Haemostasis and Haematology VIVAs (Pathology)

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2015.1.C.3

Question 3 Sickle Cell Disease Subject: Path LOA: 2	1. What is sickle cell disease? 2. What are the major pathological manifestations of sickle cell disease? 3. In general how are haemolytic anaemias classified?	**Hereditary** blood disorder **Haemoglobinopathy** • Haemolysis/Haemolytic anaemia • Microvascular occlusions (crises/Tissue ischaemia = severe pain in affected organs eg bones, lungs, liver, spleen) • Splenic enlargement, infarct and dysfunction (Increased susceptibility to infection – encapsulated organisms [eg strep pneumonia, haemophilus influenza]) **Inherited genetic defects** (RBC Membrane [spherocytosis], enzyme deficiencies [G6PD], haemoglobinopathies [thalassaemia, sickle cell disease]) **Antibody mediated destruction** (transfusion reactions, autoimmune) **Mechanical trauma** (Microangiopathic haemolytic anaemias [HUS, DIC, TTP], cardiac valves) **Infections of red cells** (malaria) **Toxic** (envenomation)	**Bold** (Prompt: is it congenital or acquired?) **2 of 3 to pass** **2 of 5 Bold** to pass

2014.2.A.1

Question 1 Anaemia (pp 639-665) **Subject:** Path LOA: 1	1. How are the causes of anaemia classified? Prompt if use RC morphology: How are the causes classified by mechanism? Prompt for example if not volunteered.	1. **Blood loss**: acute, chronic 2. **Increased RC destruction** Inherited genetic: H Spherocytosis, G6PD, Thal, Sickle cell Acq genetic: Parox noct hemo. Ab mediated: transfusion, drugs, Rh disease. Mech trauma: HUS, DIC, TTP, cardiac valves, runners. Infx: malaria; Toxic: envenom, clostridia, Pb. 3. **Decreased RC production** Inherited genetic: Fanconi's, thalassemia. Nutritional: B12/folate, iron. Erythropoietin deficit: renal failure, chronic dis. Immune: aplastic anaemia.	Bold main headings & 1 example of each to pass.
	2. Describe the pathogenesis of iron deficiency anaemia.	Causes: Chronic blood loss, poor diet, impaired absorption, incr reqs Iron stores used up first – **ferritin** haemosiderin. Once reserves depleted **serum iron & transferrin** decr. Erythroid activity increases, no iron in marrow macrophages. RCs become **hypochromic & microcytic.**	Bold to pass.
	3. (Please give examples of anaemias that are more common in specific ethnic groups.) Ask if there is time.	Hereditary spherocytosis: northern Europe G6PD: 10% African American, Africa, Middle East, Med Sickle cell: African descent, up to 30% Thalassemia trait: Africa, Asia, Med, India Pernicious: Scandinavian, Caucasian.	1 correct with example.

2014.1.A.2

Question 2 Thrombosis **Subject:** Path LOA: 1	1. What factors predispose to thrombus formation in a vessel? 2. How are hypercoaguable states categorised? What are some examples of each type? 3. What are the possible outcomes for a vessel thrombus?	Virchows triad. **Endothelial injury**; **Alteration in blood flow** (stasis or turbulence); **Hypercoaguability** of blood **Primary (Genetic)** • Mutations - Factor V Leiden, Prothrombin • Increased levels - factors VIII, IX, XI, fibrinogen • Deficiencies - AT3, Protein C, S • Fibrinolysis defects, homozygous homocystinuria **Secondary (Acquired)** • Prolonged bed rest, immobilisation, MI, AF, Tissue injury (surgery, #, burn), cancer, prosthetic valves,, DIC, HITS, Anti phospholipid antibody syndrome • Cardiomyopathy, nephrotic syndrome, hyperoestrogenic states (pregnancy, post partum), OCP, sickle cell anemia, smoking • Note: often multifactorial **Propagation** (e.g. resulting occlusion); **Embolization; Dissolution; Organisation and recanalization** (e.g. to variable degree)	3/3 bold 2 categories plus Primary - 2 examples Secondary – 3 examples 2/4 categories

