Disseminated intravascular coagulation (DIC)

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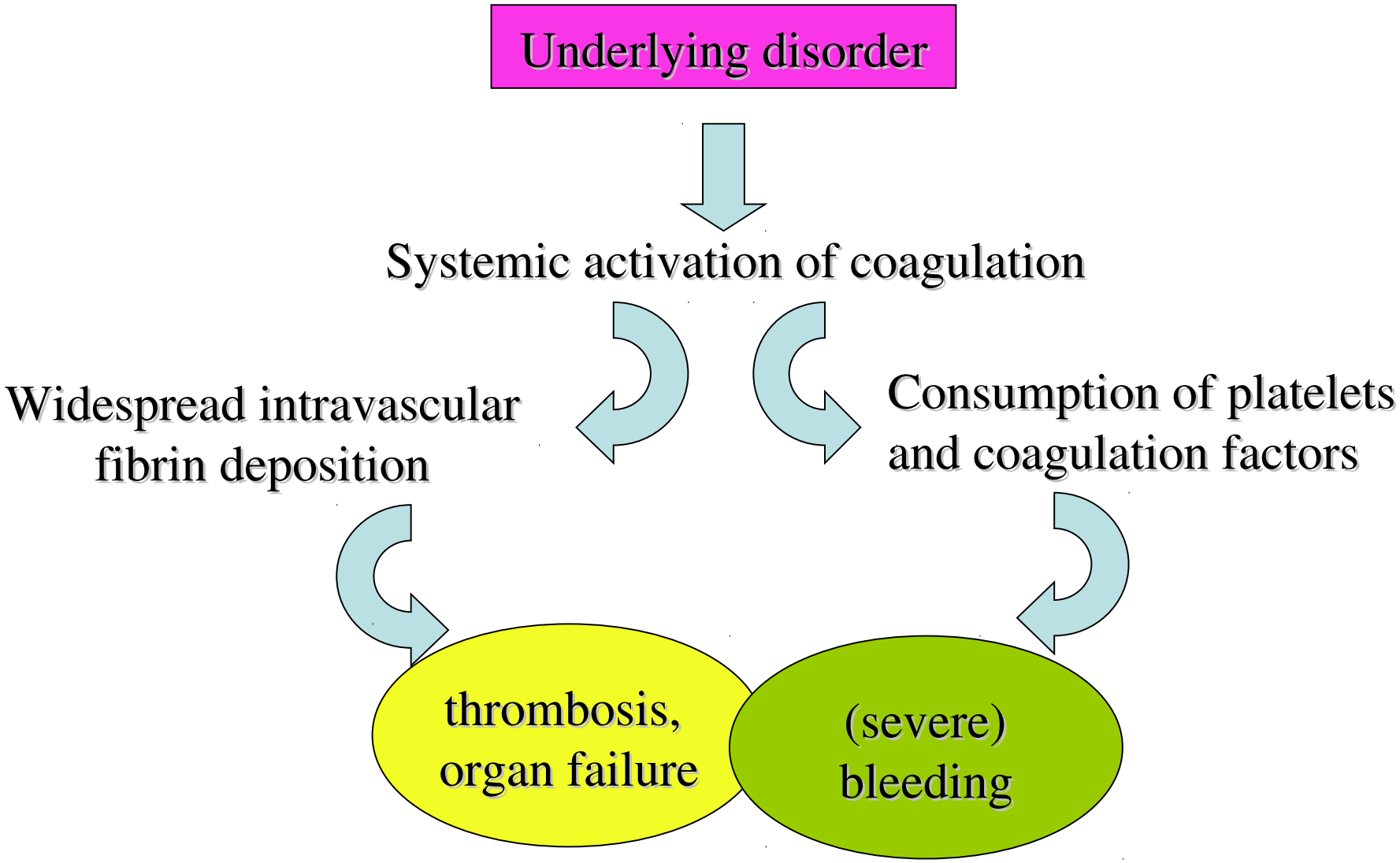
Disseminated intravascular coagulation *(DIC, consumptive coagulopathy)*

is a clinicopathologic syndrome characterized by widespread *intravascular fibrin formation* in response to a ***pathological activation of blood coagulation.***

Small vessel *thrombosis occurs,* and *ischemic organ damage* results.

