Idiopathic (Autoimmune) Thrombocytopenic Purpura(ITP)

Acute ITP

Self limited disorder following viral infection (HIV, CMV, HEPATTIS C, RTI)

1 - 4 wk after exposure to a common viral infection

The peak age is 1-4 yr

The classic presentation of ITP is a previously healthy 1-4 yr old child who has sudden onset of generalized petechiae and purpura

Recover within few weeks to 6 months

Chronic ITP

- **More common in adult woman in child Bearing age (20-40yrs)**
- **Insidious onset**
- **Associated with SLE, AIDS, Auto immune thyroiditis**

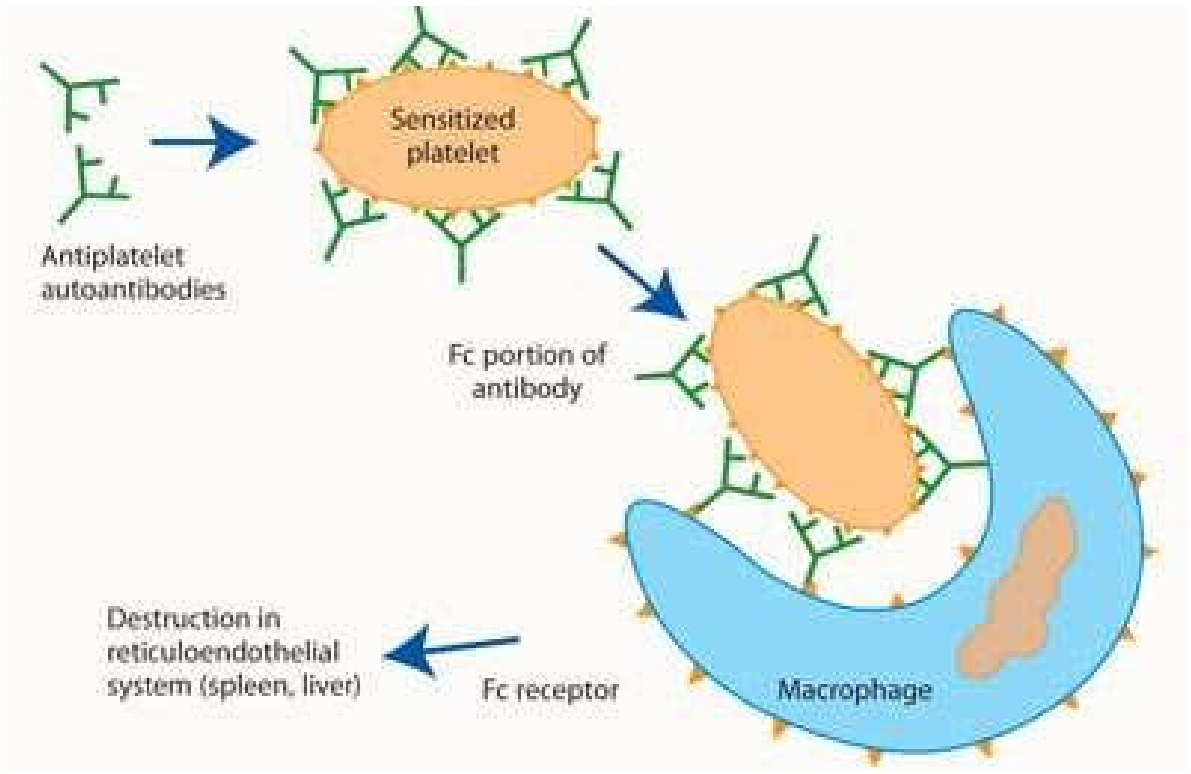
Pathogenesis of chronic ITP

Formation of Ig G humoral auto antibodies against gp IIb – IIIa / Ib – IX in spleen

In 80% cases these Ab demonstrated in plasma / on platelet surface

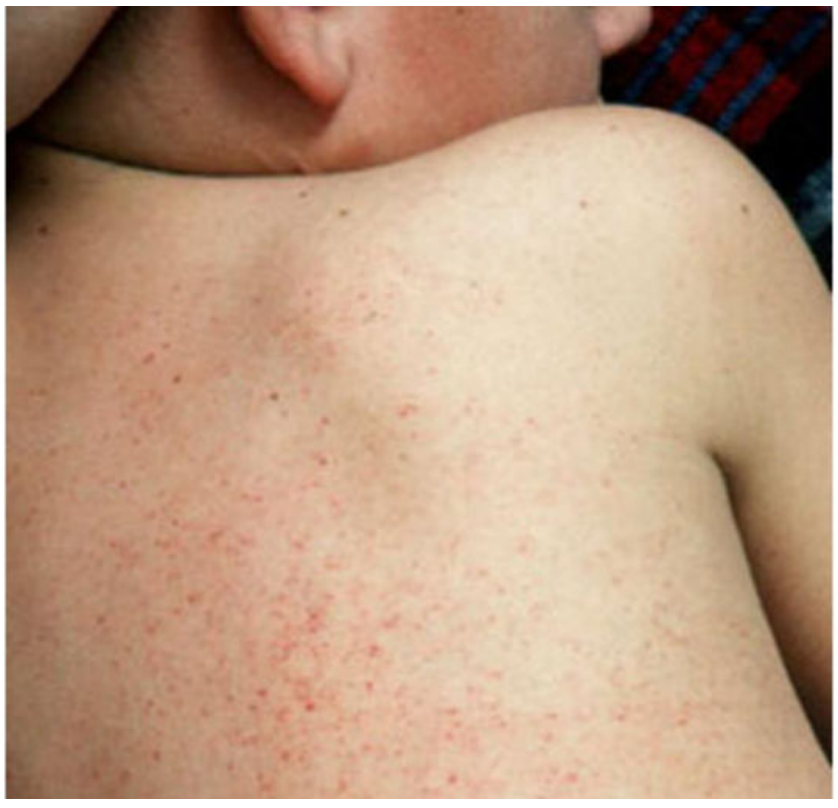
Opsonized platelet are recognized by the Fc receptor on splenic macrophages, ingested, and destroyed

ITP (Pathophysiology)(cont.)