2014.2.B.1

Question 2 Embolism (pp 125-127) **Subject:** Path LOA: 1	1. What is an embolus?	A **detached intravascular** solid/liquid/gas **mass** that is carried by the blood stream from its site of origin to a **distant site**.	Bold to pass
	2. Name the different types of embolus?	• **Thromboembolus** **1. Venous: pulmonary** **2. Arterial: systemic** • Fat embolus: from bone marrow • Gas embolus: eg air/nitrogen • Amniotic fluid embolus • Tumour fragment embolus • Foreign body embolus eg catheter	Bold + 2 to pass
	3. What is systemic thromboembolism?	**Definition: Emboli in arterial circulation**	Bold to pass
	4. From where do they arise and where do they lodge?	<u>Sources:</u> 80% from **intracardiac mural thrombi** (2/3 L vent wall infarcts, ¼ L atrial dilation/AF) Other sources: aortic aneurysms, ulcerated atherosclerotic plaques, valvular vegetation, paradoxical emboli, unknown <u>Lodgement Sites:</u> Lower limbs (75%), brain(10%), Other: intestine, kidneys, spleen, upper limbs	Bold + 2/4 sources and 2/4 sites to pass
	Bonus Question Describe the process of infarction from arterial occlusion. Prompt: What are the features that influence the development of an infarct?	Area of ischaemic necrosis: dominant histologic characteristic is ischaemic necrosis - White infarcts occur in solid organs with end-arterial circulation - Acute inflammation happens within hours; reparative response follows - Factors influencing infarct development: nature of vascular supply (end artery vs presence of collateral blood supply), rate of occlusion, vulnerability to hypoxia, oxygen content of blood, calibre of occluded vessel,	

2014.1.A.3

Question 2 DIC **Subject:** Path LOA: 2	1. On a full blood count and coagulation profile, what would you expect to find?	↓Hb (MAHA – microangiopathic haemolytic anaemia), ↑WCC, **platelets↓**, Fibrinogen↓, PT/INR↑, a/PTT↑ and **fibrin degradation products↑**	Bold to pass
	2. What are the pathological consequences of DIC?	DIC – major trauma releases tissue thromboplastins. Both sides of clotting cascade are activated. 2 major consequences – deposition of fibrin within microcirculation leading to **ischaemia/micro thrombosis** of vulnerable organs; and a **consumptive coagulopathy** - platelets and clotting factors leading to a **bleeding diathesis**.	Bold to pass 3/3
	3. What are the causes of DIC?	**Obstetric** – FDIU, amniotic fluid embolism, preeclampsia, **Sepsis** **Malignancy** – acute promyelocytic leukaemia, adenoca of lung, pancreas, stomach and colon **Trauma**- multi/burns/environmental/snakebite	Must get 3 categories

2012.2.2

Q5 Thrombocytopaenia LOA: 1	1. What are the causes of thrombocytopaenia?	**Decreased production of platelets** - Generalised diseases of bone marrow [Aplastic anaemia (congenital / acquired); Marrow infiltration : leukaemia/cancer] - Selective impairment of platelet production [Drug induced (alcohol, thiazides, cytotoxics); Infections (measles, HIV)] - Ineffective megakaryopoieis [Megaloblastic anaemia, Myelodysplastic syndromes ,parox noct Hburia] **Decreased platelet survival** - Immunological destruction [Autoimmune (ITP, SLE); Iso immune (post transfusion, neonatal); Drugs (quinidine, heparin, sulfa); Infections (mono, HIV, CMV)] - Non immunological destruction [DIC, TTP, giant haemangioma, micro-angiopathic haemolytic anaemia; Sequestration] - Hypersplenism; Dilutional	2 groups in bold 2 examples from each
	2. What is the pathogenesis of immune thrombocytopaenic purpura?	Triggers: Primary /Idiopathic ITP : acute / chronic Secondary : drugs ,HIV Chronic – more common – young adult women **Formation of antibodies against platelet** membrane glycoproteins (IIb-IIIa or Ib-IX); Antibodies evident 80% (plasma/platelet surface) Opsonised platelets susceptible to phagocytosis (mononuclear) Spleen probably major site of removal; 80% improve after splenectomy (site destruction + auto antibody synthesis) Acute – disease of childhood Viral illness – abrupt onset; Antiplatelet autoantibodies; Self-limiting, resolves usually within 6 months	Bold to pass