A ***compensatory fibrinolysis*** develops, and combined with the *exhaustion of coagulation factors and thrombocytopenia,* contributes to a *hemorrhagic diathesis.*

Pathophysiology of DIC



(Bjh guideline, 2009)

DIC is *not a disease in itself,* but it is a manifestation of an underlying disorder.

About half of DIC cases result from complications of pregnancy, and about a third result from carcinomatosis.

Causes of DIC

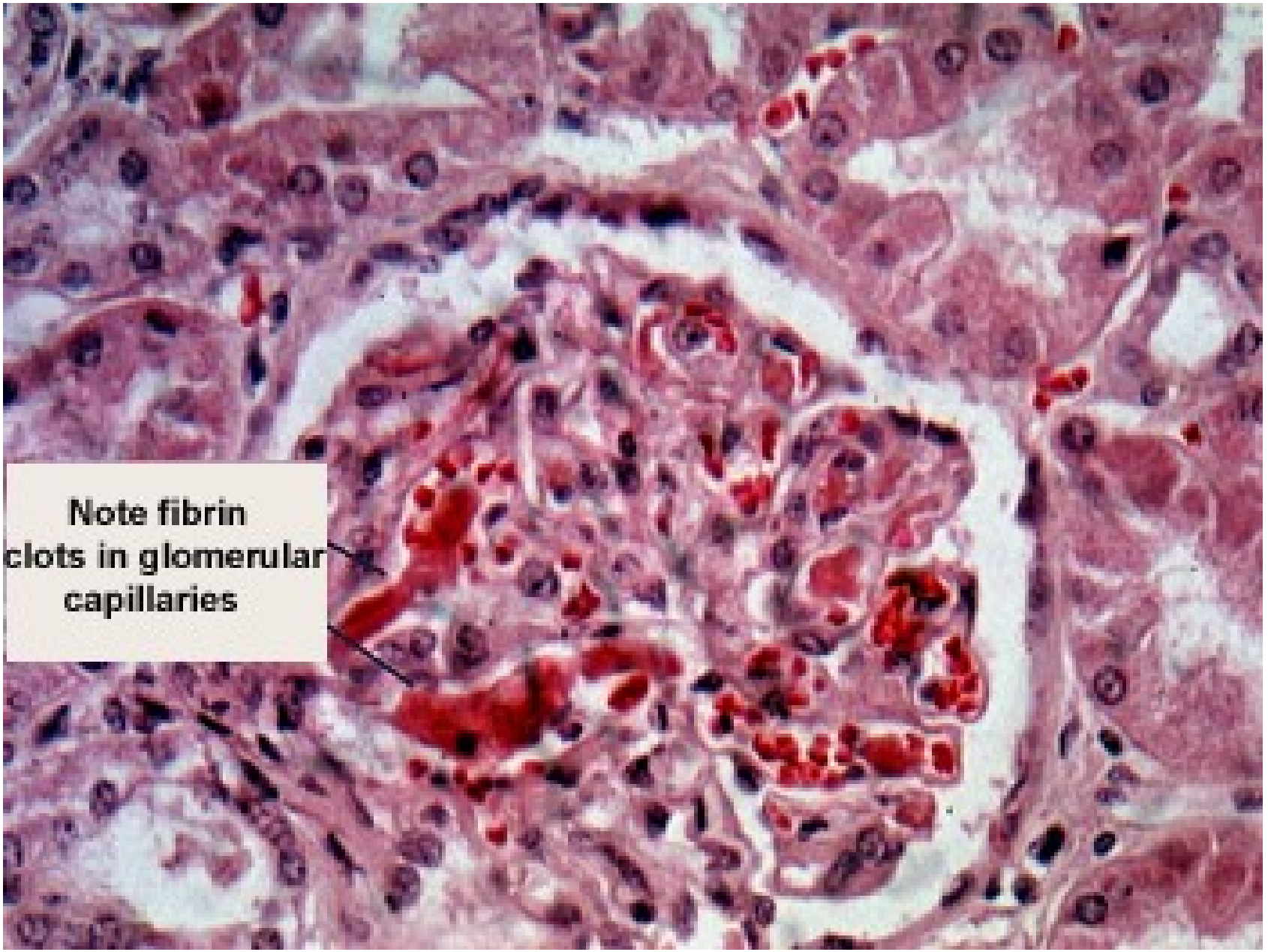
- Sepsis
  - Gram Negative (endotoxin)
  - Gram Positive (mucopolysaccharides)
- Cancer
  - APL (M-3)
  - Acute myelomonocytic (M-4)
  - Adenocarcinomas in particular and many others
- Trauma
  - Burns
  - Crush injuries
  - Extensive surgery
- Obstetrical Accidents
  - Amniotic fluid embolus
  - Placental abruption
  - Retained fetus syndrome
  - Eclampsia
  - Saline abortion
- Hemolysis
  - Acute transfusion reactions from mismatched blood
  - Chronic immune-mediated hemolysis
  - Massive transfusion
- Collagen vascular disease/ Inflammatory disease
  - Crohn's Disease
  - SLE
  - TTP
- Acute Liver Disease
  - Obstructive jaundice
  - Acute hepatic failure
- Viremia
  - HIV
  - Hepatitis
  - Varicella
  - CMV
- Envenomation
  - Insect bites
  - Snake bites
- Intravascular prostheses
  - Aortic balloon pumps
  - Shunts
- Heat Stroke
- Hyperacute Solid Organ Transplant Rejection
- Large vessel aneurysms
- Giant AVM

