PATHOLOGY

MD3

PATHOLOGY

CIRCULATORY PATHOLOGY

CIRCULATORY PATHOLOGY

Learning Objectives

- ❑ Use knowledge of edema, haemostasis, and bleeding disorders to solve problems
- ❑ Answer questions about thrombosis, embolism, and infarction
- ❑ Solve problems concerning shock

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EDEMA

Edema is the presence of excess fluid in the intercellular space. It has many causes.

- **Increased hydrostatic pressure** causes edema in congestive heart failure (generalized edema), portal hypertension, renal retention of salt and water, and venous thrombosis (local edema).
- **Hypoalbuminemia and decreased colloid osmotic pressure** cause edema in liver disease, nephrotic syndrome, and protein deficiency (e.g., kwashiorkor).
- **Lymphatic obstruction** (lymphedema) causes edema in tumor, following surgical removal of lymph node drainage, and in parasitic infestation (filariasis → elephantiasis).
- **Increased endothelial permeability** causes edema in inflammation, type I hypersensitivity reactions, and with some drugs (e.g., bleomycin, heroin, etc.).
- **Increased interstitial sodium** causes edema when there is increased sodium intake, primary hyperaldosteronism, and renal failure.
- Specialized forms of tissue swelling due to **increased extracellular glycosaminoglycans** also occur, notably in pretibial myxedema and exophthalmos (Graves disease).
- **Anasarca** is severe generalized edema. **Effusion** is fluid within the body cavities.

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EDEMA INCREASE HRDROSTATIC PORESSURE

CHF\

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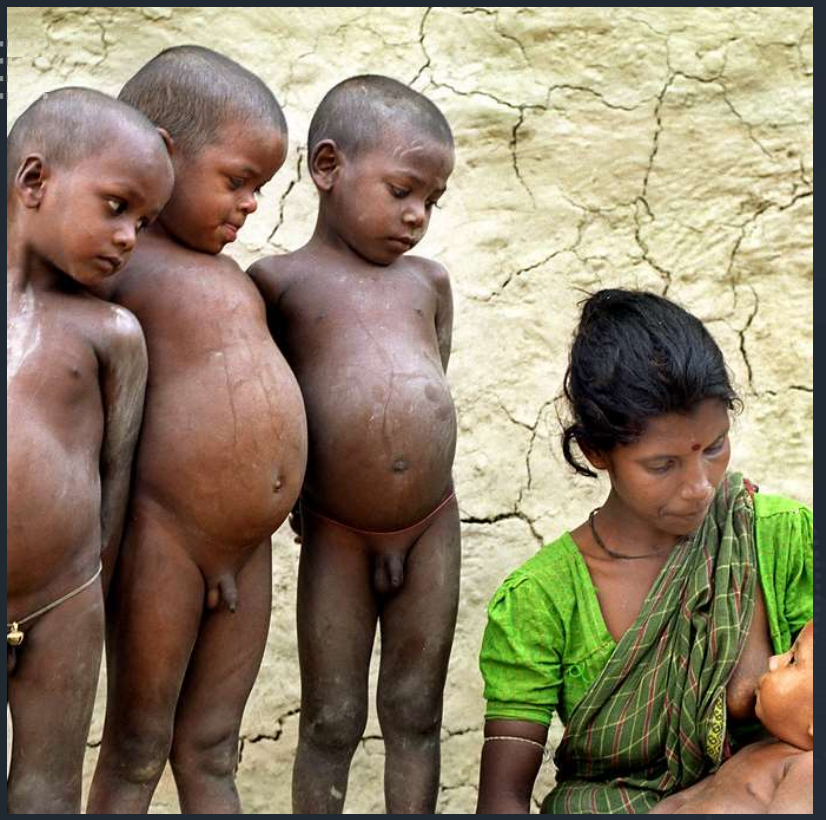
Protein energy malnutrion



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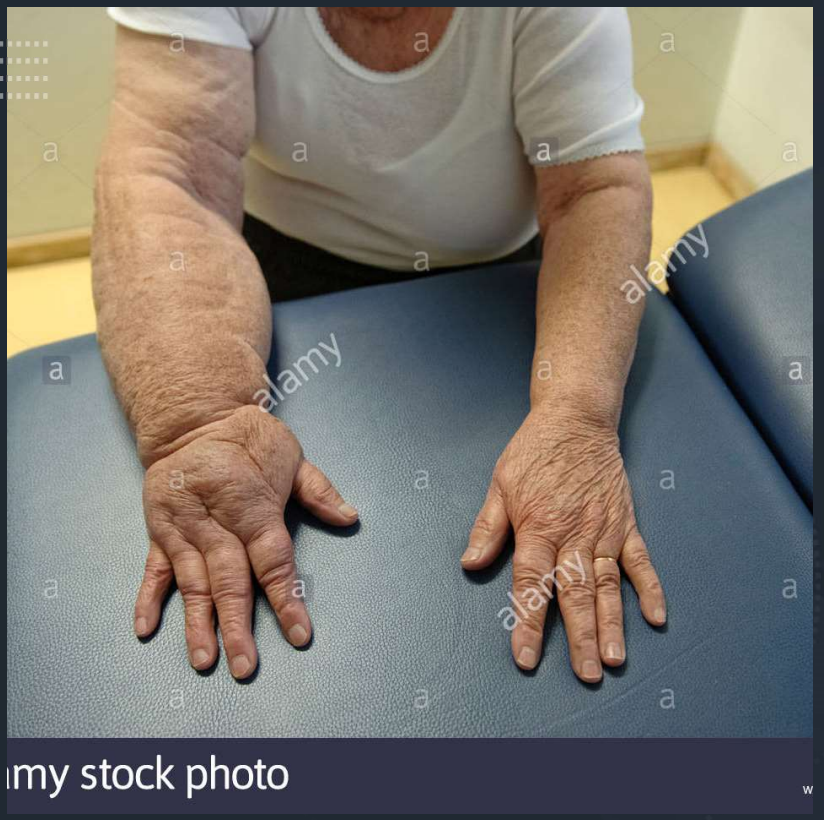
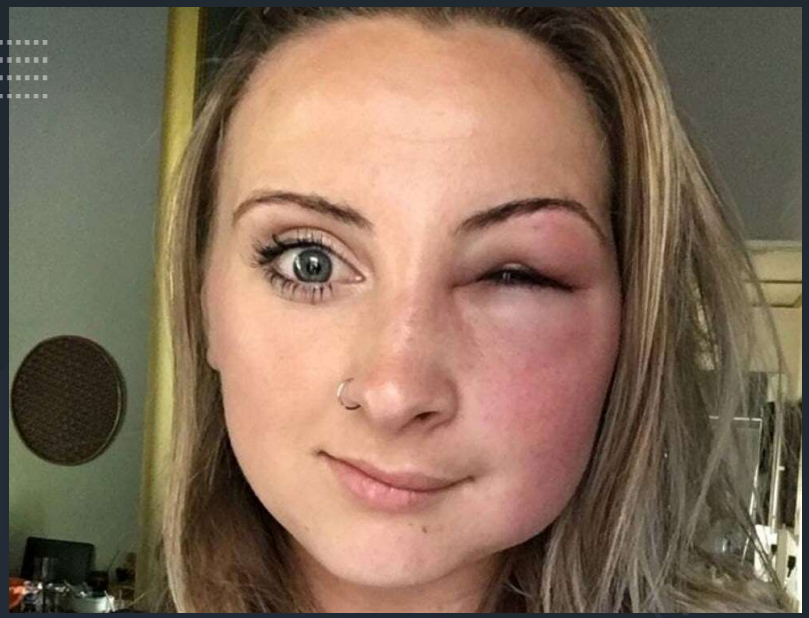
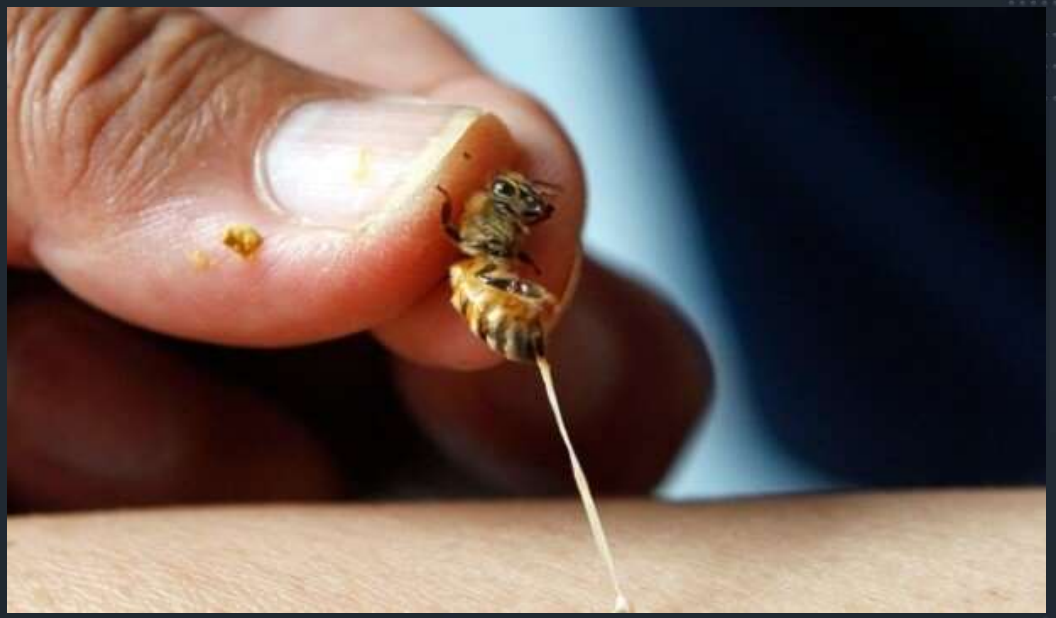
Edema due to lymphatic obstruction