2012.1.1

Question 1 Haemostasis LOA: 1	**In hemostasis, describe the sequence of events at the site of vascular injury**	• Transient **vasoconstriction** by neurogenic and via local secretion of factors eg endothelin • Endothelial damage exposes ECM, leads to • **Platelet adherence, secretion & activation** leading to the primary haemostatic plug • Tissue factor is exposed, resulting in activation of **coagulation cascade** and **thrombin** generation, converting **fibrinogen to fibrin** leading to secondary haemostasis consolidating the initial platelet plug • **Polymerised fibrin and platelet aggregates** to form permanent plug • Counter regulatory mechanisms limit plug to site of injury	**Must state** • Vasoconstriction • Platelets • Coagulation cascade • Fibrin
	What factors restrict clotting to the site of vascular injury? **Prompt:** What prevents runaway clotting of the vascular tree?	• **Endogenous anticoagulants** o **Antithrombins** eg AT III, inhibit thrombin and IXa, Xa, Xia, XIIa o **Proteins C and S** - inactivate Va, VIIIa o **TFPI** (Tissue factor pathway inhibitor) • **Fibrinolytic cascade activation** o **Plasmin** from plasminogen (via factor XII or plasminogen activators) to break down fibrin & interfere with its polymerisation o **tPA** = the most important plasminogen activator	**Must include** concepts of : • Endogenous anticoagulants • Activation fibrinolysis

2012.1.2

Question 1 Thrombosis LOA: 1	**What factors predispose to thrombus formation?** (Prompt: Give an example of a clinical situation where each factor occurs)	Virchow's triad - • **Endothelial injury** • **Alteration in blood flow** • **Hypercoagulability**	**Bold 3** Plus **1 example for each**
	Expanding on hypercoagulable states, what are the broad categories and give examples of each type?	• **Primary (Genetic)** Mutations- Factor V Leiden, Prothrombin Increased - factors VIII, IX, XI, or fibrinogen Deficiencies- AT3, Protein C, S • **Secondary (Acquired)** Prolonged bed rest, immobilisation, MI, AF, Tissue injury, prosthetic valves, cancer, DIC, HITS, Anti phospholipid Antibody Cardiomyopathy, nephrotic syndrome, pregnancy, post partum, OCP, sickle, smoking Note often multifactorial	**Bold + 2 examples** **Bold + 3 examples**

2012.1.2

Question 5 Anaemia LOA: 2	**What are the causes of intravascular haemolysis?** **What are the manifestations of intravascular haemolysis?** (Prompt: In the blood? In the urine?)	-mechanical injury to cells (valves, microthrombi, other physical trauma) - complement fixation (eg transfusion reaction) -toxic injury (eg clostridia), - parasites (eg malaria) Anaemia, haemoglobinuria, haemoglobinaemia, jaundice, haemosiderinuria	**3 causes** **3 manifestations**

2012.1.3

Question 1 Embolism LOA: 1	**What is an embolus?** **What types of emboli do you know of?** **What are the features of fat embolism syndrome?** **Prompt –** What systems may be affected in fat embolism syndrome?	A **detached intravascular** solid/liquid/gas **mass** that is carried by the blood stream from its site of origin to a **distant site**. • Pulmonary • Arterial thromboemboli • Fat emboli • Air emboli • Amniotic fluid • **Associated with long bone fractures,** rarely soft tissue injury/burns • Only 10% symptomatic • **Pulmonary insufficiency**- SOB, ↑RR,↑HR • **Neurologic symptoms**- irritability, restlessness, delirium, coma • **Anaemia**- due to RBC aggregation/haemolysis • **Thrombocytopaenia**- platelet adhesion/aggregation, leads to petechial rash	**Bold to pass** **3 examples to pass** **3/5 bold to pass**

2011.1.2

Question 2. **Normal Haemostasis**	1. List the **sequence of events in normal haemostasis after vascular injury**	1. **Transient vasoconstriction** [Neurogenic & humoral factors (include endothelin – endothelium derived vasoconstrictor)] 2. **Primary haemostatic plug - platelet.** 3. **Secondary haemostatic plug**: coagulation cascade activated by tissue factor and platelet phospholipids, fibrin polymerization "cementing" platelets 4. **Limit spread**: tissue plasminogen activator & thrombomodulin	3 of 4 bold
	2. Describe the **creation of the Primary Haemostatic Plug?**	**Platelets** bind via 1. glycoprotein Ib (GpIb) receptors to 2. von Willebrand factor (vWF) on 3. exposed extracellular matrix (ECM) are 4. activated undergo 5. shape change and 6. granule release: adenosine diphosphate (ADP) and thromboxane A_2 (TxA_2) 7. additional platelet aggregation through platelet GpIIb-IIIa receptor binding to fibrinogen	3 of 7 (plus must say **platelets**)

