COAGULATION DISORDERS

von Willebrand's Disease

- Qualitative or quantitative defect in von Willebrand's factor (vWF)
- Clinically, it is characterized by spontaneous bleeding from mucous membranes, excessive bleeding from wounds and menorrhagia.
- vWD is of three types.

	Type I	Type II	TypeIII
Frequency	70%	5-15%	Rare
Severity	Mild	Mild to Moderate	Severe
Inheritence	Autosomal Dominant	Autosomal Dominant	Autosomal Recessive
vWF	Mildly increased	N to ↑	↑ ↑↑

Type I disease:

- Autosomal dominant
- reduced quantity of circulating vWF.
- missense mutations

Type II disease:

- Autosomal dominant
- Qualitative defects in vWF
- several subtypes, type 2A is the most common
- missense mutations, the vWF formed is abnormal, leading to defective multimer assembly.
- Large and intermediate multimers, representing the most active forms of vWF, are missing from plasma.

Type III disease:

- Autosomal recessive
- extremely low levels of functional vWF
- severe deficiency of vWF has a marked affect on the stability of factor VIII, hence the patient manifests with severe bleeding as in hemophillia.
- Type 3 disease is associated with deletions or frameshift mutations

Acquired von Willibrand Disease

It can occur in various acquired disorders

- Hypothyroidism
- Autoimmune disease
- Lymphoproliferative disorder
- Monoclonal gammopathies

Mechanism:

- ✓ Autoantibodies directed against high molecular weight multimers of vWF
- ✓ Increased degradation of polymers by enzyme
- ✓ Adsorption of vWF by tumor cells.

LABORATORY FINDINGS

- Prolonged bleeding time.
- Normal platelet count.
- Reduced plasma vWF concentration.
- Defective platelet aggregation with ristocetin
- Reduced factor VIII activity.

Treatment

For significant bleeding:

- Desmopressin
- Factor VIII concentrate
- Cryoprecipitate.

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

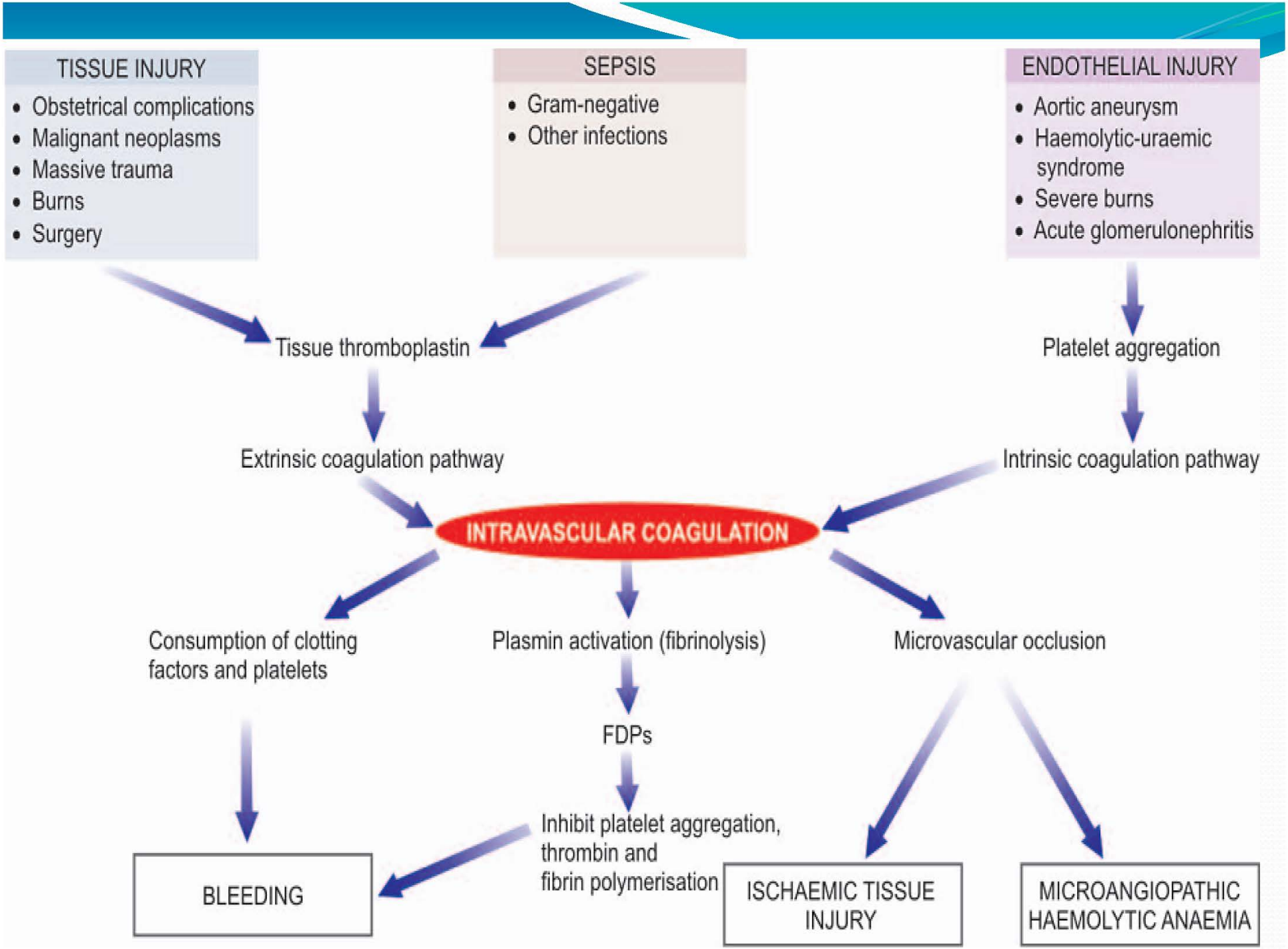
- also termed defibrination syndrome or consumption coagulopathy
- complex thrombo-haemorrhagic disorder (intravascular coagulation and haemorrhage)