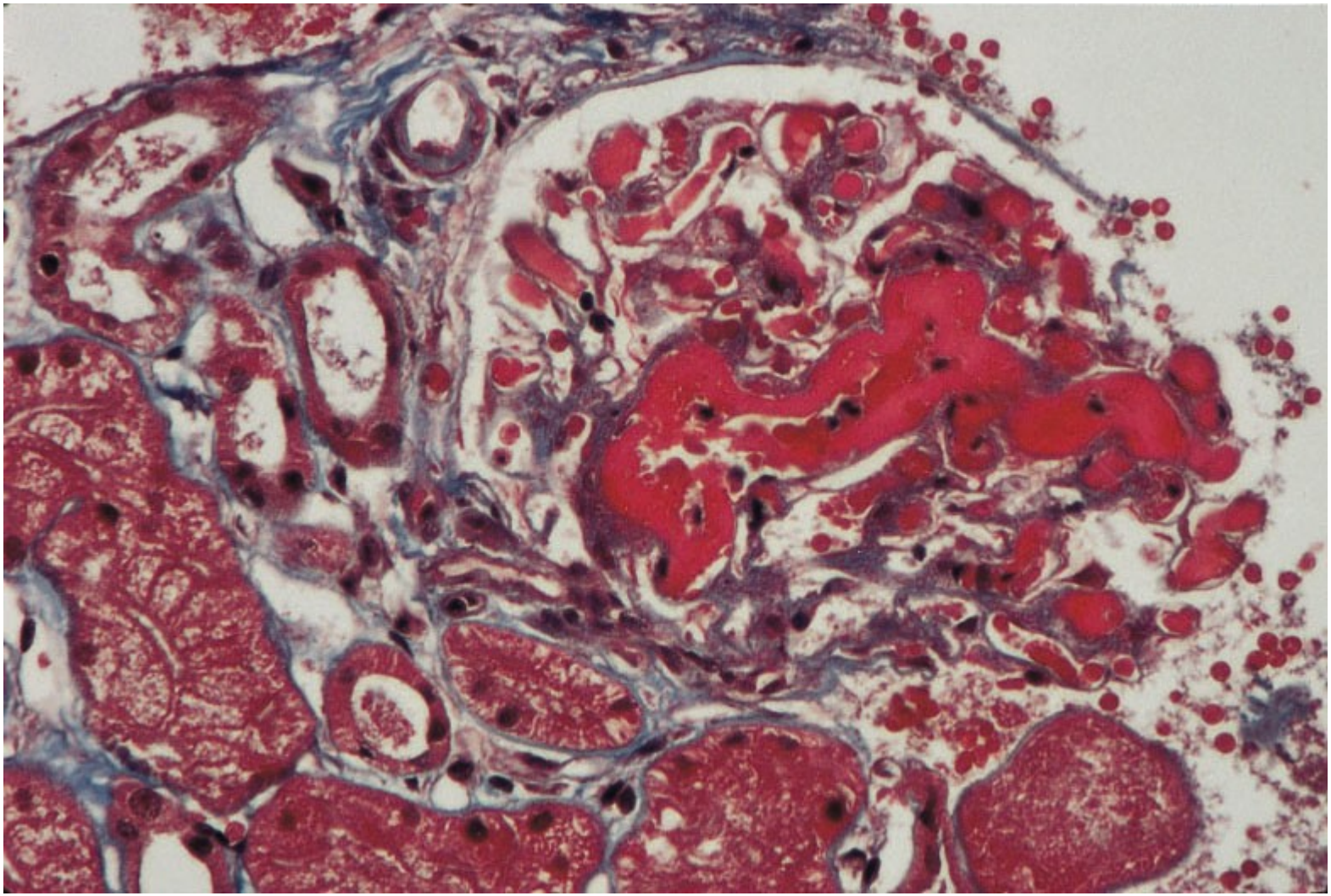
Clinical forms of DIC

- **Chronic DIC:** ***compensated***
  - **Is associated with solid tumors, connective tissue disorders, vascular diseases (giant hemangiomas, abdominal aortic aneurysms).**
  - **Clotting factors are generated at the same rate as they are consumed.**
- **Acute DIC:** ***decompensated***
  - **Generation of clotting factors cannot keep up with exseccive consumption.**