2010.2.1

Question 1.4 Disseminated Intravascular Coagulation	1. Describe the pathophysiology of "disseminated intravascular coagulation"? ("Trigger" can be a prompt) 2. What are some of the important causes and triggers of severe DIC?	1. 2 major mechanisms **trigger** DIC: 1.1 release of tissue factor into circulation 1.2 widespread injury to the endothelial cells 1.3 Acute, subacute or chronic thrombo-haemorrhagic disorder characterized by 1.3.1 excessive activation of coagulation leading to 1.3.2 formation of **thrombi in the microvascular** circulation 1.3.3 secondary activation of **fibrinolysis causing bleeding** 1.3.4 **consumption of platelets**, fibrin and coagulation factors 2.1 **Obstetric complications** (eg amniotic fluid embolism, FDIU) responsible for approx 50% cases 2.2 Malignant neoplasms (33% cases) **2.3 Sepsis** **2.4 Major trauma**, severe burns, extensive surgery 2.5 Transfusion reaction 2.6 Most mild cases probably due to sepsis, esp in elderly, but not usually diagnosed – low plts	1. 1 trigger and 2/3 bolds 3. 3/6

2010.2.2

Question 2.2 Role of Platelets in Haemostasis	1. What are the 2 main roles of platelets in haemostasis? 2. How is the primary haemostatic plug formed?	**1.1. Primary Haemostatic Plug** **1.2.** Provides surface to **recruit and concentrate activated coagulation factors** **2.** After vascular injury, platelets contact exposed ECM eg. collagen, adhesive glycoprotein, vWF 2.1. **Adhesion –** via glycoprotein 1b (GpIb) receptor to vWF forming bridge between plat and ECM collagen 2.1.1. necessary to overcome high shear force of blood flow, deficient in vW disease or Bernard-Soulier syndrome 2.2. Activation resulting in shape change and **secretion – granule release (ADP, TxA2).** 2.3. **Aggregation –** ADP potent activator of platelet aggregation and +ve feedback for more ADP release. Agonist binding causes intracellular protein phosphorylation cascade => degranulation, including dense body content release of **Ca^{++}**, required for coagulation cascade. Platelet activation causes appearance of negatively charged phospholipids on surface => bind Ca, critical nucleation sites for assembly of coagulation factor complexes. 2.4. TxA2 amplifies platelet aggregation => leads to formation of primary haemostatic plug. 2.5. Aggregation reversible at this stage but not after next stage of stabilization via coagulation cascade with formation of thrombin.	1. **Bold** to pass 2. **4/7 Bold** to pass

2010.2.4

Question 4.4 Iron Deficiency Anaemia	**1.** What is the aetiology of Fe deficiency anaemia? **2.** What are the laboratory findings in Fe deficiency anaemia? 3. What are the clinical features of Fe deficiency anaemia?	**1.1. Chronic blood loss – GIT, menorrhagia** 1.2. Increased requirement – pregnancy 1.3. Dietary deficiency – vegetarians 1.4. Impaired absorption – celiac 2. 2.1. **Microcytic hypochromic anaemia** (low Hb) 2.2. Low S. Fe levels 2.3. Low S. Ferritin levels (correlates well with body iron stores) 2.4. High TIBC (high transferrin levels) 2.5. Low Transferrin saturation levels 3. 3.1. **General -** pallor, weakness, lethargy, fatigue, SOBOE, angina 3.2. Features of blood loss – GI, menorrhagia 3.3. **Specific** features – koilonychia, alopecia, glossitis, pica	1. Bold + 1 2. Bold +3 3. At least 5 from 2 groups