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Edema due ot hypersensititvity

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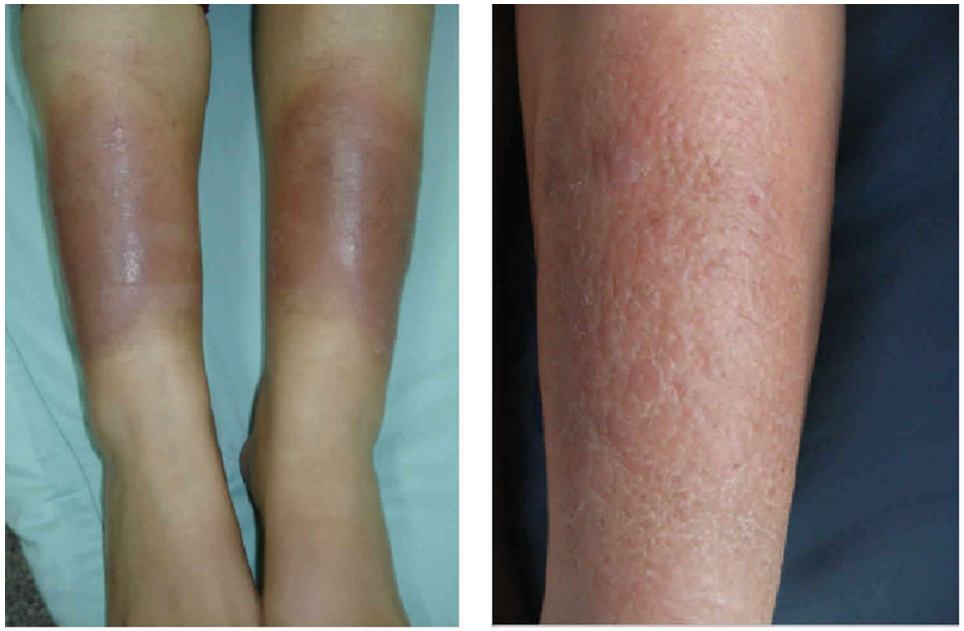
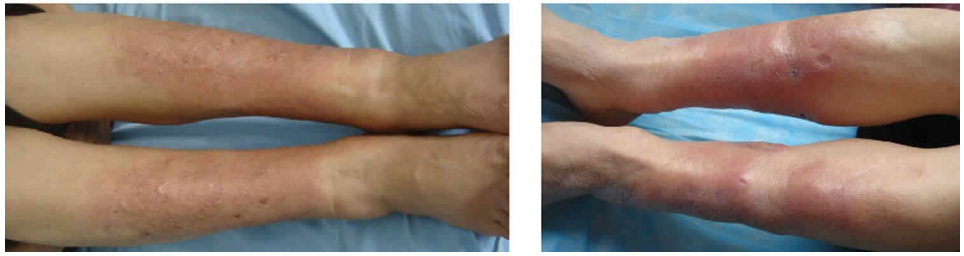
Edema in hyprthyroidism



Pretibial myxedema



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Types of Edema Fluid

- **Transudate** is edema fluid with low protein content.
- **Exudate** is edema fluid with high protein content and cells. Types of exudates include purulent (pus), fibrinous, eosinophilic, and hemorrhagic.
- **Lymphedema** related to lymphatic obstruction leads to accumulation of protein-rich fluid which produces a non-pitting edema.
- **Glycosaminoglycan-rich** edema fluid shows increased hyaluronic acid and chondroitin sulfate, and causes myxedema.

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Transudate vs exudate

FEATURE	TRANSUDATE	EXUDATE
Definition	Filterate of blood plasma without changes in endothelial permeability. Due to physiomechanical factors.	Oedema of inflamed tissue associated with increased vascular permeability, damage to serous membranes.
Character	Non-inflammatory oedema	Inflammatory oedema
Grossly	Typically clear, pale yellow fluid	Usually cloudy, yellow or bloody
Protein content	Low, no tendency to coagulate as mainly albumin, no fibrinogen.	High, readily coagulates due to high content of fibrinogen.
Glucose content	Same as plasma	Low
Specific gravity	Low	High
pH	>7.23	<7.23
LDH	Low	High
Effusion LDH/Serum LDH ratio	<0.6	>0.6
Cells	Few cells, mainly mesothelial cells and cellular debris	Many cells, inflammatory as well as parenchymal.

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Active hyperaemia versus congestion (passive hyperemia): an excessive amount of blood in a tissue or organ can accumulate secondary to vasodilatation (active, e.g., inflammation) or diminished venous outflow (passive, e.g., hepatic congestion).

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HEMOSTASIS AND BLEEDING DISORDERS

Hemostasis is a sequence of events leading to the cessation of bleeding by the formation of a stable fibrin-platelet hemostatic plug. It involves interactions between the vascular wall, platelets, and the coagulation system.

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Vascular Wall Injury

Transient vasoconstriction is mediated by endothelin-1. Thrombogenic factors include a variety of processes:

- Changes in blood flow cause turbulence and stasis favor clot formation.
- Release of tissue factor from injured cells activates factor VII (extrinsic pathway).
- Exposure of thrombogenic subendothelial collagen activates factor XII (intrinsic pathway).
- Release of von Willebrand factor (vWF) binds to exposed collagen and facilitates platelet adhesion.
- Decreased endothelial synthesis of antithrombogenic substances (prostacyclin, nitric oxide [NO2], tissue plasminogen activator, and thrombomodulin)

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Platelets

Platelets are derived from megakaryocytes in the bone marrow. They form a thrombus through a series of steps.

- **Step 1: Platelet adhesion** occurs when vWF adheres to subendothelial collagen and then platelets adhere to vWF by glycoprotein Ib.
- **Step 2: Platelet activation** occurs when platelets undergo a shape change and degranulation occurs. Platelets synthesize thromboxane A2. Platelets also show membrane expression of the phospholipid complex, which is an important substrate for the coagulation cascade.
- **Step 3: Platelet aggregation** occurs when additional platelets are recruited from the bloodstream. ADP and thromboxane A2 are potent mediators of aggregation. Platelets bind to each other by binding to fibrinogen using GPIIb-IIIa.

