ACEM Primary Examination Vivas > Pathology > Fluid & Haemodynamics Organised by edvivas.com	
Title	**Page**

Coagulation Cascade 2010-1

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**

Coagulation Cascade 2006-2

TOPIC: Coagulation cascade _____ **NUMBER:** _____

OPENING QUESTION	**Give an overview of the coagulation cascade**	**COMMENTS**
POINTS REQUIRED	**1 Component of haemostasis** resulting in thrombosis (with endothelium + platelets)	
	2 Series of enzymatic conversions	
	3 Proenzymes converted to activated enzymes resulting in formation of Thrombin	
	4 Comprises extrinsic and intrinsic pathways	
	5 Extrinsic pathway – activated by Tissue Factor (lipoprotein), exposed at sites of tissue injury	Essential to pass
	6 Intrinsic pathway – activated by Factor XII	
	7 Pathways converge where activation of Factor X occurs	Essential to pass
	8 Common pathway - factor X, Prothrombin, Thrombin, factor V, Calcium, then fibrinogen converted to fibrin and ultimately cross linked fibrin	Essential to pass
PROMPTS	**Describe the common pathway of the coagulation cascade?**	
PROMPTS		

Coagulation Cascade 2005-1

Coagulation cascade	How is the coagulation cascade limited to the site of vascular injury? (2 of a/b/c) Prompt... What natural anticoagulants?	1. Exposed phospholipids at site necessary for factor activation. 2. Natural anticoagulants generated: a. Antithrombins by binding to endothelial cell b. Proteins C and S, via thrombomodulin c. Plasmin via endothelial cell release tPA d. (FDPs also weakly anticoagulant) e. Tissue factor pathway inhibitor	

Coagulation Cascade Inhibition 2003-2

3.2 Inhibition coagulation cascade	Describe factors that inhibit activation of the coagulation cascade	1. **Antiplatelet**: Intact endothelium; endothelial PGI2, NO; adenosine diphosphatase degrades ADP 2. **Anticoagulant**: membrane associated heparins allow antithrombin 111 to inactivate factors; thrombomodulin allows thrombin to activate protein C, which requires protein S to be anticoagulant. 3. **Fibrinolytic**: endothelial cells synthesize t-PA	

Disseminated Intravascular Coagulation 2016-1-A

Stem: Moving onto Pathology. You suspect she has disseminated intravascular coagulation.			
Question 5 DIC **Subject:** Path LOA: 1 (2 min)	List some common triggers DIC? How does endothelial injury initiate DIC?? Extra question: Draw the extrinsic pathway of the coagulation cascade.	**Sepsis** (bacterial endotoxins and AgAb complexes), **major trauma/burns/surgery**, **certain cancers** (AML (promyelocitic), adenoca of lung, colon, stomach, pancreas), **obstetric complications** (placenta, amniotic fluid, dead fetal tissue) • Exposure of sub endothelial matrix activates plts and the coag cascade • TNF causes tissue factor to be expressed from endothelial cells • TNF up-regulates the expression of adhesion molecules on endothelial cells to allow leucocytes to bind and damage endothelial cells. • Direct trauma to endothelial cells from AgAb complexes, temperature extremes, or microorganisms.	3 of 4 categories required. Will accept examples. 3 points required for pass

Disseminated Intravascular Coagulation 2014-1-A

Stem: We are moving to Pathology. She has multiple wounds oozing blood due to DIC			
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

Disseminated Intravascular Coagulation 2010-2

Question 1.4 Disseminated Intravascular Coagulation	1. Describe the pathophysiology of "disseminated intravascular coagulation"? ("Trigger" can be a prompt)	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	1. 1 trigger and 2/3 bolds
	2. What are some of the important causes and triggers of severe DIC?	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	3. 3/6

Disseminated Intravascular Coagulation 2009-2

Qn 5 ACEM PRIMARY 2009/2 PATHOLOGY VIVA

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
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	

Disseminated Intravascular Coagulation 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

Disseminated Intravascular Coagulation 2003-2

2..2 Genesis of DIC	Describe the pathogenesis of Disseminated Intravascular Coagulation What major disorders might precipitate DIC?	Variety of diseases activate the coagualtion system –> **microthrombi** –> injury to microvasculature of organs; **consumption** of clotting factors; activation of **fibrinolysis** –> **bleeding**. Triggers: 1. release of tissue factor or thromboplastic substances; 2. widespread injury to endothelial cells. Obstetric complications; infections; neoplasms; massive tissue injury; miscellaneous: shock, snakebite, heat stroke, burns etc.	3/

Embolism 2017-2-A

Stem: Moving on to Pathology. His TIA is most likely embolic.			
Question 5 Embolism **Subject**: Pathology LOA: 1	a) What is an embolus?	a) An embolus is a **detached intravascular** solid, liquid or gaseous mass that is **carried by the blood** to a **site distant** from its point of origin.	Bold to pass
	b) Name the different types of emboli Prompt: what can embolise?	b) Thromboembolus Venous: pulmonary Arterial: systemic • Fat embolus • Gas embolus • Amniotic fluid embolus • Air embolus	3 out of 5 to pass
	c) What is systemic thromboembolism?	c) Systemic thromboembolism refers to emboli **in the arterial circulation.**	Bold
	(d) Name the sources of systemic thromboembolism?	d) Most (80%) arise from **intracardiac mural thrombi**, two thirds of which are associated with left ventricular wall infarcts and another quarter with left atrial dilation and fibrillation. The remainder originate from aortic aneurysms, thrombi on ulcerated atherosclerotic plaques or fragmentation of a valvular vegetation, with a small fraction due to paradoxical emboli. 10 to 15% of systemic emboli are of unknown origin.	Bold plus one other
	Bonus question What are the differences in the lodgement of venous and arterial thrombi?	Venous thrombi tend to lodge primarily in one vascular bed (the lung). Arterial thrombi can travel to a wide variety of sites; the point of arrest depends on the source and the relative amount of blood flow that downstream tissues receive. Major sites of arterial embolization are the lower extremities (75%) and the brain (10%), with the intestines, kidneys, spleen and upper extremities involved to a lesser extent.	