2010.1.2

Question 3: Coagulation Cascade	1. What is the coagulation cascade?	"The coagulation cascade is essentially a **series of conversions of inactive pro-enzymes to activated enzymes**, culminating in the formation of thrombin which then converts the soluble plasma protein fibrinogen into the **insoluble fibrillar protein fibrin**"	**Series of reactions** **Fibrin formed**
	2. What mechanisms restrict the activity of the coagulation cascade. *Prompts:* *How is fibrin broken down?*	A. **Restriction of factor activation** to sites of exposed phospholipids B. **Three types of natural anticoagulants** 1. **Antithrombins** (e.g. AT3) - Inhibit the activity of thrombin & other serine proteases (IXa, Xa, XIa, XIIa) - AT3 activated by binding to heparin like molecules on endothelium → utility heparin in thrombosis 2.**Proteins C & S** - Vit K dependant proteins characterised by ability to inactivate factors Va and VIIIa. 3. **Plasmin (fibrinolytic system)** Plasminogen to plasmin by factor XII dependant pathway or 2 groups of plasminogen activators (PA) u-PA or t-PA Breaks down fibrin & interferes with polymerisation - Resulting fibrin split products (fibrin degradation products) also act as weak anticoagulants Endothelial cells modulate the coagulation / anticoagulation cascade balance by releasing PAI - block fibrinolysis by inhibiting t-PA binding to fibrin **4. Tissue factor Pathway Inhibitor (TFPI)**	**Plasmin + 1 other** **Description of plasmin action**

2010.1.3

Question 5: Haemolytic anaemia	1. Classify haemolytic anaemias	- Intravascular/extravascular Or - extrinsic/intrinsic to the RBC. Or - hereditary/acquired	One classification,
	2. Describe the common features of haemolytic anaemias.	Features: - *Decreased RBC life span(< 120/7) due to premature destruction - ^ erythropoietin and erythropoiesis - Accumulation of products of Hb catabolism - reticulocytosis	• premature RBC destruction and one other feature
	3. Give some important causes of intravascular haemolysis. Prompt for examples	Intravascular - Mechanical injury: cardiac valves, microangiopathic. repetitive physical trauma - Complement fixation: ABO incompatible blood transfusion - Intracellular parasites: malaria - Exogenous toxins: clostridia	• 2 of 4
	If required **4. Apart from anaemia what are the results/manifestations of intravascular haemolysis?**	**- *Haemoglobinaemia** **- Haemoglobinuria** **- *Unconjugated hyperbilirubinaemia(jaundice) from catabolism of haem groups in mononuclear phagocyte system** **- Haemosiderinuria and renal haemosiderosis** **- Decreased serum haptoglobin due binding with free Hb and then cleared by monophag system.** **- Free Hb oxidized to metHb** **- Reticulocytosis**	* Hbaemia and hyperbilirubinaemia to pass and one other OR 3 of 7

2009.2

DIC	What major clinical disorders are associated with DIC ? (same words as table)	**Most common are obstetric complications, malignancy, sepsis and major trauma** **Obstetric**: abruptio, retained dead fetus, amniotic fluid embolism, septic abortion. **Infections**: G-ve sepsis, meningococcus, malaria, rickettsia, histoplasmosis, aspergillosis **Neoplasia**: pancreas, prostate, lung, stomach. **Massive tissue injury**: trauma, burns, surgery. **Miscellaneous**: snakebite, shock, heat stroke, vasculitis, liver disease, leukaemia.	3 of 5 groups and an example of each.
	What is the pathogenesis of DIC?	2 major mechanisms - **release of tissue factor or thromboplastic substances** into the circulation, shift towards pro-coagulation, extrinsic pathway - **widespread injury to epithelial cells**, causing release of tissue factor, platelet aggregation, intrinsic coag pathway	Both mechanisms to pass
	What are the consequences of DIC?	- widespread deposition of fibrin leads to ischaemia and haemolytic anaemia - hemorrhagic diathesis (consumptive coagulopathy) from consumption platelets/clotting factors & activation plasminogen	

2009.2

Question 2: Normal Haemostasis	a) In the normal coagulation cascade, what happens after factor X is activated? Prompt: tell candidate factor X is where the intrinsic and extrinsic pathways join.	1. **Conversion of Prothrombin (II) to Thrombin (IIa)** requiring Calcium (Ca) and activated factor V (Va) as cofactors. Occurs on surface of damaged endothelium or activated platelets 2. **IIa catalyses fibrinogen (I) to fibrin (Ia)** in presence of Ca 3. IIa catalyses factor XIII to XIIIa in presence of Ca leading to **cross-linking of fibrin**	**Bold** essential to pass
	b) Describe the process of normal fibrinolysis.	1. **Plasmin is produced from circulating plasma protein plasminogen**, either by factor XIIa – dependent pathway, or by plasminogen activators. (PA, see 2. below) 2. **Plasmin breaks down fibrin** to FSPs, (eg D-dimer) and disrupts polymerisation 3. a) **t-PA from endothelial cells** most important PA, and most active when attached to fibrin b) Urokinase – like TPA (u-TPA) circulating protein 4. Free plasmin inactivated by alpha 2 plasmin inhibitor	**Bold** essential