SYMPTOMS

- **Petechiae**
- **Bruises or purpura**
- **Bleeding of mucous membranes: epistaxis, gingival bleeding**
- **Acute gastrointestinal bleeding**
- **Menorrhagia**
- **Hematuria**
- **Acute CNS hemorrhage: the rarest but MOST FEARED consequence of low platelets**



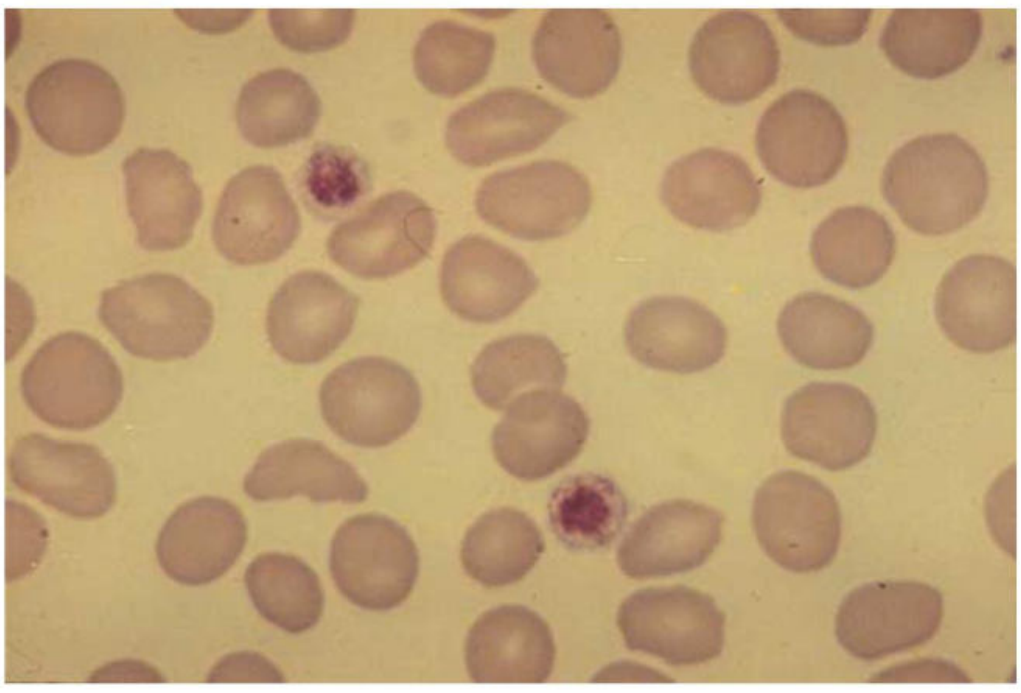
Lab diagnosis

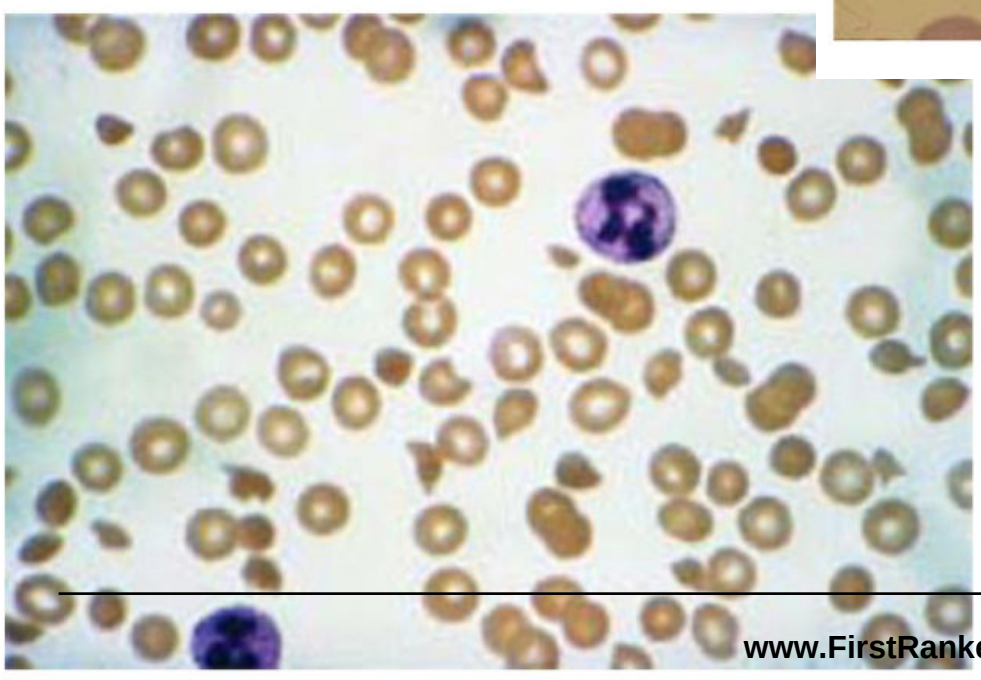
Platelet count reduced(10,000-50,000)

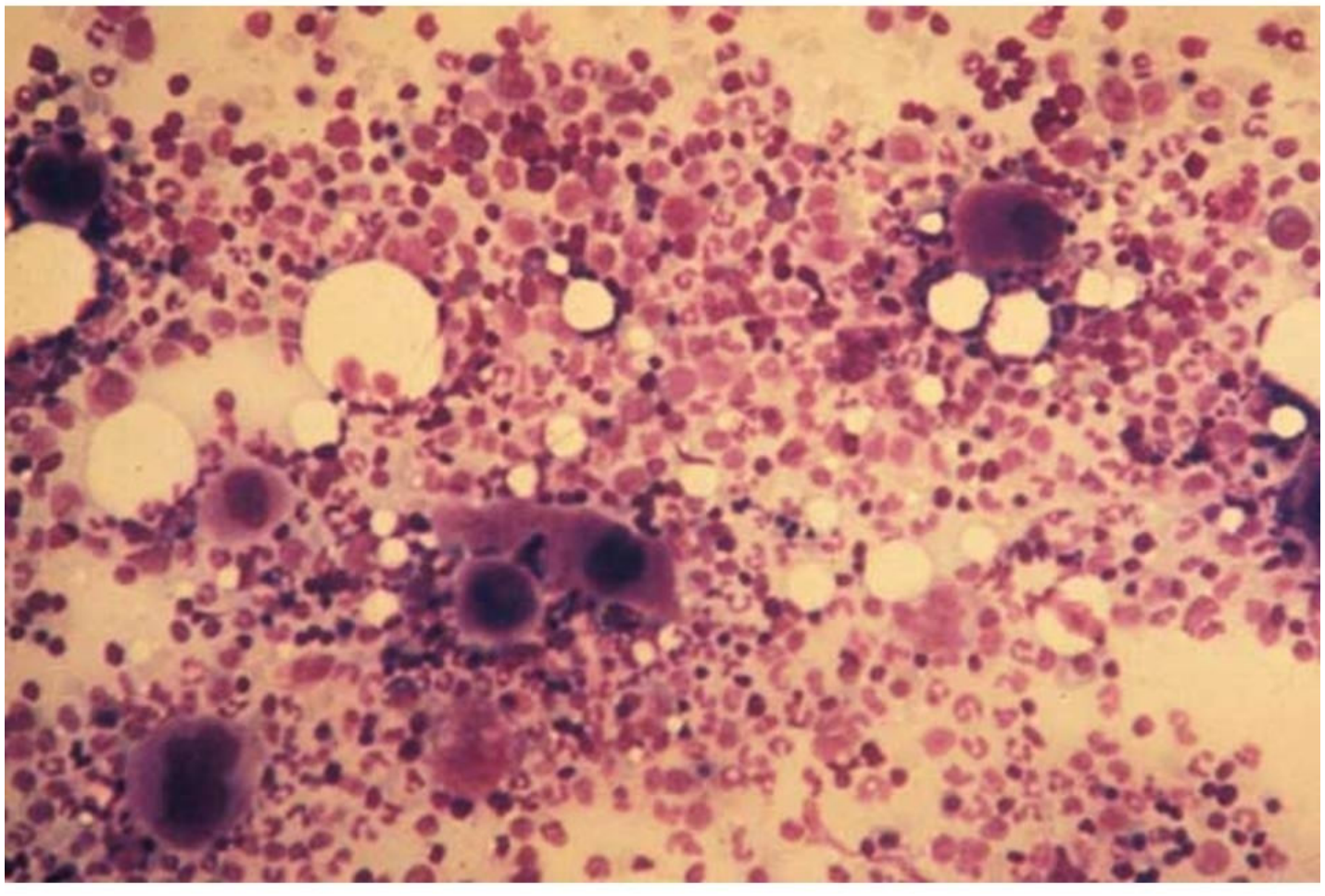
Peripheral smear-Reduced platelet with giant platelet

Bone marrow – increased megakaryocytes

Large non lobulated single nuclei (immature forms) with reduced granularity presence of vacuole







Treatment(Cont.)