Embolism 2014-2-B

Stem: We will now move on to Pathology.			
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,	

Embolism 2013-1

Question 3 Pulmonary Embolism LOA: 1	1. From where do pulmonary thromboemboli originate? 2. What are some risk factors for thrombus formation? 3. What are the clinical effects of pulmonary thromboemboli?	1/95% **arise in the deep veins of the leg** – pass up to R side of heart and into pulm vasculature. Size determines where they lodge. 2. **Primary** – (genetic factors) – factor 5 Leiden, protein C+S deficiency, antiphospholipid syn **Secondary**- (acquired) – stasis/Immobilisation, long haul flights, active malignancy, trauma/burns/surgery, pregnancy, OCP. Indwelling catheters 3. most clinically silent 60-80%, Cough, SOB, fever, CP, haemoptysis, tachy-cardia/pnoea through to sudden death,cor pulmonale,CVS collapse Pulm haemorrhage / infarction, over time multiple emboli may cause pulm hypertension & cor pulmonale	Bold to pass (exact % not required but rough idea) At least one example from Primary, and 2 from secondary 5 features

Embolism 2012-1

TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Embolism LOA: 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**
	What types of emboli do you know of?	• Pulmonary • Arterial thromboemboli • Fat emboli • Air emboli • Amniotic fluid	**3 examples to pass**
	What are the features of fat embolism syndrome? **Prompt** – What systems may be affected in fat embolism syndrome?	• **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	**3/5 bold to pass**

Haemostasis 2017-2-D

Stem: Moving on to Pathology. Her wound is oozing.			
Question 4 Haemostasis **Subject:** Pathology LOA: 1 *Robbins – Pg. 119; Chapter 4: Haemodynamic disorders* *Chapter 12: The Heart; 9th Edition;*	a) Describe the process of primary haemostasis. ***Prompt:*** *how is the primary haemostatic plug formed* b) How is the coagulation cascade activated following injury? Prompt: what happens after it is activated? c) BONUS: What does prothrombin time measure?	Primary haemostasis = formation of platelet plug • Endothelial damage exposes ECM (collagen, vWF) • Platelet activation • adhere (via Gp1b to vWF) • shape change (flat to round) • secretion (ADP, Tx A2, Ca) + negative charge phospholipid) • Platelet aggregation (platelet Gp11b-111a receptors via fibrinogen) Vascular damage and exposure of **tissue factor** converts factor VII to VIIa. This in turn causes a series of amplifying enzymatic reactions that leads to the deposition of a **fibrin clot (secondary haemostasis)**. (Factor X is converted to factor Xa, which in turn converts prothrombin (factor II) to thrombin. Which converts fibrinogen to fibrin (fibrin network)) Assesses the extrinsic and common coagulation pathways.	Platelets plus 3of 6 Bold plus concept At least one

Haemostasis 2016-2-A

Stem: Moving on Pathology. He has multiple wounds which are bleeding.			
Question 3 Haemostasis, platelet aggregation **Subject:** Path LOA: 1	1) What is the sequence of events that occurs to produce haemostasis after a vascular injury. Prompt: What happens first? 2) What laboratory tests are used to assess the function of the different pathways of the coagulation cascade? *Prompt: Which one is vitamin K dep.*	**1) Vasoconstriction**: arteriolar, reflex neurogenic, enhanced by endothelin 2) **Primary haemostasis**: extracellular matrix exposed, platelet adherence/activation -- platelets aggregate & forms a plug 3) **Secondary haemostasis**: Tissue factors exposed, Fac III, thromboplastin, Fac VII , platelet plug consolidated – thrombin/fibrin generated **4) Thrombus & antithrombotic effect** – fibrin polymerises to form permanent plug, tPA regulates **Prothrombin time – extrinsic pathway** factors VII, X, II, V, fibrinogen (including vit K dependent factors) **Partial thromboplastin time – intrinsic pathway** factors XII. XI, IX, VIII, X, V, II fibrinogen	To pass identify 3/4 steps & demonstrate understanding of concepts To pass identify test, what pathway it is testing & identify which one is vit k dependent.

Haemostasis 2015-2-A

Stem: Moving onto Pathology. He has multiple facial lacerations which are bleeding			
Question 3 Haemostasis **Subject:** Path LOA: 1	1. What are the sequence of events in haemostasis after a vascular injury? Prompt: Is there any particular sequence to the events?	a. **Vasoconstriction**: arteriolar, reflex neurogenic, enhanced by endothelin b. **Primary haemostasis**: extracellular matrix exposed, pl adherence/activation - - pl aggregates & forms plug c. **Secondary haemostasis**: Tissue factors exposed, Fac III, thromboplastin, Fac VII, platelet plug consolidated - thrombin/fibrin generated d. **Thrombus & antithrombotic effect** – fibrin polymerises to form permanent plug, tPA regulates	Q3.1 – to pass identify 3/4 steps of hemostasis (bold) in correct sequence
	2. What laboratory tests are used to assess the function of the different pathways of the coagulation cascade? Prompt: Which one is vitamin K dependant	**Prothrombin time – extrinsic pathway** factors VII, X, II, V, fibrinogen (including vit K dependent factors) **Partial thromboplastin time – intrinsic pathway** factors XII. XI, IX, VIII,X, V, II, fibrinogen	Q3.2 – to pass identify test, what pathway it is testing and identify which one is vit K dependant

Haemostasis 2012-1

TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
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** ○ **Antithrombins** eg AT III, inhibit thrombin and IXa, Xa, Xia, XIIa ○ **Proteins C and S** - inactivate Va, VIIIa ○ **TFPI** (Tissue factor pathway inhibitor) • **Fibrinolytic cascade activation** ○ **Plasmin** from plasminogen (via factor XII or plasminogen activators) to break down fibrin & interfere with its polymerisation ○ **tPA** = the most important plasminogen activator	**Must include** concepts of : • Endogenous anticoagulants • Activation fibrinolysis

Haemostasis 2011-1

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**)

Haemostasis and Fibrinolysis 2009-2

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
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

Infarction 2013-1

TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1: Infarction LOA: 1	1. What is an infarct?	1. Area of **ischaemic necrosis** caused by **arterial** or venous occlusion	Bold
	2. What mechanisms lead to infarction?	**2 Arterial thrombosis, embolism**, vasospasm, haemorrhage into plaque, extrinsic vascular compression (by tumour or oedema), torsion of vessel, traumatic rupture, entrapment in hernial sac, venous thrombosis	Bold + 2
	3. What factors determine the development of an infarct? Prompt- What influences whether an infarct will develop?	3. Factors that determine development of an infarct • *Nature of vascular supply eg dual vs end arterial* • Rate of occlusion development – time for collaterals to develop • Vulnerability to hypoxia of the tissue type • Oxygen content of blood	2 of 4