2009.1

Question 2: **Role of platelets in haemostasis**	**Describe the formation of a primary haemostatic plug after vascular injury** **How does this then become the secondary haemostatic plug?**	1.Circulating platelets exposed to extracellular matrix (esp collagen) resulting in **adhesion** via vWf /Gp1b/V/IX. 2. **Activation** – a)Secretion of granule contents (esp Ca^{++} and ADP from dense granules) and b)expression phospholipids with platelet thromboxane A_2 leads to 3. **Aggregation** = primary haemostatic plug (reversible process) 1. **Thrombin binds** to platelet with ADP/TxA2 - increased aggregation 2. **Platelet contraction** occurs ("viscous metamorphosis") = secondary haemostatic plug 3. **Fibrin** formation locks platelets into clot (irreversible process)	Need **3/3 bold** Prompt: *What is the role of platelets at the site of injury?* Need **2/3 bold**

2009.2

Question 1: Embolism	What conditions predispose to the development of pulmonary thrombo-embolism?	**Hypercoagulable States:** 1. Primary- factor V Leiden, prohtrombin 20210 A, hyperhomocysteinaemia, antiphospholipid syndrome 2. Secondary – obesity, recent surgery, cancer, oral contraceptive pill, pregnancy **Other underlying medical conditions** – hip fracture, immobilization, cardiac disease, central venous lines	Simple list of 6 = straight pass Better pass with bold groups and examples of each
Question 2	What are the potential clinical sequelae of pulmonary thrombo-embolism?	Relates to size and number of emboli and overall status of cardiovascular system 1. Asymptomatic 2. Sudden death 3. Large PE –chest pain, dyspnoea, shock 4. Small PE-transient chest pain, cough and in predisposed individuals pulmonary infarct causing tachycardia, tachypnea, haemoptysis, fever,pleural rub. 5. Pulmonary hypertension	Any 3 to pass
Question 3:	What are the non-thrombotic types of pulmonary embolism?	1. Air 2. Bone marrow or Fat 3. Amniotic fluid 4. Tumour 5. Foreign bodies	3 to pass

2009.1

Question 4: **von Willebrand Disease**	**What are the haematological and clinical effects of von Willebrand disease?** **Describe the types of von Willebrand Disease**	Haem: Increased bleeding time with normal platelets Increased PT time (Types 1 & 3) Decreased Ristocetin cofactor activity Clin: Spontaneous bleeding from mucous membranes Increased bleeding from wounds Menorrhagia Bleeding into joints rare except in Type 3 **1. Type 1** and **Type 3** associated with decreased circulating vWF. Type 1 most common (70%), autosomal dominant and usually mild. Type 3 autosomal recessive and severe **2. Type 2** has defective vWF, autosomal dominant, mild severity and 25% of cases.	Need 3/4 Need 2/3

2009.1

Question 1: **Thrombosis**	**What factors lead to formation of a thrombus?**	1. **Endothelial injury: dominant** influence, by itself can lead to thrombosis, especially in **high flow** circulation (e.g. arterial circulation; cardiac chambers). Any alteration in **dynamic balance** of pro- and anti-thrombotic effects of endothelium can influence clotting 2. **Stasis or turbulence:** Turbulence contributes to thrombosis by causing endothelial injury or dysfunction, and local pockets of stasis. Disrupts laminar flow and bring platelets into contact with endothelium; prevents dilution of clotting factors by fresh flowing blood; retards inflow of clotting factor inhibitors. Stasis is a major factor in development of **venous** thrombi. 3. **Blood hypercoagulability:** Less frequent. Any alteration of the coagulation pathways that predisposes to thrombosis. **Primary**: Genetic mutations (e.g. Factor V gene; prothrombin gene); genetic deficiencies (e.g. antithrombin III; protein C; protein S) **Secondary (acquired):** High risk for thrombosis (prolonged bed rest; immobilisation; MI; AF; tissue damage; cancer; DIC; HITS; APLA); lower risk (cardiomyopathy; nephritic syndrome; hyperestrogenic states / pregnancy; OCP use; sickle cell anaemia; smoking)	**All three plus brief description to pass** Prompt: What is **Virchow's triad**?