  - **Massive generation of thrombin and consumption of coagulation factors leads to the catastrophy of hemostasis.**
- **Septic DIC:**
  - **Endothelial damage plays an important role in the pathophysiology.**
  - **Impairment of the vital organs ⇒ multiorgan system failure (MOF).**

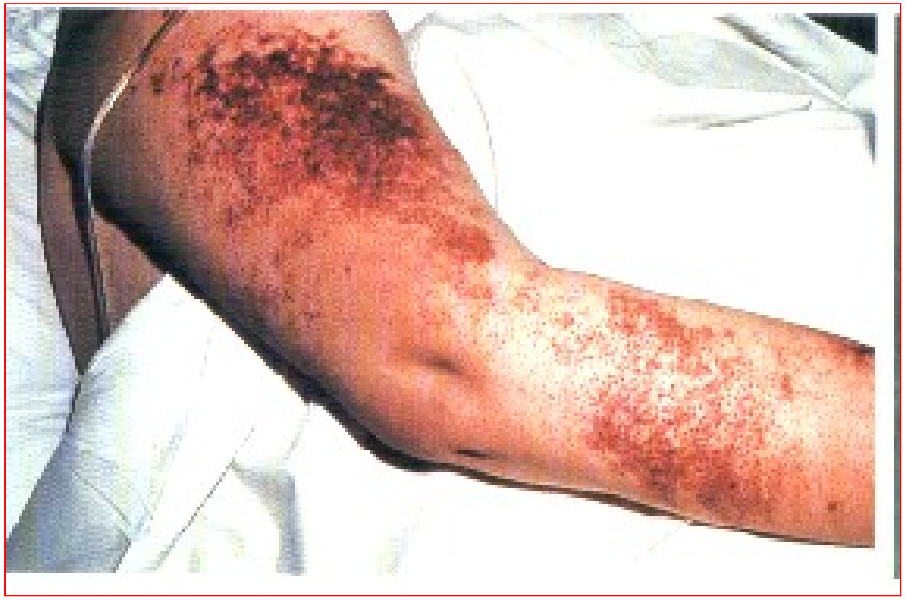
Clinical manifestations: are related to the magnitude of the imbalance of hemostasis, to the underlying disease, or to both.

