CEM PRIMARY 2009/1 PATHOLOGY VIVA Thursday am *Candidate Number*..... AGREED MARK.....

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Question 1: **Vascular changes of inflammation**	**Describe the vascular changes that occur in acute inflammation**	**1.Vasodilation & increased blood flow mediated by histamine and NO, action on vascular smooth muscle** **2. Increased permeability** 3.Stasis - incr blood viscosity and concentration of RBCs 4 Accumulation of leukocytes on vascular endothelium	Need **1** + **2** and 1 other
	What are the causes of the increased vascular permeability?	**1. Gaps due to endothelial contraction via mediators** ("immediate transient response"): histamine (fast), bradykinin, sub P, leukotrienes, cytokines(longer). Venules. 2. Direct injury to vessel: ("immediate sustained") 3. "Delayed prolonged" 2-12 hrs burn, radiation, toxins 4.. Leukocyte mediated injury: venules, pulm caps, hours 5. Incr transcytosis: vesicles, vacuoles, incr channels VEGF 6. New vessel formation; new bvs leaky; VEGF, mediators	Need **1** and 2 others
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**
Question 3: **Tumour invasion and metastasis**	**Describe the steps involved in tumour cell invasion of the extracellular matrix**	1. **Detachment** ('loosening up') of the tumour cells from each other, with breaking of intercellular bonds 2. **Attachment** to extracellular matrix (ECM) components, via laminin and fibronectin receptors 3. **Degradation** of ECM, via type IV collagenase and plasminogen activator, creating passageways 4. **Migration** of tumour cells, which may then lead to vascular dissemination	Accept ≥ 3 of 4 **bolded words** (or a similar explanation) for a pass? Prompt: "*Detachment is the first step.*"
	Describe possible mechanisms that influence the distribution of metastases	1. **Tumour cell adhesion molecules** ligands *preferentially* expressed on target organ cells 2. **Chemokines** *for* target tissues 3. **Chemoattractants** *from* target organs	Prompt: "*Chemokines have an important role*"

Question 4: **Influenza**	**How does the Influenza virus cause pneumonia?**	1. **Attachment of virus to upper resp tract epithelium** 2. Necrosis of cells followed by inflammatory response 3. Interstitial inflammation with outpouring of fluid into alveoli 4. **Secondary infection by Staph / Strep**	Need bolded
	How does Influenza A cause epidemics and pandemics	Mutations of Influenza A haemagglutinin and neuraminidase allow virus to escape host antibodies (**antigenic drift**) and epidemics, whereas replacement of these with animal-derived RNA segments leads to new virus (**antigenic shift**) and pandemics	Needs bolded
Question 5: **Hypertrophic cardiomyopathy**	**What are the characteristics of hypertrophic cardiomyopathy?**	1. **Myocardial hypertrophy without ventricular dilatation** 2. **Asymmetrical septal thickening (septum >> free wall)** 3. Impaired diastolic filling and LV outflow obstruction in 25% of cases	Need bolded Prompt: What are the structural effects on the myocardium?
	What are the complications of HCM?	1. Heart Failure 2. Sudden death, ventricular arrhythmias 3. Atrial fibrillation, mural thrombus / embolisation 4. Stroke 5. Infective endocarditis mitral valve	Need 3/5

CEM PRIMARY 2009/1 PATHOLOGY VIVA Thursday pm *Candidate Number*..... AGREED MARK.....

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Question 1: **Cellular changes following ischaemia**	**Describe the types of damage that occur inside a cell after severe ischaemia**	1. **ATP depletion** leading to NaK pump failure, anaerobic metabolism, Ca pump failure, reduced protein synthesis and protein misfolding 2. **Membrane damage** - mitochondria, lysosomes and plasma membrane 3. **Increased intracellular Ca^{++}** / loss **Ca^{++} homeostasis** 4. **Accumulation of reactive O_2 species** **5. Defects in membrane permeability**	Need 3/5 bold Prompt: What would happen to energy production in the cell?
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**
Question 3: **Hepatitis C**	**What are the routes of transmission of Hepatitis C virus?** **What are the potential outcomes of infection?**	1. **Blood inoculation with IV drug use** 60%. 2. Unknown 3. Transmission via blood products pre1991 10% 4. Dialysis < 5% 5. Occupational exposure < 5% 6. Sexual transmission infrequent 7. Vertical transmission very low. 1. Acute Infection generally asymptomatic, rarely fulminant hepatitis 2. **85% progress to chronic persistent hepatitis** 3. 15% resolve completely 4. **20% of chronic infection progress to cirrhosis** 5. Some cirrhotics develop **Hepatocellular carcinoma**	Need bold and 2 other? Need bold