2009.1

Question 1:	**Assuming a patient survives the immediate effects, what is the fate of the thrombus itself?**	Some combination of the following four events: 1.**Propagation** (accumulates more platelets and fibrin, eventually leading to vessel occlusion); 2. **Embolisation** (dislodges and travels to other sites); 3. **Dissolution** (removal by fibrinolytic activity); and 4. **organisation** (inflammation leading to fibrosis) and **recanalisation** (vascular flow re-established or thrombus incorporated into a thickened vascular wall)	3 out of four to pass

2008.1

Q5. Sickle cell disease	What is sickle cell disease?	Hereditary haemoglobinopathy	An abnormal haemoglobin HbS is formed because of a point mutation in the beta globin chain
		(Generally heterozygous (about 40% HbS) is asymptomatic unless severe hypoxia. Homozygous most haemoglobin is HbS – leads to alteration of the Hb when deoxygenated – sickling (morphological alteration), as well as red cell membrane changes)	Pass criteria: Must state it is an abnormal haemoglobin.
	What are the major clinical features of sickle cell disease?	1.Haemolytic anaemia (anaemia, reticulocytosis, hyperbilirubinaemia) 2.Vaso- occlusive complications/crises 3. Splenomegaly/dysfunction Prone to infections esp pneumococcus/haemophilus	Pass criteria: 2 minimum
	What are the major precipitants for a sickle cell crisis in a prone individual?	1.hypoxia 2. dehydration 3. Drop in pH	2 of 3 Optional depending on time

2008.1

Q2. Embolism	What clinical conditions may cause fat embolism?	1. (Microscopic) fat globules travelling in the circulation. 2. Long bone # 3. Soft tissue trauma/burns –rare 4. Very common with severe skeletal injury but rarely (<10%) of clinical significance	Pass criteria: 2 to pass.
	What is the pathogenesis of fat embolism syndrome?	1. Mechanical obstruction of microvasculature (lungs & brain): fat globules/aggregated platelet and RBCs. 2. Biochemical injury: FFAs from fat globules > endothelial injury, platelet activation & mediator release.	Main 2 points to pass
	What are the potential clinical sequelae of fat embolism?	1. Asymptomatic (Majority) 2. Neurological: altered LOC. 3. Pulmonary: Inc RR, SOB, hypoxia. 4. Haem: thrombocytopenia & anaemia.	2/4 to pass

2008.1

Q5. Disseminated intravascular coagulation	What is Disseminated Intravascular Coagulation?	1 Intravascular activation of the coagulation sequence by a variety of processes and clinical conditions 2 resultant formation of micro-thrombi throughout the circulation, often uneven in distribution 3 consumption of platelets, fibrin & coagulation factors 4 coagulopathy secondary to loss of platelets, fibrin & coagulation factors 5 activation of fibrinolytic mechanisms aggravates haemorrhagic potential 6 clinical picture of tissue/organ hypoxia/infarction as well as haemorrhage 7 microangiopathic haemolytic anaemia (MAH) secondary to intravascular fibrin traumatising RBC	Pass criteria: 4 from 7 Prompt: In broad terms what occurs in DIC?
	List the major clinical disorders associated with DIC.	1.Obstetric: a. Abruption b. Retained dead fetus c. Septic abortion d. Amniotic fluid embolus e. Toxaemia 2.Infection/Sepsis a. Meningococcaemia b. Malaria c. Gram negative sepsis d. Aspergillosis e. Histoplasmosis 3.Neoplasm a. Ca pancreas, prostate, lung & stomach b. Acute promyelocytic leukaemia 4.Trauma a. Major diffuse b. Burns c. Extensive surgery c. Others a. Liver disease b. Heat stroke c. Shock d. Snakebite e. AAA	Pass criteria: suggest need two from at least 4 groups
	What are the major mechanisms which trigger Disseminated Intravascular Coagulation?	Pathological activation of the extrinsic and/or intrinsic coagulation pathways. OR impairment of clot-inhibition (RARE) 1. Release of tissue factor or thromboplastic substances into the circulation (placental origin in obstetric disorders; mucus from adenocarcinoma; endotoxins in gram negative sepsis) 2. Widespread / diffuse injury to endothelial cells (TNF is extremely important mediator), seen with heat stroke, burns, diffuse trauma, meningococcal & rickettsial infection	Underlined processes essential