Ischaemia 2006-1

TOPIC: Reversible v Irreversible changes of ischaemia
NUMBER: Question 1 - Thursday 6 April pm

OPENING QUESTION	What is "irreversible injury" in cells after a period of ischaemia?	**COMMENTS**
POINTS REQUIRED	1 The irreparable structural and intracellular damage that results in sequelae of necrosis or apoptosis.	Definition
	2 Two consistent characteristics – severe disturbance of membrane function, and inability of mitochondria to generate energy \ ATP.	
	3	
	4	
	5	
PROMPTS		
SECOND QUESTION (if needed)	What changes are observed in these cell's structure and contents?	3 to pass
POINTS REQUIRED	1 Extensive damage to all cell membranes.	
	2 Increased cell swelling.	
	3 Lysosomal swelling and disruption.	
	4 Swelling in mitochondria with amorphous densities.	
	5 Nuclear condensation, then fragmentation \ dissolution	
	6 Laminated structures (myelin figures) appear.	
PROMPTS		

COMMENTS

Expect a definition and then at least 2-3 of second question list for pass.

Ischaemia 2005-2

TOPIC: Ischaemic Injury _____ **NUMBER:** 1a

OPENING QUESTION	Describe the mechanisms of ischaemic cell injury	**COMMENTS**
POINTS REQUIRED	1 Hypoxia → Loss of Ox Phos and ↓ATP in mitochondria	Most of 3 of 4
	2 Failure of Na pump, loss of glycogen and ↓protein synthesis	
	3 Cellular swelling, loss of microvilli, ER swelling, cell surface blebs, myelin figures	
	4 Irreversible changes – swollen mitochondria, plasma membrane damage, lysosome swelling, Ca influx	
	5	
	6	
	7	
PROMPTS		
SECOND QUESTION (if needed)	What are the differences between ischaemic cell injury and hypoxic cell injury?	One of two
POINTS REQUIRED	1 Ischaemia prevents delivery of energy substrates, while hypoxic tissue can still produce energy by anaerobic glycolysis	
	2 Ischaemia tends to injure tissues faster than hypoxia	
	3	
	4	
	5	
	6	
PROMPTS		

Ischaemia 2004-2

TOPIC: Initial cellular changes in acute ischaemia _____ **NUMBER: 1**

OPENING QUESTION	Describe the morphological changes that occur in cells during acute ischaemia.	**PROMPTS**	**COMMENTS**
POINTS REQUIRED	<u>Reversible changes</u> *Cellular Swelling*: failure to maintain ionic and fluid haemostasis; organs become swollen; 1. plasma membrane blebs, intramembranous aggregations 2. mitochondrial swelling, small densities. 3. distended segments of ER; dispersion of ribosomes 'vacuolar degeneration. 4. Clumping of nuclear chromatin. Fatty change: lipid vacuoles in cytoplasm. <u>Irreversible changes</u> *Cell membrane defects*, Myelin figures in cytoplasm, rupture of lysosymes and autodigestion Mitochondrial large densities, lysis of ER Nuclear pyknosis, karyolysis or karyorrhexis.	Need both reversible & irreversible changes to pass, need 5 or 6 points to pass.	

Ischaemia 2003-2

3.1 Cell irreversible ischaemia	Describe the morphological changes seen in cells with irreversible ischaemia. What metabolic changes occur in irreversible ischaemia?	**Mitochondrial swelling**: influx of Ca, loss of proteins, enzymes, RNA, through hyperpermeable membranes. Lysosomal injury – leakage of enzymes into cytoplasm. – **autodigestion**. Cell membrane leakage in both directions, fluid in, eg CK,Trop out.. **Nuclear changes** (pyknosis/karyolysis/karyolexis). **Inability to reverse mitochondrial dysfunction** causing **ATP depletion**. Disturbances of cell membrane. Contributing mechanisms: mitochondrial dysfunction; loss of membrane phospholipids; cytoskeletal abnormalities; reactive oxygen species; lipid breakdown products; loss of intracellular amino aids.	2/

Ischaemia and Hypoxic Injury 2008-2

1.1 Cell reversible ischaemia	Describe the morphological changes seen in cells with reversible ischaemia. What metabolic changes occur in reversible ischaemia?	**Cellular swelling**: failure to maintain ionic and fluid homeostasis; organelles become swollen; 1.plasma membrane alterations. 2. mitochondrial changes. 3. distended segments of ER; 'vacuolar' degeneration. 4. nuclear alterations. Fatty change: lipid vacuoles in cytoplasm. **Depletion of ATP –> sodium pump reduction –> swelling**, Na into cells. Increased. catabolites in cells –> increased. osmotic load –> swelling. Anaerobic metabolism. –> **lactic acidosis**, decreased pH. Detachment of ribosomes from ER –> decreased protein synthesis	2/4

Ischaemia, reversible 2003-2

1. Ischaemic Injury	1. What is the difference between ischaemic and hypoxic injury?	Ischaemic involves disruption or reduction in blood supply resulting in reduced oxygen delivery, reduced delivery of substrate and reduced removal of metabolic products Hypoxic involves reduced oxygen delivery only. I hypoxic, anaerobic (glycolytic metabolism can continue as new substrate is being delivered). As a result cellular, hence tissue injury is much more rapid in ischaemic injury.	Candidate to clearly differentiate the 2 processes
	2. Describe the morphologic intracellular changes that occur in ischaemic injury	**Reversible**; Cell swelling, ultrastructural changes including loss of microvilli and cell surface 'bleb' formation. Swelling of ER and mitochondria, Myelin figure formation, and clumping of nuclear chromatin **Irreversible**; severe mitochondrial swelling, plasma membrane damage, swelling of lysosomes	Mention of reversible & irreversible changes with examples from each

Odema 2017-2-C

1.1 Cell reversible ischaemia	Describe the morphological changes seen in cells with reversible ischaemia. What metabolic changes occur in reversible ischaemia?	**Cellular swelling**: failure to maintain ionic and fluid homeostasis; organelles become swollen; 1.plasma membrane alterations. 2. mitochondrial changes. 3. distended segments of ER; 'vacuolar' degeneration. 4. nuclear alterations. Fatty change: lipid vacuoles in cytoplasm. **Depletion of ATP –> sodium pump reduction –> swelling**, Na into cells. Increased. catabolites in cells –> increased. osmotic load –> swelling. Anaerobic metabolism. –> **lactic acidosis**, decreased pH. Detachment of ribosomes from ER –> decreased protein synthesis	2/4