1. IVIG
2. High-dose corticosteroids
3. splenectomy
4. Platelet transfusion

Thrombotic Thrombocytopenic Purpura

Definition

- **Syndrome of Coomb's negative microangiopathic hemolysis and thrombocytopenia in the absence of an alternative explanation for these manifestations.**
- **Presence of Fever, Neurological and renal abnormalities : classic Pentad.**

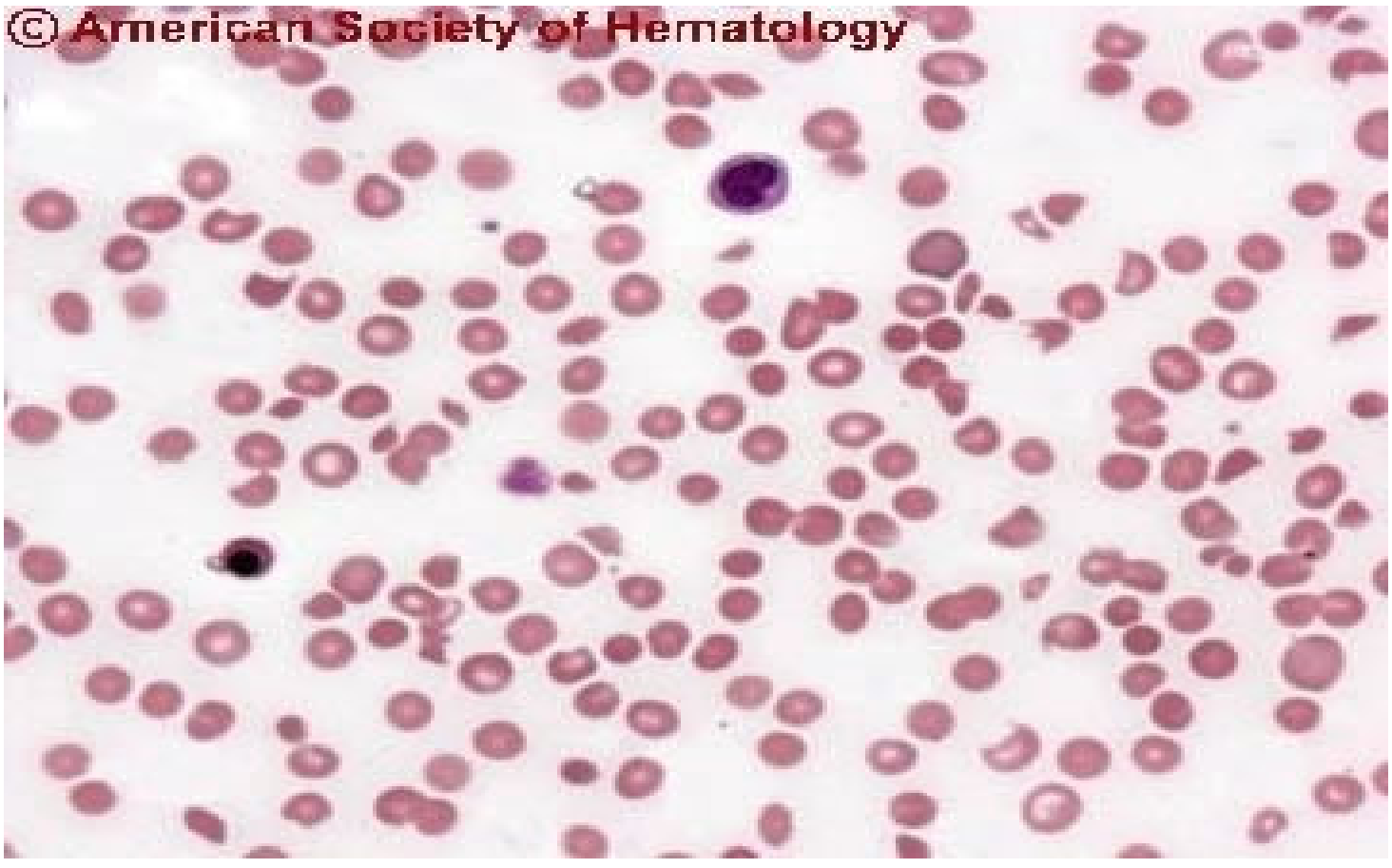
Pathogenesis

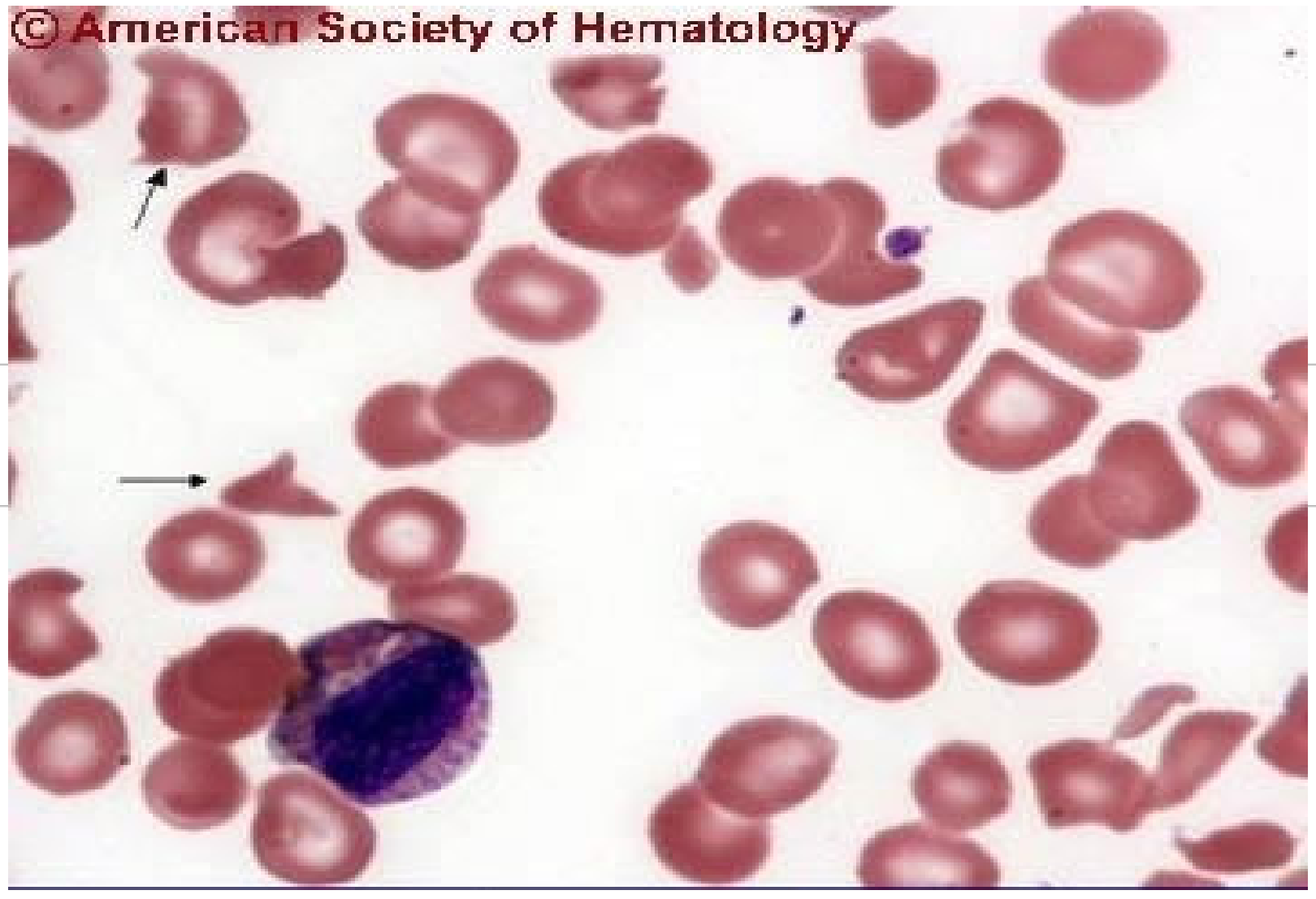
- Endothelial damage from immunological damage by diverse condition like pregnancy metastatic cancer chemotherapy hiv
- Release of procoagulant like vwf from endothelium
- Formation of micro thrombi