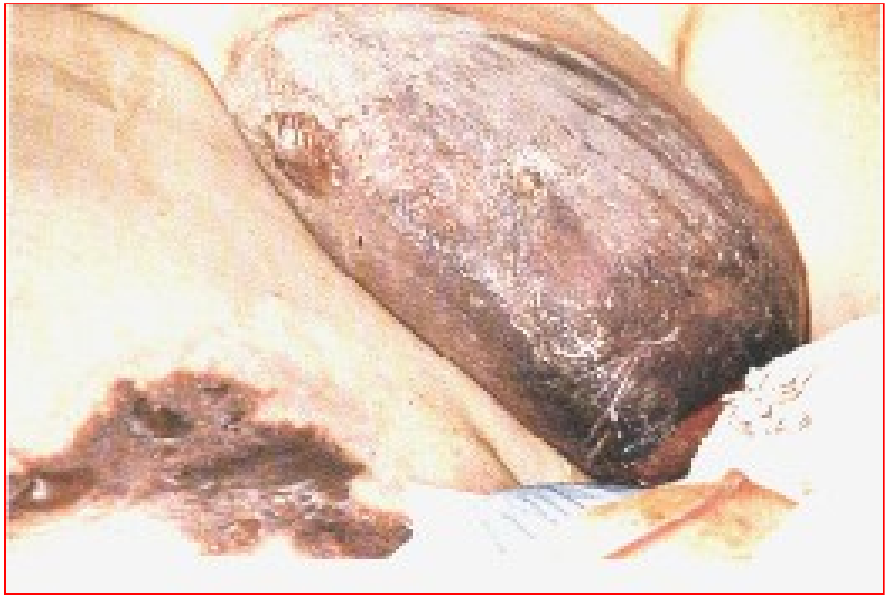
- **Chronic DIC:**
  - *It most often manifests clinically with **thrombosis rather than hemorrhage**.*
  - **Hypercoagulability manifests as the occlusion of vessels in the microcirculation (resulting organ failure). Thrombosis of large vessels and cerebral embolism can also occur.**