Odema 2017-1-C

Stem: Moving on to Pathology. The knee swells over several hours following the injury			
Question 2 Oedema Robbins 9th edition pages 113-115 **Subject:** Path LOA: 1	a) What is oedema b) What are some of the causes of oedema *(prompt, what are the non-inflammatory causes)* c) What is the difference in the composition of the fluid, between inflammatory and non-inflammatory oedema	**Increased interstitial fluid** **Inflammatory** (acute / chronic):- infection, tissue necrosis, foreign body, immune, traumatic **Non-inflammatory**: - increased hydrostatic pressure (eg cardiac failure, DVT), hypoproteinaemia (chronic liver disease, nephrotic syndrome), lymphatic obstruction, sodium retention **Inflammatory**: - exudate**, high protein** conc, **Non-inflammatory**: - transudate, **low protein** conc (effectively an ultrafiltrate of plasma)	**Bold** **2 examples from each to pass** Must know

Odema 2013-1

Stem: The patient is in heart failure. Moving on to Pathology.			
Question 4 Fluid and oedema **Subject:** Path LOA: 1	a) What factors govern the movement of fluid between the vascular and interstitial spaces?	**1. Hydrostatic pressure** **2. Colloid osmotic pressure** **3. Normal capillary walls** - most protein remains intravascular, fluid leaks out. Fluid out of vessel at arteriolar end. Most fluid returned to vessel at venular end. Small amount of fluid returns via lymphatics.	2 bold plus concept
	b) What are the major mechanisms of oedema formation? Give examples of each.	**1 Increased hydrostatic pressure** (i) Local venous; venous obstruction, compression, thrombosis (ii) Local arteriolar; dilation, heat, neurohumeral dysregulation (iii) Systemic; CCF, constrictive pericarditis, impaired venous return 2. **Reduced plasma oncotic pressure** (mainly protein loss e.g. nephrotic syndrome or poor production e.g. cirrhosis, malnutrition, gut loss). **3. Inflammation -** acute or chronic inflammation, angiogenesis **4. Lymphatic obstruction** - Inflammatory, neoplastic, post-surgical, post irradiation, **5. Sodium retention with water** - renal insufficiency, activation of renin-angiotensin system, renal hypoperfusion.	3 out of 5 bold, must include hydrostatic and COP. 5 conditions covering three groups
	c) What are the clinical features of heart failure?	1. Lung - dyspnoea, orthopnoea, PND, APO, pleural effusions. 2. Cardiac - 3rd heart sound, displaced apex beat, AF, murmurs, JVP elevation. 3. Renal - fluid retention, pedal oedema, AKI. 4. Brain - confusion secondary to hypoxia. 5. Hepatic - congestion, ascites, cirrhosis late	3 of 5 organ system symptoms to pass

Odema 2011-2

TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1: **Oedema formation** LOA: 1	1. What are the mechanisms of oedema formation?	**1.↑ hydrostatic pressure –** impaired venous return, eg CHF,Constrictive pericarditis,ascites,venous obstruction(internal/external +immobility), arteriolar dilatation eg heat **Decr plasm oncotic pressure (hypoproteinaemia)** – nephrotic syndrome, ,malnutrition, protein losing enteropathy. **Lymphatic obstruction** - inflammatory, neoplastic, post-surgery/radiation **Sodium and water retention** –XS salt with renal insufficiency, incr renin-angiotensin-aldosterone secretion **Inflammation** –acute/chronic, angiogenesis	3 out of 5 bold, example from each
	2. What is the pathogenesis of cardiogenic oedema?	**2.** Decreased cardiac output, decr renal perfusion, secondary aldosteronism, Incr blood volume, incr venous pressure	At least 3 steps.

Odema 2010-2

Question 1: LOA: 1	1) What is the pathogenesis of oedema?	**1.Hydrostatic pressure** and **osmotic pressure** normally balance to ensure that net fluid into and out of capillaries remains relatively equal with the little over removed by **lymphatics. Increased HP or diminished OP or overload of the lymphatics** will result in oedema.	Bold to pass
	2) How is oedema categorised and provide some examples?	**2.Increased hydrostatic pressure** - impaired venous return, eg. CCF, constrictive pericarditis, ascites, venous obstruction (internal or external + immobility); arteriolar dilatation eg. heat, neurohumeral dysregulation **Reduced plasma osmotic pressure (hypoproteinaemia)** - nephrotic syndrome, ascites, malnutrition, protein losing gastroenteropathy **Lymphatic obstruction** - inflammatory, neoplastic, postsurgical, postirradiation **Sodium retention** - excessive salt with renal insufficiency, increased tubular reabsorption of sodium (renal hypoperfusion, increased renin-angiotensin-aldosterone secretion) **Inflammation** - acute, chronic, angiogenesis	3 of 5 bold to pass with one example each category quoted

Odema 2007-1

a) What factors govern the movement of fluid between the vascular and interstitial spaces? (30%)	Hydrostatic Pressure – Osmotic Pressure- protein/ Na Normal capillary walls- most protein retained Small fluid out art end Most back venous end Small amount back via lymphatics	3 concepts mentioned A > c >V May know some Pressures, may mention gravity/ leg v head. Capillaries are fluid leak vessels. Normal tissue flow important. Thoracic duct return of lymphatics
b) What are the major mechanisms of oedema formation (with examples)? 70%	>**Increased Hydrostatic Pressure** (local- DVT/ systemic- CCF)/venous obstruction < **Oncotic P** (mainly prot loss e.g. Nephrotic syndrome or poor production eg cirrhosis/ malnutrition or loss via gut) **Capillary leak**- (inflammatory injury/ systemic / infection) **Obstructive lymphatics**- e.g. lymphodema/ tumour/ op etc **Na retention with H2O** (renal insuff/ renin angio)- mainly dilutional	3 key features + a couple of examples
1. What is type 2 hypersensitivity?	"Type 2 hypersensitivity is mediated by antibodies directed toward	