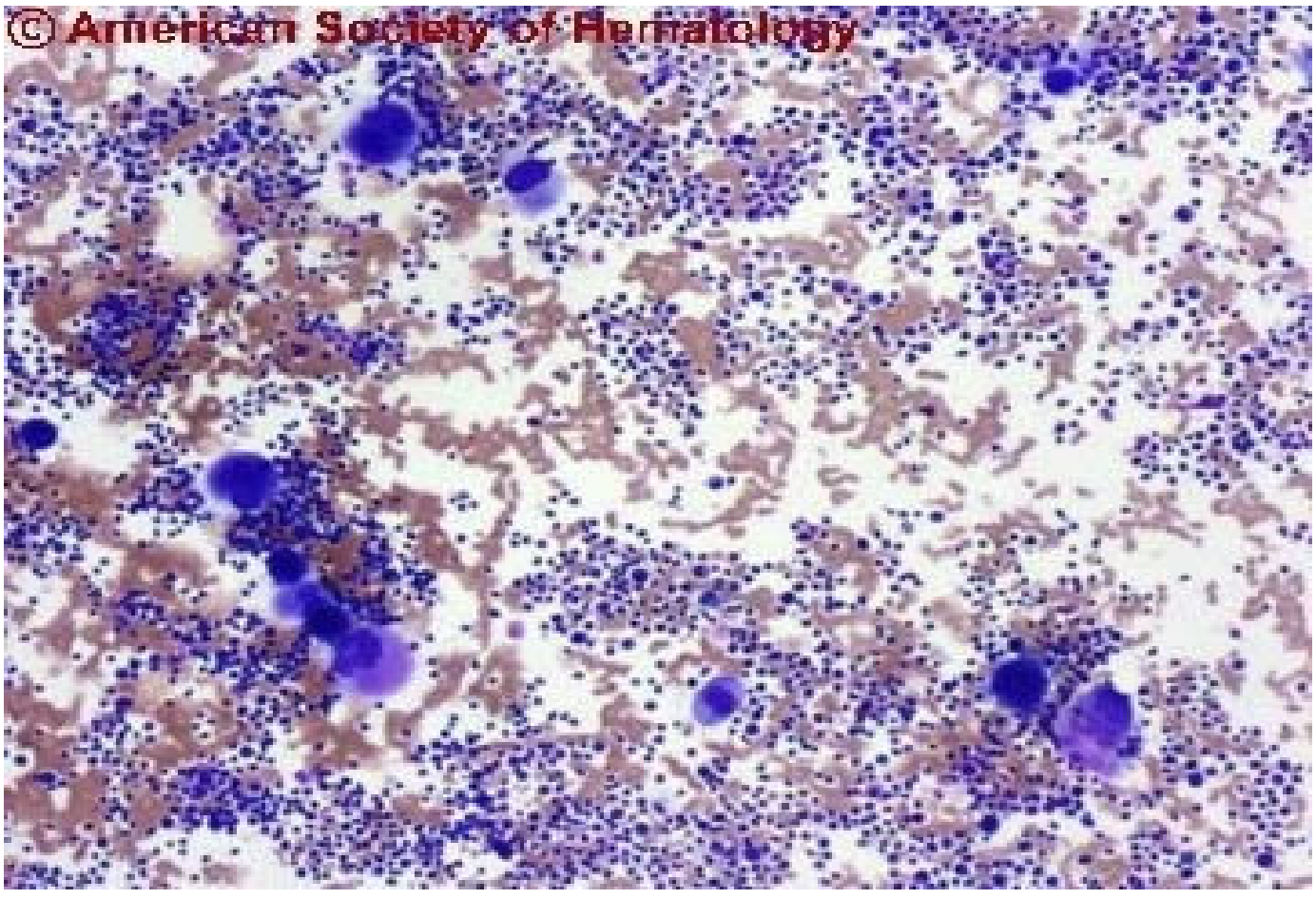
Diagnosis

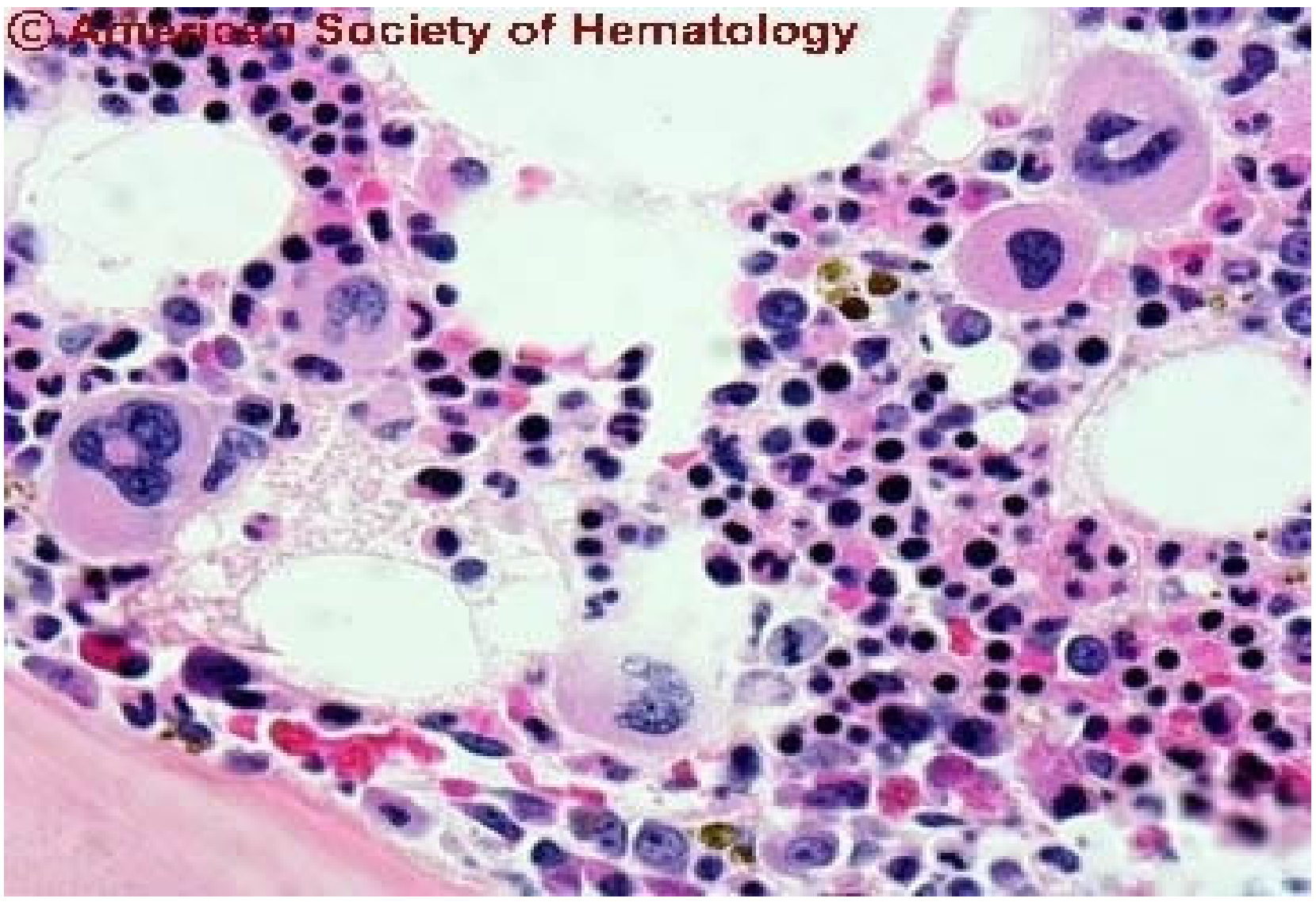
- **Primary diagnostic criteria**
  - **Thrombocytopenia (often below <20,000)**
  - **Microangiopathic hemolytic anemia**
    - **Negative Coomb's test.**
    - **Fragmented red cells (schistocytes) on peripheral smear**
    - **LDH elevation is the hallmark of RBC destruction and tissue injury related to ischemia.**
- **examination of biopsy (gingival) demonstrate microthrombi in arterioles, capillary and venules not associated with inflammatory changes in vessel wall**
- **Bone marrow shows mild myeloid and megakaryocytic hyperplasia**

George,Blood Aug 2000









ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13)—also known as von Willebrand factor-cleaving protease (VWFCP)—is a zinc-containing metalloprotease enzyme that cleaves von Willebrand factor (vWf), a large protein involved in blood clotting.

The unprocessed form of von Willebrand factor interacts easily with **cell** fragments called **platelets**, which circulate in the bloodstream and are essential for blood clotting

- Tests for ADAMTS13 deficiency or inhibitors are not readily available and lack standardization.

Differential Diagnosis

- Disseminated intravascular coagulation.
- Sepsis: cytomegalovirus, rocky mountain spotted fever, meningococcemia.
- Preeclampsia/eclampsia, HELLP.
- Disseminated malignancy.
- Hemolytic-uremic syndrome
- Evans syndrome
- Malignant hypertension.

Treatment

- Plasma exchange:
  - Untreated TTP has 80-90% mortality.
  - Removes ULvWF multimers, autoantibody and replaces metalloproteinase.
  - Randomized controlled trial (Rock et al, 1991)
  - FFP as the replacement fluid is most widely used and cost effective.

