ACEM 2007.1 PRIMARY VIVA EXAMINATION. PATHOLOGY 10 April 2008 am *Candidate Number……..*

	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Q1. Hypertrophy vs hyperplasia.	What are the differences between hyperplasia and hypertrophy?	1 Hyperplasia - increase in number of cells in organ/tissue - usually resulting in increase in volume - occurs if cellular population capable of synthesising DNA thus permitting mitotic division. 2 Hypertrophy - increase in size of cells - causes increase in size of organs. 3 Hypertrophy and hyperplasia often co-exist.	Prompt: What are the differences at a cellular level Pass criteria: 2/3 to pass
	Describe the different types of hyperplasia and give an example of each.	1 Physiologic: Hormonal, Compensatory. 2 Pathological - hormonal stimulation excessive e.g. oestrogen and effect on uterus, benign prostatic hypertrophy caused by androgens - growth factors e.g. proliferation of connective tissue cells and blood vessels in aiding wound repair.	Pass criteria: Need basic classification to pass
Q 2. Pathological calcification	Please describe the 2 different forms of pathological calcification and give an example of each.	1. Dystrophic calcification – normal serum calcium - in necrotic or dying tissue 2. Metastatic calcification - normal tissue - abnormal (raised) calcium	Prompt: "What is meant by dystrophic calcification / metastatic calcification" ?
	Prompt: Please give an example(s) of dystrophic calcification, and metastatic calcification.	1. Dystrophic calcification – atherosclerosis; calcific aortic stenosis; tuberculous node 2. Metastatic calcification – nephrocalcinosis; pulmonary calcinosis; gastric mucosal	Prompt: "What type of abnormal calcification is nephrocalcinosis" ?

	"Describe the different principal pathological causes of hypercalcaemia, with some clinical examples.	1. Increased PTH secretion + bone resorption - hyperparathyroidism 2. Destruction of bone tissue – skeletal metastases, myeloma, Paget's 3. Vit-D related disorders – sarcoidosis, hypervitaminosis D 4. Renal failure – secondary hyperparathyroidism + phosphate retention	Prompt: "Hyperparathryoidism from increased PTH secretion is one example. Can you give another" ? Pass criteria: 2/4
Q3. Hepatitis A	Describe the clinical course of Hepatitis A infection.	1) Oral faecal transmission. 2) Incubation period: 2-6 weeks. 3) No carrier state or chronic hep or cause hepatocellular Ca. 4) Rarely causes fulminant hepatitis, and so the fatality rate is about 0.1%.	Pass criteria: provide 3/4 Prompt: mode of transmission.
	How do the serological markers change with time in Hep A infection?	1) IgM anti HAV appears at the onset of symptoms. 2)Faecal shedding of the virus ends as IgM titre rises (2-12 weeks). 3) IgM Ab (months) 3) Replace by IgG anti HAV (years) . Encourage graph	Encourage graph.
Q 4. Nephrotic syndrome	What are the manifestations of the nephrotic Syndrome?	1. Massive proteinuria, with the daily loss of 3.5 gm or more of protein (less in children) 2. Hypoalbuminemia, with plasma albumin levels less than 30 gm/L 3. Generalized oedema 4. Hyperlipidemia and lipiduria	Pass criteria:3 out of 4
	What are the mechanisms of the oedema?	1. Loss of colloid osmotic pressure 2. Loss of serum albumin 3. Accumulation of water and sodium in tissues 4. Due to compensatory secretion of aldosterone Mediated by - Hypovolaemia - ↑ ADH - ↑ Sympathetic system	Pass criteria: 3/4