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- Laboratory tests for platelets include platelet count (normal 150,000–400,000 mm3) and platelet aggregometry.
- Bernard-Soulier syndrome and Glanzmann thrombasthenia present as mucocutaneous bleeding in childhood.

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Content sin platelet granules

Alpha Granules	Dense Bodies
• Fibrinogen	• ADP (potent platelet aggregator)
• Fibronectin	• Calcium
• Factor V and vWF	• Histamine and serotonin
• Platelet factor 4	• Epinephrine
• Platelet-derived growth factor (PDGF)	

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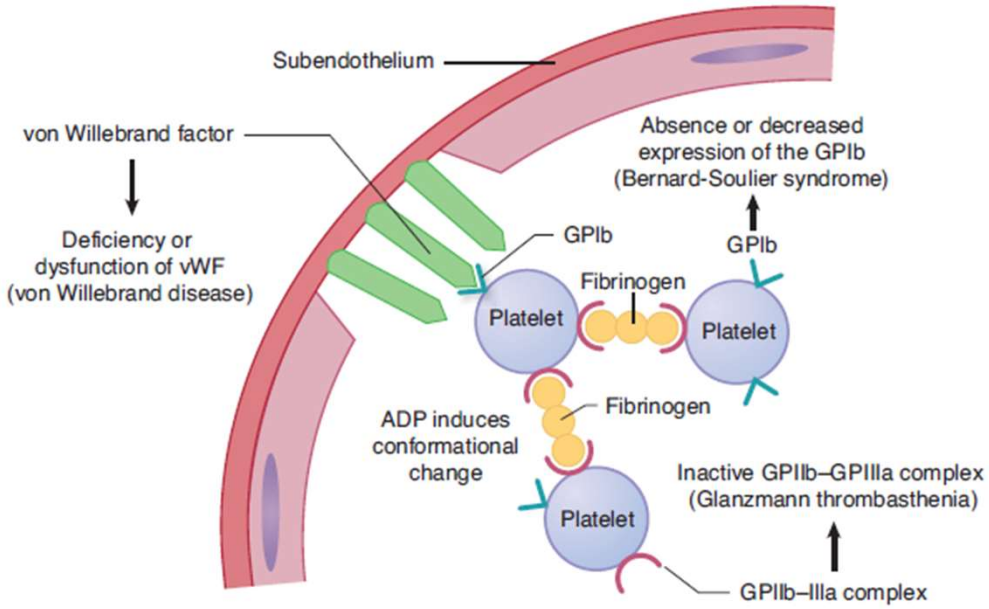
Platelet aggregation



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Disorder in platlets aggregation

Thrombocytopenia	Qualitative Defects
Decreased production • Aplastic anemia (drugs, virus, etc.) • Tumor	• von Willebrand disease • Bernard-Soulier syndrome • Glanzmann thrombasthenia • Drugs (aspirin) • Uremia
Increased destruction • Immune thrombocytopenia (ITP) • Thrombotic thrombocytopenic purpura (TTP) • Disseminated intravascular coagulation (DIC) • Hypersplenism	

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Bernard-Soulier Syndrome

- Usually autosomal recessive
- Defects of the GPIb IX-V
- Defective platelet adhesion

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Glanzmann Thrombasthenia

- Autosomal recessive
- Defective GPIIb-IIIa receptor
- Defective platelet aggregation

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Coagulation factors

The majority of the clotting factors are produced by the liver. The factors are proenzymes that must be converted to the active form. Some conversions occur on a phospholipid surface, and some conversions require calcium.

- The **intrinsic coagulation pathway** is activated by the contact factors, which include contact with subendothelial collagen, high molecular weight kininogen (HMWK), and kallikrein.
- The **extrinsic coagulation pathway** is activated by the release of tissue factor.

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Immune thrombocytopenia purpura (ITP)

Is an immune-mediated attack (usually IgG antiplatelet antibodies) against platelets leading to decreased platelets (thrombocytopenia) which result in petechiae, purpura (bruises), and a bleeding diathesis (e.g., hematomas).

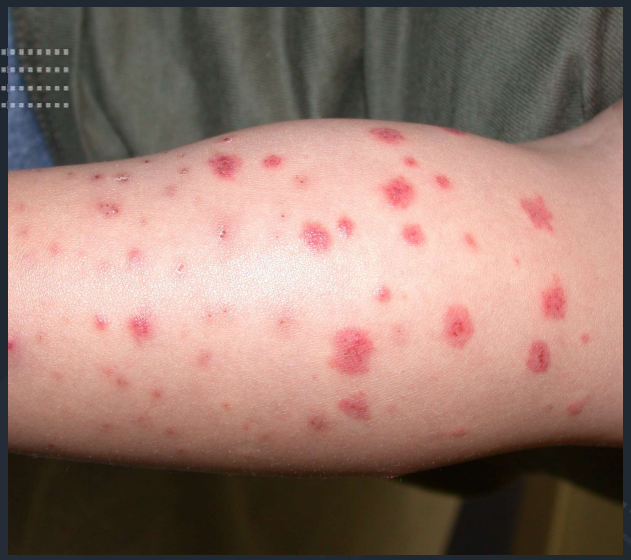
The Etiology involves antiplatelet antibodies against platelet antigens such as GPIIb-IIIa and GPIb-IX (type II hypersensitivity reaction). The antibodies are made in the spleen, and the platelets are destroyed peripherally in the spleen by macrophages, which have Fc receptors that bind IgG-coated platelets.

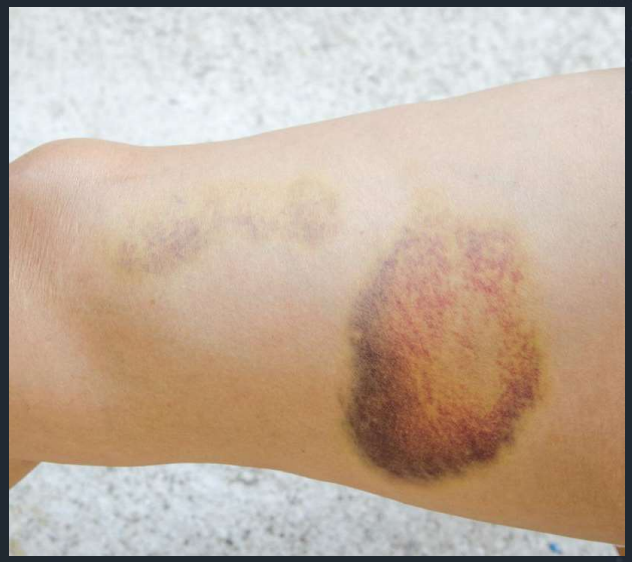
Forms of ITP include:

- Acute ITP, seen in children following a viral infection and is a self-limited disorder.
- Chronic ITP, usually seen in women in their childbearing years and may be the first manifestation of systemic lupus erythematosus (SLE). Clinically, it is characterized by petechiae, ecchymoses, menorrhagia, and nosebleeds.

Lab studies usually show decreased platelet count and prolonged bleeding time but normal prothrombin time and partial thromboplastin time. Peripheral blood smear shows thrombocytopenia with enlarged immature platelets (megathrombocytes). Bone marrow biopsy shows increased numbers of megakaryocytes with immature forms.

Treatment is corticosteroids, which decrease antibody production; immunoglobulin therapy, which floods Fc receptors on splenic macrophages; and/or splenectomy, which removes the site of platelet destruction and antibody production.





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PURPURA, PETHICAE AND HEMATOMA

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Thrombotic thrombocytopenic purpura (TTP)

Is a rare disorder of haemostasis in which there is widespread intravascular formation of fibrin-platelet thrombi. It is sometimes associated with an acquired or inherited deficiency of the enzyme ADAMTS13, responsible for cleaving large multimers of von Willebrand factor.

Clinically,

TTP most often affects adult women. The inclusion criteria are

- Microangiopathic
- Hemolytic anaemia and
- Thrombocytopenia, with or without renal failure or neurologic abnormalities.
- Pathology includes widespread formation of platelet thrombi with fibrin (hyaline thrombi) leading to intravascular haemolysis (thrombotic microangiopathy).