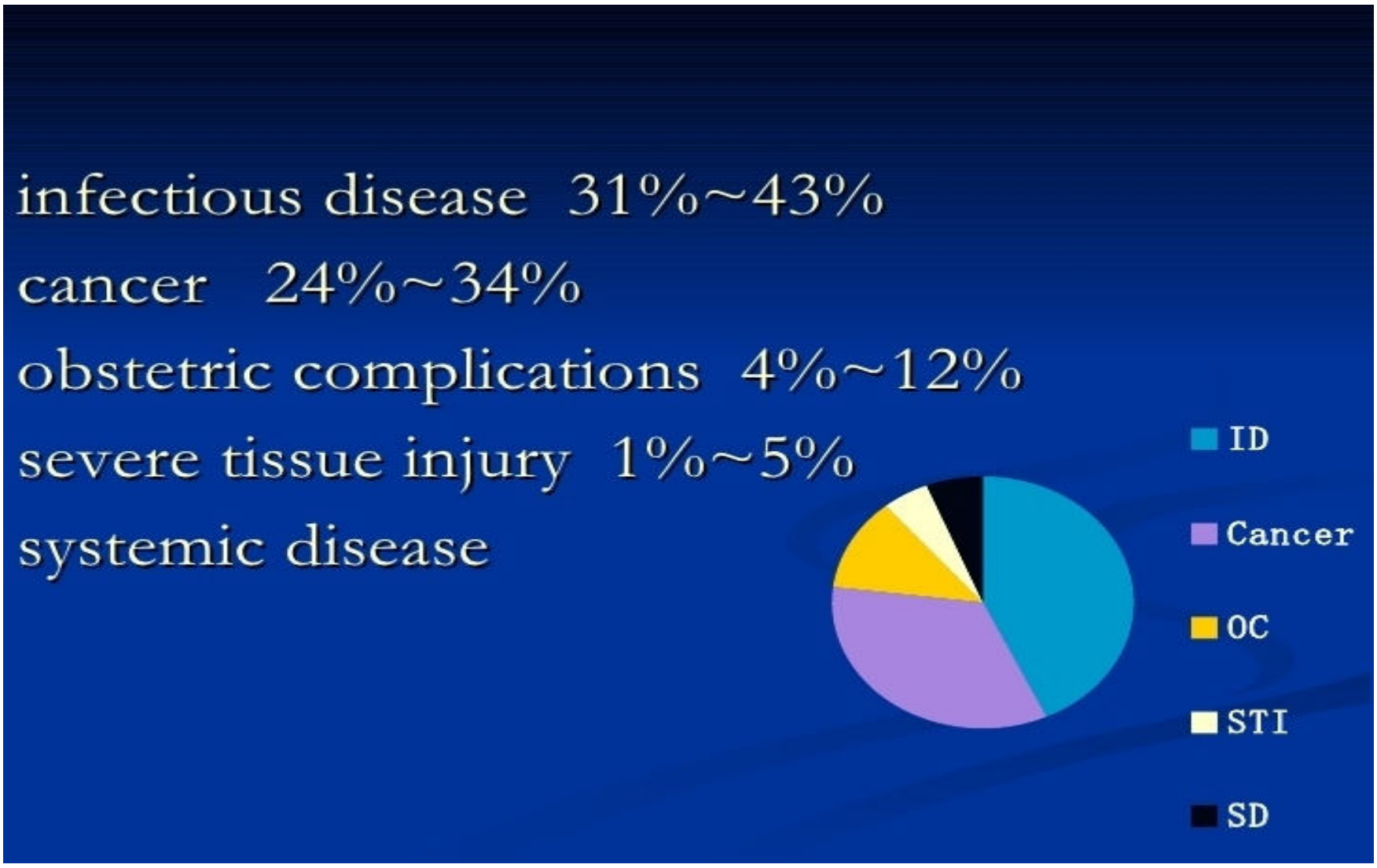
Treatment

- Cryosupernatant plasma (Rock et al 2000)
  - Theoretically superior to FFP in refractory disease
  - Removal of cryoprecipitate from donor plasma results in removal of vWF (only 18%), with no change in metalloproteinase concentration.
- Solvent-detergent plasma (Moake et al 1998)
  - Lacks high molecular weight forms of VWF
  - Inactivates lipid-enveloped viruses.
  - Drawback: parvovirus & hep A not inactivated.

DIC (Disseminated Intravascular Coagulation)

- **An acute, subacute or chronic thrombo hemorrhagic disorder occurring as a secondary complications in a variety of diseases.**
- **As a consequence of the thrombotic diathesis, there is consumption of platelets, fibrin & Clotting Factors & secondary activation of fibrinolytic mechanism.**