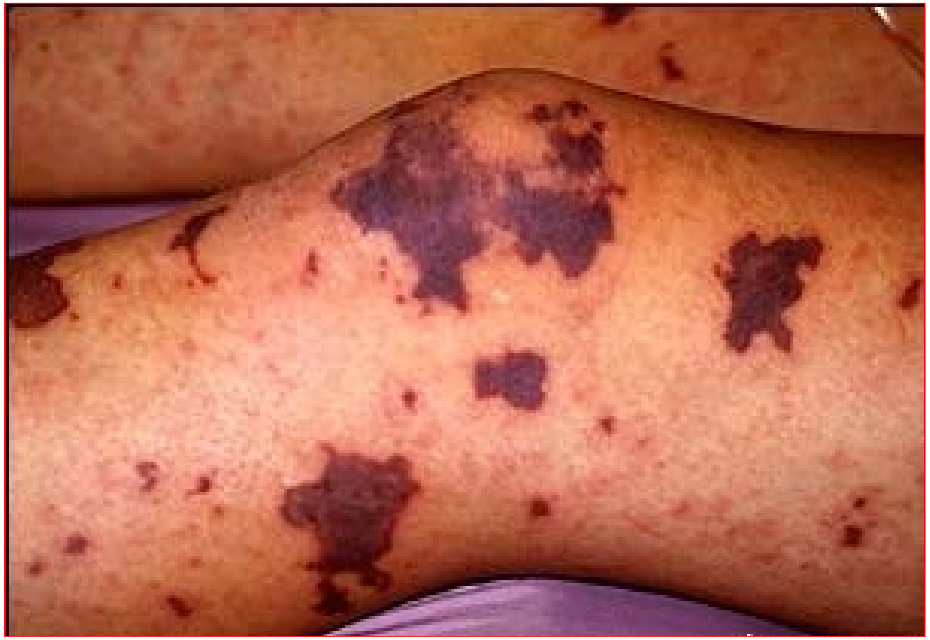

Note fibrin clots in glomerular capillaries

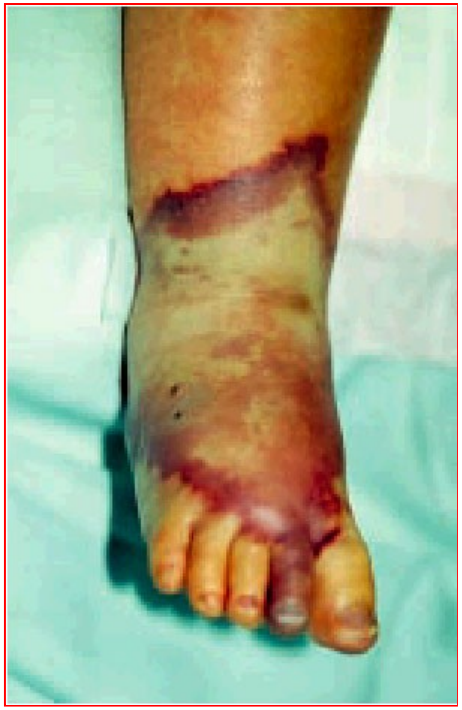


- **Acute DIC:**
  - ***It appears to be primarily a hemorrhagic disorder.***
  - **The most common findings are bleeding ranging from oozing from venipuncture sites, petecchiae, and ecchimoses to severe hemorrhage from gastrointestinal tract or lung or into the central nervous system.**
  - **Mortality: 30-80 % (depending on the underlying disease, severity of the DIC, and the age of the patient).**

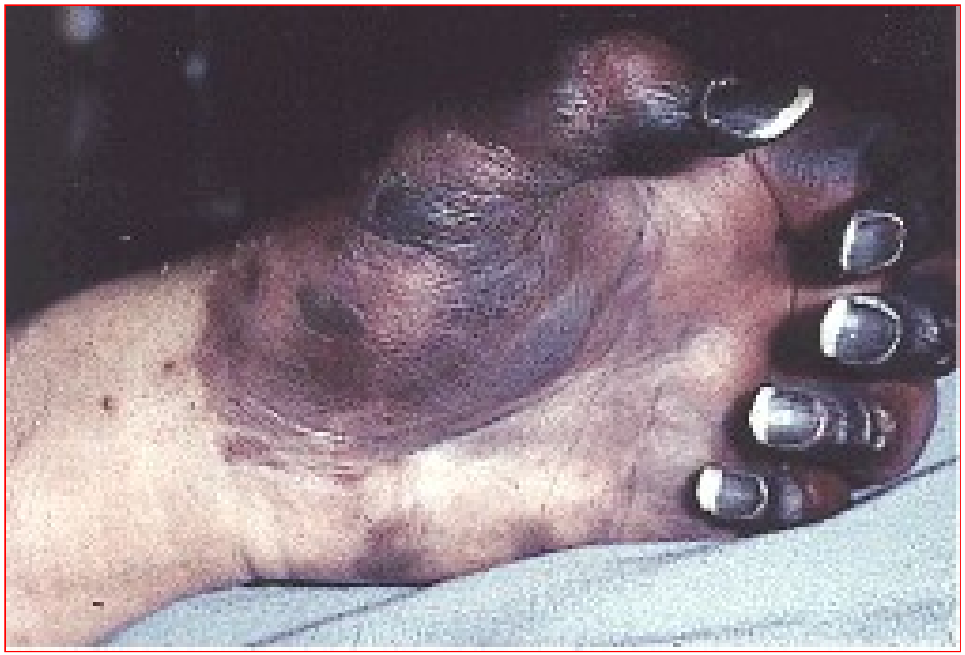








- **Septic DIC:**
  - **Symptoms are similar to acute DIC.**
  - **Hypotension, shock, microthromboses, organ failure.**
  - **Bleeding often mild.**
  - **High mortality rate.**