Lab studies typically show decreased platelet count and prolonged bleeding time but normal prothrombin time and partial thromboplastin time. Peripheral blood smear shows thrombocytopenia, schistocytes, and reticulocytotic.

Treatment is Plasma exchange.

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Hemolytic uremic syndrome (HUS)

Is a form of thrombotic microangiopathy due to endothelial cell damage. It occurs mostly in children, typically after a gastroenteritis (typically due to Shiga toxin-producing *E. coli* 0157:H7).

Typical HUS presents with

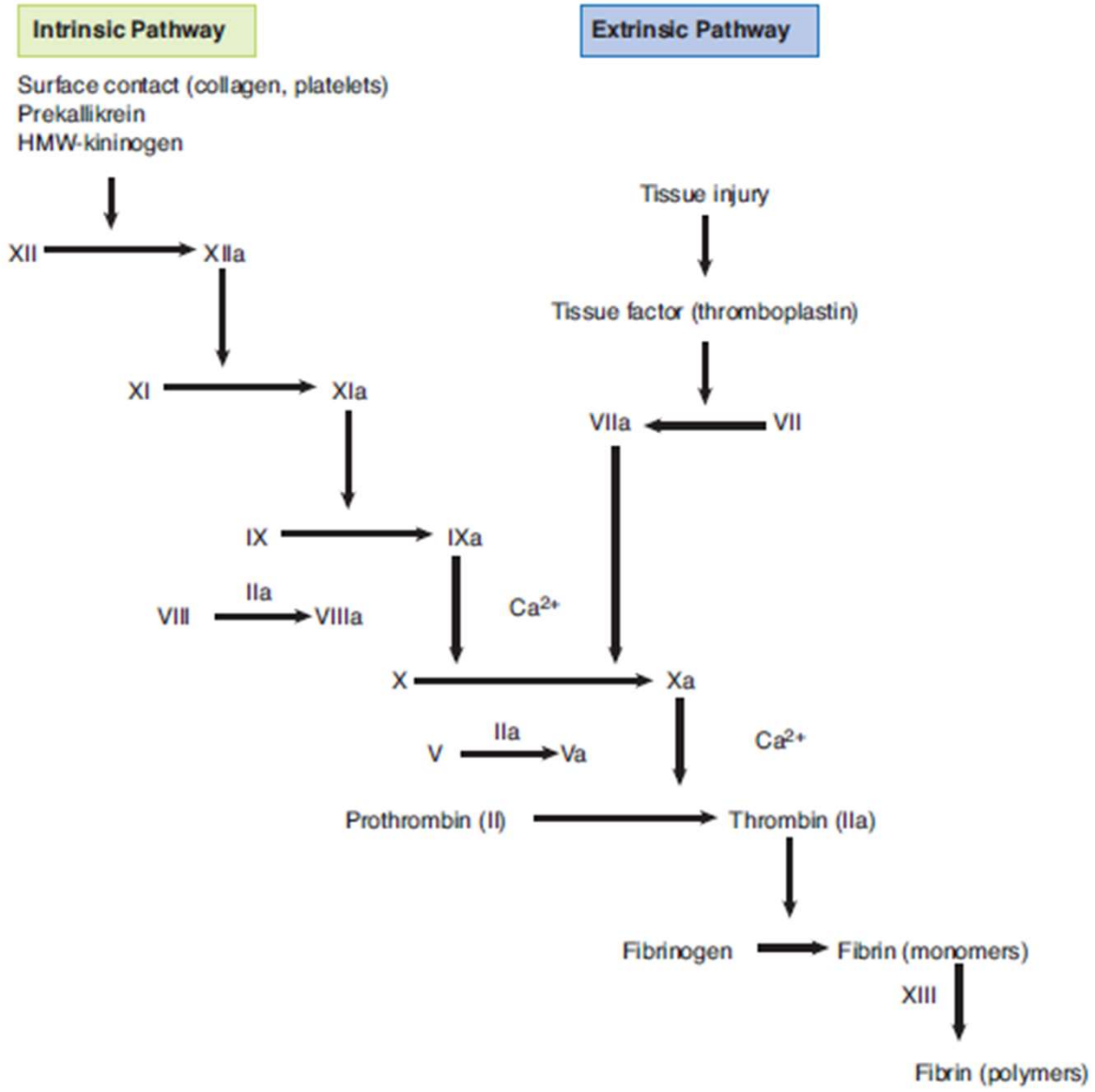
- Abdominal pain,
- Diarrhoea (an atypical variant is diarrhea-negative),
- Microangiopathic hemolytic anemia,
- Thrombocytopenia, and
- Renal failure.

Renal involvement is seen more commonly than in TTP. The kidney shows fibrin thrombi in the glomeruli. Renal glomerular endothelial cells are targeted by the bacterial toxin. Glomerular scarring may ensue.

Treatment is supportive (fluid management, dialysis, erythrocyte transfusions); plasma exchange is only used for atypical cases.

Circulatory pathology

Clotting mechanism



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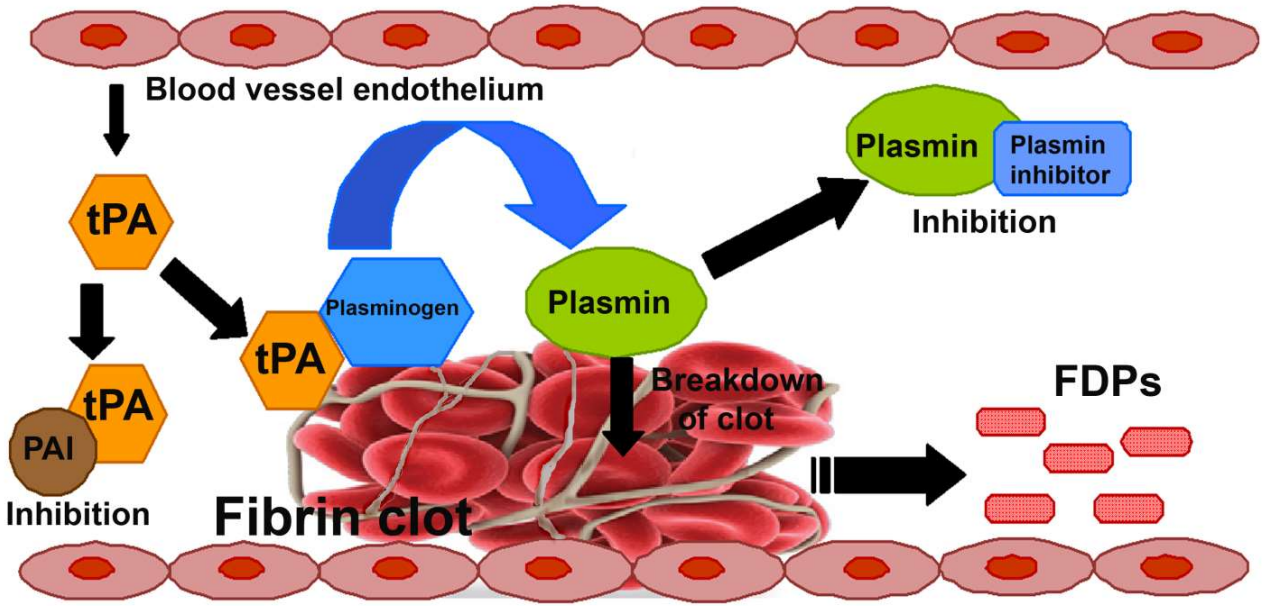
Clotting Mechanism



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Note

- Patients on warfarin therapy should be monitored using prothrombin time (WEPT = warfarin, extrinsic PT).
- Patients on heparin therapy should be monitored using partial thromboplastin time (HIPTT = heparin, intrinsic PTT).

