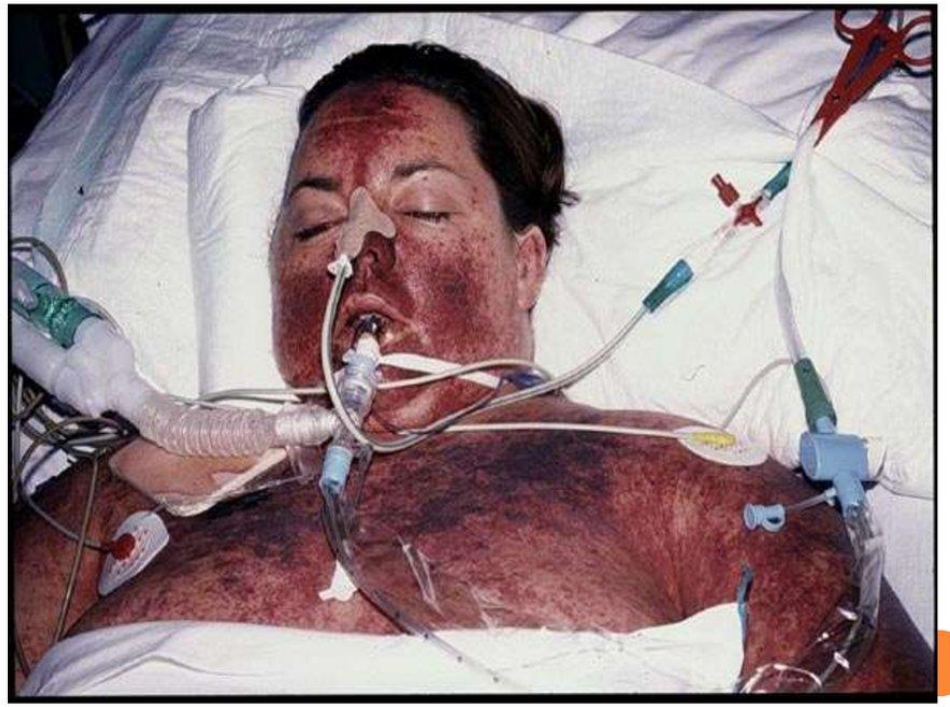
BLEEDING

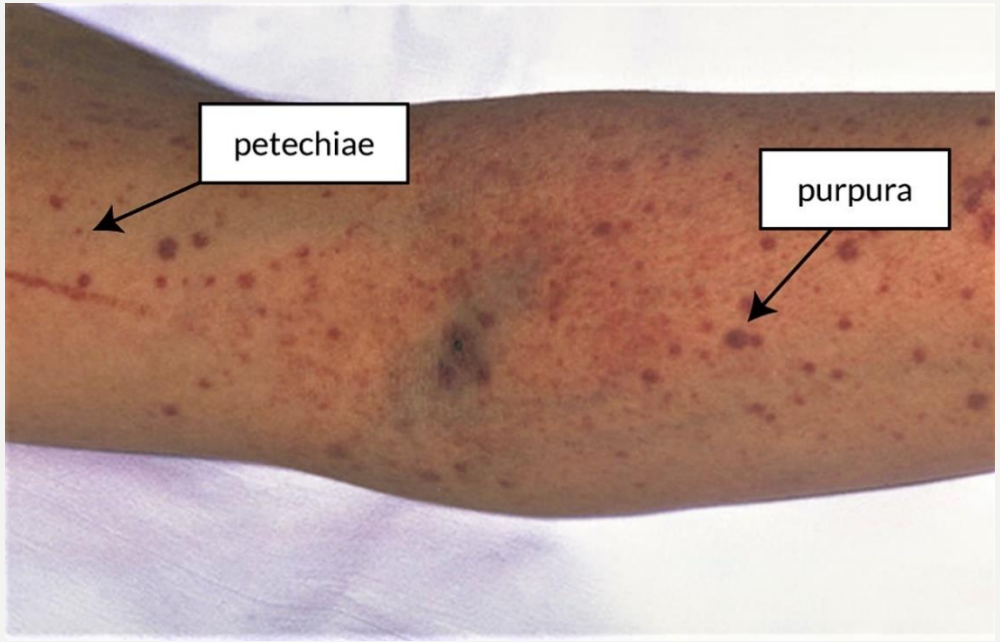


ECCYHMOSIS

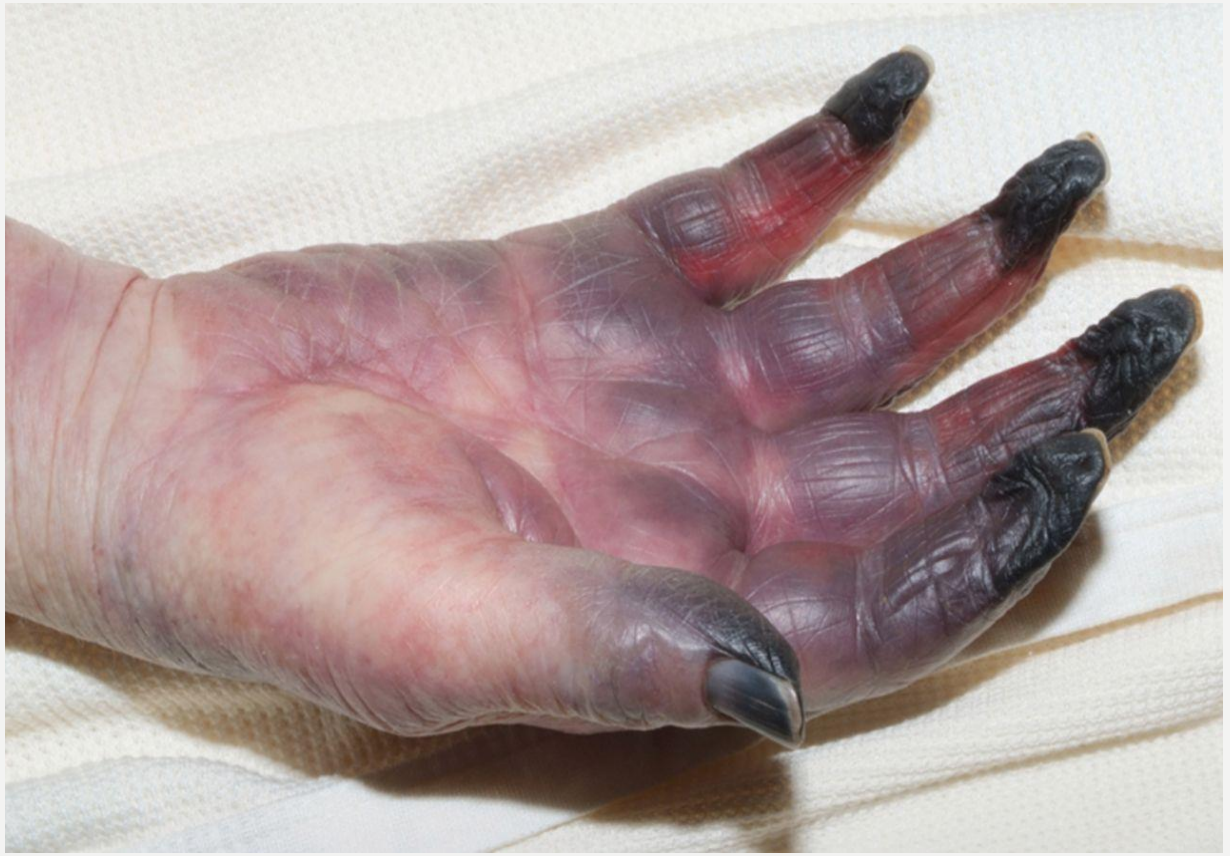


PURPURA AND PETECHIAE





NECROSIS AND GANGRENE



INVESTIGATION

- No single history, physical exam, or laboratory component can lead to a diagnosis of or rule out DIC; therefore, a combination of both ***subjective, objective, and laboratory findings*** should be utilized to make a diagnosis of DIC.

- A specific scoring system to assess for the presence of DIC was established in 2007. This score **includes platelet count, fibrin markers such as D-dimer**, **prolonged PT, and fibrinogen level** with a **score over five** indicating a high likelihood for overt DIC.

Test	Result	Points
Platelet Count	> 100 x 109/L	0 points
	51-99 x 109/L	+1 point
	≤ 50 x 109/L	+2 points
Prothrombin time (PT)	< 3 seconds	0 points
	3-6 seconds	+1 point
	> 6 seconds	+2 points
Fibrinogen level	> 1 g/L (2.94 mcmol/L)	0 points
	< 1 g/L (2.94 mcmol/L)	+1 point
Fibrin-related makers	No increase	0 points
	Moderate increase	+2 points
	Strong increase	+3 points
DIC score ≥ 5 sensitive and specific for DIC diagnosis		

TREATMENT

- The treatment for DIC centers on **addressing the underlying disorder**, which ultimately led to this condition, such as:-

1. **antibiotics and human activated protein C for severe sepsis.**

2. **possible delivery for placental abruption.**
3. **possible exploratory surgical intervention for trauma.**

- **Platelet and plasma transfusions** should only be considered in patients with **active bleeding or a high risk of bleeding or those patients requiring an invasive procedure**

- Likewise, **fresh frozen plasma**, typically at a dose of 15 mL/kg to 30 mL/kg, and **cryoprecipitate** can be transfused to replenish coagulation factors.