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

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	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Q1. Apoptosis	What is apoptosis?	1.Pathway of cell death. 2.Induced by tightly regulated intracellular programme 3. Cells that are destined to die activate enzymes that degrade the cells' own nuclear DNA and nuclear/cytoplasmic proteins. 4. The cell's plasma membrane remains intact. 5. Apoptotic cell becomes target for phagocytosis. 6. Dead cell rapidly cleared before contents leak out so this does not elicit an inflammatory reaction in the host. 7. Cell shrinks	Prompt: What are the features at a cellular level? Pass criteria: 3/6 to pass Must get no.1 and cell contents don't leak out.
	Describe the physiologic situations where apoptosis occurs.	1.Programmed destruction of cells during embryogenesis. 2. Hormone dependent involution in adult such as endometrial breakdown. 3. Cell deletion in proliferating cell populations e.g. intestinal crypt cells. 4. Death of host cells that have served their purpose e.g. neutrophils in acute inflammation. 5. Elimination of potentially harmful self reactive lymphocytes. 6. Cell death induced by cytotoxic T cells.	Pass criteria: 2/6 required
Q2. Angiogenesis	Describe how angiogenesis occurs.	1)Mobilisation of Endothelial precursor cells (EPC) from the bone marrow & from pre-existing vessels. 2)EPC migrate to a site of injury or tumour growth. 3) EPC differentiate & form a mature network by linking with existing vessels. 4)Stabilisation: Endothelial cells from pre-existing vessels become motile & proliferate to form capillary sprouts. 5)Vessels mature involving pericytes & smooth muscle cells to form periendothelial layer.	Pass criteria: underlined

	Factors: VEFG Angioproteins 1 and 2 PDGF TGFB Receptors: $VEGFR^{-2}$ FGF^{-2} EC receptor Tie 2	1. Haemangioblast generates haemopoietic stem cells and angioblasts. Angioblasts like EPC are stored in adult bone marrow initiate antiogenesis. Participate in replacing lost endothelial cells, in vascular impant endothelization and in neovascularising ischaemic organs, cutaneous wounds and tumours. 2. Vasodilatation of pre-existing vessels, increased permeability, degradation of basement membrane, disruption of endothelial cell to cell contact, proliferation and migration towards angiogenic stimulus, and endothelial cell maturation/growth inhibition/remodelling capillary beds.	
Q3. Hepatitis C	Describe the potential outcomes of acute hepatitis C infections in adults.	1)Acute fulminant rare 2)15% resolve 3)85% chronic - >80% stable/20% cirrhosis (50% mortality) hepatocellular Ca	3 major points with most > chronic fulminant) and potential for cirrhosis/Ca
	How does the serology for Hepatitis C infection change in case of resolution?	1)Incubation period (2-26 weeks) 2)HCV-RNA (detectable for 1-3 weeks co-incident with transaminitis) 3)Anti HCV antibodies emerge. Only about 50% detectable during symptomatic acute infection. Remainder after 3-6 weeks. IgG/IgM. IgG persists.	All major points & 'window' when both virus & Ab may be – ve. Diagram encouraged.
10/4/2008 Q4	Describe the pathological features of gout	**Hyperuricaemia**	
		Acute arthritis Precipitation of urate crystals into the joint/s An event (sometimes minor trauma) releases crystals into synovial fluid Cascade occurs resulting in intense inflammatory reaction (complement activated, chemotaxis of neutrophils and macrophages with phagocytosis and activation of lysosymal enzymes, leukotrienes, prostaglandins and free radicals **Chronic arthritis and formation of tophi** which are urate deposits in synovium and periarticular areas **Nephropathy** – deposition of urate in kidney as well as formation of **uric acid stones**	Pass criteria: 3/4

	What are the causes of gout?	**Primary –** enzyme defect unknown (90%) (overproduction, underexcretion or increased excretion) - rare enzyme defect (HGPRT deficiency) **Secondary** (10%) Increased nucleic acid turnover e.g leukaemias (overproduction and excretion) Chronic renal disease (decreased excretion) Inborn error metabolism (complete HGPRT deficiency – Lesch-Nyhan syndrome) overproduction and excretion	Need primary & 1 secondary to pass.
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