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Lab tests for coagulation include the following:

- Prothrombin time (PT), which tests the extrinsic and common coagulation pathways (more specifically, it tests factors VII, X, V, prothrombin, and fibrinogen). The international normalized ratio (INR) standardizes the PT test so that results throughout the world can be compared. A longer time means blood takes longer to clot.
- Partial thromboplastin time (PTT), which tests the intrinsic and common coagulation pathways (more specifically, it tests factors XII, XI, IX, VIII, X, V, prothrombin, and fibrinogen).
- Thrombin time (TT), which tests for adequate fibrinogen levels.
- Fibrin degradation products (FDP), which tests the fibrinolytic system (increased with DIC).

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Haemophilia A (classic haemophilia)

- X-linked recessive condition
- Deficiency of factor VIII.
- Clinically, haemophilia A predominately affects males.

Symptoms vary depending on the degree of deficiency.

- New-born may develop bleeding at the time of circumcision.
- Spontaneous haemorrhage into joints (hemarthrosis),
- Easy bruising and hematoma formation after minor trauma,
- Severe prolonged bleeding after surgery or lacerations.

Laboratory studies

- Normal platelet count and
- normal bleeding time,
- normal PT and
- prolonged PTT.

Treatment is factor VIII concentrate.

CIRCULATORY PATHOLGY

Haemophilia B (Christmas disease)

X-linked recessive condition resulting from a deficiency of factor IX that is clinically identical to haemophilia A.

Treatment is recombinant factor IX.

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Acquired coagulopathies include vitamin K deficiency (decreased synthesis of factors II, VII, IX, X, and protein C & S) and liver disease (decreased synthesis of virtually all clotting factors).

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Von Willebrand disease

Is an autosomal dominant bleeding disorder characterized by a deficiency or qualitative defect in von Willebrand factor. vWF is normally produced by endothelial cells and megakaryocytes.

Clinical features include

- Spontaneous bleeding from mucous membranes,
- Prolonged bleeding from wounds,
- Menorrhagia in young females.
- Hemarthrosis is uncommon.

Lab studies show

- Normal platelet count,
- Prolonged bleeding time,
- Normal PT, and
- Often prolonged PTT.
- Abnormal platelet response to ristocetin (adhesion defect) is an important diagnostic test.

Treatment for mild classic cases (type I) is desmopressin (an antidiuretic hormone analog), which releases vWF from Weibel-Palade bodies of endothelial cells.

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Disseminated intravascular coagulation (DIC)

Is always secondary to another disorder. Causes are diverse.

Most common etiologies

- Obstetric complications can cause DIC because placental tissue factor activates clotting.
- Gram-negative sepsis can cause DIC because Tumor necrosis factor activates clotting.
- Microorganisms (especially meningococcus and rickettsia)
- AML M3 (cytoplasmic granules in neoplastic promyelocytes activate clotting)
- Adenocarcinomas (mucin activates clotting)

DIC causes widespread microthrombi with consumption of platelets and clotting factors, causing haemorrhage.

Laboratory studies show decreased platelet count, prolonged PT/PTT, decreased fibrinogen, and elevated fibrin split products (D dimers).

Treat the underlying disorder.

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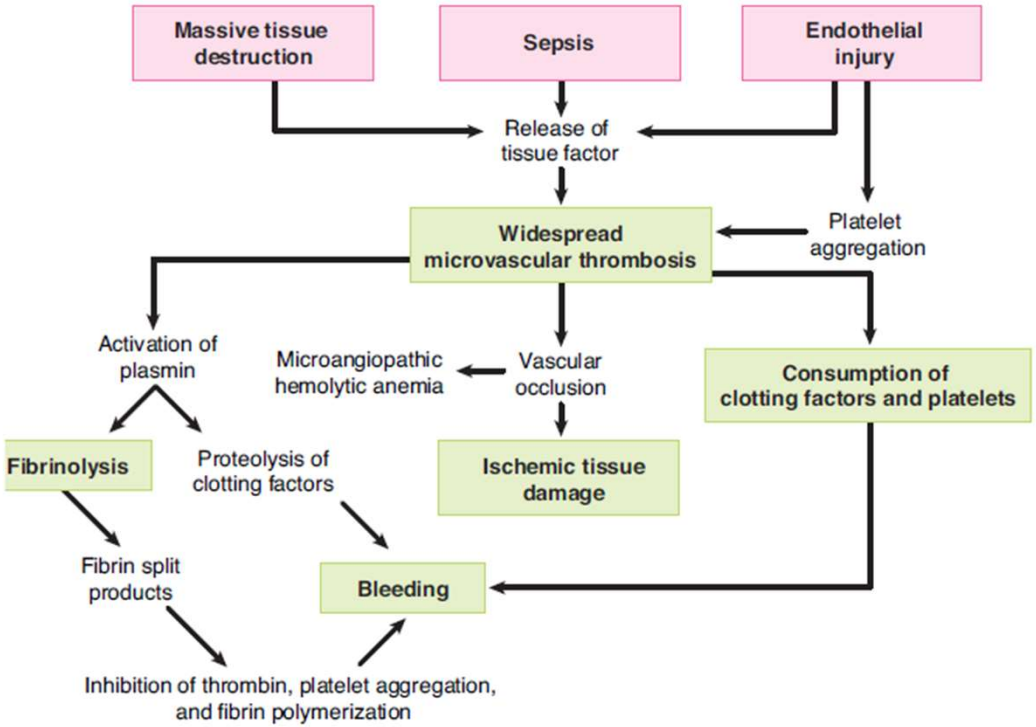
Mechanism of DIC



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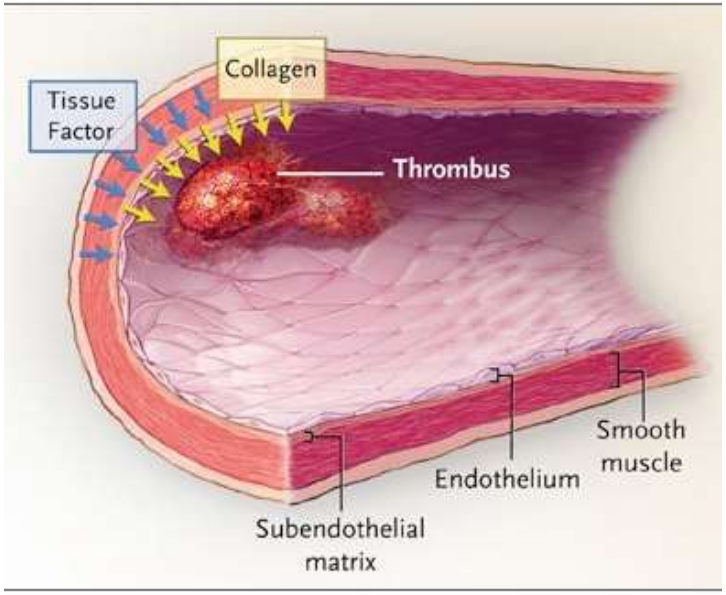
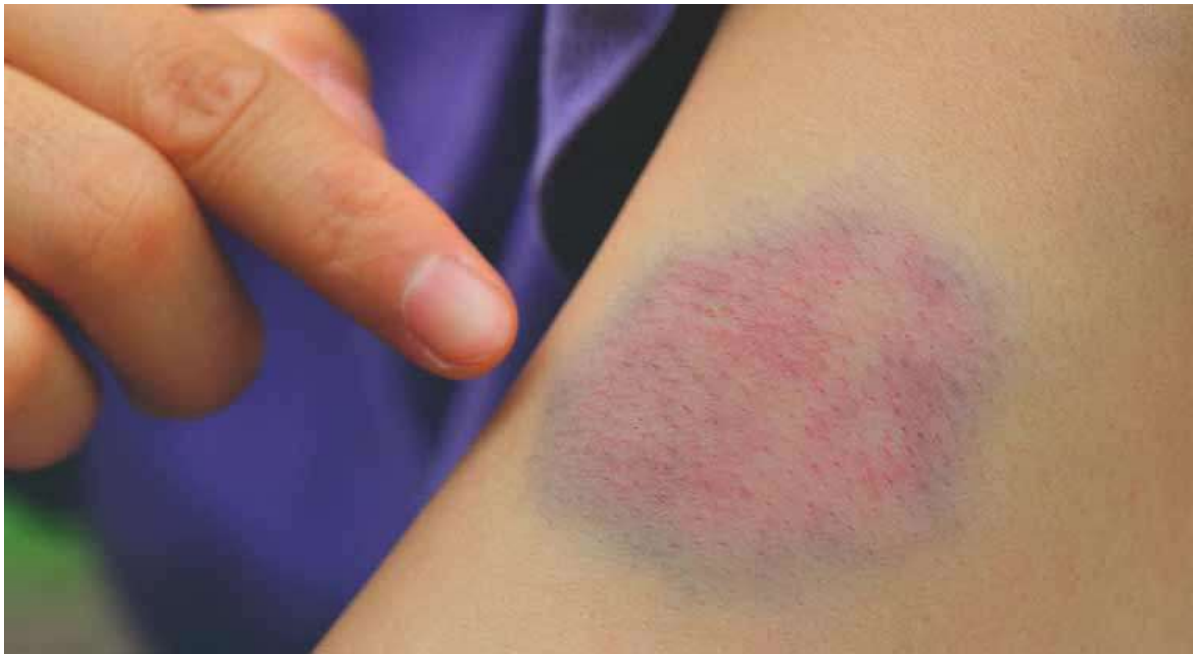
THROMBOSIS