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
Question 5: **Malignant mesothelioma (pleural)**	**Describe the relationship between asbestos exposure and malignant mesothelioma** **Where can malignant mesothelioma arise?**	1. **Increased incidence among people with heavy exposure to asbestos.** Lifetime risk up to 7-10%. 2. **Asbestos bodies** found in increased numbers in lungs of patients with mesothelioma. 3. **Long latent period** for mesothelioma (25-45 yrs). 4. No increased risk in asbestos workers who smoke (in contrast to asbestos related lung carcinoma). Asbestos workers more at risk of dying from lung carcinoma (especially if they smoke). 1. **Pleura** 2. **Peritoneum** 3. pericardium 4. tunica vaginalis 5. genital tract	**2/4** **Bold**

ACEM PRIMARY 2009/1 PATHOLOGY VIVA Friday am *Candidate Number*…… **AGREED MARK**……

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
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**?
Question 2: **Type 4** **Delayed type hypersensitivity**	**What are the cellular events in delayed type hypersensitivity** in a previously sensitised individual? **How does it differ in a naïve individual?**	1. Delayed type hypersensitivity T_H1cells are activated and secrete cytokines that are responsible for the delayed type reaction - IL-12, IFN-γ, TNF, lymphotoxin, chemokines. Accumulation of mononuclear cells around small veins and venules, p**erivascular cuffing,** increased **microvascular permeability, escape of plasma proteins** and **deposition of fibrin** in interstitium Typical example = tuberculin reaction 2. T cell mediated cytotoxicity Sensitised CD 8+ T cells (cytotoxic T lymphocytes) kill Ag bearing target cells In naïve individual, **CD4+T cells** differentiate into T_H 1cells after recognising antigen presented on APCs in association with class II MHC molecules. **T_H1cells** can enter the circulation and remain in the **memory** pool of T cells for long periods (years)	2/4 bold

Question 3: **Neisserial infections**	**What are the two clinically significant *Neisseria*?** **Describe the pathogenesis of a *N. meningitidis* infection**	1. *meningitidis* 2. *gonorrhoeae* 1. Respiratory spread 2. Common coloniser of the oropharynx 3. (10% of the population at any one time) 4. Colonisation lasts for months 5. Immune response leads to protection against that strain 6. Invasive disease crosses respiratory epithelium to enter blood 7. Capsule of *Neisseria* reduces opsonisation & protects against destruction by complement proteins 8. Outbreaks in young people living in crowded quarters who encounter new strains	Both Need 5/8 Prompt: How does it spread?
Question 4: **Vitamin K**	**What is the function of Vitamin K?** **What are the causes of Vitamin K deficiency?**	1. Required co-factor for a liver microsomal carboxylasewhich carboxylates a glutamate residue in Factors VII, IX, X & prothrombin (PLUS Proteins C & S and a few others) 2. Necessary for binding calcium and thus functional activity of the proteins 1. Fat malabsorption syndrome 2. Destruction of endogenous Vitamin K-synthesizing flora in the gut by broad spectrum antibiotics 3. Neonates (small liver reserves, no bacterial flora and low Vitamin K in breast milk) 4. Diffuse liver disease (hepatocyte dysfunction interferes with synthesis of Vitamin K dependent factors)	Need 3/4 Should know all the clotting factors and Protein C & S
Question 5: **Crohn disease**	**What are the pathological features of Crohn disease?** **What are the extraintestinal manifestations of Crohn disease?**	**1. Transmural inflammation of bowel with skip lesions** **2. Noncaseating granulomata** **3. Fissures and fistulae** Migrating polyarthritis, sacroiliitis, ank spondylitis, erythema nodosa, finger clubbing, sclerosing cholangitis (uncommon), Uveitis, mild hepatic pericholangitis, renal disorders due to trapping of the ureters (uncommon). Systemic amyloidosis (rare) GI tract cancer (less common than UC). May occur prior to intestinal symptoms.	2/3 Bold needed At least three systems Prompt: What other inflammatory conditions may be seen in Crohn disease?

ADDITIONAL QUESTIONS IF REQUIRED

ACEM PRIMARY 2009/1 PATHOLOGY VIVA Friday am ***Candidate Number*****…… AGREED MARK……**

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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
Question 2:			
Question 3:	**What are the microbiological features of *Neisseria*?**	1. Aerobic 2. Gram negative diplococci 3. Coffee bean shaped 4. Require chocolate blood agar 5. 13 serotypes of *N. meningitidis*	Prompt: What are the staining characteristics of *Neisseria?*
Question 4:			
Question 5:			