Causes of DIC



Major disorders associated with DIC

1. Obstetric complications
- **Abruptio Placentae**
- **Retained dead fetus**
- **Septic abortions**
- **Amniotic fluid embolism**
- **Toxemia**

2. Infections
- **Gm –ve sepsis**
- **Meningococcemia**
- **Rocky mountain spotted fever**
- **Histoplasmasis**
- **Aspergillosis**
- **Malaria**

3. Neoplasms
- **Carcinoma of pancreas, stomach, prostate & lung**
- **AML – M3**

4. Massive Tissue injury
    Traumatic
    Burns
    Extensive injury

5. Miscellaneous
    Acute intravascular hemolysis, snake bite, giant hemangiomas, shock, stroke, liver disease.

PATHO-PHYSIOLOGY

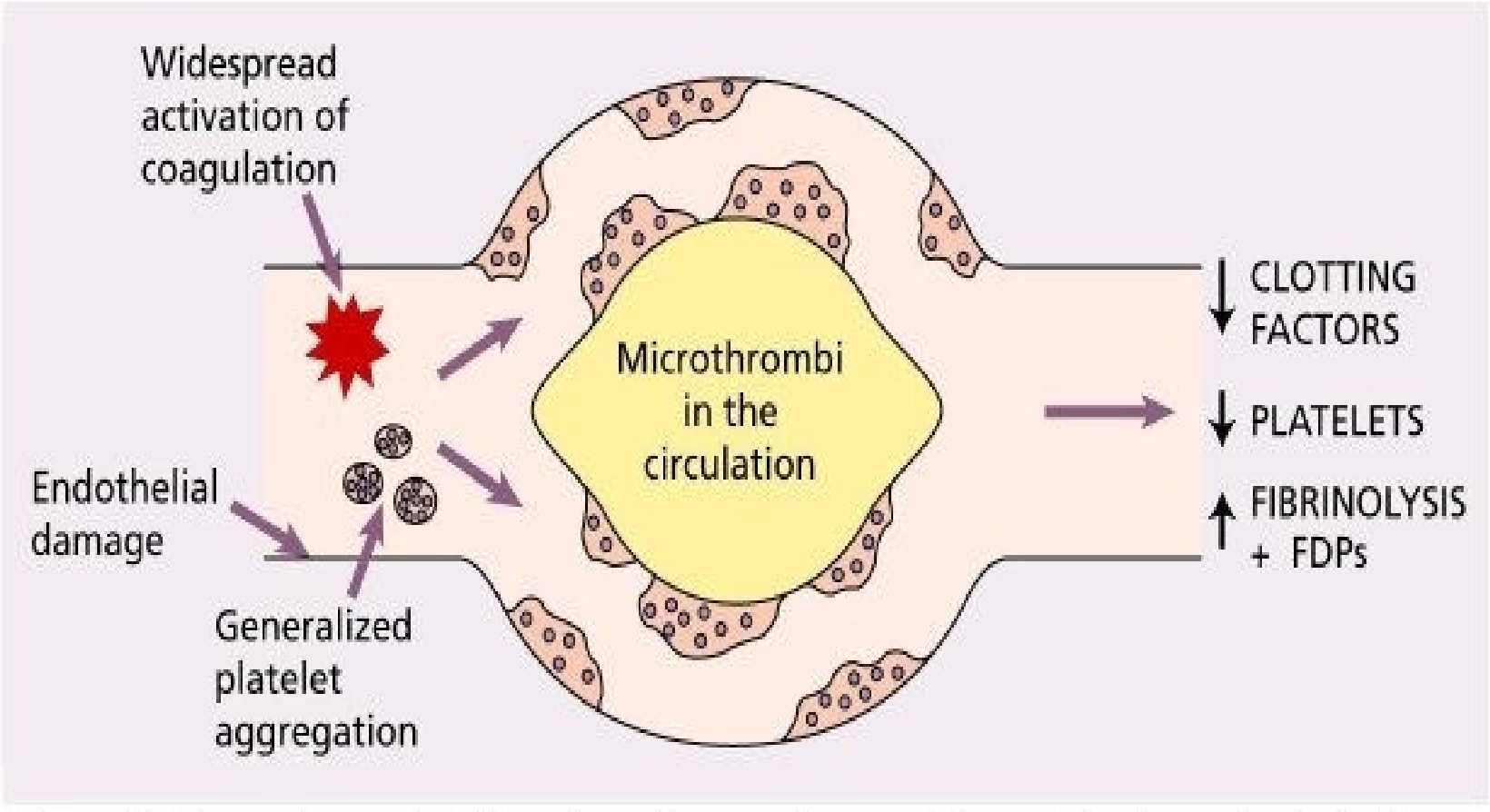
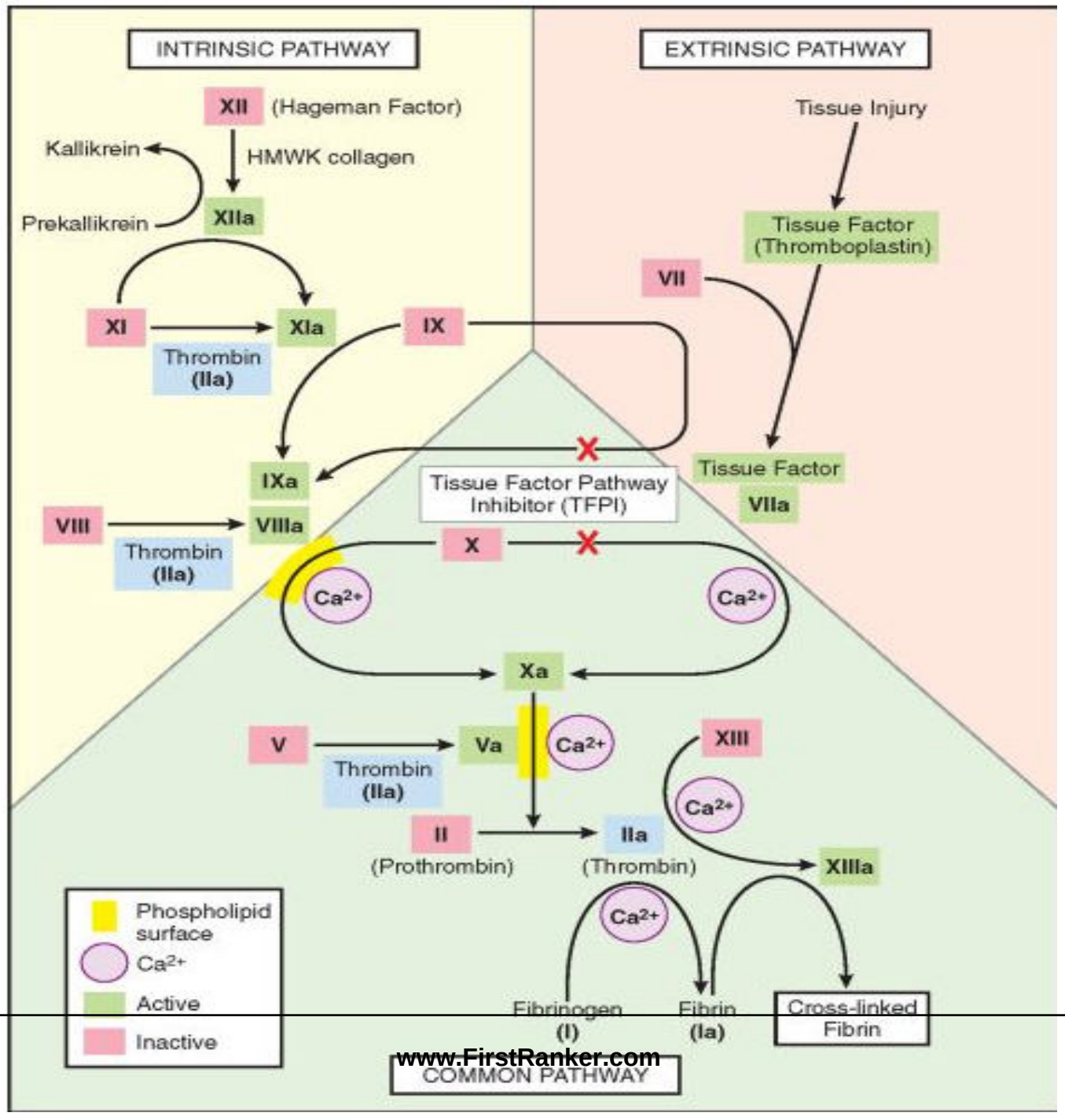