Thrombosis is the pathologic formation of an intravascular fibrin-platelet thrombus during life.

Factors involved in thrombus formation (**Virchow's triad**) include:

- Endothelial injury due to atherosclerosis, vasculitis, or many other causes
- Alterations in laminar blood flow predisposing for DIC occur with stasis of blood (e.g., immobilization); turbulence (e.g., aneurysms); and hyperviscosity of blood (e.g., polycythemia vera)
- Hypercoagulability of blood can be seen with clotting disorders (factor V Leiden; deficiency of antithrombin III, protein C, or protein S); tissue injury (postoperative and trauma); neoplasia; nephrotic syndrome; advanced age; pregnancy; and oral contraceptives (estrogen increases synthetic activity of the liver, including clotting factors)





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Thrombus and Clot

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Thrombi and blood clot

	Thrombus	Blood Clot
Location	Intravascular	Extravascular or intravascular (postmortem)
Composition	Platelets	Lacks platelets
	Fibrin	Fibrin
	RBCs and WBCs	RBCs and WBCs
Lines of Zahn	Present	Absent
Shape	Has shape	Lacks shape

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Common locations of thrombus formation include coronary and cerebral arteries; heart chambers in atrial fibrillation or post-MI (mural thrombus); aortic aneurysms; heart valves (vegetations); and deep leg veins (DVTs).

Outcomes of thrombosis include vascular occlusion and infarctions; embolism; thrombolysis; and organization and recanalization.

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EMBOLISM

An embolism is any intravascular mass that has been carried down the bloodstream from its site of origin, resulting in the occlusion of a vessel. There are many types of emboli:

- **Thromboembolism:** most common (98%)
- Atheromatous emboli (severe atherosclerosis)
- Fat emboli (bone fractures and soft tissue trauma)
- Bone marrow emboli (bone fractures and cardiopulmonary resuscitation [CPR])
- Gas emboli cause decompression sickness ("the bends" and caisson disease) when rapid ascent results in nitrogen gas bubbles in the blood vessels
- Amniotic fluid emboli are a complication of labor that may result in DIC; fetal squamous cells are seen in the maternal pulmonary vessels
- Tumor emboli (metastasis)
- Talc emboli (IV drug abuse)
- Bacterial/septic emboli (infectious endocarditis)

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Pulmonary emboli (PE)

Often clinically silent and are the most commonly missed diagnosis in hospitalized patients. They are found in almost 50% of all hospital autopsies. Most PE (95%) arise from deep leg vein thrombosis (DVT) in the leg; other sources include the right side of the heart and the pelvic venous plexuses of the prostate and uterus.

Diagnosis of a PE can be established when

- V/Q lung shows a scan V/Q mismatch.
- Doppler ultrasound of the leg veins can be used to detect a DVT.
- Plasma D-dimer ELISA test is elevated.

Most cases are clinically silent and resolve.

Infarction is more common in patients with cardiopulmonary compromise.

Symptoms include shortness of breath, haemoptysis, pleuritic chest pain, and pleural effusion.

On gross examination there is typically a haemorrhagic wedge-shaped infarct. The infarction heals by regeneration or scar formation.

• Sudden death can occur when large emboli lodge in the bifurcation (saddle embolus) or large pulmonary artery branches.

• Chronic secondary pulmonary hypertension is caused by recurrent PEs, which increase pulmonary resistance and lead to secondary pulmonary hypertension.

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INFARCTION

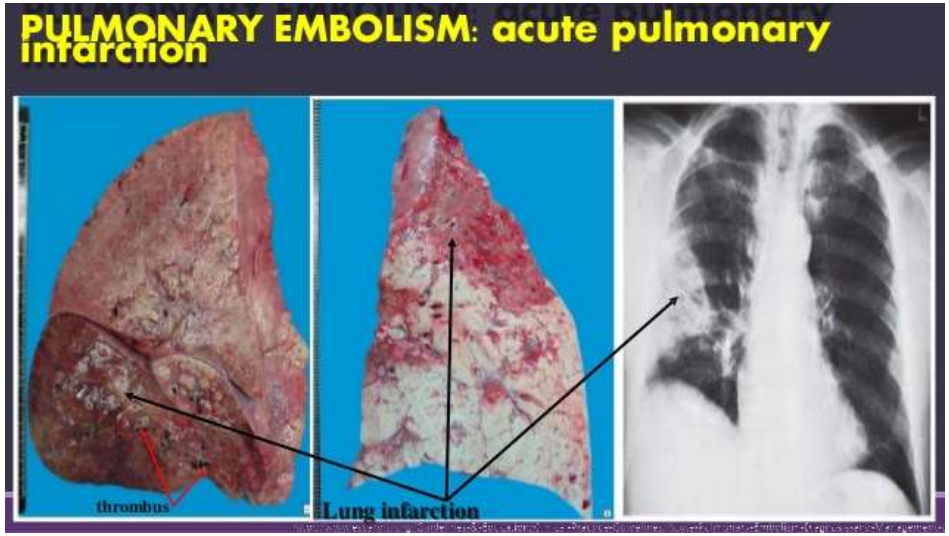
Infarction is a localized area of necrosis secondary to ischemia. Common sites of infarction include heart, brain, lungs, intestines, kidneys. Infarcts have multiple causes.

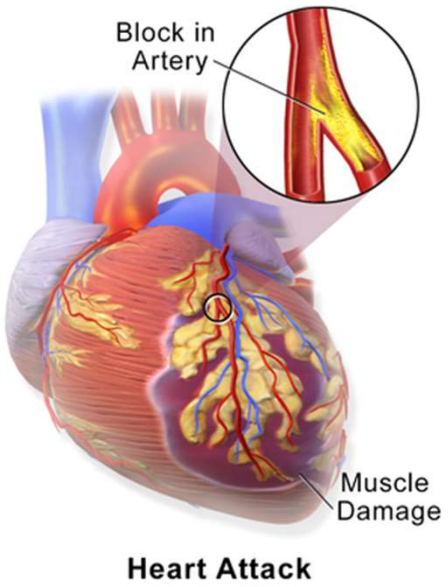
- Most infarcts (99%) result from thrombotic or embolic occlusion of an artery or vein.
- Less common causes include vasospasm and torsion of arteries and veins (e.g., volvulus, ovarian, and testicular torsion).
- On gross examination infarctions typically have a wedge shape, with the apex of the wedge tending to point to the occlusion.

Anaemic infarcts (pale or white color) occur in solid organs with a single blood supply such as the spleen, kidney, and heart.

Haemorrhagic infarcts (red color) occur in organs with a dual blood supply or collateral circulation, such as the lung and intestines, and can also occur with venous occlusion (e.g., testicular torsion).