- Patients with DIC **who are not actively bleeding** should receive prophylactic

anticoagulation with heparin or low molecular weight heparin (LMWH).

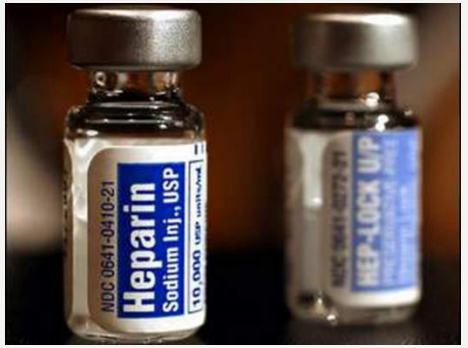
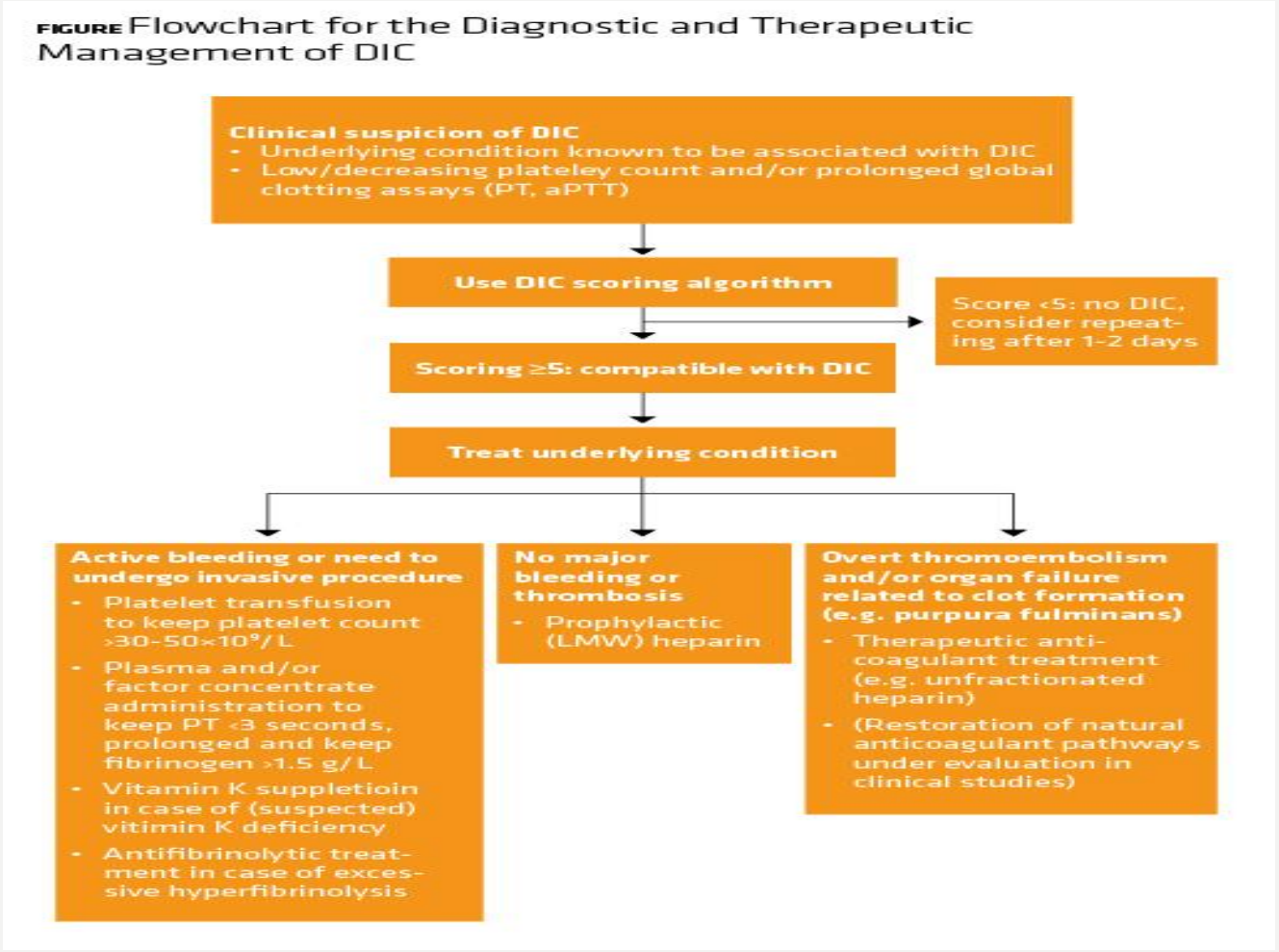


FIGURE Flowchart for the Diagnostic and Therapeutic Management of DIC



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