Figure 26.9 The pathogenesis of disseminated intravascular coagulation and the changes in clotting factors, platelets and fibrin degradation products (FDPs) that occur in this syndrome.



Two major mechanism triggers DIC

1) Release of TF/ thromboplastin substances into circulation

TF – Released from placenta, Granules of leukemic cells (AML)

Mucus released from adenocarcinomas(Directly activate Factor X)

2) Endothelial Injury

Release of TF, Pl- aggregation, increased intrinsic pathway activity.

widespread endothelial injury may be produced by deposition of Ag – Ab complexes (SLE),

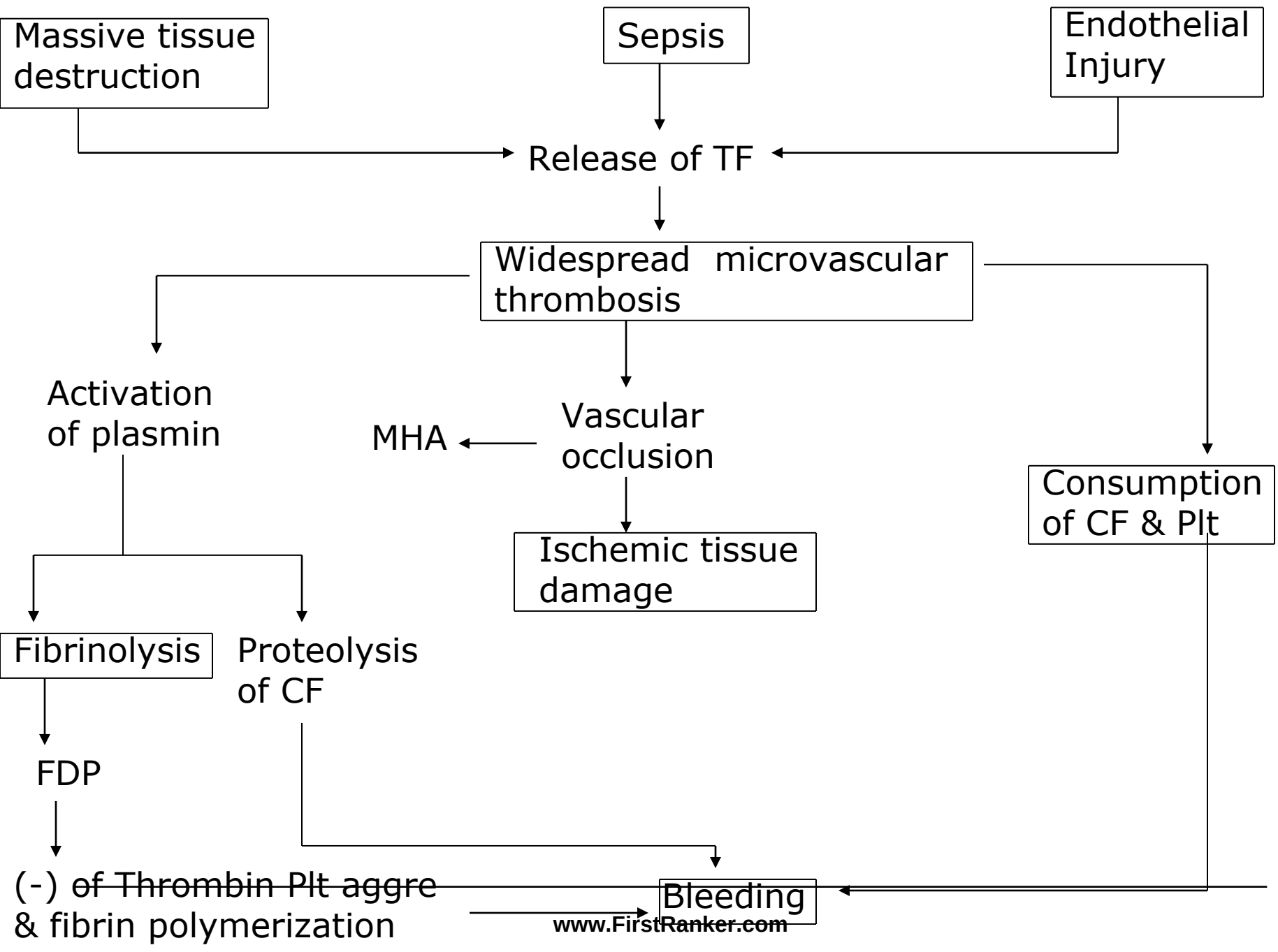
Temperature extremes (burns, heat stroke) or micro-organisms (meningococci, rickettsiae)