Odema 2003-1

2. Oedema formation	1. Describe the causes of oedema formation	**1. Hydrostatic pressure; 2. Decreased plasma oncotic pressure;** 3. Lymphatic obstruction; 4. Sodium and water retention; 5. Inflammation	First 2 + 1 more
	2. How does increased hydrostatic pressure causes oedema? Prompt: What are some examples?	1. Local: Impaired venous outflow – Thrombosis, External pressure, Prolonged dependency with inactivity 2. Generalised impaired venous return – CCF, Constrictive pericarditis, Ascites 3. Arteriolar dilatation – Heat, Neurohumeral dysregulation	2/3 categories, At least 4 examples
	3. What is the pathogenesis of cardiac oedema?	**Decreased cardiac output**, Decreased renal perfusion, Secondary aldosteronism, Increased blood vol, inc venous pressure	At least 3

Platelets in Haemostasis 2010-2

TOPIC: OEDEMA **NUMBER:** _____

OPENING QUESTION	Define Oedema	**COMMENTS**
POINTS REQUIRED	1 Increased fluid in interstitial space	
	2	
	3	
	4	
	5	
	6	
	7	
PROMPTS	Increased fluid WHERE	
SECOND QUESTION (if needed)	What mechanisms contribute to oedema	
POINTS REQUIRED	1 Increased Hydrostatic pressure	4 of 5
	2 Reduced Plasma Osmotic Pressure	
	3 Impaired Lymph flow	
	4 Renal Retention Salt & water	
	5 Inflammation	
	6	
PROMPTS		
THIRD QUESTION (if needed)	How do these mechanisms contribute to development of oedema in congestive cardiac failure	
POINTS REQUIRED	1 Decreased cardiac output	2 of 3
	2 Increased Venous pressure	
	3 Renal Retention of salt & fluid (renin-Angiotensin)	
	4	
	5	
	6	
PROMPTS		

Platelets in Haemostasis 2009-1

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**

Platelets in Haemostasis 2006-2

Question 2: **Role of platelets in haemostasis**	**Describe the formation of a primary haemostatic plug after vascular injury**	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)	Need **3/3 bold** Prompt: *What is the role of platelets at the site of injury?*
	How does this then become the secondary haemostatic plug?	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 **2/3 bold**

Platelets in Haemostasis 2005-1

Role of platelets in hemostasis	(a) How do platelets adhere at the site of a vascular injury?	(a) Von Willebrand's factor on endothelium most important, * bridging platelet surface receptors (Gp1b) and collagen Also collagen direct to platelet collagen receptors, and interaction with extracellular fibronectin.	
	(b) How is a primary haemostatic plug formed?	(b) Mass of aggregated platelets formed under influence of released ADP and TXA_2 Detail...thrombin etc to follow on	

Platelets in Haemostasis 2003-2

1.2 Platelets in coagulation	Describe the role of platelets in coagulation	• Vascular injury – extracellular matrix constituents, especially **collagen.** • **Adhesion**: vWF bridges, stabilises initial platelet adhesion; • Secretion (release reaction): from two types granules: - **Ca, ADP** key to aggregation; phospholipid complex key to intrinsic path. • **Aggregation**: - primary hemostatic plug. Coagulation cascade –> thrombin –> then platelet contraction. Fibrin stabilises the aggregate.	3/4

Reperfusion Injury 2012-2

Q2 Reperfusion Injury LOA: 1	1. What is reperfusion injury? 2. What are the mechanisms of reperfusion injury?	It is when reperfused tissues sustain loss of cells in addition to the cells that are irreversibly damaged at the end of ischaemia. a. **Reactive O2 and N species** produced from incomplete reduction of the incoming O2 by damaged mitochondria in parenchymal and endothelial cells b. **Inflammation –** increased cytokine production and adhesion molecule expression by hypoxic cells recruits inflammatory cells (neutrophils) causing further injury c. **Activation of complement**. IgM Abs may deposit in ischaemic tissues - complement binds and activate – further injury and inflammation	Broad concept expressed Concept of 2 of 3 bolded

Reperfusion Injury 2010-1

QUESTION	ESSENTIAL KNOWLEDGE	NOTES
(a) What is reperfusion injury?	Further **cell death** in ischaemic tissues following **restoration of blood flow**	(a) Highlighted
(b) What are the proposed mechanisms of reperfusion injury?	1. **Generation of oxygen free radicals** – formed from incomplete reduction of in-coming O2 by damaged mitochondria in affected tissue and action of oxidases (generated from ischaemic cells and leucocytes) 2. **Associated inflammation** - cytokines, adhesion molecules generated by hypoxic cells; they recruit neutrophils etc in re-perfused tissue; ensuing inflammation causes additional injury 3. **Activation of complement system** – IgM Ab deposit in ischaemic tissue; restored blood flow brings complement proteins that bind to Ab and are activated; causing further cell injury and inflammation 4. Mitochondrial permeability transition – via reactive O2 species – effects mitochondrial function - precludes recovery of ATP / energy supplies for the cell	(b) 2 for pass

Reperfusion Injury 2006-2

TOPIC: Reperfusion injury _____ **NUMBER:** _____

OPENING QUESTION	What is reperfusion injury?	**COMMENTS**
POINTS REQUIRED	1 Further injury to ischaemic tissue that occurs after restoration of blood flow.	Must give concept
PROMPTS		
SECOND QUESTION (if needed)	What are the proprosed mechanisms of reperfusion injury.	
POINTS REQUIRED	1 Oxygen free radicals	2/4 to pass
	2 Mitochondrial permeability transition	
	3 Inflammation: cytokine production and increased expression of adhesion molecules, recruitment polymorphs	
	4 Complement pathway activation	

Reperfusion Injury 2006-1

TOPIC: Reperfusion injury **NUMBER:** Question 1 - Thursday 6 April am

OPENING QUESTION	**What is "Reperfusion injury" after blood flow is restored to an ischaemic tissue?**	**COMMENTS**
POINTS REQUIRED	1 New damaging processes are triggered by **reperfusion** which effect ***additional*** cell injury and necrosis to that caused by the period of ischaemia itself.	Not injury due to ischaemia
	2	
	3	
	4	
	5	
	6	
	7	
PROMPTS		
SECOND QUESTION (if needed)	**What mechanisms are involved?**	At least one for pass
POINTS REQUIRED	1 Oxygen free radical generation	
	2 Increased "Mitochondrial permeability transition" -> mitochondrial failure and loss of intracellular energy production.	
	3 Inflammatory response with neutrophil influx (in response to cytokines and increased expression adhesion molecules)	
	4 Activation of complement	
	5	
	6	
PROMPTS		

COMMENTS

Opening question , so first a definition, then expect at minimum, say two of the mechanisms for a pass?