- Microscopic pathology of infarction can show either coagulative necrosis (most organs) or liquefactive necrosis (brain). The general sequence of tissue changes after infarction is as follows:





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Infarction

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SHOCK

Shock is characterized by vascular collapse and widespread hypoperfusion of cells and tissue due to reduced blood volume, cardiac output, or vascular tone.

The cellular injury is initially reversible; if the hypoxia persists, the cellular injury becomes irreversible, leading to the death of cells and the patient.

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Major Causes of Shock

- **Cardiogenic shock** (pump failure) can be due to myocardial infarction, cardiac arrhythmias, pulmonary embolism, and cardiac tamponade.
- **Hypovolemic shock** (reduced blood volume) can be due to haemorrhage, fluid loss secondary to severe burns, and severe dehydration.
- **Septic shock** (viral or bacterial infection) causes cytokines to trigger vasodilatation and hypotension, acute respiratory distress syndrome (ARDS), DIC, and multiple organ dysfunction syndrome. Mortality rate is 20%.
- **Neurogenic shock** (generalized vasodilatation) can be seen with anaesthesia and brain or spinal cord injury.
- **Anaphylactic shock** (generalized vasodilatation) is a type I hypersensitivity reaction.

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Stages of Shock

The stages of shock are arbitrarily defined as follows.

Stage I: compensation

Perfusion to vital organs is maintained by reflex mechanisms. Compensation is characterized by increased sympathetic tone, release of catecholamines, and activation of the renin-angiotensin system.

Stage II: decompensation

There is a progressive decrease in tissue perfusion, leading to potentially reversible tissue injury with development of a metabolic (lactic) acidosis, electrolyte imbalances, and renal insufficiency.

Stage III: Irreversible tissue injury and organ failure

This ultimately results in death.

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The organs show various manifestations of shock:

- Kidneys show fibrin thrombi in glomeruli and ultimately, acute tubular failure ensues, which causes oliguria and electrolyte imbalances.
- Lungs undergo diffuse alveolar damage (“shock lung”).
- Intestines show superficial mucosal ischemic necrosis and haemorrhages, and with prolonged injury, bacteraemia may ensue.

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A 34-year-old obese man presents to your office complaining of fatigue, daytime sleepiness and occasional headaches. When you inquire about his sleeping habits, he reports that he sleeps in a separate room from his wife because she finds his snoring annoying. On physical examination, his blood pressure is 160/90 mmHg and his heart rate is 80fmin. His abdomen is soft and non-tender, his liver span is 9 cm, and his spleen is not palpable. Laboratory findings are:

Haematocrit 57%

WBC count 9000

Platelet 190,000

Decreased oxygen delivery to which of the following organs is responsible for his increased haematocrit?

A. Brain

B. Liver

C. Spleen

D. Bone marrow

E. Lungs

F. Kidneys

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A mother brings her 12-year-old son to his pediatrician for evaluation of easy bruising. Physical examination is notable only for the presence of multiple bruises. There is no lymphadenopathy or hepatosplenomegaly. laboratory studies show:

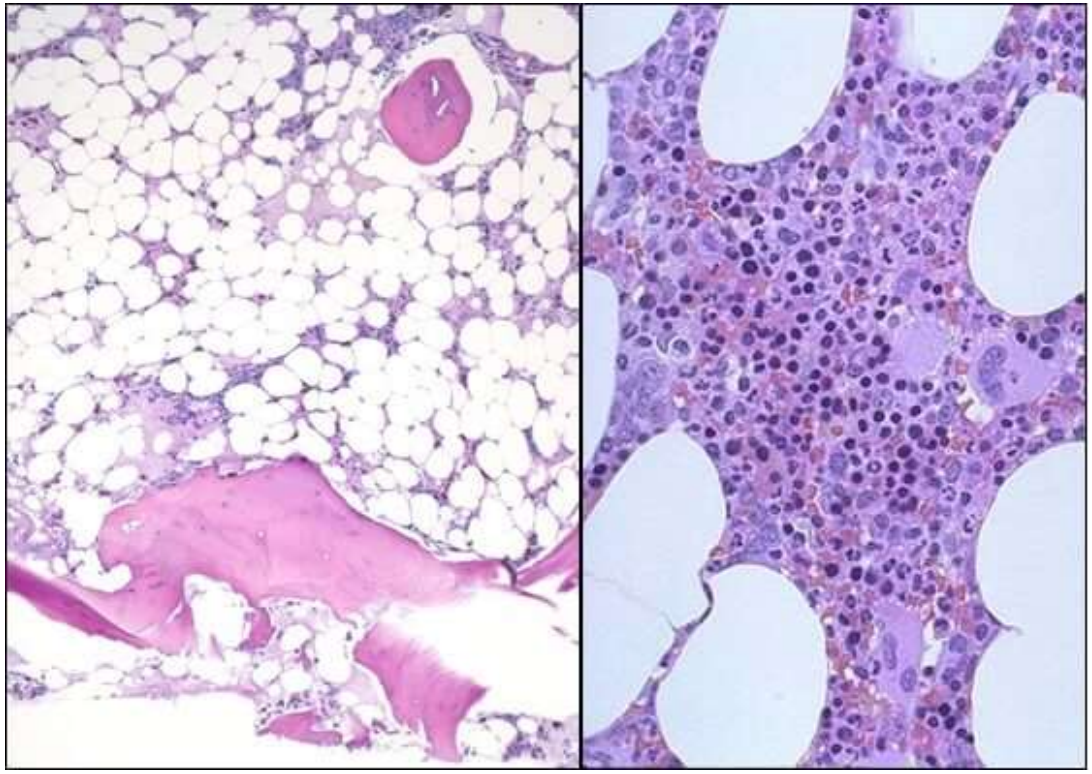
HB 9.2 gm per Dl

Platelet count: 80000 mm/cm3

Leucocyte count: 2100

What is the most likely diagnosis?

A. Myelofibrosis
B. Hiary cell leukaemia
C. Myelodysplastic syndrome
D. Aplastic anaemia
E. Acute lymphocytic leukaemia
F. Folic acid deficiency
G. Myelophithisic Anaemia



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A 70-year-old female presents to your office complaining of easy fatigability, exertional dyspnoea and weight loss. She also complains of frequent falls. Physical examination reveals symmetrically decreased vibratory sensation to the lower extremities. Her haemoglobin is 7.8 g/dl and a peripheral blood smear shows hyper segmented neutrophils. Which of the following is the best treatment for this patient?

A. Iron Preparations
B. Vitamin B12
C. Pyridoxin
D. Vitamin C
E. Folic Acid
F. Erythropoietin
G. Filgrastim
H. Interleukin 2
I. Antithymocyte granule

CIRCULATORY PATHOLOGY

A 16-year-old female comes to the physician because of fatigue. She is not sexually active, and her menstrual cycles are irregular. She eats a balanced diet and works out regularly in a gym. She admits to drinking one or two cans of beer on occasion. Physical examination reveals pale conjunctivae. Her blood haemoglobin level is 9.2 g/dl. Which of the following additional findings would you expect most in this patient?

	Serum Ferritin	Transferrin	MCV	Hyper segmented Neutrophils	Folate
A.	Low	High	76	None	Normal
B.	Low	High	76	None	Normal
C.	Low	Low	84	None	Normal
D.	Normal	Normal	95	None	Present
E.	Normal	Normal	115	Present	Low

CIRCULATORY PATHOLOGY

A 63-year-old man comes to the office due to fatigue and easy bruising. He has no lymphadenopathy on physical examination. Laboratory results are as follows: The patient's peripheral blood smear is shown in the image below:

Which of the following is the most likely diagnosis?