Clinical course

Acute DIC associated with Bleeding diathesis initially

obstetric complications
Trauma
endotoxic shock
Amniotic fluids embolism

Chronic DIC associated with thrombotic disorders (cancer)
Retained dead fetus
Carcinomatosis



Thrombi are most often found in the brain, heart, lungs, kidneys, adrenals, spleen, and liver, in decreasing order of frequency, but any tissue can be affected.

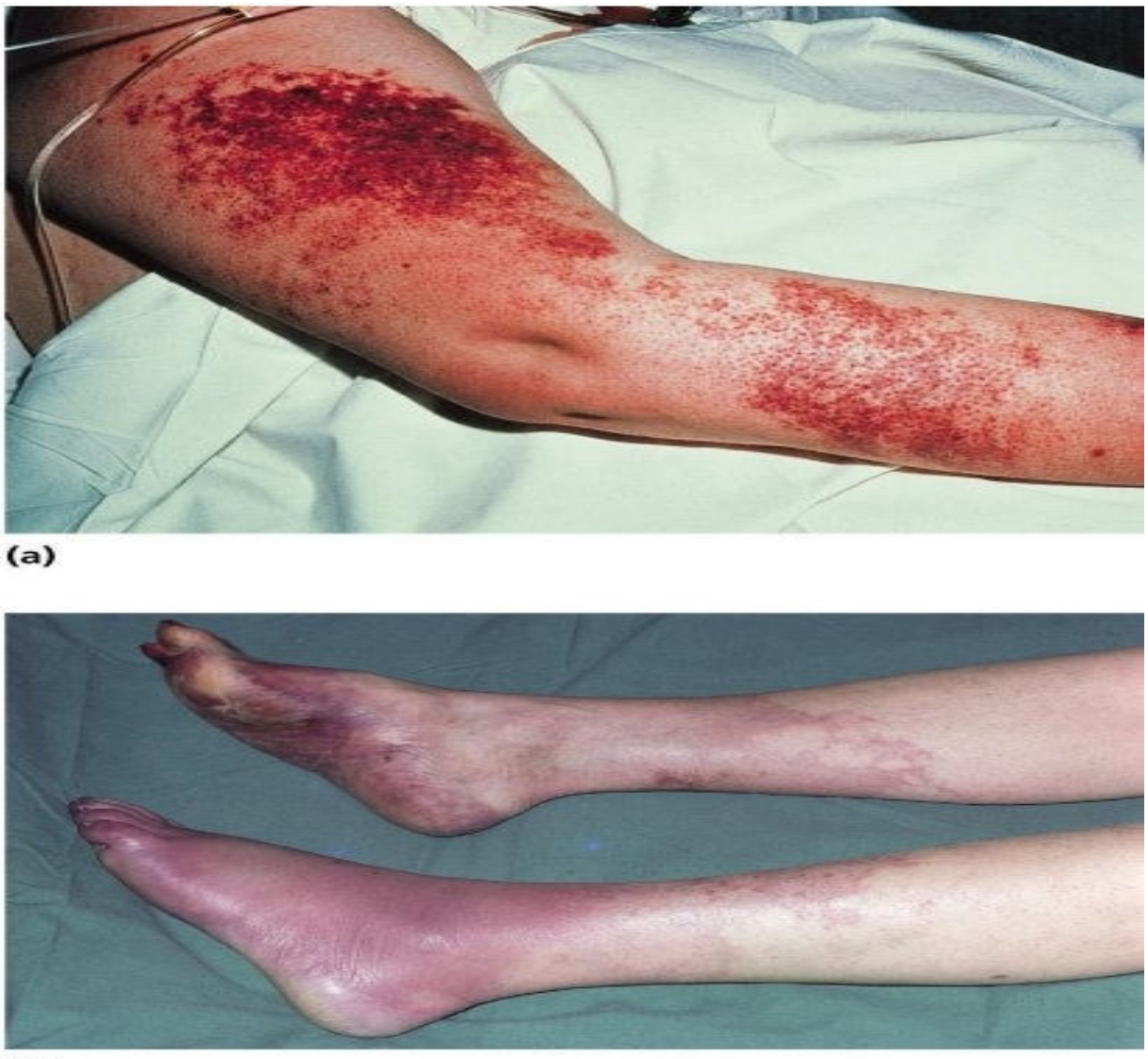
Affected kidneys may have small thrombi in the glomeruli that evoke only reactive swelling of endothelial cells or, in severe cases, microinfarcts or even **bilateral renal cortical necrosis**.

Numerous fibrin thrombi may be found in alveolar capillaries associated with pulmonary edema and fibrin exudation, creating “hyaline membranes” reminiscent of acute respiratory distress syndrome

In the central nervous system, fibrin thrombi can cause microinfarcts, occasionally complicated by simultaneous hemorrhage, which can sometimes lead to variable neurologic signs and symptoms.

In meningococcemia, fibrin thrombi within the microcirculation of the adrenal cortex are the probable basis for the massive adrenal hemorrhages seen in **Waterhouse-Friderichsen syndrome**.

An unusual form of DIC occurs in association with giant hemangiomas (**Kasabach-Merritt syndrome**), in which thrombi form within the neoplasm because of stasis and recurrent trauma to fragile blood vessels



(a)

Figure 26.10 Clinical features of disseminated intravascular coagulation: **(a)** indurated and confluent purpura of the arm; **(b)** peripheral gangrene with swelling and discolouration of the skin of the feet in fulminant disease.

LAB FINDINGS IN DIC

TEST	RESULTS
PLATELET COUNT	MARKEDLY REDUCED
PROTHROMBIN TIME	MARKEDLY INCREASED
APTT	MARKEDLY INCREASED
FDP	MARKEDLY INCREASED
FIBRINOGEN	NORMAL / DECREASED
AT III	MARKEDLY DECREASED
PROTEIN C	MARKEDLY DECREASED

- R_X Fresh frozen plasma
  Heparin