Reperfusion Injury 2005-2

TOPIC: Reperfusion Injury **NUMBER: 1b**

OPENING QUESTION	What are the possible mechanisms for ischaemia-reperfusion injury?	**COMMENTS**
POINTS REQUIRED	1 O_2 free radicals from cells and leukocytes	Q 1 = 60% of overall weighting
	2 Mitochondrial permeability transition	2 of 4 to pass
	3 Inflammation from cytokines and expression of adhesion molecules	
	4 Complement activation	
	5	
	6	
	7	
PROMPTS	Prompt to talk about reperfusion injury	
SECOND QUESTION (if needed)	Describe how oxygen free radicals contribute to this injury	1 of 2 to pass
POINTS REQUIRED	1 Derived for parenchymal cells, endothelial cells and leucocytes	
	2 Superoxide anions – damaged mitochondria - action of oxidases	
	3	
	4	
	5	
	6	
PROMPTS		

Stem: A 51-year-old male has presented with abdominal pain and vomiting. He is tachycardic and hypotensive. We will start with Pathology			
TOPIC	QUESTIONS	KNOWLEDGE	NOTES
Question 1 Shock **Subject:** Path LOA: 1 Robbins 9th edition P131-134	(a) What is the definition of shock?	Reduction in cardiac output or the effective circulating blood volume; the result is hypotension followed by **impaired tissue perfusion** and **cellular hypoxia.**	Bold to pass
	(b) What are the major categories of shock? Please give examples.	Cardiogenic e.g. AMI, cardiotoxins, arrhythmia Hypovolaemic e.g. haemorrhage, burns, GI losses Septic/ systemic inflammation e.g. sepsis, pancreatitis, trauma (independent of haemorrhage) Distributive e.g. anaphylactic, adrenal crisis, Neurogenic e.g. spinal injury, spinal anaesthetic Obstructive e.g. tension pneumothorax, cardiac tamponade, PE	3 categories with 1 example of each

Stem: He becomes shocked. Moving onto Pathology.			
Question 5 Haemorrhagic Shock **Subject**: Path LOA: 1	a) Define shock	**Tissue hypoperfusion due either** 1 Reduced Cardiac Output, or 2 Reduced effective Blood volume	**Bold** to pass **plus 1 or 2**.
	b) Describe the stages of haemorrhagic shock *Prompt : describe what happens during each stage?*	▪ Non-progressive – reflex compensatory mechanisms maintain vital organ perfusion ▪ Progressive – tissue hypo-perfusion and onset metabolic disturbances (lactic acidosis) ▪ Irreversible – non reversible tissue and cellular injury, MOF	All 3 stages to pass plus some detail for each
	c) Describe initial clinical presentation of shock	Narrowed pulse pressure / ↑CPR time / Tachycardia / Hypotension / Tachypnoea /Cool Clammy Skin / Cyanotic Skin / Oliguria / Altered mental state	3/5 to pass
	d) What other types of shock are there – with an example of each?	Distributive (septic, anaphylactic), Obstructive (PE, PTX, tamponade), Cardiogenic (MI, cardiomyopathy, arrhythmia), Neurogenic (spinal trauma), Dissociative (poisoning), Hypovolaemic (burns, GI losses)	3 to pass

TOPIC: Haemorrhagic Shock **NUMBER:** _____

OPENING QUESTION	Define Shock	**COMMENTS**
POINTS REQUIRED	1 Tissue hypoperfusion	
	2 Reduced Cardiac Output OR	
	3 Reduced effective Blood volume	
	4	
	5	
	6	
	7	
PROMPTS		
SECOND QUESTION (if needed)	Describe the stages of haemorrhagic shock	
POINTS REQUIRED	1 Non-progressive	
	2 Progressive	
	3 Irreversible	
	4	
	5	
	6	
PROMPTS		
THIRD QUESTION (if needed)	Can you draw a graph showing the relationship between proportion of blood loss and cardiac output in haemorrhagic shock	
POINTS REQUIRED	1 Something like the picture (turns down around 20%, dead at 45%)	
	2	
	3	
	4	
	5	
	6	
PROMPTS		

Shock, Hypovolaemia 2013-2-D

Stem: Moving on to Pathology: The patient becomes hypotensive.

PATHOLOGY Question 3 LOA: 1	1. What is hypovolaemic shock?	1. **Systemic hypoperfusion due to reduced effective circulating blood volume** resulting in **impaired tissue perfusion** and cellular hypoxia	Bold to pass
	2. Describe the stages of hypovolaemic shock Prompt: What compensatory mechanisms are involved?	2. A. **Non- Progressive phase** – reflex **compensatory mechanisms** activated to **maintain vital organ perfusion.** Variety of neurohumoral mechanisms activated to help maintain cardiac output and blood pressure (baroreceptors reflexes, release of catecholamines, activation of renin-angiotensin axis, ADH release and increased sympathetic output resulting in: tachycardia, peripheral vasoconstriction, and renal conservation of fluid with decreased urine output. Coronary and cerebral vessels less sensitive to sympathetic response and blood flow/ O_2 delivery spared.	All 3 phases to pass. 2A. Bold to pass + 3 features (prompt if necessary)
		B. **Progressive phase- tissue hypoperfusion** and worsening circulatory and metabolic imbalance including **acidosis.** Widespread tissue hypoxia resulting in anaerobic glycolysis with excess lactic acidosis production blunts vasomotor response → peripheral pooling, hypoxic injury, DIC, vital organs begin to failure	2B Bold to pass.
	3. What happens at the cellular and tissue level during the irreversible phase?	C. **Irreversible phase** - after body has incurred **cellular and tissue injury so severe** that even if haemodynamic defects are corrected, **survival is not possible** - Widespread cell injury - lysosomal enzyme release - nitric oxide → decreased myocardial contractility - acute tubular necrosis -> acute renal failure, - ischaemic gut→ bacteraemic shock - severe hypotension, unconscious, anuric - pre-cardiac arrest - > death	2C Bold to pass 3 features to pass