Peripheral gangrene in Meningococcal sepsis

Diagnosis of DIC is based on the presence of *clinical and/or laboratory abnormalities*.

Laboratory tests in DIC

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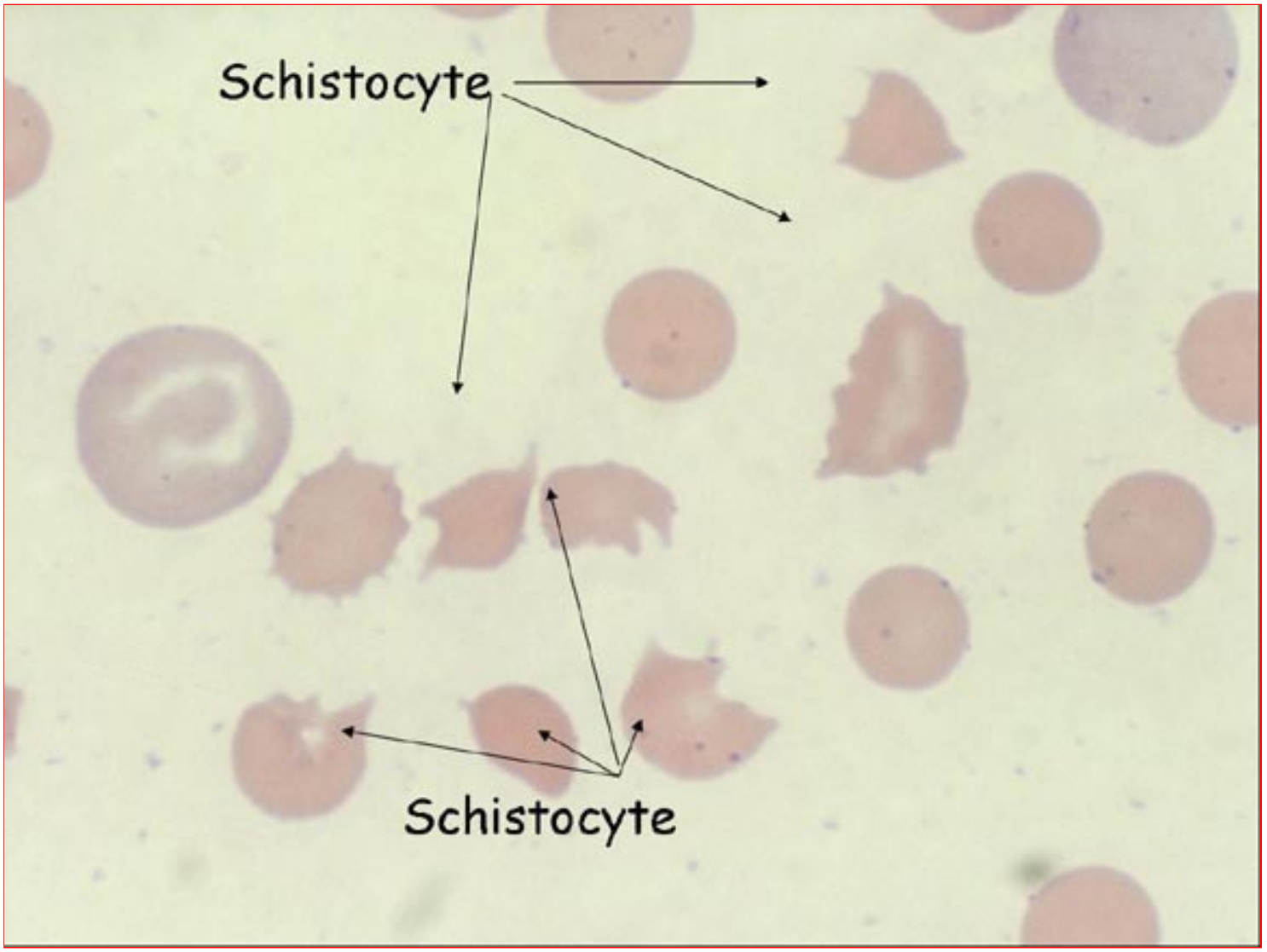
LABORATORY TEST	NORMAL RANGE	SUGGESTIVE OF DIC
Platelets	140,000–400,000/mm³	< 50,000/mm³ and/or falling
Fibrinogen degradation products	< 10 mcg/ml	> 40 mcg/ml and/or rising
D-dimer	< 1mcg/ml	Elevated, > 4 mcg/ml suggestive of deep vein thrombosis
Fibrinogen	150–400 mg/dl	< 100 mg/dl and/or falling
Prothrombin time	10–15 seconds	> 20 seconds
Partial prothrombin time	60–70 seconds	> 100 seconds
Activated partial prothrombin time	20–36 seconds	> 70 seconds
Thrombin time	Within 2 seconds of 9- to 13-second control value	Prolonged
Blood smear	Normal	Cells are abnormal in number, size, shape, or color; schistocytes may be seen.
Antithrombin III	Plasma: > 50% of control value Serum: 15%–35% lower than plasma values	Decreased