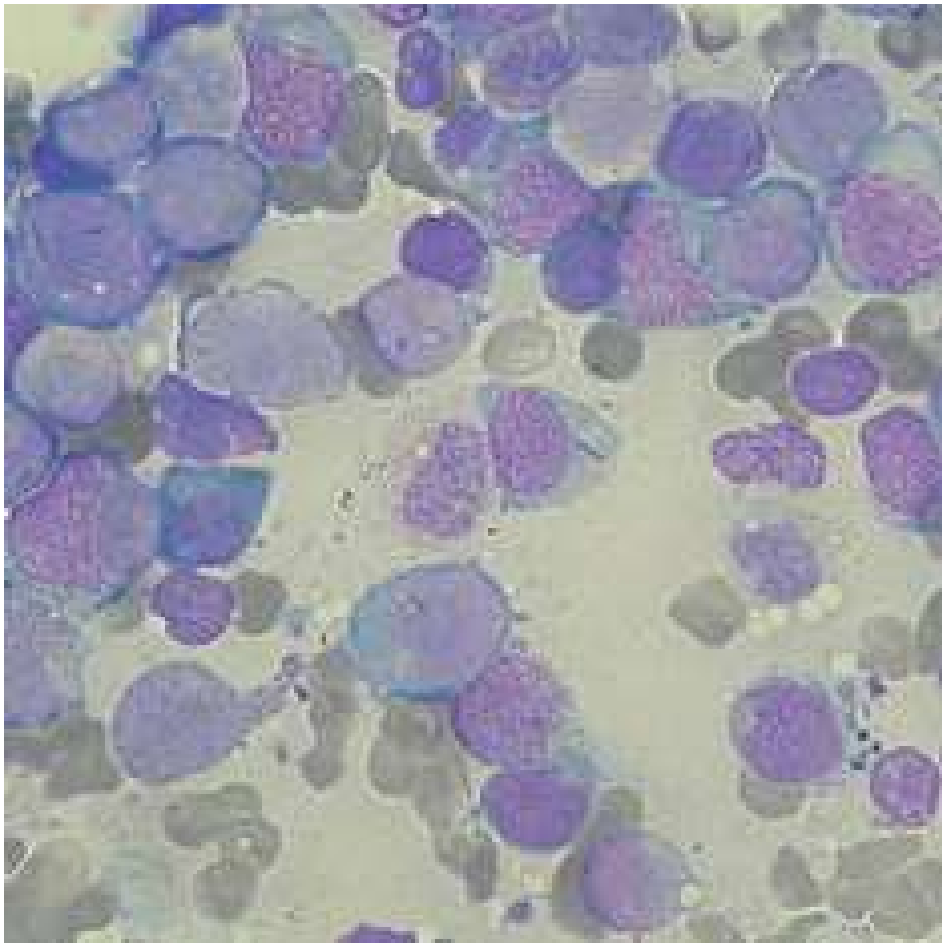
A. AML

B. ALL

C. CML

D. CLL

E. Myeloproliferative disorders



CIRCULATORY PATHOLGY

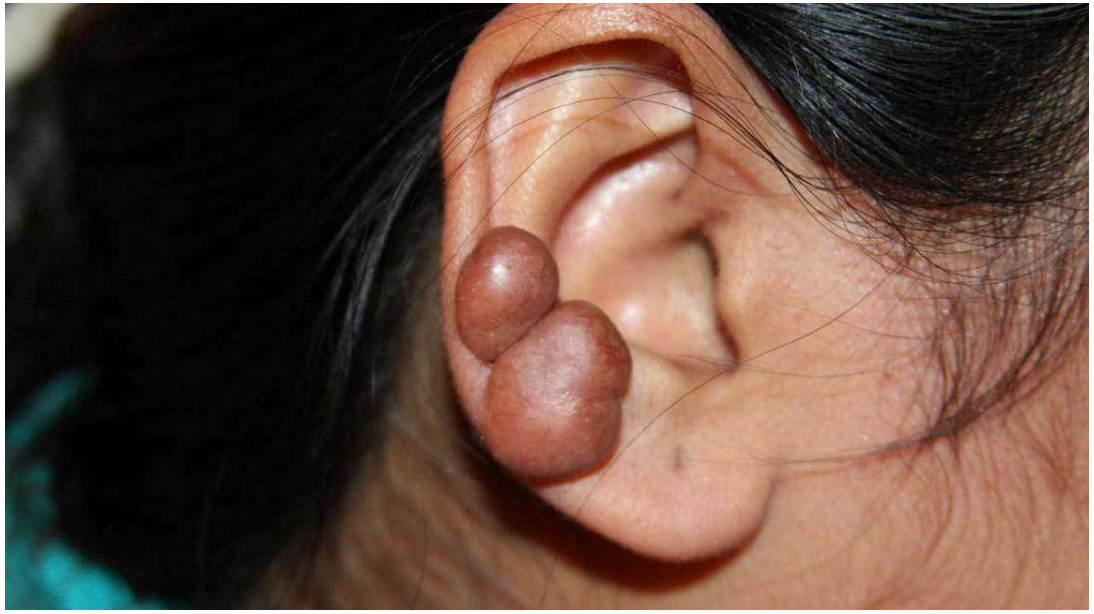
Atherosclerotic lesions involving the coronary arteries limit blood flow to portions of the myocardium supplied by the affected vessels. The administration of certain medications can cause a redistribution of blood flow away from ischemic areas, exacerbating existing myocardial ischemia. A drug that causes which of the following effects is most likely to be associated with this phenomenon?

A. Epicardial vaso dilatation
B. Coronary arteriolar dilatation
C. Systemic venous dilation
D. Systemic arteriolar dilatation
E. Mixed arterial and venous dilatation

CIRCULATORY PATHOLGY

An 18-year-old woman comes to the office due to a slowly enlarging, irregularly shaped mass on her left ear. The mass is often itchy and painful. She had an ear piercing at this site 6 months ago, but there were no immediate complications such as bleeding. The patient has smaller, similar lesions on her right knee and elbow that have been present for several years. Her ear is shown in the image below.

A. Chronic venous insufficiency
B. Deficiency of type V collagen
C. Excess collagen formation
D. Healing by primary intention
E. Retained foreign body
F. Wound contraction



CIRCULATORY PATHOLGY

A new drug developed for the treatment of congestive heart failure demonstrates favourable effects in both animal experiments and human studies. The drug dilates arterioles and veins and promotes diuresis. The drug described above is most likely an analog of which of the following endogenous substances?

A. Endorphins
B. TGF
C. Brain natriuretic peptide
D. Bradykinin
E. Endothelin
F. Angiotensin II

CIRCULATORY PATHOLGY

Platelets	120,000/mm³
Prothrombin time	26 sec
Activated partial thromboplastin time	38 sec

A 50-year-old man with a long-standing history of alcoholism is admitted to the hospital with difficulty breathing. His blood pressure is 90/40 mm Hg, pulse is 114/min, respirations are 22/min, and pulse oximetry is 92% on room air. Physical examination shows bilateral basal crackles, increased jugular venous pressure, hepatomegaly, ascites, and peripheral pitting Edema. Chest x-ray demonstrates cardiomegaly. Scattered ecchymoses are present across each extremity. Laboratory results are as follows:

The patient is given intramuscular vitamin K. Two days later, his laboratory results are unchanged. Which of the following is the most likely cause of this patient's laboratory abnormality?

A. Dietary vitamin K difeciency
B. Factor VII Def
C. Factor VIII def
D. Intrinsic pltlet def
E. VW F Deficiency

CIRCULATORY PATHOLGY

The following Vignette applies to the next 2 items. The items in the set must be answered in sequential order. Once you click Proceed to Next Item. you will not be able to add or change an answer.

A 24-year-old woman is being evaluated for chronic fatigue. She has a history of heavy menstrual periods since menarche and also recalls frequent nosebleeds as a child. Her past medical history is otherwise insignificant and she takes no medications. Laboratory studies show a hemoglobin level of 9.2 g/dl, a mean corpuscular volume of 72 fl, and decreased levels of ferritin.

Item 1 of 2

Which of the following is the most likely diagnosis?

A. Antiphospholipid syndrome

B. Factor VIII def

C. Factor XIII def

D. Immun thrombocytopenia

E. Protein C def

F. VWF Def

CIRCULATORY PATHOLGY

Further evaluation shows decreased von Willebrand factor activity in the patient's serum. This protein normally binds to which of the following?

A. Collagen
B. Fibrin Polymer
C. Prostacyclin
D. Protein c
E. Thrombin