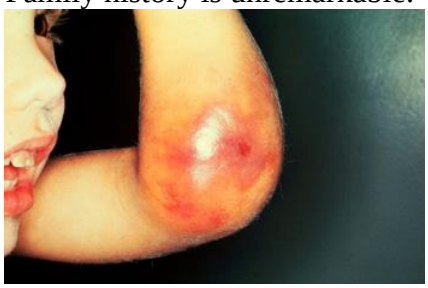
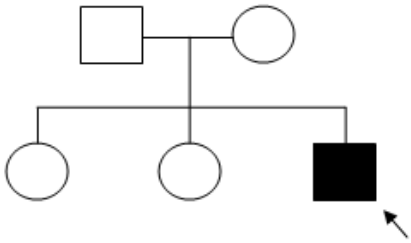
- **Case 1**: a 5 years old boy presents with swelling of the left elbow for 1 day duration which was caused by a minor trauma. The patient has a limitation of movement, but no fever, no hematuria, no mucosal bleeding and normal bowel. There is a history of easy bruising. Family history is unremarkable.





- **Lab investigations:**

PT	Normal
APTT	↑
Bleeding time	Normal
Platelet count	Normal
Factor VIII	↓

- **What is your diagnosis?**
  - ✓ Hemarthrosis due to hemophilia A
- **Definition**: it is an inherited bleeding disorder (X-linked recessive) in which factor VIII is missing and is seen in males.
- **Classification:**

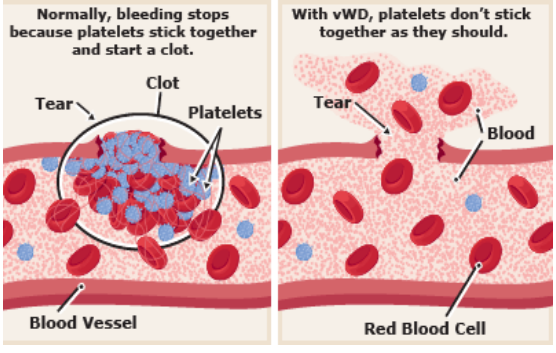
Mild (> 5% factor VIII protein activity)	Bleeding only after surgery or major trauma
Moderate (1%-5% factor VIII protein activity)	Bleeding only with trauma
Severe (< 1% factor VIII protein activity)	Spontaneous bleeding

- **Complications**: Central Nervous System (CNS) bleeding.
- **Management**: replacement with recombinant factor VIII. Desmopressin acetate (DDAVP) can be used with mild hemophilia.

- **Case 2**: a 15 years old girl presents with menorrhagia for 16 days, epistaxis that started at the 10th day of her menstruation, some ecchymosis, fatigue and decreased appetite. There is a history of family bleeding disorder.
- **Lab investigations:**

PT	Normal
APTT	↑
Bleeding time	↑
Platelet count	Normal
Factor VIII	↓

- **What is your diagnosis?**
  - ✓ von Willebrand's disease.
- **Definition**: it is an autosomal dominant disease in which there is a deficiency in vWf portion of factor VIII complex.
- **Diagnosis (other than lab values mentioned above):** can be done via quantitative assay for vwF antigen and activity (ristocetin cofactor assay).



- **Management**: DDAVP (for mild-moderate disease); factor VIII and vWf concentrates (for severe disease).

- **Vitamin K deficiency and liver diseases:**
  - **Vitamin K is a fat soluble vitamin essential for synthesis of the following factors; II, VII, IX, X in addition to proteins C and S.**
  - **Causes of vitamin K deficiency:**
    - ✓ Nutritional deficiency (unusual).
    - ✓ Pancreatic insufficiency, biliary obstruction (both resulting in diminished ability to absorb vitamin K).
    - ✓ Medications (such as warfarin).
    - ✓ Hemorrhagic disease of newborn (rare nowadays because prophylactic vitamin K injection is given to all newborns).
  - **Clinical features of vitamin K deficiency**: bruising, oozing from skin puncture wounds and bleeding into organs (deep tissue bleeding).
  - **Lab investigations of vitamin K deficiency:**

PT	↑
APTT	↑
Bleeding time	Normal
Platelet count	**Normal**

  - **Management of vitamin K deficiency**: administration of vitamin K.

  - **Liver disease**: the liver is the major site of production of most coagulation factors. Notice that vitamin K-dependent factors are most severely affected.
  - **Lab investigations of liver diseases;**

PT	↑
APTT	↑
Bleeding time	↑
Platelet count	↓

  - **Management**: vitamin K, fresh frozen plasma and platelets as needed.