Shock, Hypovolaemic 2011-2

Question 2 LOA: 1	1 What is hypovolaemic shock?	**Systemic hypoperfusion due to reduced effective circulating volume,** cellular hypoxia	Bold
	2 Describe the stages of hypovolaemic shock.	**Non Progressive phase**. Reflex compensation, vital organ perfusion. Baroreceptors, catechol, renin/angiotensin, ADH, sympathy stim.(↑HR, periph vasocons, ↓ urine)	3 phases to pass with details 4/9
		Progressive Phase Anaerobic glycolysis, lactic acidosis, ↓ vasomotor response, → periph pooling, hypoxic injury, DIC, vital organ failure	3/7
		Irreversible Phase lysosomal enz release., NO→ ↓ myocardial contractility, ATN, bacteraemic shock from isch gut.	2/4

Shock, Septic 2017-1-A

Stem: Moving onto Pathology. He has confirmed Gram Negative sepsis.			
Question 5 Gram-negative sepsis **Subject:** Path LOA: 1	a) What are the mechanisms of Gram negative sepsis? *Prompt :what other immune components are involved?"* *Prompt : what other blood components are involved?"*	a) Combination of **direct microbial injury** and activation of host inflammatory responses e.g. by **endotoxins** (lipid A, O Ag) 1. Inflammatory mediator release TNF, IL (1, 6,8,10), PGs, NO, PAF, reactive O2 species, PAI-1 (Plasminogen activator inhib 1) 2. Activation innate cells of immune system- neutrophils. macrophages and monocytes 3. Humoral interaction to activate complement and coagulation pathways 4. Direct endothelial injury and activation 5. Metabolic abnormalities (insulin resistance and hyperglycaemia, glucocorticoid excess/def) 6. Immune suppression (activation counter-regulatory mechanisms with anti-inflamm mediators, lymphocyte apoptosis, hyperglycaemia inhibits neutrophils)	**Bold** **2 of 6**
	b) What are the potential outcomes of septic shock?	End organ and systemic dysfunction, incl a) Cardiomyopathy b) Hypotension c) ARDS d) DIC e) Renal failure f) MSOF g) Death	**3 of 7**

Shock, Septic 2015-1-A

Stem: A 50 year old man presents in septic shock. The cause of this is unclear on initial assessment. We will start with Pathology.			
TOPIC	QUESTIONS	KNOWLEDGE (essential in bold)	NOTES
Question 1 Septic Shock (pp 129-133) Subject: Path LOA: 1	What is Shock?	State where reduced cardiac output or effective blood volume results in **impaired tissue perfusion** and **cellular hypoxia**	Bold concepts
	How do microbes initiate septic shock? *Prompt: What are the mechanisms*	1 Interaction with innate cells of immune system – examples neutrophils, macrophages, monocytes 2 Interaction with Humoral cells of immune system to activate complement & coag pathways 3 Direct action on endothelium (complex, not fully understood) Toll-like receptors recognise microbial elements, and other mechs End result is **mediator release** examples TNF,IL-6, 8, 10, PAF PAI-1, HMGB1	2 of 3 plus examples of each (at least 1) + understand role of mediators
	When DIC develops, what is the process?	Induction of procoagulant state by: **1 Increased TF** production **2** Decreased production of **Protein C** **3** TF pathway inhibitor **Thrombomodulin** **4 Decreased fibrinolysis** by increasing plasminogen activator inhibitor, Combined with stasis (decr washout of activated coag factors) results in activation of thrombin & and fibrin rich thrombi	2 of 4 & understanding of process
	What factors determine the severity and outcome of septic shock in an individual?	Extent and virulence of infection Immune status of host Presence of other co-morbid conditions Pattern and level of mediator production	Bonus Q – no pass criteria

Shock, Septic 2012-1

Question 2. **Septic Shock**	1. How do microbial constituents initiate septic shock?	1. Interact with **cells of the innate immune system** (Neutrophils/Macrophages/Others) to release inflammatory mediators (& immunosuppressants) 2. Interact with **humoral elements of innate immunity** to activate complement and coagulation pathways 3. Act on **endothelium**	2 of 3 bold
	2. What is the **effect of endothelial cell activation and injury during septic shock?** PROMPT; What happens in the vessel?	**1. Thrombosis** 2. Increased **vascular permeability** **3. Vasodilation**	2 of 3
	3. **How does endothelial activation result in DIC (disseminated intravascular coagulation)?** **PROMPT; what mechanisms contribute to the coagulapathy in DIC**	1. Sepsis favours coagulation a. Increased tissue factor production b. Decreased fibrinolysis c. Stasis **d.** Decreased washout of activated coagulation factors e. Results in multiple fibrin rich thrombi 2. Increased hypoperfusion **Consumption Coagulopathy = DIC**	Consumptive and some detail

Shock, Septic 2011-1

Question 2. **Septic Shock**	1. How do microbial constituents initiate septic shock?	1. Interact with **cells of the innate immune system** (Neutrophils/Macrophages/Others) to release inflammatory mediators (& immunosuppressants) 2. Interact with **humoral elements of innate immunity** to activate complement and coagulation pathways 3. Act on **endothelium**	2 of 3 bold
	2. What is the **effect of endothelial cell activation and injury during septic shock?** PROMPT; What happens in the vessel?	**1. Thrombosis** 2. Increased **vascular permeability** **3. Vasodilation**	2 of 3
	3. **How does endothelial activation result in DIC (disseminated intravascular coagulation)?** **PROMPT; what mechanisms contribute to the coagulapathy in DIC**	1. Sepsis favours coagulation a. Increased tissue factor production b. Decreased fibrinolysis c. Stasis **d.** Decreased washout of activated coagulation factors e. Results in multiple fibrin rich thrombi 2. Increased hypoperfusion **Consumption Coagulopathy = DIC**	Consumptive and some detail

Shock, Septic 2009-1

Question 2: **Septic shock**	**What is an endotoxin?** **How does an endotoxin cause septic shock?**	**Bacterial cell wall Lipopolysaccharides** usually from Gram -bacilli. Consists of a generic fatty acid core and a complex polysaccharide coat unique for each species. **Dose dependent activation of neutrophils, macrophages and monocytes** → mediator release → local/systemic inflam. response. Activation via: LPS binding prot. + CD14 receptor via IC toll I receptor. Mediators: TNF, IL-1, 6, 8, chemokines → cytokine release Low dose: enhanced local inflammatory response and clearance of infection. Moderate dose: fever, procoagulant activity. **High dose: Syndrome of septic shock** • Systemic vasodilatation • Decreased myocardial contractility • Widespread endothelial injury → alveolar capillary damage (ARDS) • Activation coag system → DIC	**Bold** **3/4 needed**