Note. Based on information from Chernecky and Berger, 2004; Geiter, 2003; Teal, 2007.

Laboratory tests in DIC (n= 65) (Carr JM et al, 1989)

	Sensitivity (%):	Specificity (%):	Predictive value (%):
Platelet count <150xG/l	73	48	66
Fibrinogen <150 mg/dl	22	87	64
FDP >10 mg/dl	100	56	70
D-dimer >0,5 mg/dl	85	97*	96

*positiv: DVT, PE, cancer, AMI, peripheral vascular disorder, sepsis, infections, postoperative period, gravidity (3th trimester)


Schistocyte
Schistocyte

Diagnosis of DIC:

- **Clinically significant DIC:**
  - **PT, APTT: prolonged, fibrinogen level: reduced, FDP: high levels , D- dimer: elevated thrombocytopenia, schistocytes (fragmented red blood cells) in blood film**
- **Mild cases without bleeding:**
  - **PT, APTT, platelet count: normal, FDP, D- dimer: elevated, schistocytes**

Treatment of DIC:

The only effective treatment is the reversal of the underlying cause!

Attempts to treat DIC without accompanying treatment of the causative disease are likely to fall.

I. Management of hemorrhagic symptoms:

The control of bleeding due to marked (< 5-10 x 10^9/l) thrombocytopenia and low levels of coagulation factors will require replacement therapy.

The PT (>1,5x normal) provides a good indicator of the severity of the clotting factor consumption.

- **FFP:** 1 unit increases most coagulation factors by 3% in an adult without DIC

- **Platelet concentrates:** 1-2 U/10 kg body weight

- Clotting factor concentrates are not recommended (aggrevate the disease)

II. Replacement of coagulation or fibrinolysis inhibitors:

- **Heparin:** low doses of continuous infusion (5-10 U/kg per h) may be effective in patients with low-grade DIC (associated with solid tumors or APL), or in recognized thrombosis. *In acute DIC heparin aggrevates bleeding!*

- **Antithrombin concentrate:** in early phase studies are promising.

- **Antifibrinolytic drugs:** in DIC with hyperfibrinolysis. They can increase the risk of thrombosis, and concomitant use of heparin is indicated.

- **Protein C concentrate:** in meningococcemia has been proved effective.

Prognosis:

varies depending on the underlying disorder.