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	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Q1.Scar formation	What are the phases involved in scar formation?	1. Fibroblast migration and proliferation 2. Extracellular matrix (ECM) deposition 3. Tissue remodelling	Prompt: "One phase is fibroblast migration and proliferation. Can you name another phase" ? Pass criteria 2/3
	What are the local triggers of fibroblast migration and proliferation (at the site of an injury)?	1. Growth Factors- TGF-β; PDGF; EGF; FGF Cytokines – IL-1; TNF	Prompt" Can you name a growth factor / cytokine involved" ? Pas criteria: 2 to pass
	What are the sources of these local triggers?	1. Platelets 2. Macrophages and other inflamm cells such as mast cells, eosinophils, lymphocytes 3. Endothelium	Prompt: "Which blood cells or constituents are involved. Platelets are one example. Can you give another" ? Pass criteria: 2 to pass.
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
Q3. Clostridial infections	Name some clostridial diseases and causative organisms.	1) Tetanus (lockjaw) – Clostridium tetani 2) Botulism (paralytic food poisoning) – Clostridium botulinum 3) Gas gangrene, necrotizing cellulitis – Clostridium perfringens, C. septicum 4) Pseudomembranous colitis – Clostridium difficile	Pass: Require 2 out of 4

	What is the pathogenesis of gas gangrene (C. perfringens, C. septicum)	Release enzymes – hyaluronidase; collagenase Virulence factors – TOXINS <u>α-toxin</u> - multiple actions - phospholipase C: degrades membranes; muscle; RBC - release phospholipid derivatives: ITP; prostaglandins - these cause derangement in cell metabolism and cell death	At least 2 & α-toxin
	Optional		
Q4. Peptic ulcer disease.			
	By what mechanisms may Helicobacter pylori cause peptic ulcers?	*1.H. pylori* secretes **<u>urease</u>**, which generates free ammonia; and a **<u>protease</u>** which breaks down glycoproteins in the gastric mucosa. 2. *H.* pylori makes **<u>phospholipases</u>** →damage surface epithelial cells glycoprotein complexes. *3.H.* pylori enhances gastric secretion and impairs duodenal bicarbonate secretion. This enhances metaplasia. 4. Several H. pylori proteins are immunogenic→evokes **<u>strong immune response</u>** in the mucosa. Activated T and B cells are both seen in chronic gastritis caused by *H. pylori.* 5. Thrombotic occlusion of surface capillaries is promoted by a **<u>bacterial platelet activating factor.</u>** 6. Other antigens (including **<u>lipopolysaccharide</u>**) recruit inflammatory cells to the mucosa. 7. Damage to the mucosa is thought to permit **<u>leakage of tissue nutrients</u>** into the surface microenvironment, thereby sustaining the bacillus.	**Prompt:** What does *H. pylori* produce which can help cause ulceration? Pass criteria: need to say it involves immunogenic response.
	What complications may arise from peptic ulcer disease?	1. **<u>Bleeding</u>** (15-20%of patients), →25% of ulcer deaths 2. **<u>Perforation</u>** ~ 5% of patients →2/3 of ulcer deaths 3. **<u>Obstruction</u>** from oedema and or scarring ~ 2% of patients Mostly due to pyloric channel ulcers Rarely causes complete obstruction with intractable vomiting & incapacitating, crampy abdominal pain	Pass criteria: 2/3
Q5. Pre-eclampsia	What are the proposed pathogenesis and consequences of pre-eclampia?	<u>Placental ischaemia</u> is the key feature leading to 1.Reduction in PGI2, PGE2, 2.Inc renin/angiotensin II, 3.Inc thromboxane and endothelial dysfunction, 4.Resulting in systemic hypertension & DIC.	Pass criteria: placental ischaemia & 1 other point.

	Describe the clinical course of pre-eclampsia.	Usually starts after 32 weeks gestation, charcaterised by 1.Hypertension, oedema and proteinuria. 2.Headache and visual disturbances are common. 3.Ecclampsia is characterised by convulsion and coma.	Need 2/3 to pass.
	Describe the morphological changes in the placenta.	1. Placental infarcts, 2. retroplacental haematoms, 3. villous ischaemia, 4. prominent syncytial knots, 5. thickened trophoblastic basement membrane, 6. villous hypovascularity, 7. fibrinoid necrosis , 8. intramural lipid deposition.	Needs to give 3 to pass.