Etiology

TABLE 13–10 Major Disorders Associated with Disseminated Intravascular Coagulation

Obstetric Complications
Abruptio placentae
Retained dead fetus
Septic abortion
Amniotic fluid embolism
Toxemia
Infections
Gram-negative sepsis
Meningococcemia
Rocky Mountain spotted fever
Histoplasmosis
Aspergillosis
Malaria
Neoplasms
Carcinomas of pancreas, prostate, lung, and stomach
Acute promyelocytic leukemia
Massive Tissue Injury
Traumatic
Burns
Extensive surgery
Miscellaneous
Acute intravascular hemolysis, snakebite, giant hemangioma, shock, heat stroke, vasculitis, aortic aneurysm, liver disease

PATHOGENESIS


TISSUE INJURY
• Obstetrical complications
• Malignant neoplasms
• Massive trauma
• Burns
• Surgery
SEPSIS
• Gram-negative
• Other infections
ENDOTHELIAL INJURY
• Aortic aneurysm
• Haemolytic-uraemic syndrome
• Severe burns
• Acute glomerulonephritis
Tissue thromboplastin
Platelet aggregation
Extrinsic coagulation pathway
Intrinsic coagulation pathway
INTRAVASCULAR COAGULATION
Consumption of clotting factors and platelets
Plasmin activation (fibrinolysis)
Microvascular occlusion
FDPs
Inhibit platelet aggregation, thrombin and fibrin polymerisation
BLEEDING
ISCHAEMIC TISSUE INJURY
MICROANGIOPATHIC HAEMOLYTIC ANAEMIA

Sequence of events:

Activation of coagulation

Thrombotic phase

Consumption phase

Secondary fibrinolysis

CLINICAL FEATURES

- BLEEDING- most common symptom
- THROMBOSIS
- Sites involved in decreasing order of frequency: brain, heart, lungs, kidneys, adrenals, spleen, and liver.
- Kidneys reveal small thrombi in the glomeruli that evoke reactive swelling of endothelial cells or, in severe cases, microinfarcts or even bilateral renal cortical necrosis.
- Lungs – numerous fibrin thrombi- pulmonary edema and fibrin exudation creating Hyaline memberane

- CNS- microthrombi causes microinfarct formation.
- Adrenal cortex- microthrombi formation- leads to massive adrenal hemmorhage- Water-house-Friderichsen syndrome.
- Sheehan syndrome- pituitary necrosis secondary to DIC complicating labor and delivery.

LABORATORY FINDINGS

- The platelet count is low.
- Blood film shows the features of microangiopathic haemolytic anaemia (schistocytes and fragmented red cells).
- Prothrombin time, thrombin time and activated partial thromboplastin time- prolonged.
- Plasma fibrinogen levels are reduced due to consumption in microvascular coagulation.
- Fibrin degradation products (FDPs) are raised due to secondary fibrinolysis.

Treatment

- Treatment of underlying cause.
- Transfusion of blood products- cryoprecipitate (Factor VIII, fibrinogen, F XIII, and fibronectin), FFP or platelet concentrate depending upon deficient component.
- Heparin therapy- controversial