- **Disseminated Intravascular Coagulation (DIC):**
  - **DIC is a secondary phenomenon to systemic factors such as: sepsis, hypothermia, malignancy, heat stroke, snake bite and burns.**

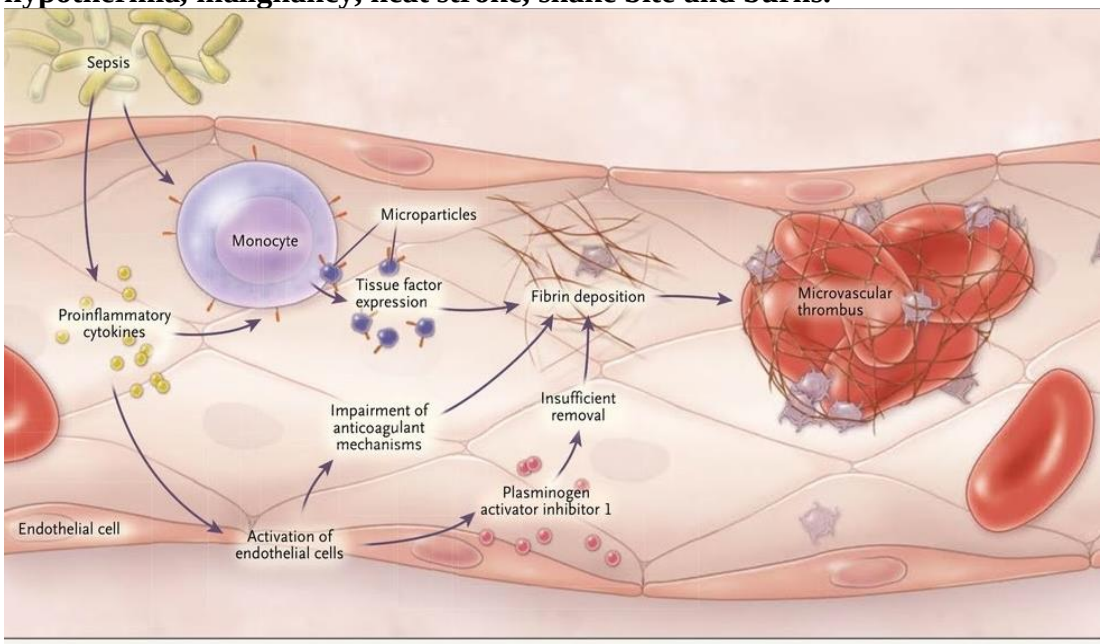


Figure 2. Pathogenesis of Disseminated Intravascular Coagulation in Sepsis.
Through the generation of proinflammatory cytokines and the activation of monocytes, bacteria cause the up-regulation of tissue factor as well as the release of microparticles expressing tissue factor, thus leading to the activation of coagulation. Proinflammatory cytokines also cause the activation of endothelial cells, a process that impairs anticoagulant mechanisms and down-regulates fibrinolysis by generating increased amounts of plasminogen activator inhibitor.

- **Clinical features**: cutaneous bleeding (bleeding from venepuncture sites) and internal organ bleeding.
- **Lab investigations:**

PT	↑
APTT	↑
Bleeding time	↑
Platelet count	↓
Fibrinogen	↓
D-dimer	↑

- **Management**: treatment of underlying cause (being most important), fresh frozen plasma and platelets as needed.

- **Immune Thrombocytopenic Purpura (ITP):**
  - **Etiology**: in most cases it is idiopathic but can be preceded by a viral infection 2 weeks before which will stimulate autoantibodies to bind to platelets resulting in their destruction by the spleen.
  - **Clinical presentation**: sudden cutaneous or mucous membrane bleeding (petechia, bruising, epistaxis or gum bleeding).
  - **Lab findings**: thrombocytopenia.
  - **Management**: IV immunoglobulin or corticosteroids. Notice that platelet transfusion are generally avoided because transfused platelets are rapidly destroyed.
  - **Prognosis**: 70-80% of cases resolve spontaneously within months.
- **Henoch-Schonlein purpura:**
  - It is an IgA-mediated vasculitis in which patients present with palpable purpura (especially on lower extremities and buttocks), renal insufficiency, arthritis and abdominal pain. Notice that platelet count is normal.