Shock, Septic 2007-2

TOPIC: Pathogenesis of septic shock **NUMBER: Q2**

OPENING QUESTION	**Describe the pathogenetic sequence of events in septic shock**	**COMMENTS**
POINTS REQUIRED	**Infection**, producing particularly **gram negative endotoxin (bacterial wall lipopolysaccharides LPS)** but also **gram positive exotoxin** binds with leucocytes and endothelial cells causing **cell damage as well as initiating a cascade of mediators** from plasma or cells . **Major mediators** from the mononuclear phagocyte system are IL-1 and TNF- α. Others include PAF,NO, complement prostaglandins, leukotrienes etc Effects on **multiple organ systems**	
SECOND QUESTION	How are specific organ systems affected in septic shock	
POINTS REQUIRED	• Heart – dysfunction/depression/dilation • Vascular system – hypotension and vasodilation • Microcirculation – endothelial injury and activation, leucocyte aggregation • Coagulation system – DIC • Lungs – ARDS • Liver - failure • Kidney - ARF • CNS – confusion/coma	

Shock, Septic 2005-2

TOPIC: Pathogenesis of septic shock **NUMBER: 2c**

OPENING QUESTION	Outline the pathogenesis of septic shock	**COMMENTS**
POINTS REQUIRED	1Bacterial toxin (endotoxin or exotoxin) binds to LPS binding protein in serum	Must have 1 plus 2 of rest
	2 complex binds to receptors on leucocytes, and endothelial cells	
	3 induce release and synthesis of inflammatory mediators	
	4 induce direct cell damage	
PROMPTS		
SECOND QUESTION (if needed)	What chemical mediators are involved	At least 4 to pass
POINTS REQUIRED	1 Vasoactive amines Histamine, Serotonin	
	2 Plasma proteases – complement, Kinins	
	3 arachadonic acid metabolites – prostaglandins, leucotrienes	
	4 Platelet activating factor	
	5Cytokines - IL1 and TNF	
	6 Lysosomal constituents – proteases, lysozymes,	
PROMPTS	7 Oxygen free radicals, neuropeptides, Nitric oxide	

Thrombosis 2017-2-C

Stem: Moving on to Pathology. Venous thrombosis is considered to be the most likely cause for his leg swelling.			
Question 5 **Subject**: **Path** **Thrombosis** LOA: 1	1. What pathological mechanisms may contribute to venous thrombus formation in a vessel? 2. What are some of the different risk factors for venous thrombosis? *Prompt: You have named one genetic risk factor, can you name another one?* *Prompt: You have named one relating to X (e.g. stasis), can you name others with different mechanisms?* 3. What are possible outcomes of a venous thrombus in a vessel?	**Endothelial injury (damage to vessel)**, **alteration in blood flow** (stasis, turbulence), **hypercoagulability** of blood. <u>Primary (genetic)</u> • Mutations – Factor V Leiden, prothrombin gene • Increased levels – factors VIII, IX, XI, fibrinogen • Deficiencies – AT3, protein C, S • Fibrinolysis defects, homozygous homocysteinuria • Non O blood group <u>Secondary (acquired)</u> • Stasis – (e.g. prolonged bed rest, immobilization, long distance travel) • Tissue injury (e.g. MI, surgery/burns/fractures) • AF • Cancer • Prosthetic cardiac valves/devices • Indwelling vascular devices (e.g. PICC, CVC etc) • External vessel compression (e.g. pregnancy (>20 weeks) May Thurner syndrome, etc) • Platelet abnormalities (e.g. DIC, HITS, Thrombocytosis) • Cardiomyopathy, nephrotic syndrome, • Hyperoestrogenic states (pregnancy, post-partum, OCP etc.) • Sickle cell anaemia • Smoking • Antiphospholipid syndrome • Hyperviscosity states (PCRV, leukaemia, hyperproteinaemia) **Propagation** (eg resulting occlusion), **embolisation**, **dissolution, organization, recanalisation.**	All bolded to pass. 2 examples of genetic causes and 2 non genetic causes with *different mechanisms* (i.e. from a different line) to pass. 3 of 5 to pass.

Thrombosis 2014-1-A

TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
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**

Thrombosis 2012-1

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
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

Thrombosis 2009-1

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
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

Thrombosis 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**?

Thrombosis 2006-2

TOPIC: Thrombosis _____ **NUMBER:** _____

OPENING QUESTION	**Describe the pathogenesis of thrombosis**	**COMMENTS**
POINTS REQUIRED	1 **(Virchows triad) endothelial injury** – most important, may alone result in thrombosis eg heart and arterial circulation where flow is high	3/3 factors to pass
	2 **Blood flow stasis / turbulence** eg turbulence over atheromatous plaques, aneurysms, AMI with poor contractility, left atrial dilatation	
	3 **Blood hypercoaguability** eg primary hypercoaguability (factor V mutation, protein C/S resistance, hyperhomocysteinemia) / secondary hypercoaguability (CCF, trauma, OCP, pregnancy, Ca)	
PROMPTS	1. **What factors predispose to thrombus formation?** 2. **Give examples where each of these factors operate?**	
SECOND QUESTION (if needed)	**What are the potential fates of a thrombus?**	¾ in list to pass
POINTS REQUIRED	1 **Propagation** – accumulate more platelets / fibrin and lead to vessel obstruction	
	2 **Embolisation** – eg pulmonary or systemic (arterial)	
	3 **Dissolution** – by fibrinolytic activity	
	4 **Organisation and recanalisation** - inflammation, fibrosis then recanalised	
PROMPTS	Are there any other possible fates?	

Thrombosis 2005-1

Thrombosis	What are the potential fates of an intravascular thrombus? What are the primary causes of a hypercoagulable state? (prompt: "1^0 = genetic or inherited" if need be)	Propagation Embolisation Dissolution Organisation \ Recanalisation Factor V (Leiden) mutation Antithrombin 111 deficiency Protein C or S deficiency Other: Homocysteinaemia, Fibrinolysis defects, Increased prothrombin	